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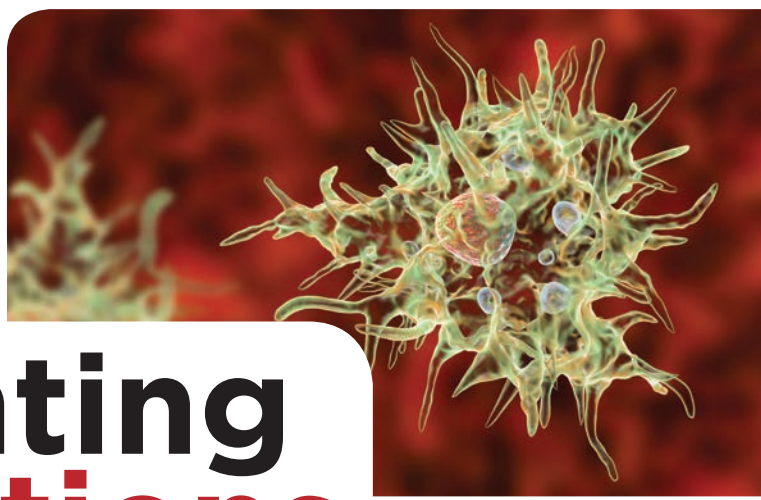
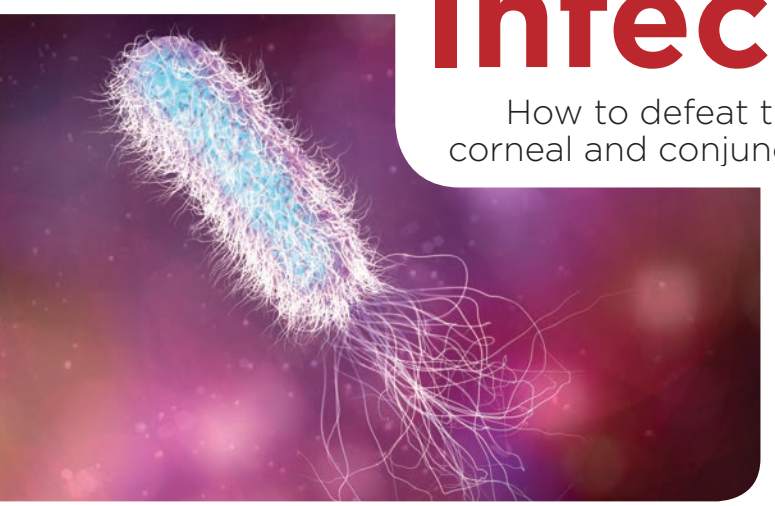
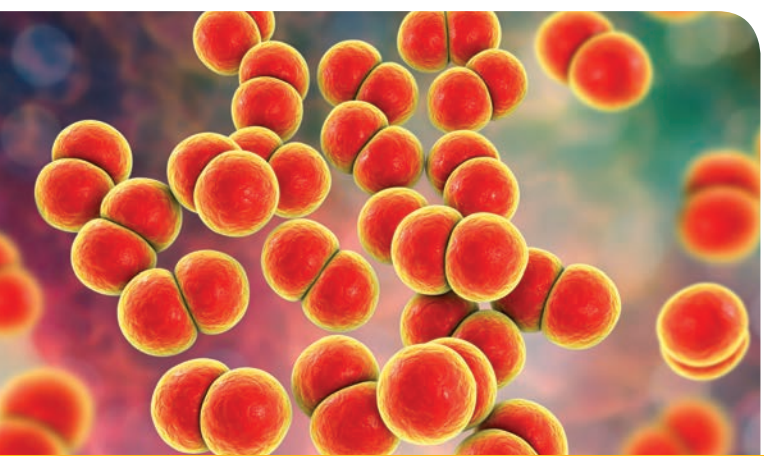
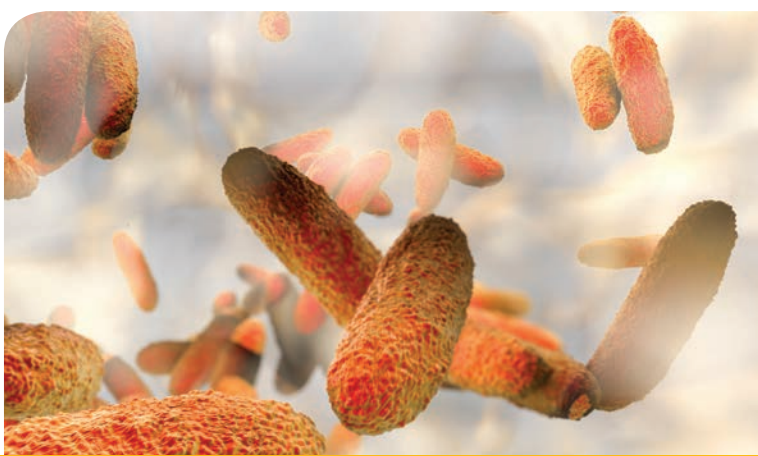
REVIEW OF CORNEA & CONTACT LENSES
SEPTEMBER/OCTOBER 2018

Fighting Infections

How to defeat the bugs behind corneal and conjunctival compromise.



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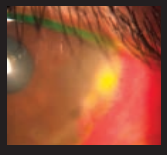

Even if they aren't infectious, these are no laughing matter. In fact, many ocular and systemic conditions may be at play.

By Elizabeth Escobedo, OD, and Nate Lighthizer, OD

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Fighting Corneal Infections with CXL: A New Ally?

Evaluate the strengths and weaknesses of this newfound application before considering it an alternative treatment for keratitis.

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Take the Anxiety Out of Specialty Lens Fittings

Smarter clinical strategies and useful new technologies help ensure a smoother process.

By Clark Chang, OD, and Jeffrey Sonsino, OD

IN BRIEF

■ Research suggests **decreasing the center thickness of a high Dk, low modulus miniscleral lens** from 350µm to 150µm **results in less than a 0.25D increase in lens flexure**. Nine healthy patients with normal corneas were fit with miniscleral lenses with center thicknesses of 150µm, 250µm and 350µm. On average, lens flexure increased as center thickness decreased, but remained below 0.50D. In addition, scleral toricity was positively correlated with *in vivo* flexure for the 150µm and 250µm lenses, and eyes with greater than 200µm of scleral toricity exhibited greater *in vivo* flexure than eyes with less than 200µm, on average.

Vincent SJ, Kowalski LP, Alonso-Caneiro D, et al. Importance of decreasing the center thickness on miniscleral lens flexure. Cont Lens Anterior Eye. July 12, 2018. [Epub ahead of print].

■ Data from 3,851 pterygium eyes that underwent excisional surgery revealed that **1.4% developed conjunctival granuloma (CG)** within a 13-year period—although most arose within 12 to 90 days. All the CGs developed around the free conjunctival flap and involved large amounts of inflammatory cell infiltration. Treatment, which was successful for all patients, included surgical resection combined with corticosteroid eye drops.

Zhang Z, Yang Z, Pan Q, et al. Clinicopathologic characteristics and the surgical outcome of conjunctival granulomas after pterygium surgery. Cornea. 2018;37(8):1008-12.

■ Researchers recently looked at **monthly injections of platelet-rich plasma (PRP)**, which is known to be beneficial for ocular surface restoration in dry eye patients when in topical form. Of 30 patients with Sjögren's syndrome, 15 received monthly injections of PRP in conjunction with hyaluronic acid five times per day for three months. The 15 control patients only received hyaluronic acid five times daily. The investigational group had **improvements in all dry eye parameters**, including reduced corneal staining, increased mean Schirmer value and increased tear break-up time.

Avila MY, Igua AM, Mora AM. Randomized, prospective clinical trial of platelet-rich plasma injection in the management of severe dry eye. Br J Ophthalmol. July 3, 2018. [Epub ahead of print].

A Call for Standardized DED Monitoring

While diagnostic testing for dry eye disease (DED) in Sjögren's syndrome (SS) is well described, the same cannot be said for monitoring, as it's not uniform across and between academic and private practice sites in North America. A multi-centered retrospective study analyzed 123 SS charts to describe the customary DED monitoring practices at six sites. Although DED symptoms were the most common chart entry (98.4% of charts), the absence of standardized DED questionnaires was noteworthy.

The next three frequently recorded variables were meibomian gland dysfunction (76.4%), corneal staining with fluorescein (75.6%) and anterior blepharitis (73.2%).

Private practice sites were more likely to use symptom questionnaires and grading scales and to describe anterior blepharitis, while academic sites were more likely to record tear break-up time and tear meniscus height.

The lack of a standardized symptom assessment, wide differences in ocular surface stains and scales and lack of a tear flow assessment concerned researchers considerably. They suggested applying the Dry Eye Workshop II report's recommended testing protocol to test the proscribed testing's validity in SS.

"How to implement a protocol such as this is challenging," says Jillian F. Ziemanski, OD, MS, clinical assistant professor at University of Alabama at Birmingham's School of Optometry. "First, 'standardizing care' is not necessarily synonymous with standardizing our approach to care. Instead of implementing a strict battery of tests for all Sjögren's patients, a flexible protocol with options for different types of tests would be more practical."

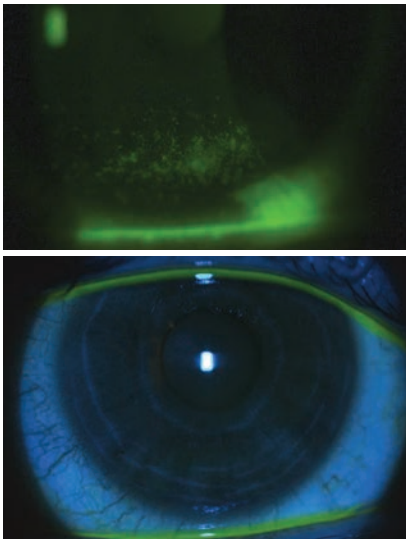

Photo: Chandra Mickles, OD

Sodium fluorescein in an SS patient before scleral contact lens wear, top, and three weeks post-scleral lens wear, bottom.

She suggests a thorough follow-up with a slit lamp exam, symptom assessment, staining and tear production test. But clinicians choose a range of options in each category: an OSDI in one patient but the DEQ-5 for another, or phenol red thread for quicker follow-up and Schirmer's every six to 12 months.

"Standardizing the types of tests may ultimately allow us to more sensitively detect change—improvement or worsening—so that we know whether to maintain or alter our current therapy," she says.

Acs M, Caffery B, Barnett M, et al. Customary practices in the monitoring of dry eye disease in Sjögren's syndrome. J Optom. July 17, 2018. [Epub ahead of print].

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Scleral Lens Wear Raises IOP

Now that scleral lenses are back in vogue, researchers are busy trying to update their assessment of this modality's risk profile. Recent findings of a group from the Université de Montréal may provide cause for concern: intraocular pressure (IOP) during scleral lens wear may increase by an average of 5mm Hg, regardless of the lens diameter.

A prospective randomized study conducted with 21 Caucasian subjects (16 female, five male) evaluated the variation of IOP during scleral lens wear and the influence of lens diameter. Researchers compared one eye randomly fit with a 15.8mm diameter scleral lens with the fellow eye fit with an 18mm lens of the same design, thickness and material. Anterior segment tomography was taken pre- and post-lens removal.

In those wearing the 15.8mm lens, transpalpebral IOP (IOPt) rose from 10.1 ±1.9mm Hg to 14.4 ±5.5mm Hg after 4.5 hours, while those fit with the 18mm lens saw IOPt rise from 9.2 ±2.1mm Hg to 14.4 ±4.8mm Hg. Researchers found the difference based on wear time, but not on the lenses themselves, to be statistically significant.

Anterior segment parameters did not vary except for the anterior chamber volume and the corneal thickness. Baseline Goldmann-correlated IOP revealed no significant diurnal variations.

The researchers conclude that more work is needed to confirm if practitioners should be warned when using scleral lenses on populations at risk for glaucoma.

Studies such as this one tend to create more questions than they answer, says Melissa Barnett, OD, who practices at the UC Davis Eye Center in Sacramento, CA. "Should different scleral lens designs be manufactured that rest differently on the scleral conjunctiva to prevent IOP elevation? Should scleral lenses not be fit in patients with glaucoma? Are other parameters, such as ocular blood flow or corneal hysteresis, valuable in this population?" she adds. "Of utmost importance is that there are numerous studies that need to be performed."

Until then, clinicians simply need to exercise good judgment. "When fitting scleral lenses in patients with glaucoma, ocular hypertension or status post a filtration device, caution may be advised," says Dr, Barnett. "It is important to establish baselines parameters of IOP, visual fields, OCT and pachymetry prior to fitting scleral lenses and habitually with scleral lens wear. At each visit, monitor IOP in those diagnosed with and at risk for glaucoma. If scleral lens wear is of substantial concern or is contraindicated, other options may be considered." RCCL

Michaud L, Samaha D, Giasson CJ. Intra-ocular pressure variation associated with the wear of scleral lenses of different diameters. Cont Lens Ant Eye. July 24, 2018. [Epub ahead of print].

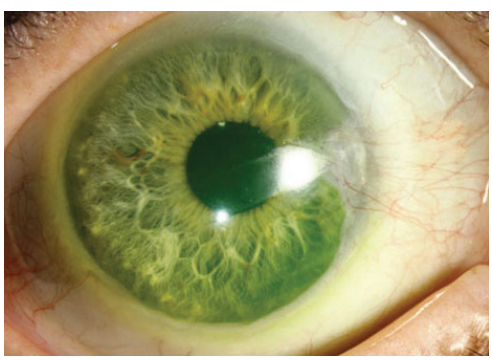

Photo: Christine W. Sindt, OD

While a great option for many patients, scleral lenses may pose some problems for patients already at risk for glaucoma.

HZO: Prevention is the Best Therapy

Clinicians must participate in the discourse regarding the importance of vaccination.

Of the more than one million new cases of herpes zoster virus (HZV) reported each year, about 20% result in ocular complications, including corneal insult.[1] As eye care providers, we should be prepared to recommend the vaccine to patients older than 50, considering HZV is a relatively common cause of ocular disease.

WHAT'S AT STAKE

Herpes zoster ophthalmicus (HZO) presents with a long list of ocular complications both infectious and inflammatory in nature, such as persistent keratitis, conjunctivitis, scleritis, uveitis, acute retinal necrosis, cranial nerve palsies and optic neuropathy.[1] Long-term complications include cataracts, glaucoma, corneal scarring and postherpetic neuralgia (PHN). At least 30% and as many as 50% of HZO patients will experience chronicity.[1] Associated complications include a 4.5x increased risk of stroke within the first year of being infected.

To ward off these ill effects, clinicians should recommend vaccination when the opportunities arise. The Shingles Prevention Study showed reasonable efficacy for the vaccine Zostavax (live-attenuated vaccine, Merck).[2] Studies estimate a 38% to 70% reduction in HZV after vaccination (age-dependent) and a 60% to 70% reduced risk of PHN. Cost analysis studies suggest younger patients accrue the greatest benefit, as the vaccine's effect wanes in older patients—most studies suggest five to eight years of protection that decreases after five years.[3] Patients with a history of HZO may have recurrent ophthalmic, dermatologic or even disseminated disease after vaccination.

Despite the benefits this vaccines provides, health care providers have done a poor job educating patients on the benefits of shingles vaccination; only 28% of eligible patients have been vaccinated with Zostavax.

A NEW OPTION

Recent approval of a new vaccine, Shingrix (recombinant, sub-unit vaccine, GlaxoSmithKline), has renewed interest in shingles vaccination. The vaccine combines an antigen (glycoprotein E) and an adjuvant system (AS01B) to generate a strong, long-lasting immune response. Shingrix has shown an incredible age-independent efficacy of 92.7% and an 88.8% efficacy against PHN.[4] The vaccination stimulates the cellular immune system for at least one year. The new vaccine requires a two-dose schedule (two to six months apart) with an 11% adverse event rate (severe headache, pain and fatigue).[4] Because up to 6% of those affected by HZO may experience recurrent eye disease, patients with active disease should hold off vaccination for a year or two.

QUESTIONS AND CONCERNS

Uncertainties and controversies can cause widespread falsehoods, most of which can be easily explained:

- ***Vaccination after shingles.*** The CDC has not made a formal statement except to say that the vaccine shouldn't be given during the acute phase.
- ***Stopping antivirals before/after vaccination.*** This is not necessary for Shingrix since it maintains over 70% "potency," even when patients are on antivirals.[2] Zostavax requires cessation two days prior to and two weeks following vaccination.[4]
- ***Vaccination for patients with active keratoweitis or corneal dendritiform.*** Authorities suggest waiting until there is some improvement with chronic or recurrent disease states; beyond one to two years is reasonable.
- ***Shingrix after Zostavax.*** Because they have different formulations, Shingrix can still be given.
- ***Vaccination for immunosuppressed or compromised patients.*** While no formal recommendation against vaccination has been issued for Shingrix, immunocompromised or compromised patients should not receive Zostavax since it's a live-attenuated vaccine and comes with concern for disseminated disease.

Considering the overall morbidity of this potentially devastating disease, we should definitely advise eligible patients to receive the new vaccine for herpes zoster. Taking the opportunity to have the appropriate discussion with patients might just prevent a debilitating disease. Prevention is the only foolproof treatment. RCCL

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2. Gelb LD. Preventing herpes zoster through vaccination. Ophthalmology. 2008;115(2):35-8.

3. Merck Medical Advisory, April 2016. Personal communication.

4. GlaxoSmithKline Medical Advisory, January 2018. Personal communication.

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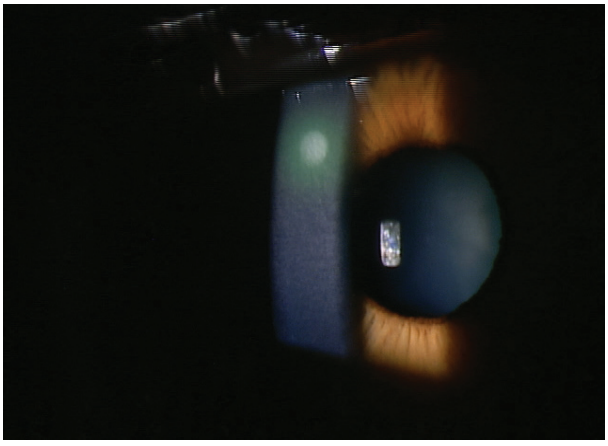
By Robert Ensley, OD, and Heidi Miller, OD

Climb on the Health Bandwagon

Known primarily for their quality of vision, an easily overlooked benefit of GP lenses is their excellent ocular health profile.

Although the gas-permeable (GP) lens market has been stable for the past several years, there is no denying the general decline in GP lens fitting since the introduction of soft contact lenses.[1,2] Compared with the soft lens fitting experience, a survey found eye care practitioners often cite initial discomfort and increased chair time as reasons for hesitation with fitting GPs.[3] Despite these perceived drawbacks, GP lenses are still highly regarded for their ocular health profile.



Extended wear of SiHy lenses increases risk of symptomatic CIEs, such as a sterile marginal ulcer.

AVOIDING THE LIMBUS

Anatomically, the limbus is the junction between corneal and conjunctival tissue. In addition to containing a vascular supply and aqueous humor pathways, the limbus is also home to limbal epithelial stem cells (LESCs).[4] These supply basal cells that migrate and proliferate into corneal epithelial cells. Mechanical disruption or hypoxia of these LESCs can lead to limbal hyperemia and corneal neovascularization.[5] In the event of significant insult or injury, limbal stem cell deficiency (LSCD) can also occur. Although this condition is rare, the resultant epitheliopathy, corneal conjunctivalization and scarring can be devastating.[6,7]

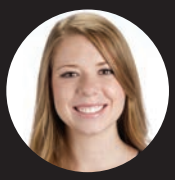
While soft lenses drape over the entire cornea, small-diameter corneal GPs have minimal interaction with the limbus and typically avoid compression entirely. A review of the literature reveals only one case of LSCD attributed to GP lenses, while the remaining cases involve soft lenses.[8] The incidence of corneal neovascularization is also lower with GP lenses than soft lenses, which may be attributed in part to the lack of limbal disruption.[9]

THE ROLE OF OXYGEN

In an open-eye environment, the atmosphere is the main supply of oxygen to the cornea. Placing a contact lens on the eye can reduce this supply by 8% to 15% depending on the oxygen permeability (Dk) of the lens.[9] If oxygen levels decrease enough to leave the cornea in a hypoxic state, multiple physiological changes can occur, including epithelial defects, neovascularization, acute stromal edema and endothelial polymegethism.[9]

Commonly associated with hypoxia, corneal inflammatory events (CIEs) include infiltrative keratitis, sterile marginal ulcers and contact lens-associated red eye (CLARE). In the non-contact lens-wearing population, the prevalence of asymptomatic CIEs can be as high as 4%.[10] Although incidence rates vary among studies, the relative risk of symptomatic CIEs increases significantly with extended contact lens wear for both higher Dk silicone hydrogel (SiHy) lenses and hydrogel lenses.[11-13] One study compared the clinical success of 30-day continuous wear high Dk GP lenses with extended wear SiHy lenses. The GP group contained half as many adverse events as the SiHy group, with the study classifying two events as a CIE for the GP group and nine events for the SiHy group.[14] Other studies have also confirmed lower rates of CIE for GP lenses.[12,15]

Even with similar Dk between GP and SiHy lenses, some speculate GPs are safer due to tear exchange. Compared with the general tear stasis underneath a soft lens, the smaller diameter of a GP lens promotes a flushing mechanism that improves oxygen tension reaching the corneal surface.[16] Additionally, research shows tear film has bacteriostatic activity, although the exact mechanism is unknown.[17]

REDUCED MICROBIAL LOAD

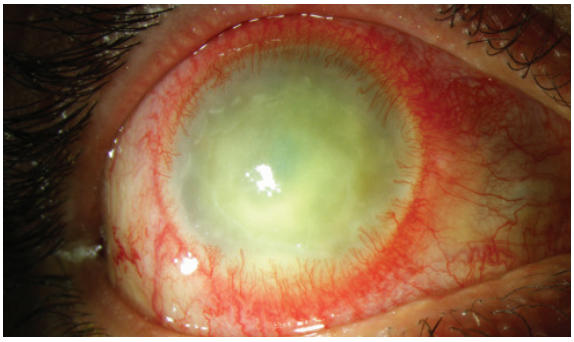
When comparing SiHy and hydrogel lenses, SiHy lenses actually have higher risk of CIEs—suggesting hypoxia is not the only risk factor.[18] While CIEs are considered sterile, many think bacterial bioburden plays a part to their pathogenesis. However, the larger concern of bacterial exposure is microbial keratitis (MK), which, although rare, can be sight threatening.

In one study, the annual incidence rate of MK among all contact lens wearers was 4.2 per 10,000.[19] When comparing modalities, the rate for soft lens wearers was 1.9 per 10,000 and 11.9 for SiHys.[19] When worn as extended wear, these rates increased to 19.5 for soft lenses and 25.4 for SiHys.[19] However, in GP daily wearers the rate was only 1.2 per 10,000.[19] An earlier study had similar annual incidence rates of 2.0 per 10,000 for GP lenses and 2.2 to 4.1 per 10,000 for daily soft lenses.[20]

All of this boils down to the fact that GP lenses have a lower risk profile for MK than soft lenses. In addition to having a 10 to 20 times greater tear exchange than a soft lens, GP lens surfaces have lower adherence rates of bacteria, according to at least one study.[21,22]

Another major concern for contact lens wearers is the exposure to *Acanthamoeba* present in most forms of water, including tap water. GP lens wearers are far more likely to rinse and store their lenses with tap water than soft lens wearers.[23] Although the literature investigating *Acanthamoeba* keratitis and GP lenses have typically involved orthokeratology lenses, there are still relatively few reports of *Acanthamoeba* keratitis among GP wearers.[24] The lack of water content in GP lenses, compared with soft lenses, is one contributing factor that significantly reduces the rate of *Acanthamoeba's* adherence.[25]

Like any contact lens, GP lenses are not without risk or complication; however, when weighing the benefits of different lens modalities, practitioners should strongly consider GP lenses for their safety profile. RCCL



***Acanthamoeba* keratitis seldom occurs in GP wearers.**

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By Vivian P. Shibayama, OD

Hard Case, Hard Lenses

Although RGPs can be difficult to fit, the right technique can provide challenging patients clearer vision.

Congenital cataracts can lead to deprivational amblyopia in children. However, a good visual prognosis is possible with early detection and removal of infantile cataracts—as long as the subsequent visual rehabilitation with contact lenses is successful.[1,2] Children should be fit in lenses that provide the best optical quality and the highest oxygen permeability because the lenses are usually of a high plus power and, consequently, are thicker.

The initial contact lens fitting often occurs during infancy and is sometimes done under anesthesia. Infants are relatively easy to swaddle, which makes taking measurements easier. If the fitting occurs when the child is older, however, ocular measurements can be more difficult to obtain due to a lack of cooperation.

As a solution, creative fitting techniques are designed to help successfully fit these patients in the rigid gas permeable (RGP) lenses they need. This case highlights a method of fitting aphakic bitoric lenses using spherical diagnostic aphakic lenses in a toddler when keratometry (K) readings are unattainable.

THE CASE

The parents of a two-year-old aphakic child with developmental delay presented and claimed that their child was unable to see clearly in his soft aphakic lenses. They had noticed a decrease in his visual attention and felt he was relying more on his hearing than his sight.

The child had been born full-term but was diagnosed soon after with polymicrogyria, which is a condition associated with abnormal brain development before birth.[3] The patient has a history of infantile spasms and is psychologically and physically delayed in his development.

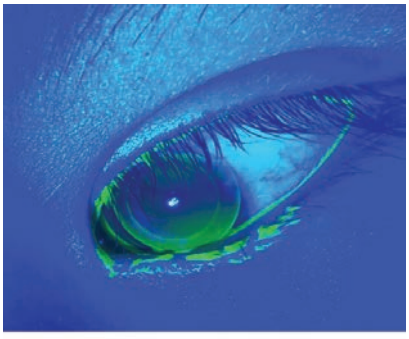

Fig. 1. To determine this patient's K readings, I first had to find the flat K. Note the light horizontal band touch with excessive edge lift at the vertical axis. This is a spherical RGP lens fit on flat K: 8.33 BC/10.0D lens.

When he was four months old, the child developed cataracts (from an unknown origin) that progressed rapidly within a short period of four weeks. Cataract surgery was performed, and the child was fit with soft spherical lenses that he has been wearing with no issues for the past 16 months.

Currently at 24 months, he does not speak and is not ambulating. He regularly receives behavioral, speech and physical therapy.

During the child's most recent visit with his pediatric ophthalmologist six weeks ago, findings showed that his eyes had experienced an increase in the amount of cylinder, from 1.00D to 1.75D OU. The child was corrected for full distance in his contact lenses while wearing bifocal glasses to correct for near vision. He currently wears Alden HP 49 lenses at 8.3/+22.00/14.5 OD, 8.4/+20.00/14.5 OS.

CONTACT LENS EVALUATION

Subjective visual acuity was not measurable; however, the patient was able to fix and follow OU. Retinoscopy over contact lenses revealed:

- -2.50+2.50x090 OD
- -2.00+2.00x100 OS

On exam, the child's pupils were equally round and reactive to light; no afferent defect was noted OU. Extraocular muscles were unrestricted in all gazes, and nystagmus was noted. The patient's intraocular pressures were 11mm Hg OD and 12mm Hg OS, as measured by a Tonopen (Reichert). His anterior segment evaluation was unremarkable. The dilated view of the posterior fundus was also within normal limits, with a cup-to-disc ratio of 0.1/0.1 OU. Due to the cataract surgery, natural lens was absent in both eyes. I did not perform a confrontation visual field exam because of age limitations.

After assessing the patient, I diagnosed him with aphakia OU and progressing astigmatism.

I discussed the pros and cons of three lens options with the patient's parents:

Soft toric lenses *pros*: no change in lens modality, familiarity with soft lenses; *cons*: variable retinoscopy due to soft lens movement, low Dk, not easily verified in-office.

Cylinder-correcting glasses (worn over soft lenses) *pros*: more control of astigmatism (does not change with rotation), do not dislodge easily, no change in lens modality, familiarity

with soft lenses; *cons*: must be updated to match prescription changes, not as precise optics as RGP lenses,[4] soft lenses are not easily verified in-office, low Dk.

***Bitoric RGP lenses** pros*: more consistent retinopathy, high Dk, better optical quality, easily verified in-office, extensive parameters, easy to insert and remove; *cons*: must learn insertion and removal techniques, more challenging to fit, K readings are not attainable, lens may eject more easily, risk of corneal abrasions.

CONTACT LENS FITTING

The parents were most interested in contact lenses that would provide their son with the best optical quality. Bitoric RGP lenses may be a challenge to fit, but they are the lens of choice when fitting patients with high astigmatism.[5,6] K readings were unattainable due to poor cooperation, so I used diagnostic spherical RGP lenses from a Pediasite aphakic fitting set (Advanced Vision Technologies) and fluorescein patterns to estimate the patient's K readings through the following steps:

Step 1. Determine the flat K reading. Spherical lenses should exhibit band-like astigmatism fluorescein patterns (*Figure 1*).

Step 2. Estimate the toricity based on the amount of cylinder in the glasses prescription or the amount of edge lift in a spherical lens fitting. A 2D steep spherical RGP lens was chosen as a starting point to reduce vertical edge lift (*Figure 2*).

Fig. 3. These bitoric contact lenses are properly aligned OU.

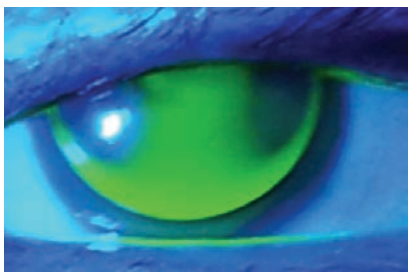

Fig. 2. A 2D steep (7.94D) spherical RGP lens on a toric cornea.

Step 3. As outlined in the fitting guide, find the diameter by subtracting 1.0mm from the horizontal visible iris diameter (HVID).

After estimating the K readings, I ordered Pediasite SPE bitoric optimum extreme lenses (Advanced Vision Technologies) with the following parameters:

- 8.33/7.94 (drum reading) +20.00/+18.00 (back vertex power) 10.5 (diameter) OD
- 8.33/7.94 (drum reading) +18.00/+16.00 (back vertex power) 10.5 (diameter) OS

CONTACT LENS DISPENSING

The patient returned, and I placed the lenses on his eyes. I observed good centration, peripheral fit and alignment (*Figures 3 and 4*). The parents were trained on insertion and removal techniques, which weren't a problem; in fact, they were able to handle the rigid lenses better than the soft lenses. They were then instructed to use Unique pH multipurpose GP cleaning solution (Menicon) to clean and store the lenses.

By Vivian P. Shibayama, OD

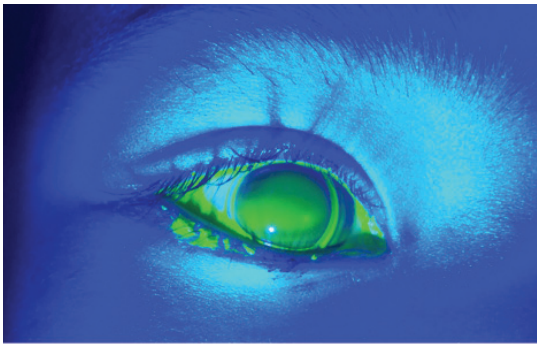

Fig. 3. Above is a close-up of the right eye fit with a bitoric lens.

FOLLOW-UP

Two weeks later, the patient and his mom presented with no new complaints. The child's visual attention had noticeably improved, according to his mom and behavioral therapist. The patient's parents were happy with his new contact lenses, and a follow-up appointment was scheduled for six weeks later.

Six years later, the patient is still doing well in his bitoric RGP lenses. Some modifications were made to flatten the lens and change the power as the patient aged.

DISCUSSION

Although they are optically superior to soft contact lenses, RGP lenses can be challenging to fit in young patients due to a lack of cooperation and an inability to obtain K readings. Bitoric lenses can be especially challenging because most are fit empirically.[7] While not usually necessary, performing an exam under anesthesia may be required if a child is uncooperative and measurements are unattainable.

For aphakic contact lenses, in-office diagnostic fitting with high plus lenses is highly recommended because these lenses are heavy, which changes the dynamics of the fit and may require clinicians to manipulate the contact lens parameters to achieve better centration. If the cornea is highly astigmatic, bitoric diagnostic sets are not always available. However, as presented in this case, bitoric lenses can be designed using spherical diagnostic lenses.

After determining the flat curvature reading, the practitioner must then determine how much toricity to add by either matching the amount of cylinder in the spectacle prescription or observing the amount of edge lift and lens rock with the spherical diagnostic contact lens. Toricity should be increased if the lens is dislodging or exhibiting excessive edge lift. Toricity should be decreased if the lens is not exhibiting enough movement.[4] Against-the-rule corneas should be fit as close to alignment as possible for stability, and with-the-rule corneas can be fit with low toric simulation to allow for adequate tear exchange.[7]

Ejection, a common challenge with pediatric RGP lens fittings, could occur for a number of reasons. A lens that is too steep will eject on blink and requires a flatter base curve that will need to be adjusted as the child grows. A sudden increase in eye pressure can also cause the lens to eject and should be carefully monitored in aphakic patients. Excessive toricity of the cornea can cause lens rock and decentration. In this case, a clinician should fit the patient in a bitoric lens or increase the toricity of the current lens. For heavy lenses that displace easily, the optic cap size or center thickness of the lens should be reduced.[8] Lastly, the diameter should be large enough to optimize lens stability.

Spherical diagnostic contact lenses are valuable tools for fitting both spherical and bitoric RGP lenses on infants and children when K readings are unavailable. When managing aphakic lenses in young patients, the optic cap, lens thickness and diameter size can be manipulated by clinicians to improve stability and centration. Although initially more challenging, RGP lenses can provide more stable and precise vision for young patients. As these children age, clinicians should consider a secondary lens implantation for better results. RCCL

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Advertorial

AIR OPTIX® PLUS HYDRAGLYDE® CONTACT LENSES AND HYDRAGLYDE® LENS CARE: COMFORT, VISION AND LENS SURFACE MOISTURE ALL MONTH LONG

Susan J. Gromacki, OD, MS, FAAO, FSLS
Silver Spring, MD

Dr. Gromacki was compensated by Alcon for her participation in this advertorial.

I recently welcomed a longtime wearer of frequent-replacement contact lenses to my practice. After finding that she wore an older brand of lenses, I explained that the latest lens technologies—especially if paired with the right lens care—may offer an improved experience. Newer lens designs, I explained, include advanced materials and wetting agents to better "keep up" with a modern lifestyle.[1,2] My patient agreed to try something new, and—as I expected—she was amazed. The regimen we tried? AIR OPTIX® plus HydraGlyde® monthly replacement contact lenses paired with CLEAR CARE® PLUS Cleaning and Disinfecting Solution.

A modern lifestyle is a digitally-connected lifestyle, but devices like computers and smartphones can stress our eyes, drastically decreasing our blink rate—from a normal 19 to 23 blinks/min to between 4 and 8 blinks/min while concentrating on a digital device.[3,4] I recommend this regimen because AIR OPTIX® plus HydraGlyde® contact lenses—which combine two unique technologies—are designed to work synergistically with either CLEAR CARE® PLUS or OPTI-FREE® PureMoist® Multipurpose Disinfecting Solution. This provides my patients with comfort and subjective visual quality throughout the 30-day wearing period—even during digital device use.[1]

Exclusive SmartShield® technology, present in all AIR OPTIX® contact lenses, is an advanced plasma surface technology that creates an ultra-thin protective shield around the outer surface to minimize exposed silicone at the lens surface.[5] This helps provide lipid deposit resistance and supports consistent comfort from Day 1 to Day 30.[6-10*]

HydraGlyde® Moisture Matrix is a proprietary lens wetting agent, a block copolymer that attracts and retains moisture on the lens surface of AIR OPTIX® plus HydraGlyde® lenses in an envelope of long-lasting moisture.[11] The premium lens care solutions from Alcon—CLEAR CARE® PLUS and OPTI-FREE® PureMoist®—also contain HydraGlyde® Moisture Matrix, so pairing AIR OPTIX® plus HydraGlyde® lenses with one of these solutions for daily cleaning and disinfection helps provide consistent comfort and long lasting lens surface moisture during the entire month-long wearing period.[1]

In a recent clinical study and patient survey, habitual wearers of other contact lenses tried AIR OPTIX® plus HydraGlyde® lenses along with a HydraGlyde®-containing lens care solution for daily cleaning and disinfection for 1 month. Patients in both cases agreed their trial lenses stayed comfortable, even during challenging real-life situations like long work days,[1] outdoor activity and active environments,[1,12] during digital device use[1,2] and in air-conditioned environments.[12] Additionally, in the survey, 4 times as many patients preferred AIR OPTIX® plus HydraGlyde® lenses to their habitual brand after trying them for 1 month while using a lens care solution containing HydraGlyde® Moisture Matrix (73% vs 18%, respectively; $p<0.05$).[12]

New lens materials and wetting technologies have brought us very far in the realm of contact lens comfort. So, even if patients are used to their habitual brand, they should be presented the opportunity to experience all the benefits of the latest technologies. AIR OPTIX® plus HydraGlyde® contact lenses paired with HydraGlyde® lens care solutions offer a unique combination of technologies that meets the needs of the modern lifestyle, providing outstanding comfort, vision and lens surface moisture during the entire wearing period.[1,11] Recommend AIR OPTIX® plus HydraGlyde® contact lenses paired with either CLEAR CARE® PLUS or OPTI-FREE® PureMoist® to help your frequent-replacement lens wearers see, look and feel their best.

*Based on clinical studies with AIR OPTIX® AQUA, AIR OPTIX® AQUA Multifocal and AIR OPTIX® for Astigmatism contact lenses.

Important information for AIR OPTIX® plus HydraGlyde® (lotrafilcon B) contact lenses: For daily wear or extended wear up to 6 nights for near/far-sightedness, presbyopia and/or astigmatism. Risk of serious eye problems (i.e., corneal ulcer) is greater for extended wear. In rare cases, loss of vision may result. Side effects like discomfort, mild burning or stinging may occur.

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CONJUNCTIVITIS: **Making the Call**

Good judgment and a comprehensive look beyond signs and symptoms are integral to knowing whether it's allergic, bacterial or viral.

By Stephanie Fromstein, OD

Conjunctivitis is a common, costly and, at times, confounding condition. It accounts for 1% of all primary care visits and costs the healthcare system anywhere from $377 to $857 million dollars annually.[1] Known colloquially as "pink eye," it can present with non-specific symptoms, such as lacrimation, grittiness, stinging and burning. Signs include hyperemia, chemosis and hemorrhages.[2]

While clinicians tend to rely on traditional signs—papillae, follicles, discharge, etc.—to distinguish the etiology, a recent meta-analysis suggests that these familiar signs and symptoms do not correlate with any one specific etiology of conjunctivitis.[3] Consequently, clinicians are frequently misjudging viral, bacterial and sterile causes, with one study showing only 50% accuracy in diagnosing viral conjunctivitis when confirmed with laboratory testing.[1] With so few standard tests available, a more thoughtful diagnosis requires knowledge of the prevalence, pathogens and clinical experience—with an eye for atypical presentations. Here, we take a look at what we know—and what remains to be resolved—about conjunctivitis and how best to distinguish between the condition's various forms.

RECOGNIZING THE USUAL SUSPECTS

Conjunctivitis has a host of etiologies, both infectious (viral and bacterial) and sterile (allergic, toxic, contact lens-related, etc.). The most common cause of infectious conjunctivitis is viral, responsible for up to 80% of acute cases of conjunctivitis.[1,4] Bacterial conjunctivitis, while less common, is more likely to cause infection in children (50% to 75% of cases).[1,5] Allergic conjunctivitis is the most common overall (up to 40% of all cases) but vastly under-diagnosed, with only about 10% of allergy sufferers with acute ocular symptoms seeking medical care.[1,5] With each case of conjunctivitis, clinicians must carefully judge the whole clinical picture to uncover the true etiology.

Viral conjunctivitis. While a wide variety of viruses are implicated in this condition, the most common culprit by far is the adenovirus.[6] Viruses that infect the conjunctiva less frequently include herpes simplex virus (often with associated keratitis), varicella-zoster, picornavirus, influenza A, Epstein-Barr, poxvirus, Newcastle disease and, rarely, HIV.[7,8]

Adenovirus is a nonenveloped, double-stranded DNA virus that can survive on dry surfaces for up to seven weeks.[2] The incubation period for the virus is five to 12 days, meaning that patients often shed the active virus in advance of symptoms. Carriers are contagious for a period of 10 to 12 days, with symptoms sometimes lasting up to three weeks, an ample amount of time to spread the condition. Patients and family should be counseled accordingly.

The consequent non-specific acute follicular conjunctivitis is the most common type of viral conjunctivitis and usually results in mild ocular involvement with concurrent systemic findings, such as a sore throat or cold. Pharyngoconjunctival fever (PCF), caused by adenovirus strains 3, 4 and 7, most commonly affects children. It is usually associated with mild pharyngitis and a low-grade fever and often spreads within families.[2,6] Epidemic keratoconjunctivitis (EKC), caused by adenovirus strains 8, 19 and 37, is the most

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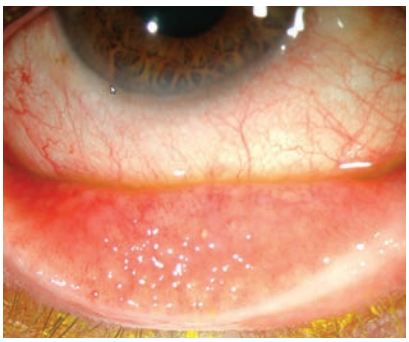

Photo: Marc Bloomenstein, OD

Filled with lymphocytes and plasma cells, follicles tend to localize to the fornices and lack a central vessel.

severe type of viral conjunctivitis, typically occurs in middle-aged adults (men and women equally) and is most likely to involve corneal changes.[2,6]

Signs of viral conjunctivitis include prominent conjunctival hyperemia and follicles, lid edema and pre-auricular lymphadenopathy.[2] In severe cases, conjunctival hemorrhages, pseudomembranes and true membranes may also be observed. Keratitis is seen in a third of cases and ranges from punctate staining to subepithelial infiltrates—signs representative of an immune response to the virus. Watery discharge may also be noted.[2]

Acute bacterial conjunctivitis. This is a common, often self-limiting condition that affects all races and genders. It is caused by direct contact with infected secretions, most commonly *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Staphylococcus aureus* and *Moraxella catarrhalis*, with the first two agents comprising 85% to 98% of all infections.[9] However, hyperacute infections with *Neisseria gonorrhoeae* pose a far greater threat to sight.[1] Infections with methicillin-resistant *Staph. aureus* (MRSA) are also of increasing concern in the general population. *Molluscum contagiosum* and *microsporidia* should be considered as possible etiologies as well.[10]

The condition typically presents with conjunctival injection, papillae and mucopurulent discharge. In severe cases, the patient may present with eyelid edema and erythema. Hyperacute purulent discharge is associated with infections by gonococcal or meningococcal bacteria, predominantly in infants born to infected mothers or adults infected via sexual contact.[1] This is a serious infection that may develop a perforating keratitis within 48 hours.[1] *Chlamydia trachomatis* infections are also possible, often with corneal involvement.[1] Coinfection with gonorrhea and chlamydia is common, and clinicians should initiate treatment for both conditions if either is found.

Finally, blepharoconjunctivitis, often mild and overlooked, involves the interaction between lid margin secretions, microbial organisms and tear film abnormalities. This causes a chronic and episodic conjunctivitis.[11]

Allergic conjunctivitis. This comes in several varieties, each mediated by a type 1 hypersensitivity reaction to an environmental immune mediator. The allergen reacts with IgE antibodies, stimulates mast cell degranulation and the release of inflammatory modulators and causes a host of symptoms traditionally associated with allergic conjunctivitis.[6]

Simple allergic conjunctivitis is caused by a reaction to an environmental allergen, such as pollen, or to eye medications or solutions or to the preservatives contained within.[2,6] Seasonal conjunctivitis refers to the exacerbation of allergic symptoms most frequently in the spring and summer as the result of tree and grass pollens, while perennial conjunctivitis presents symptoms year-round as the result of house dust mites, animal dander and fungal allergens.[2]

Vernal keratoconjunctivitis (VKC) is a severe allergic inflammatory condition that mainly affects young males, with an average onset of five to seven years old.[3] The condition is often associated with personal or family history of VKC or other atopies (e.g., asthma or eczema). While the condition often resolves in their late teens, some of these patients go on to develop atopic keratoconjunctivitis (AKC), a rare, bilateral disease with onset in late adolescence to adulthood.

The Treatment Dilemma

Proper diagnosis is critical to avoid unnecessary therapy and antibiotic resistance. Since both types of infectious conjunctivitis resolve spontaneously in seven to 14 days, clinicians should use antibiotic therapy judiciously. Unfortunately, treatment is often mandatory before children can return to school; this approach encourages unnecessary therapy and can send the child back to school well within the period of contagion. Furthermore, patients of all ages often expect therapy regardless of etiology and efficacy and will seek care at another provider's office if not properly educated before leaving your office empty-handed.

If treatment is indicated for bacterial infections, fluoroquinolones can combat the most common causative agents with little resistance. A potent antibiotic at the appropriate dosage is critical in eliminating the pathogen before it has the opportunity to mutate. Antibiotic therapy should never be reduced below the therapeutic dose, as this can further contribute to antibiotic resistance.

The condition is marked by chronic and unremitting conjunctival inflammation in patients with a history of atopy elsewhere, often dermatologic.[2,6] Symptoms of VKC and AKC are similar, though those associated with AKC are more severe and unremitting.

Giant papillary conjunctivitis (GPC) involves a combination of an allergic reaction and a mechanical irritation from a foreign body (in most cases, a contact lens).

Signs of allergic conjunctivitis include redness, itching and chemosis. Watering may also be noted and is associated with nasal discharge. VKC may present with a collection of eosinophils at the limbus (Horner-Trantas dots) and large papules under the conjunctiva. No preauricular node is typically noted.

ATYPICAL PRESENTATIONS

Other non-infectious forms of conjunctivitis can include contact lens-related, mechanical/traumatic (including trichiasis, ectropion and entropion), toxic, and neonatal.[6]

EXAM POINTERS

Clinicians performing adnexal exam should look at the periorbital skin and lymph nodes. Herpetic conjunctivitis may present with lid involvement before (simplex) or after (zoster) conjunctival involvement. Periorbital edema could point to a viral etiology. Lymphadenopathy is also most likely to occur in viral infections (EKC more so than PCF), though it may be noted in severe bacterial infections, chlamydial infections and Parinaud's oculoglandular syndrome as well. The preauricular node is typically affected, though clinicians should also check the submandibular in all cases of conjunctivitis of unknown etiology. Tonsillar nodes may also give an indication of previous or current infection with influenza or non-influenza viruses. Clinicians should also perform an out-of-slit lamp view of the pattern of injection, so as not to lose the proverbial forest for the trees; viral infections may initially have more inflammation and injection inferiorly than superiorly, though severe cases will appear more diffuse.[1]

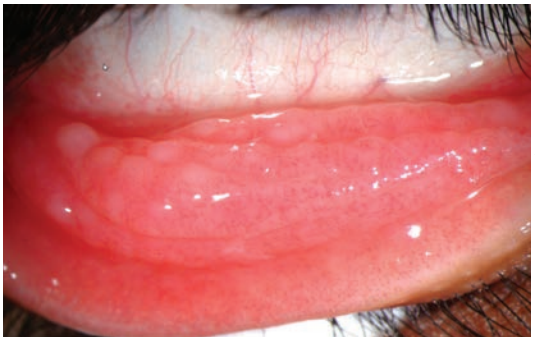

Photo: Marc Bloomenstein, OD

Papillae often arrange in a cobblestone configuration of flattened nodules with a central vascular core.

Conjunctival lumps and bumps may point to a cause, though not always. Bacterial and allergic conjunctivitis tend to present with a papillary reaction—a cobblestone arrangement of flattened nodules with central vascular cores.[10] Papillae are more generalized markers of inflammation, while follicles are more diagnostic of a particular brand of inflammation, occurring mainly in viral, toxic and chlamydial infections. Follicles—filled with lymphocytes and plasma cells—tend to localize to the fornices, be smaller and lack a central vessel.[2,12] As follicles associated usually tend to present inferiorly, while papillary reaction are often most pronounced on the upper tarsal plate, lid eversions can hold important diagnostic clues and should be performed on every patient. Chlamydial conjunctivitis classically presents with a mixed papillary or follicular response, worse inferiorly, in the context of a chronic, low-grade conjunctivitis.

Discharge can narrow the differential causes, as watery discharge is more indicative of viral conjunctivitis, while purulent or mucopurulent discharge is often associated with bacterial conjunctivitis. Hyperacute conjunctivitis tends to be associated with copious amounts of discharge that reappears immediately after wiping it away. Allergic conjunctivitis is also associated with nasal discharge due to the systemic association. The type of discharge should not be considered in isolation, as research shows it is not specific to any class of conjunctivitis.[1] Any eye under stress will self-lubricate as a means of protection.[13,14]

Corneal changes may give further insight as well. Subepithelial infiltrates are associated with EKC and present several days into the infectious period. Bacterial conjunctivitis typically does not present with corneal findings, though serious infections can cause infiltrates and, in some cases, hypopyon.[15] VKC can present with a shield ulcer secondary to the close apposition between the conjunctiva and the cornea. Chlamydial infections may present with peripheral corneal infiltrates.[1]

Even knowing these common signs and symptoms, clinicians often have to look beyond the obvious to ensure the right diagnosis by obtaining the following:

Patient history. While signs and symptoms may not be diagnostic for an etiology, patient history can provide invaluable clues about the cause of conjunctivitis.

Data as simple as a patient's age or the time of year can help to narrow down the differential diagnosis. Viral conjunctivitis is more common in adults, while bacterial conjunctivitis is more common in children. One in eight children has

an episode every year, with five million pediatric cases reported annually.[9] Allergic conjunctivitis has little preponderance for age, though certain types (e.g., VKC) tend to target younger patients.[2] The time of year can also give a clue; viral and allergic conjunctivitis are most common in the spring and summer, while bacterial conjunctivitis is most common in the winter.

History of present illness questions may also point toward an etiology. As viral cases are often connected with upper respiratory tract infections, asking whether the patient feels sick or has in the recent past can help differentiate between PCF and EKC, respectively. Patients with viral conjunctivitis will often report recent contact with a sick individual. Bacterial infection is moderately less contagious and more likely to arise de novo. Both bacterial and allergic causes are less commonly linked to an acute bout of illness.

The disease course can also be a good diagnostic clue. While allergic conjunctivitis likely is associated with a long course of exacerbation and remission, both bacterial and viral likely have an acute presentation and a protracted (fewer than 14 days) course to improvement. As such, sudden onset of symptoms may point to an infectious cause. Viral infections tend to last longer than bacterial, but neither is likely to recur several times in succession.

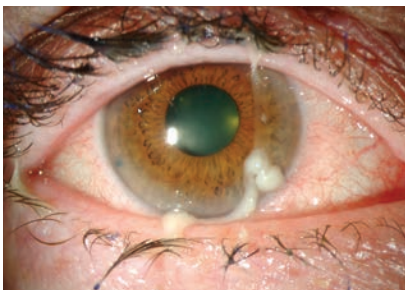

Photo: Marc Bloomenstein, OD

Purulent or mucopurulent discharge is often associated with bacterial conjunctivitis.

Laterality can also be indicative of etiology. Viral conjunctivitis pathognomonically starts in one eye and spreads to the other within a few days, almost always with varying severity. Bacterial conjunctivitis has no clear pattern of laterality and can be unilateral, bilateral or asymmetric. If presenting bilaterally, allergic cases almost always present with varying severity.

Visual acuity. Vision can be notably reduced in adenoviral infections compared with other forms of conjunctivitis, especially in cases with corneal involvement or significant inflammation.

Additional tests. Some cases may warrant specific testing to pinpoint the underlying etiology. AdenoPlus (Quidel Corporation), a point-of-care immunochromatography test for adenoviral infection, takes 10 minutes in-office and is highly sensitive to adenoviral infections. Specificity ranges widely in studies, with some showing high false-negatives. Additional testing is typically not indicated in bacterial conjunctivitis, although severe cases—including those with corneal findings and those suspected to be hyperacute, recurrent or recalcitrant cases—may warrant conjunctival swabs to rule out gonococcal and meningococcal infection. While false-positives are possible (*Staphylococcus* and *Streptococcus* are found in normal lid flora and will often show up on the swabs), atypical findings can be diagnostic. Investigations are typically not performed for allergic conjunctivitis.

The most common causes of conjunctivitis are difficult to distinguish based on signs and symptoms alone. With a broader understanding of the various distinguishing factors, clinicians will be prepared to diagnose every case of conjunctivitis with relative accuracy. Certain combinations have been shown to be predictive; bilateral matting of the eyelids, no itching and no history of conjunctivitis are indicative of a bacterial infection.[5] On the other hand, if the patient is also older than six, is presenting between April and November, has watery or no discharge and does not have glued eyes in the morning, this is highly predictive of a negative bacterial culture. Signs and symptoms only form part of the diagnostic picture; other factors, including patient history, are just as crucial to diagnosing the various forms of conjunctivitis. RCCL

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Your Corneal Infection Care Questions—ANSWERED

Here's how you can overcome your top three microbial keratitis challenges.

By Doan Huynh Kwak, OD

Microbial keratitis is a well-known condition that has the potential to cause visual impairment and blindness. Corneal opacities, typically a sequela of infectious keratitis, are responsible for 5.1% of visual impairments worldwide and up to 10% of avoidable blindness in the world's least developed countries.[1,2] Diagnosis and timely initiation of appropriate antimicrobial treatment are imperative in patients presenting with a red, painful eye indicative of infection, as researchers speculate only 50% of eyes heal with good visual outcome without either.[2,3] However, treating corneal infections is fraught with challenges and uncertainties that can make a clinician hesitant to move forward with any one management plan, even when confident of the diagnosis. This article addresses several of these roadblocks to help you treat microbial keratitis patients promptly and correctly.

SHOULD I CULTURE?

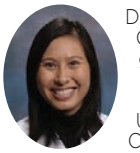
In the past, textbooks and guides such as the *Wills Eye Manual* recommended culturing suspicious infectious keratitis prior to treatment.[4] However, in practice, many start empirical treatment without culturing. The most recent edition of the *Wills Eye Manual* reflects this trend and recommends culturing infiltrates that are larger than 2mm, of a suspected unusual organism, in the visual axis or unresponsive to initial treatment.[5]

For example, a survey of community ophthalmologists in southern California found that 48.7% of corneal ulcers were treated without taking cultures.[6] The discrepancy between formal recommendations and community practice may be due to the time and cost associated with performing cultures and maintaining materials and the high success rate of empirical antibiotic therapy.

In a comparison of a tertiary cornea clinic and general ophthalmology clinic, 10% of ulcers in the cornea clinic were resistant to empirical antibiotics, did not improve clinically and needed a therapy modification based on the culture and sensitivity testing. However, culture results in the general ophthalmology clinic did not lead to an alteration of therapy for patients.[7] This discrepancy is likely due to the varying patient presentations between the cornea clinic and general ophthalmology clinic, the researchers note.[7] The general clinic patients had smaller peripheral ulcers and were treated within three days of the onset of symptoms; the cornea clinic patients, however, were older, more likely to have corneal disease or previous surgery, larger central ulcers and referred an average of nine days after the onset of symptoms.[7] Of the ulcers that needed modified treatment based on their culture and sensitivity testing, several were of unusual etiology (*Aspergillus*, *Acanthamoeba* and *Actinomyces*) and others were of *S. epidermidis* and resistant to fortified cefazolin.[7] This study recommends those who treat severe cases culture most ulcers and general practitioners culture if the patient presents with a significant corneal ulcer.[7]

When initial treatment fails, patients are usually referred to a cornea specialist for further investigation or treatment. However, current antibiotic therapy often complicates the question of whether to culture. Studies found that patients on antibiotic therapy were only slightly more likely to be culture negative. Nevertheless, the pathogen recovery may be somewhat delayed compared with cultures that were not

ABOUT THE AUTHOR



Dr. Kwak is an Illinois College of Optometry graduate and completed her primary care residency at Salus University's Pennsylvania College of Optometry. After years at an anterior segment practice, she recently joined Salus University as a clinical faculty member.

pretreated. The delay in diagnosis does not necessarily lead to a negative outcome.[8] In corneal ulcers with delayed healing, the causative organism may be fungal or protozoan. Thus, in patients not responsive to treatment, it is imperative to make a quick referral to a cornea specialist or have the patient cultured.

Patients with corneal ulcers that are central in location, have a significant anterior chamber reaction or have corneal infiltrates larger than 4mm should be cultured, referred to a cornea specialist or both.[3] In practice, clinicians should start considering culturing infiltrates larger than 2mm.[9]

HOW SHOULD I CHOOSE THE RIGHT ANTIBIOTIC?

Factors to consider when choosing an antibiotic treatment include broad-spectrum coverage, toxicity, availability, cost and region-specific epidemiology of pathogens.[2] First-line treatment for most keratitis is topical and empirical. For bacterial keratitis, fourth-generation fluoroquinolone monotherapy is a common treatment approach. Fluoroquinolones are broad-spectrum antibacterials that cover gram-negative and anaerobic species responsible for ocular infections. They are also effective against a variety of gram-positive organisms; the spectrum of activity has improved with the modification in molecular structure of fourth-generation fluoroquinolones.[10]

Fortified topical antibiotics such as cefazolin sodium (50mg/mL) and fortified tobramycin sulfate (14mg/mL) are an alternate empirical treatment option. A randomized controlled trial found gatifloxacin monotherapy was equivalent to combination therapy with cefazolin and tobramycin treatment for nonperforated bacterial corneal ulcers.[11] For patients with high-risk characteristics, another study recommends treatment with a fortified antibiotic, such as vancomycin, for gram-positive coverage, in addition to a fourth-generation fluoroquinolone, fortified aminoglycoside or fortified third- or fourth-generation cephalosporin for broad-spectrum gram-negative coverage.[12]

Because tetracyclines have anticollagenolytic activity and inhibit metalloproteinases, they can suppress connective tissue breakdown.[2,13] Thus, oral tetracyclines such as doxycycline may help to stabilize the corneal melting possible in aggressive infections such as *Pseudomonas aeruginosa*.[2,13] Despite the widespread use of adjuvant oral doxycycline among cornea specialists, high quality randomized controlled trials in humans do not exist to support its use.[2]

Patients with suspected fungal keratitis should be treated with topical natamycin 5%. Topical voriconazole, a newer generation triazole, has excellent ocular penetration compared with natamycin and is a good alternative. However, results from the Mycotic Ulcer Treatment Trial I demonstrate that natamycin was superior to voriconazole for topical treatment of fungal keratitis, and *Fusarium* keratitis in particular.[2] The Mycotic Ulcer Treatment Trial II found no significant difference in the rate of perforation, visual acuity or rate of re-epithelization between adjuvant oral voriconazole or oral placebo. Subgroup analysis showed there may be a possible benefit to oral voriconazole in *Fusarium* ulcers. Thus, topical natamycin remains the treatment of choice for filamentous fungal keratitis, and the addition of oral voriconazole should be considered in *Fusarium* ulcers.[2] Intrastromal injection of antifungal agents, such as voriconazole, may be useful for patients with deep recalcitrant fungal keratitis.[2,14] While successful cases with intrastromal injections exist, randomized controlled trials are necessary to determine their benefit.[2,14]

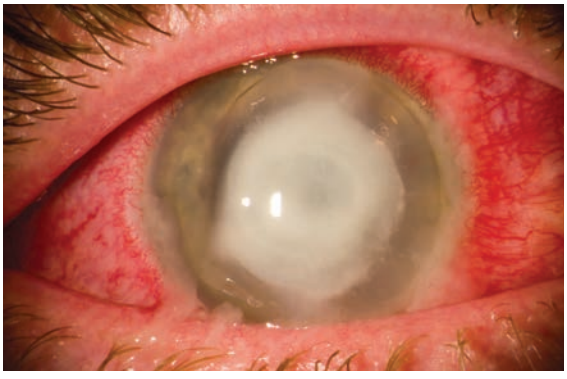


Photo: Christopher Croasdale, MD

This patient has an advanced *P. aeruginosa* corneal ulcer.

Begin with Questions

Gathering a thorough case history will help categorize a patient as having risk factors of infection. High-risk characteristics include a history of trauma, contact lens use, recurrent topical steroid use, immunosuppression and ocular surface disease.[4] Patients without these histories are categorized as low risk.

From here, clinicians can differentiate between a sterile infiltrate and an infectious keratitis and then plan the appropriate treatment approach. An epithelial defect overlying an infiltrate is generally present in microbial keratitis, although some *Acanthamoeba* keratitis and fungal infections, especially molds, can have an intact epithelium. The defect should be as large or larger than the infiltrate.

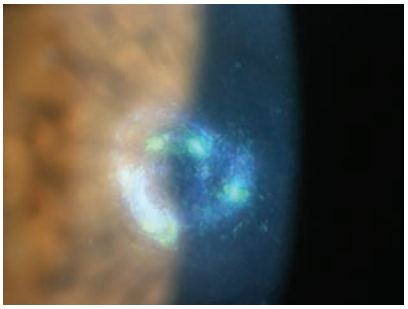


Photo: Scott G. Hauswirth, OD, Richard Mangan, OD

Here is an example of a *Nocardia*-induced keratitis.

In patients with suspicious herpes simplex virus (HSV) keratitis, topical treatments include antiviral medications such as trifluridine and ganciclovir. Topical corticosteroids are added in patients with HSV stromal keratitis. Steroids are typically avoided in HSV keratitis during the active infectious stage. Oral treatments such as oral acyclovir and valacyclovir have become more common in HSV keratitis secondary to the ocular toxicity that may develop with topical therapy. Topical medications may be added when oral medications are not adequate or in patients who are not good candidates for systemic therapy.[2]

Contact lens wearers are at risk of *Acanthamoeba* keratitis (AK). Biguanides and diamidines are the most effective cysticidal antiamebics for these cases. Commonly used biguanides include polyhexamethylene biguanide 0.02% to 0.06% and chlorhexidine 0.02% to 0.2%. Biguanides disrupt the cytoplasmic membrane and damage cell components and respiratory enzymes, all with low levels of corneal epithelial toxicity. They provide a synergistic effect when used in combination with diamidines, which include propamidine isethionate 0.1% and hexamidine 0.1%. Diamidines are effective against both the trophozoite and cystic forms of *Acanthamoeba*. First-line therapy is the combination of a biguanide and diamidine. Treatment with oral nonsteroidal anti-inflammatory drugs, systemic steroids or other systemic immunosuppressive drugs such as cyclosporine may be needed in patients with extracorneal manifestations.[15]

WHEN SHOULD I ADD CORTICOSTEROIDS?

The use of these medications in the treatment of infectious keratitis is controversial and, despite many studies researching the benefits of adding a corticosteroid to an antibiotic treatment, no formal standard of care exists for the use of steroids in bacterial keratitis.

Supporters for their adjunctive use rationalize that the addition will help minimize corneal scarring and opacification. Both infection and inflammation play a role in the pathogenesis and resulting clinical signs of infectious keratitis.[16] In addition to the corneal injury induced by the bacteria, the host inflammatory response to the infection contributes to decreased corneal healing, ultimately leading to scarring.[16] In the host, T-cells and macrophages respond to the bacterial invaders, producing cytokines. These then facilitate neutrophil migration and degranulation, leading platelet-activating factors to upregulate metalloproteinases and cause stromal necrosis.[16] Because corticosteroids decrease inflammatory factors, using them in addition to antibiotics in the treatment of bacterial keratitis can limit the host's inflammatory response and target the infection.[16]

Others believe the addition of a steroid may potentiate the bacterial infection and lead to corneal thinning and, possibly, stromal melt. Additionally, steroids may increase the duration of an infection or the risk of recurrent infection. Inappropriate addition of a steroid to antibiotic treatment may occur in patients with a fungal or *Acanthamoeba* infection, infections that are thought to be exacerbated by topical steroid use.[16,17] However, no conclusive evidence exists to demonstrate whether the adjunctive use of topical steroids in bacterial keratitis is harmful or beneficial.

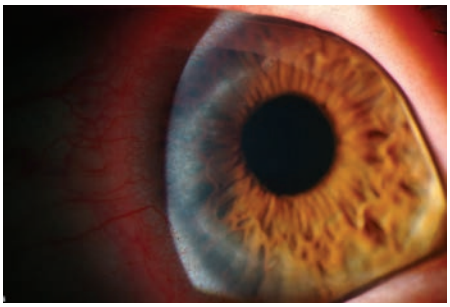
The Steroids for Corneal Ulcers Trial (SCUT), a large randomized, double-masked, placebo-controlled trial that aimed to determine whether adjunctive topical steroids for bacterial keratitis improve long-term clinical outcomes, found no significant difference in best spectacle-corrected visual acuity (BSCVA), scar size or rate of perforation at three months between patients in the placebo and topical steroid adjunctive therapy groups.[17] It also found no differences in healing rates or safety concerns with the use of adjunctive steroids.

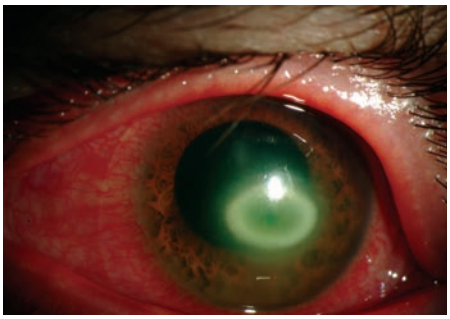
The timing of adding a steroid may be crucial, research suggests. After studying the duration of topical antibiotic treatment before adding topical steroids, research shows a significant improvement in visual acuity when the topical steroid treatment was administered within two to three days of initiation of topical antibiotic treatment. Therefore, in non-*Nocardia* ulcers, steroids are beneficial when administered earlier, within two to three days, and neutral when administered later.[18] Because the original SCUT results were inconclusive and the timing of steroid use was a non-prespecified group analysis, the authors recommend considering the results with caution and do not recommend changing clinical practice protocols.[18]

Clinicians should take these factors into consideration when treating various cases of bacterial keratitis with steroids:

***Nocardia* infections.** Subgroup analyses showed that ulcers caused by *Nocardia* species had worse

Photos: Christine W. Sindt, OD





These images depict the progression of AK over two months.

clinical outcomes with adjunctive steroid use. However, they found that patients in the adjunctive steroid treatment arm with worst baseline visual acuity (counting fingers or worse), ulcers located in and covering the central 4mm or ulcers with the deepest infiltrates at baseline experienced significant positive effects on their BSCVA.[17] Subsequent analysis at 12 months revealed that steroids may be associated with improved long-term visual outcomes among non-*Nocardia* ulcers.[17] Thus, it is possible that steroids require longer periods of time to reveal clinical benefits.[19]

Pseudomonas aeruginosa. Often associated with contact lens use in developed countries such as the United States, *P. aeruginosa* is a causative agent in a large proportion of bacterial keratitis.[20] *P. aeruginosa* corneal ulcers are more severe, highly virulent, more difficult to treat and result in worse visual outcomes compared with other bacterial corneal ulcers. Because of this and animal studies describing increased recurrence rates of *P. aeruginosa* ulcers treated with steroids, many clinicians remain uncertain about using steroids in these corneal infections. However, the SCUT subanalysis found that when compared with other bacterial ulcers of similar severity, *P. aeruginosa* corneal ulcers responded better to treatment, resulting in greater improvement in visual acuity from presentation to three months.[20] Additionally, the study did not find a significant difference in three-month BSCVA or infiltrate/scar size among the *P. aeruginosa* ulcers treated with adjunctive steroids compared with placebo, nor was there an increase in adverse events with steroid treatment.[20]

In practice, clinicians may consider adding a steroid to the antibiotic treatment of *P. aeruginosa* but should use clinical judgment and consider the specific corneal ulcer.

Acanthamoeba keratitis. In one review, researchers state that steroids are usually not required in AK cases that are diagnosed early and respond to antiamebic therapy. However, steroids may be useful when significant anterior segment inflammation exists to facilitate rapid resolution of symptoms. Again, clinicians should proceed with caution as steroids may worsen the condition by dampening the host's inflammatory response.[15] Evidence also suggests that steroid use may result in increased pathogenicity of the amoebas.[15]

Clinicians will never be able to avoid seeing corneal infections in their practice. While many controversies in corneal ulcer treatment can make these some of the toughest patients, a healthy mix of literature review and clinical acumen can go a long way. Knowing who needs a culture and how to tailor therapy based on initial response or the culture results will ensure patients receive the care they need and avoid negative outcomes. RCCL

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How to Overcome Cost by Offering Value

Practitioners share advice on how to help patients recognize the many benefits of silicone hydrogel 1-day lenses.

Research shows that, if costs were equivalent, 95% of eye care practitioners would choose silicone hydrogel over hydrogel for their 1-day contact lens patients. This obviously demonstrates that doctors recognize the true **value** of silicone hydrogel 1-day lenses and understand that they can offer more oxygen[1], healthier[2] corneas, and added convenience. However, many doctors struggle with how to convey this message to patients without getting hung up on price.

We asked three optometrists who regularly refit wearers into silicone hydrogel 1-day lenses to share advice on how they move the conversation from price to value. Here, they share their strategies on how to more effectively engage wearers, strengthen the doctor-patient relationship, and overcome perceived cost barriers.

The Practitioners

Melanie Frogozo
OD, FAAO, FSLS
The Contact Lens Institute of San Antonio
San Antonio, Texas

Ethan E. Huisman
OD, FAAO
Elite Eye Care
West Des Moines, Iowa

Steve Rosinski
OD
Crozet Eye Care
Charlottesville, Virginia

Some doctors are uncomfortable with the transactional nature of making a contact lens recommendation, which makes them hesitant to suggest lens upgrades. What is your advice for overcoming this hesitation?

Dr. Rosinski: Contact lens dispensing is, by nature, transactional—no matter what lens you fit. It's also important to note that there is value to what we do as doctors. It's up to us to explain why we prescribe certain things. Being honest and knowledgeable makes you a doctor, not a salesman. Furthermore, it earns trust and patients will be more likely to come back on a regular basis.

Dr. Frogozo: I believe silicone hydrogel is the healthiest option. In fact, 87% of eye care professionals agree with me that silicone hydrogel material should be the first choice of material for daily disposable lenses.

Dr. Huisman: Be confident. Steer your focus away from cost and focus instead on the professional service you provide when you prescribe what you believe is best for the patient's ocular health.

How do you introduce patients to silicone hydrogel 1-day contact lenses?

Dr. Huisman: By asking the right questions, you can get patients to identify their needs. For example, ask patients if they LOVE their contact lenses. Or, ask what they would change about their lenses if they could. This opens the door and creates connections to the benefits of 1-day silicone hydrogel lenses.

Dr. Rosinski: The reputation I've built with my patients plays a significant role. They expect me to always have the newest and greatest products and anticipate that I will tell them about it every year. You don't need to make it complicated; just deliver the facts. I simply explain that silicone hydrogel 1-day contact lenses offer high oxygen, all-day comfort and great vision for a few cents more per day.

Dr. Frogozo: The patient education in my practice focuses on ocular health and the importance of oxygen transmission. Beyond that, I strive to be frank with my patients. I tell them what I think is best for them and they trust me.

Research shows that 56% of eye-care professionals view the cost to the patient as the greatest barrier to the increased adoption of silicone hydrogel 1-day contact lenses[3]. How do you overcome price barriers in your practice?

Dr. Rosinski: I find it's helpful to tell patients that the cost disparity has dropped dramatically over the years. Plus, they'll receive rebates. I also point out that patients won't have to spend approximately $100 per year for solutions and cases. And, if a lens tears or becomes lost for some reason, they are only out a single use 1-day lens. All of this combined makes the conversation surrounding 1-day much easier. With regard to material, patients want to know why it is better for their eyes, so

Four Steps to Converting Patients to Silicone Hydrogel 1-Day Lenses

- ☑ **1.** Ask the patient to describe a typical day
- ☑ **2.** Ask the patient to describe how the current lenses feel. Listen carefully for identifiers such as discomfort, dryness, reduced wearing time, or redness
- ☑ **3.** Propose a better experience and why
- ☑ **4.** Trial a silicone hydrogel 1-day lens

share with them what you know about silicone hydrogel and how it compares to hydrogel. The key is to believe it yourself and share your honest opinion. My patients trust what I have to say and take my recommendations seriously. Yours will too.

Dr. Frogozo: There is not a huge cost difference. As with many things that relate to our wellbeing, healthier options can be more cost effective in the long run.

Dr. Huisman: I say, "this is more money, but here is why I'm prescribing it for you." While cost is a genuine concern for many patients, it's not the doctor's job to make assumptions about what patients value or how they choose to spend their money. The doctor's job is to educate patients.

If a patient is satisfied with a less expensive lens, is presenting silicone hydrogel 1-day worthwhile, or might it jeopardize the doctor-patient relationship?

Dr. Huisman: Patients prefer honesty and candor. The greater risk to the relationship occurs when a patient suspects you're holding something back.

Dr. Rosinski: The greater detriment stems from failure to offer the best options to our patients. They should hear it from us first instead of hearing about new technology online, via social media or by word-of-mouth.

Dr. Frogozo: You also jeopardize retention if the patient is uncomfortable or develops a problem. Silicone hydrogel 1-day lenses help us to keep patients comfortable in their lenses, which is good for them and for our practice.

What role does the lens trial process have in moving patients to silicone hydrogel 1-day lenses?

Dr. Huisman: Trials are the tipping point, but I believe in educating patients on the benefits of silicone hydrogel 1-day lenses prior to fitting them in trial lenses.

Dr. Frogozo: I agree. The trial is important, but the patient education is a more significant driving force in my practice. I educate up front, so the patient understands why I am selecting a particular lens. The trial is secondary—although it is great to hear patients describe how happy they are with their new lenses.

Dr. Rosinski: Patients are usually willing to try new technology. We just need to do our part by giving them the opportunity! You may be surprised by how many patients ask to switch to silicone hydrogel 1-day lenses after trialing them. My patients come back saying their eyes feel better and they have better vision. And when this happens, they start referring more family and friends.

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1 Manufacturer stated oxygen transmissibility values (Dk/t): MyDay® daily disposable (100), clariti® 1 day (86), 1-DAY ACUVUE® MOIST® (25.5), SofLens® daily disposable (24).
2 With higher oxygen permeability than hydrogel materials, silicone hydrogel contact lenses minimize or eliminate hypoxia-related signs and symptoms during lens wear.
3 Cello Health Insight. June 2017. Base: All US ECPs (n=61); US committed SiHy users (n=28); US non-committed SiHy users (n=33) Q203. Q204A/B/C/D. Question text in notes.

* With manufacturer's rebate. $200 rebate applies to patients new to CooperVision contact lenses.. 6047 04/18

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Corneal Ulcers: Sterile But Not Benign

Even if they aren't infectious, these are no laughing matter. In fact, many ocular and systemic conditions might be at play.

By Elizabeth Escobedo, OD, and Nate Lighthizer, OD

Consider this clinical encounter: a patient presents to the emergency room with a red left eye that has persisted for several days (*Figure 1*). The patient denies any vision changes or photophobia. Slit lamp examination reveals a severely injected temporal bulbar conjunctiva located near an area of corneal thinning and opacification. Upon questioning regarding the clinical history and events leading up to the symptoms, the patient reports minimal pain and denies both contact lens wear and any mucus discharge.

This patient has a corneal ulcer, a condition eye care providers encounter on a routine basis. Ulcers are defined as tissue loss located within the stroma or subepithelial layers of the cornea and are often accompanied by infiltrates, an influx or migration of white blood cells. The definition purposefully does not mention whether an ulcer is infectious or sterile—because it can be either. Thus, in cases such as this, clinicians should always ask, "Is this condition infectious or sterile?" The first step to answering this question is to analyze critical components such as pain, epithelial defect, anterior chamber reaction and location.

While practitioners often concern themselves with infectious etiologies, it's imperative they be familiar with the possible causes of each and know how to differentiate between the two presentations, as the treatments can be drastically different. This discussion zeroes in on the different types of non-infectious ulcers and reviews their etiologies, presentations and treatments.

NO BUGS HERE

Cases with a non-infectious etiology tend to have variable presentations but often share a few similar components such as location and progression, keeping in mind that any systemic condition contributing to the ulceration is being controlled. Most sterile ulcerations involve infiltration or thinning of the cornea near the limbus and have an associated injection of either the bulbar conjunctiva or sclera.

This peripheral location is a critical factor in determining an infectious vs. sterile etiology, with a peripheral location strongly pointing more toward a sterile cause. Pain, mucopurulent discharge and anterior chamber reaction all tend to be much less prominent, or even non-existent, compared with infectious etiologies. In addition, because these ulcerations are commonly associated with other conditions, such as irregular eyelid anatomy, malfunction of the nervous system and many systemic conditions, progression and management can become complex. Here is a look at many common ocular sterile etiologies and how to treat them:

Marginal keratitis. This is a type IV hypersensitivity reaction to bacterial antigens in the presence of Staphylococcal blepharitis. Patients will commonly present with red, irritated eyelid margins that are thickened, with prominent blood vessels.[1] Anterior segment examination can also reveal peripheral corneal infiltrates that can be unilateral or bilateral and are found near the limbal area. These infiltrates are often accompanied by sectoral conjunctival injection.

In cases where the etiology is indeterminate, it is helpful to

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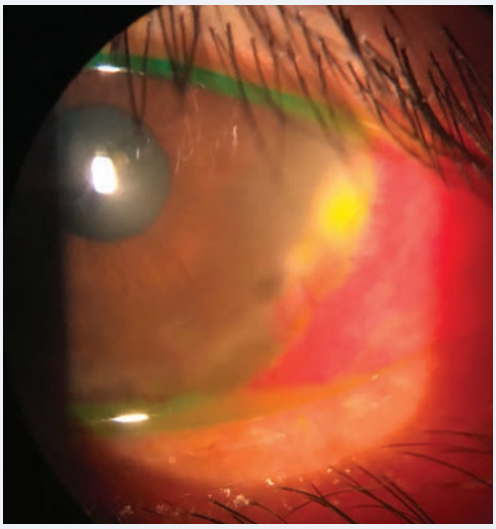

Fig. 1. Peripheral corneal ulceration with adjacent bulbar conjunctival injection.

investigate whether the patient has ever been diagnosed with rosacea. These patients commonly present with poor eyelid hygiene along with associated facial symptoms such as facial flushing and papular skin lesions.[1]

Treatment for these patients begins with lid scrubs and warm compresses to improve lid margin presentation. Antibiotic ointment, such as erythromycin, can also help to reduce the over-proliferation of eyelid bacteria. Patients who present with corneal involvement should be prescribed a topical antibiotic, and possibly a topical steroid, to reduce inflammation and irritation. Due to the chronic nature of rosacea, it is likely these patients will experience recurrent episodes of marginal keratitis. In these cases, clinicians should consider prescribing oral antibiotics, such as doxycycline, to help counteract damaging chronic inflammation. They should follow up in two to seven days to manage lid hygiene and corneal presentation for mild to moderate cases.

Clinicians should also manage intraocular pressure in patients who are prescribed topical steroids. Severe and chronic cases, especially those managed with oral antibiotics, should be followed more closely with a tapering over the course of three to six months, depending on presentation and the patient's overall systemic health.[1]

Contact lens-associated ulcer. A similar presentation is that of a contact lens peripheral sterile infiltrate, a hypersensitivity reaction to bacterial antigens or chemicals involved in lens care (*Figure 2*).[2] Infiltrates can also occur secondary to functional changes in the corneal tissue, such as a reduction in epithelial mitosis and a decrease in the density of terminal nerve endings due to contact lens wear.[3] Like marginal keratitis, a contact lens-associated ulcer presents with peripheral corneal infiltrates commonly accompanied by sectoral conjunctival injection and minimal to no epithelial defects. If epithelial defects are present, they tend to be much smaller than the underlying infiltrate.

With the exception of oral antibiotics, treatment is similar to that of marginal keratitis. While the patient is being treated, contact lens wear should be discontinued, and switching to a daily disposable lens should be considered following resolution of the acute event. In the event sterility is questionable and contact lens wear is a contributor, the recommended approach for treatment is a broad-spectrum antibiotic to cover for any possible infectious pathogens.

Neurotrophic keratopathy. This is a rare degenerative corneal disease caused by impairment of trigeminal innervation, leading to corneal epithelial breakdown, impairment of healing and development of corneal ulceration, melting and perforation. The hallmark of neurotrophic keratitis is decreased corneal sensitivity, which can result from acquired damage to the trigeminal ganglion, stroke, aneurysm or tumor.[4] Systemic diseases and congenital disorders, including diabetes, multiple sclerosis and Goldenhar syndrome, are also associated with neurotrophic keratopathy.[5] Ocular conditions that can lead to a decrease in corneal sensitivity include herpes simplex, herpes zoster keratitis, chronic use of eye drops such as nonsteroidal anti-inflammatory drugs (NSAIDs) and anesthetics, chemical burns and refractive corneal surgeries.

The clinical presentation of neurotrophic keratitis is a persistent, non-healing epithelial defect with

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Goal Statement: While practitioners often concern themselves with infectious etiologies of corneal ulcers, it is imperative they be just as familiar with the possible causes of sterile ulcers and know how to differentiate between the two presentations, as the treatments can differ drastically. This discussion zeroes in on the different types of non-infectious ulcers and reviews their etiologies, presentations and treatments.

Faculty/Editorial Board: Elizabeth Escobedo, OD, and Nate Lighthizer, OD

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heaped-up edges that stains readily with fluorescein. If progression occurs, stromal haze, scarring and thinning can present and lead to corneal melting.

Due to the decrease in corneal sensitivity, patients often present with few symptoms. The management of neurotrophic keratitis can be complex, depending on the severity. In any case, heavy lubrication with artificial tears is highly recommended to improve the health of the corneal surface.

Topical steroid and nonsteroidal drops should be avoided due to the inhibition of stromal healing and increased risk of corneal melting.[5] In severe cases with stromal involvement, collagenase inhibitors, such as tetracyclines and acetylcysteine, should be considered.

Other possible treatments include therapeutic corneal or scleral contact lenses with consideration of autologous serum and amniotic membranes to promote corneal healing.[4]

Exposure keratopathy. This is a result of an unhealthy corneal surface and irregular anatomical function, such as ocular surface dryness secondary to abnormal eyelid blinking or incomplete eyelid closure.[2,5] Possible causes of exposure keratopathy include Bell's palsy or a facial nerve palsy secondary to surgery of an acoustic neuroma or parotid tumor, reduced muscle tone associated with Parkinsonism and severe proptosis due to thyroid eye disease or orbital tumor. Abnormal anatomical structural causes can include ectropion, nocturnal lagophthalmos and tight facial skin following blepharoplasty or eyelid excision of tumors.[2]

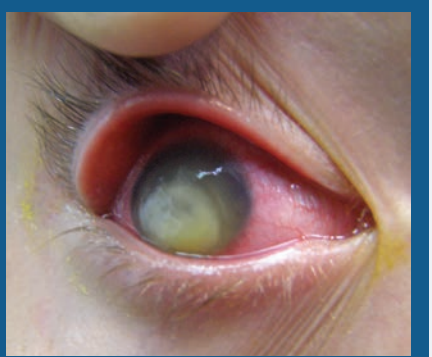
With similar etiologies, neurotrophic keratitis and exposure keratopathy may be difficult to distinguish without a clear history. However, clinical presentation and patient symptoms are two key components that help differentiate the conditions. Unlike neurotrophic keratitis, patients that present with exposure keratopathy will be symptomatic of severe dryness, ocular injection and possibly pain depending on the chronicity and severity of the condition. Punctate epithelial defects will be noted in the inferior third of the corneal surface and, in severe cases, pannus, sterile ulceration or infectious keratitis may occur. Under rare circumstances, stromal melting can eventually lead to perforation.[1]

Treatment for these patients is based on the severity of the condition and expected timeline of recovery.[5] In mild to moderate cases, causes of exposure are commonly reversible, and treatment can involve heavy lubrication during the day and ointment application at night. Taping of the eyelids or the use of a patch can be alternatives to ointment with a sterile presentation. Other viable options for these cases include bandage silicone hydrogel lenses, scleral contact lenses and temporary tarsorrhaphy. Severe and chronic cases that lead to permanent exposure can be treated with a permanent tarsorrhaphy, gold weights or conjunctival flaps. When managing exposure keratopathy in patients with severe proptosis, orbital decompression is also an option.

MORE THAN MEETS THE EYE

When dealing with a suspected sterile corneal ulcer, clinicians should always consider systemic

The Other Side of the Coin



This suspected *Acanthamoeba* ulcer (based on clinical presentation) has a central location and a significant amount of ulceration.

Infectious corneal ulcers, better known as infectious keratitis, are those that become infiltrated by either a bacterial or non-bacterial pathogen (i.e., fungus, protozoan or herpes virus). The most ubiquitous of all pathogens is *Pseudomonas aeruginosa*, covering 60% of contact lens-related keratitis.[5] Other common pathogens include *Moraxella, S. pneumonia, S. epidermidis, Serratia* and *Klebsiella*. Common symptoms of infectious keratitis include pain, photophobia, blurred vision and mucopurulent or purulent discharge.[5] Anterior segment signs tend to present in a certain chronological order that can help determine causation. Early stages include an epithelial defect with a large infiltrate that is often accompanied by stromal edema and anterior uveitis. Severe, chronic cases can result in rapid progression of infiltration with an enlarging hypopyon.[5]

Early treatment is critical for these patients to prevent aggressive inflammation and possible perforation. First-line therapy usually consists of a broad-spectrum fluoroquinolone; however, advanced central corneal ulcers suspicious of methicillin-resistant *Staphylococcus aureus* will require either fortified tobramycin or vancomycin. Lastly, depending on the pathogen and severity, some cases may need surgical intervention or hospital admission.

conditions, such as these, as a potential cause:

Peripheral ulcerative keratitis (PUK). This is a severe peripheral corneal infiltration, ulceration or thinning that cannot be explained by evident ocular disease. These cases should be highly suspicious for associated collagen vascular diseases, which account for 50% of PUK cases.[6] Rheumatoid arthritis, which can lead to some of the worst presentations of sterile corneal ulceration, is the most common associated systemic disorder, presenting in 34% of noninfectious cases, with 30% of patients having bilateral findings (*Figure 3*).[6] Wegener's granulomatosis is the second most common associated systemic condition and almost always presents with scleritis.[6] Less common systemic conditions that can lead to PUK include relapsing polychondritis and systemic lupus erythematosus.

PUK presents clinically with a crescent ulceration and stromal infiltration located at the limbus and is commonly associated with episcleritis or scleritis. Chronic cases of PUK can spread centrally on the cornea and extend into the sclera. The depth of peripheral corneal thinning is variable, with severe cases leading to perforation, with or without trauma.[6]

The goal of treatment for these patients is to reduce ocular inflammation, promote epithelial healing and minimize stromal loss. Unfortunately, unless the associated systemic disease is appropriately managed, treatment results are not promising.[6] In Wegener's, comanagement with a rheumatologist is indicated to manage a potentially life-threatening systemic vasculitis.

Treatment for PUK can be further broken down into local, systemic and surgical options. Solely local treatments are reserved for the few patients without an underlying systemic disease who have an associated marginal or peripheral ulcerative keratitis. These patients should be given topical antibiotics along with education on the importance of eyelid hygiene. Topical corticosteroids can also be prescribed and tapered based on clinical response.[6]

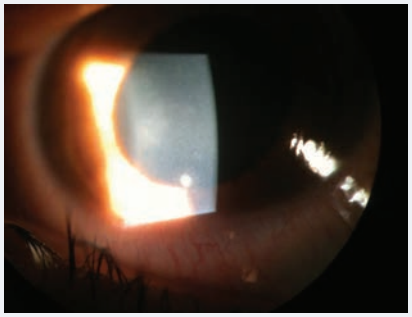


Fig. 2. This peripheral infiltrate is due to contact lens wear.

Systemic corticosteroids are the traditional first-line therapy for acute PUK and are often accompanied by an immunosuppressant due to their inability to inhibit disease progression or overcome the systemic autoimmune disease.[6]

Surgical treatment options include the use of a tissue adhesive, bandage contact lens, lamellar graft, tectonic corneal grafting and amniotic membrane transplant.[6]

Despite the improvements that have been made in cytotoxic therapy, studies show ulcerative keratitis has the highest likelihood of a regraft.[6] Overall, controlling ocular inflammation is critical in these patients, but making sure the underlying systemic disease is controlled can be life saving. Due to potential side effects from the use of corticosteroids and immunosuppressants, it is important to follow up with these patients regularly and stay up to date with lab testing.[6]

Shield ulcer. This is a sterile corneal ulceration found in patients with vernal keratoconjunctivitis (VKC). The condition mainly affects young boys in their first decade of life, and the sequelae may result in permanent visual impairment.[7] These patients have a family history of atopic diseases in 49% of cases and a personal medical history of other atopic conditions such as asthma (26.7%), rhinitis (20%) and eczema (9.7%).[7]

Clinical presentation of a shield ulcer is commonly associated with palpebral VKC, which primarily involves the upper tarsal conjunctiva and is characterized by diffuse papillae that eventually progresses into giant papillae, greater than 1mm in size, with mucus discharge between the papillae. The close apposition of the superior conjunctival papillae to the corneal epithelium results in corneal surface disease, including shield ulcers and Trantas' dots, an aggregate of epithelial cells and eosinophils at the limbus. VKC generally subsides with the onset of puberty, but some therapeutic measures may be required beyond this age to control the course of the disease.[7]

Treatment options begin with a prophylactic approach for seasonal atopic conditions and extend into surgical procedures for more devastating cases involving sterile ulceration. Prophylactic measures include patients becoming aware of their vulnerability, commonly by an allergy specialist, and avoiding the triggering allergen to reduce the chances of inflammation. Common triggers include sun, dust, wind and other general environmental factors.[7]

In these cases, cold compresses and proper lid hygiene are recommended to help with symptoms of irritation and signs of possible *Staphylococcal* hypersensitivity, respectively. Topical antihistamines are commonly used in acute episodes but are less effective when used alone during chronic disease.

Mast-cell stabilizers are frequently used in combination with NSAIDs for the long-term.[5] Topical steroids are considered when a quick tapering is expected and are often prescribed in heavy doses, with the possibility of a supratarsal steroid injection in cases with severe palpebral disease. Immune modulators, such as cyclosporine and tacrolimus, are viable options for high-risk steroid patients.[5]

Surgical treatments such as superficial keratectomy are considered for the removal of plaques or the debridement of a corneal ulcer. Furthermore, patients being treated with topical steroids should be strictly monitored due to the incidence of glaucoma in VKC patients (2%). Once the acute phase runs its course, steroids should be discontinued and replaced with alternatives such as mast-cell stabilizers, antihistamines or NSAIDs.[7]

Patients with VKC generally have spontaneous resolution of the disease after puberty without any further symptoms or visual complications. However, corneal ulcers, which are reported to develop in 9.7% of patients, can produce a permanent visual impairment.[7]

Mooren's ulcer. Unfortunately, clinicians may sometimes encounter a case in which etiology is controversial or indeterminate, as is often the case with this presentation. Mooren's ulcer is a rare, idiopathic disease thought to have an autoimmune component and possibly be associated with environmental factors of corneal insult such as surgery, trauma or infection. The disease may present itself unilaterally or bilaterally. It is rare in the northern hemisphere but common in the southern hemisphere and other geographical locations such as China, Africa and India.[8]

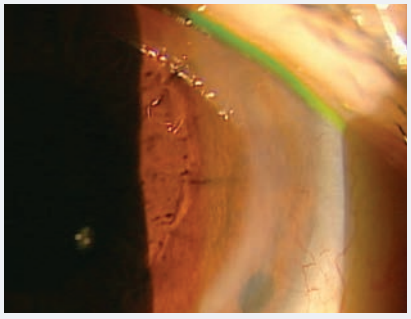


Fig. 3. Stable PUK in a long-standing RA patient.

Clinically, Mooren's ulcer is characterized by a progressive circumferential peripheral stromal ulceration, which has the potential to spread centrally. There are two types of presentations, with the first being unilateral and more benign. It predominantly affects the elderly and responds well to treatment. The second type is more aggressive, predominantly affects young males, has a bilateral presentation and does not respond well to medical therapy. Vascularization of the stromal bed can also be present in terminal stages of the condition and eventually leads to scarring as the cornea begins to heal.[5] Mooren's ulcer is a diagnosis of exclusion and is often diagnosed once other etiologies, such as PUK, have been eliminated.

Topical treatments for Mooren's ulcer include combinations of steroids, antibiotics, artificial tears and, in some cases, collagenase inhibitors such as acetylcysteine. Unfortunately, for those within the second group, visual prognosis is poor, even with treatment.

Systemic therapy includes immunosuppressants and collagenase inhibitors such as doxycycline. Surgical options include conjunctival resection and lamellar keratectomy, as well as penetrating keratoplasty. Post-surgical intervention includes vision rehabilitation once inflammation has settled.[5] During follow-up exams, these patients should be monitored for secondary infections. Eye care providers should comanage with the patient's primary care physician to make sure any underlying systemic conditions are being addressed.

Pain, photophobia and discharge are common signs and symptoms a patient mentions when they present with a corneal ulcer. While infectious causes are often the focus of discussion, sterile ulcers come with their own concerns worth understanding—as the right treatment depends on it. A widely agreed upon treatment approach with an unknown etiology is a broad-spectrum antibiotic, such as a fluoroquinolone, to cover for severe pathogens such as *Pseudomonas*. However, treatment must be far more tailored to ensure successful resolution.

Once an infectious etiology has been eliminated due to a lack of common findings such as mucus discharge, anterior chamber reaction and contact lens wear, clinicians should then consider the possibility of an associated systemic condition and other ocular surface diseases, as both are common with a sterile ulcer. Knowing the etiologies of sterile ulcers will guide the clinician through potential treatment options, both systemic and topical, to best care for each and every patient. RCCL

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CE TEST ~ SEPTEMBER 2018

1. **Which of these is the etiology of marginal keratitis?**
   a. Type I hypersensitivity.
   b. Chemical burns and trauma.
   c. Type IV hypersensitivity.
   d. Rheumatoid arthritis.
2. **Which of the following is not a management option for a contact lens-related infiltrate?**
   a. Fit patient in a lower oxygen permeable lens.
   b. Discontinue lens wear.
   c. Prescribe a broad-spectrum antibiotic when suspicious for an infection.
   d. Switch patient into a daily lens.
3. **What is the most common pathogen responsible for infectious keratitis in contact lens wearers?**
   a. *S. epidermidis.*
   b. *Klebsiella.*
   c. *Pseudomonas.*
   d. *Moraxella.*
4. **Which of the following is not a clinical sign of vernal keratoconjunctivitis (VKC)?**
   a. Shield ulcer.
   b. Trantas' dots.
   c. Giant papillae.
   d. Pseudodendrites.
5. **Which of the following statements is true regarding Mooren's ulcer?**
   a. It is more common in the northern hemisphere.
   b. The second type is more severe and commonly affects young males.
   c. The second type responds well to treatment.
   d. There is no systemic condition associated with Mooren's ulcer.
6. **Which of the following is not a surgical treatment option for PUK?**
   a. Amniotic membrane transplant.
   b. Bandage contact lens.
   c. Corneal collagen crosslinking.
   d. Corneal lamellar graft.
7. **Exposure keratopathy is a result of:**
   a. Facial nerve palsy.
   b. Severe proptosis.
   c. Reduced muscle tone.
   d. All of the above.
8. **What percentage of VKC patients develop glaucoma?**
   a. 10%.
   b. 15%.
   c. 2%.
   d. 5%.
9. **What percentage of noninfectious PUK cases is associated with RA?**
   a. 50%.
   b. 70%.
   c. 62%.
   d. 34%.
10. **Which of the following is the hallmark of neurotrophic keratitis?**
    a. Corneal perforation.
    b. Corneal melting.
    c. Decrease in corneal sensation.
    d. Corneal ulceration.

EXAMINATION ANSWER SHEET

Corneal Ulcers: Sterile But Not Benign
Valid for credit through August 16, 2021

Online: This exam can also be taken online at www.reviewofoptometry.com/ce. Upon passing the exam, you can view your results immediately. You can also view your test history at any time from the website.

Directions: Select one answer for each question in the exam and completely darken the appropriate circle. A minimum score of 70% is required to earn credit.

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Answers to CE exam:

1.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	4.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	8.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
2.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	5.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	9.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
3.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	6.	Ⓐ	Ⓑ	Ⓒ	Ⓓ	10.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
					7.	Ⓐ	Ⓑ	Ⓒ	Ⓓ					

Post-activity evaluation questions:
Rate how well the activity supported your achievement of these learning objectives:
1=Poor, 2=Fair, 3=Neutral, 4=Good, 5=Excellent

11. Better understand how to differentiate between infectious and sterile corneal ulcers.	①	②	③	④	⑤
12. Improve my knowledge of the common ocular etiologies of sterile ulcers.	①	②	③	④	⑤
13. Increase my diagnostic acumen for systemic etiologies of sterile ulcers.	①	②	③	④	⑤
14. Better recognize the common presentations of corneal sterile ulcers.	①	②	③	④	⑤
15. Increase my knowledge of the treatment approaches for each sterile etiology.	①	②	③	④	⑤
16. Increase my ability to properly manage sterile corneal ulcers, regardless of etiology.	①	②	③	④	⑤

Rate the quality of the material provided:
1=Strongly disagree, 2=Somewhat disagree, 3=Neutral, 4=Somewhat agree, 5=Strongly agree

17. The content was evidence-based.	①	②	③	④	⑤
18. The content was balanced and free of bias.	①	②	③	④	⑤
19. The presentation was clear and effective.	①	②	③	④	⑤

20. Additional comments on this course:

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Signature: _____ Date: _____

Please retain a copy for your records. LESSON 117046, RO-RCCL-0918

FIGHTING CORNEAL INFECTIONS WITH CXL: A NEW ALLY?

Evaluate the strengths and weaknesses of this newfound application before considering it an alternative treatment for keratitis.

By Aaron Bronner, OD

Corneal infections continue to trouble patients of all ages and lifestyles worldwide. Infectious keratitis occurs in 20 to 50 people per 100,000 in the United States, and the risk increases following any compromise to the corneal epithelium.[1] These infections resist conventional therapies and can be difficult to differentiate clinically, adding to the challenges posed by this already sight-threatening group of pathologies. If you were to create an ideal treatment for corneal ulcers, you'd probably want something like this:

- The treatment should be safe to the patient's own tissue.
- Its efficacy should cover a broad spectrum of pathogens, eliminating the need to differentiate clinically or with cultures prior to treating.
- The treatment's dosage should allow patients to have a relatively normal schedule compared with hourly, or more frequent, administration of topical antimicrobials.
- Cost should be affordable to allow use as needed, without worry of reimbursement or patient finances.

On paper, corneal collagen crosslinking (CXL) for microbial keratitis, a treatment known as photo-activated chromophore for infectious keratitis (PACK-CXL), checks all of these boxes. In application, PACK-CXL, vaguely recognized by optometry as a treatment option for infectious keratitis, has several limitations that stymie its widespread use.

THE HYPE

PACK-CXL follows the same general protocol as crosslinking for keratoconus. The cornea is saturated with riboflavin, a UVA source of 365µm is applied to the cornea for a period of time and then the patient recovers at home. More so than with traditional crosslinking, the exact protocol for PACK-CXL varies from center to center and relies on surgeon preferences, fluences of the UV lamp and the exact topical riboflavin concentration. Case-dependent features such as ulcer depth and degree of thinning also play a part.

Regardless of the precise protocol, the mixture of UV radiation, riboflavin and oxygen creates reactive oxygen species (ROS). In conventional crosslinking, these ROS lead to the activation of the lysyl oxidase pathway and the development of "crosslinks." This activation also takes place with PACK-CXL, and the result is a stiffer cornea.[2-4] This bolsters it against proteolytic melts common with infectious keratitis.

The "photo-activated riboflavin" in PACK-CXL disrupts base pairing of both pathogenic RNA and DNA, thereby inhibiting replication. In addition, oxidative destruction of the pathogen occurs via the ROS.[2-4] PACK-CXL therefore theoretically kills the pathogen, blocks its replication and makes the cornea more resistant to further tissue destruction.

In addition, effectiveness of PACK-CXL should be independent of the specific pathogen, as all ulcers are going to benefit from increased tectonics, and all free-living pathogens (i.e., non-viral), in theory, would be susceptible to the massive quantities of ROS. One meta-analysis of the available literature shows good susceptibility to the ROS across bacterial, fungal and protozoan sources of corneal infection. In this analysis, 85.7% of bacterial keratitis cases, 91.7% of *Acanthamoeba* cases and 78.1% of fungal cases healed.[3] Both cases of herpes simplex virus (HSV) keratitis in this review went on to melt and required a therapeutic keratoplasty, so PACK-CXL is probably best avoided in HSV cases.[3]

Ignoring the terrible outcomes reported with HSV, this review indicates that PACK-CXL actually has a broad spectrum of activity that isn't affected by the pathogenic group (fungal, *Acanthamoeba* or bacterial) or its antimicrobial resistance profile, meaning, it should work on methicillin-resistant *Staphylococcus aureus* (MRSA) just as effectively as on Methicillin-susceptible *Staphylococcus aureus* (MSSA). These attributes and strengths could present a significant benefit to the clinician who, in theory, would

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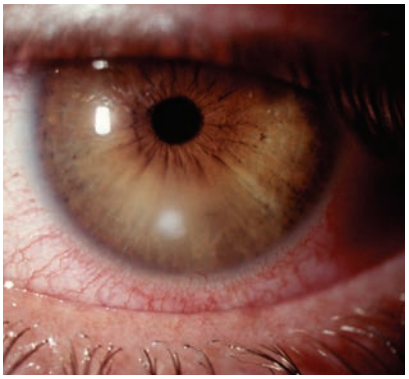

Photo: Joseph W. Sowka, OD, and Alan G. Kabat, OD

PACK-CXL may be more successful for early corneal ulcers such as this, rather than more severe presentations.

no longer be required to accurately differentiate based on clinical features or culture results. As an effective one-size-fits-all treatment, PACK-CXL could possibly take the guesswork out of selecting the initial management.

If PACK-CXL were effective as a standalone treatment, patients could avoid the need to adhere to the challenging drop regimen characteristic of microbial treatment. Regimens that require some level of continuous therapy are standard in the early management of microbial keratitis and can stretch on for several weeks. In all cases, those treatments create a significant burden to the patient regarding both quality of life and compliance. If a single in-office treatment with PACK-CXL could eliminate or at least reduce the frequency of topical antimicrobial use, it would present a tangible benefit to the patient management.

The potential to reduce or eliminate an extensive eye drop regimen is the theoretic impact on cost. Treatments often take several weeks, and occasionally months, with frequent follow-up. In addition to cost of clinic care, the expense of conventional antimicrobial treatment can be high and, in certain parts of the world, cost prohibitive. For PACK-CXL, on the other hand, riboflavin is inexpensive and UV lamps are widely available. For most of the world, PACK-CXL as a standalone therapy would represent a significant improvement in average cost of therapy compared with conventional treatment. In fact, Farhad Hafezi, MD, past chair of Ophthalmology at University of Geneva and a primary proponent of PACK-CXL, has pointed out that the benefit of CXL as a treatment for infectious keratitis to impoverished parts of the world is potentially greater than CXL's global benefit in treating keratoconus.

THE REALITY

On a cursory review and ignoring the details, PACK-CXL seems like an amazing treatment option that could address nearly all of the shortcomings and headaches associated with modern antimicrobial regimens for corneal infections. But as is often the case, the devil is in the details, and significant limitations exist with what exactly the research of PACK-CXL is suggesting in regards to efficacy, protocol and practical hurdles practitioners face—all of which may be barriers to its widespread use.

Protocol. There has been little formal standardization of the actual treatment protocol of the PACK-CXL procedure. "Dresden protocol" CXL (UVA fluence of 3mW/mm^2 for 30 minutes) has been the most common published approach, but others have advocated for accelerated treatments with greater fluences, as well as longer treatments with standard fluences but a lower concentration of riboflavin.[3] The postoperative course for PACK-CXL has also yet to be defined as well. Clinicians often use corticosteroids in the early postoperative period with conventional CXL to control inflammation, but given their potentially confounding effects on microbial keratitis, corticosteroids aren't used in studies on PACK-CXL, which may have led to unnecessary, untreated exacerbations of sterile inflammatory problems. In fact, one large study found a transient increase in the size of hypopyon following PACK-CXL in some patients, likely indicating not a worsening of infectious inflammation but a sterile inflammation.[2]

Efficacy. While most research of PACK-CXL has been positive for the most part, there are some important holes in the research. Probably most important for understanding reports of the procedure's efficacy is that the majority of available research has not directly compared PACK-CXL with conventional topical antimicrobial treatment. Instead, the bulk of the research compares the combination of PACK-CXL plus antimicrobials with topical antimicrobials alone. In one large meta-analysis, only 16 of the 175 eyes received PACK-CXL alone; all others continued with combined typical antimicrobials and PACK-CXL.[3] With this in mind, the most we can say about these eyes is the addition of PACK-CXL to conventional therapy did not worsen outcomes compared with conventional therapy alone. This is starkly different than suggesting that PACK-CXL alone is equivalent to conventional therapy. So if a center uses PACK-CXL, the patient should still expect to use topical antimicrobials (with all the associated cost and inconvenience),

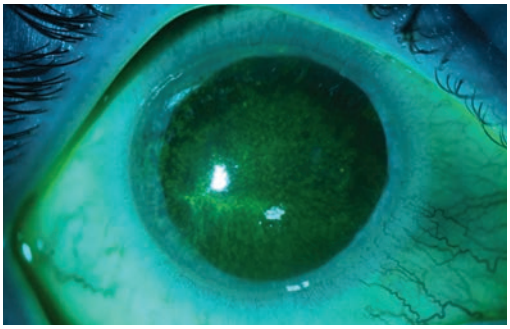

Photo: Christine W. Sindt, OD

While research suggests good efficacy for AK, seen here, animal studies are less promising.

selection of appropriate antimicrobials is still important, and clinical- and culture-based differentiation of infectious etiologies is still necessary. Obviously, this reduces some of the appeal of PACK-CXL.

Further, the available research on PACK-CXL seems to suggest that the procedure works best with early superficial ulcers that are bacterial in nature and works poorly in severe ulcers, most particularly with those that are fungal in nature—not surprising given the expected depth of treatment with conventional CXL. One article makes a compelling argument about the expected efficacy of PACK-CXL being relative to the depth of the ulcer. Pointing to previously determined depth of irradiance studies, the authors remind clinicians that 50% of irradiance is absorbed in the anterior 100µm of the cornea, 25% in the second 100µm and the remaining 25% irradiates the remaining cornea at increasingly low levels, and it could be expected that dense ulcers may reduce the penetrance of UV energy even further.[2] The authors note that the procedure could produce better results for early and anterior ulcers and worse results with increasing depth of involvement. This concept corresponds with results of other studies that suggest the procedure's efficacy diminishes with increasingly severe ulcers.[3,5]

Compounding its greater efficacy with superficial ulcers is the fact that it seems to perform differently among pathogen groups. For bacterial sources, most agree that PACK-CXL produces a bacteriocidal and bacteriostatic effect.[2-4] This concept supports the clinical outcomes seen with PACK-CXL for bacterial keratitis. For fungal keratitis, both lab and animal models appear split on UVA+riboflavin producing any antifungal effect, and it is worth noting that a study of eyes with deep fungal keratitis treated with PACK-CXL was halted due to an increasing rate of perforation in the treatment arm.[6] In addition, we also know that fungal keratitis treated with PACK-CXL is less likely to resolve than bacterial keratitis.[3]

For *Acanthamoeba* keratitis (AK), the 10 out of 11 successfully treated eyes mentioned in the meta-analysis contradict animal studies of the disease. One rabbit study of AK marked worsening of keratitis after CXL with riboflavin and UVA compared with those that did not receive treatment.[6] These discrepancies between clinical- and lab-based research should give pause to those widely embracing the procedure for these more uncommon forms of keratitis.

Practice hurdles. In the US, the only FDA-approved platform for crosslinking is the Avedro KXL System with Photrexa riboflavin drops. While PACK-CXL is an off-label application of the device, most US centers offering CXL use the Avedro system. Recently, the cost of Photrexa drops has increased significantly, a material cost to a center that is then passed on to the patient. Because of this, PACK-CXL, in the United States at least, is almost certainly not going to offer a cost savings compared with conventional antimicrobials. However, with the availability of lower-cost systems across the globe, PACK-CXL still may offer savings in other countries.

THE VERDICT

Based on the current research, PACK-CXL might fit in nicely to the therapeutic algorithm for microbial keratitis treatment in well-chosen cases (namely, superficial bacterial ulcers). Its efficacy and wide spectrum of activity against bacteria (regardless of antibiotic resistance) and lesser activity against fungus and AK makes it not a one-size-fits-all treatment, but perhaps the next best thing. That said, it is not currently advocated as a replacement of conventional therapy but as an adjunct treatment. Further, the exact place of PACK-CXL in the therapeutic paradigm is hard to pin down. The procedure seems to perform better with early ulcers, making it more of a first-line therapy. However, its cost, off-label and experimental status and poorly defined protocol all serve to undermine its use as a first-line treatment. As costs come down and the protocol becomes more defined, this may change. Currently, however, the dissemination of PACK-CXL in the United States will probably remain a secondary treatment option, likely to the detriment of its effectiveness. RCCL

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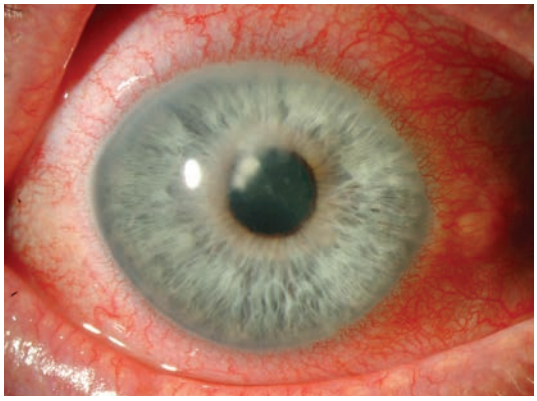

Photo: Christine W. Sindt, OD

PACK-CXL is least effective for severe cases of fungal keratitis, seen here secondary to *Fusarium*.

Take the *Anxiety* out of Specialty Lens Fittings

Smarter clinical strategies and useful new technologies help ensure a smoother process.

By Clark Chang, OD, and Jeffrey Sonsino, OD

Even though soft contact lenses dominate the market, gas permeable (GP) lenses remain essential for many patients, providing superior optics, durability, higher oxygen transmissibility and a lower propensity for surface deposits and microbial inoculations within the GP lens matrix. Modern specialty lenses, especially scleral-fit GP lenses, offer better outcome expectations for patients with a wide range of visual and clinical needs—from optical rehabilitation in patients with corneal irregularities to therapeutic protection in patients with dry eye and other ocular surface diseases.[1,2] As such, global clinical trends demonstrate a growing rate of GP contact lens use.[3-5] This finding especially holds true for scleral lenses specifically.[3-5]

While specialty lenses are becoming more popular, fitting them can sometimes intimidate clinicians who are less familiar with custom designs. This is primarily due to the perceived extensive chair time and potential patient discomfort with corneal GP lenses. However, as corneal GP technology advances, new lens designs—like the design of a scleral lens, for example—make it possible to improve initial lens comfort and reduce adaptation time.

The on-eye position and associated fitting characteristics of scleral lenses are heavily influenced by the corneo-conjunctival junction angle and scleral shape profile. Consequently, if a scleral GP cannot be customized to align with these anatomical features, fitting- and vision-related adverse reactions may develop.[6] To make matters worse, slit lamp findings alone do not usually offer sufficient clinical clues for clinicians who are looking to take advantage of the latest lens customization concepts.

Fortunately, numerous technologies are available to help overcome some of these challenges and deliver optimal results. This article walks through five key steps clinicians should take to successfully complete a specialty contact lens fitting and explains how several newer diagnostic instruments can be clinically helpful for novices and veterans alike.

Strictly speaking, you do not need any of these devices to be successful with scleral lenses in a number of routine cases. But these tools will help you solve problems, save time and fine-tune results to give each patient the most customized experience possible. An important mark of expertise in all contact lens specialists is whether they use the best available tools of the trade and stay both well equipped and well versed in their product knowledge.

1 MEASURE THE VAULT

The long-term objectives of a contact lens fit are to meet metabolic requirements of the corneal tissue and reduce hypoxic risks. Compared with the vaulting abilities of corneal-fit GP lenses and soft lenses, a scleral lens's ability to vault over the cornea helps avoid epithelial trauma and, in turn, improves comfort. Vaulting also allows the accumulation of tears to neutralize anterior corneal toricity and irregularities. The vaulting distance of a scleral lens, however, may act as a pathway that resists efficient oxygen permeation. Researchers tend to agree that long-term monitoring and using lens materials with high oxygen permeability (>100 Dk/l)

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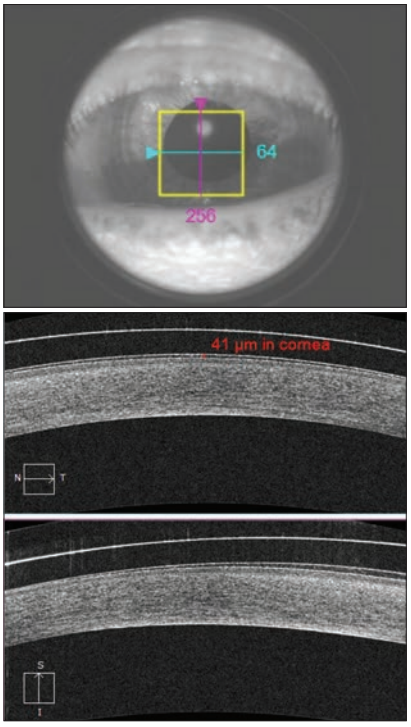


Fig. 1. This hybrid lens shows a mild amount of corneal clearance (41µm). The patient needs an increased lens vault to properly compensate for the lens settling throughout the day.

are prudent practices when fitting scleral GP lenses.[7-10]

A team of researchers suggests three clinical criteria must be checked off to achieve maximum oxygenation under a scleral lens: (1) the lens must be constructed from a material with the highest Dk available, (2) it must have a maximum center thickness of 250µm and (3) it must be fit with no more than 200µm of clearance.[7] Perhaps surprisingly, the third criterion appears to have the largest clinical significance; another group of researchers also concludes that tear vault has a bigger impact on corneal oxygen tension than lens Dk.[9] To support previous findings, a follow-up study demonstrates that corneal oxygenation levels drop by as much as 30% when scleral vault increases from 200µm to 400µm.[10]

Despite the clinical importance of the recommended 200µm clearance guideline, this proposed fitting condition might be the most challenging to fulfill. This is largely due to the variability in tear lens measurement via slit lamp biomicroscopy. Research shows that a variance of up to 207µm may occur when estimating scleral lens vault using a slit lamp.[11] Thus, if clinicians are expected to follow the 200µm clearance suggestion but must rely on slit lamp observations to guide vaulting modifications, patients may be exposed to undue risk of hypoxia.

A more precise and objective method of measuring corneal vault is anterior segment optical coherence tomography (AS-OCT). The technology's caliper tool is accurate within 6µm, offering more precise clearance data in multiple locations under scleral lenses and other specialty lenses (*Figure 1*). Nonetheless, this technology comes with limitations; it assumes the measurement path travels from the refractive indices of air to cornea and does not currently account for the additional medium of contact lens material. Despite this, AS-OCT is still substantially more accurate and repeatable than slit lamp biomicroscopy.

If you do not currently have access to AS-OCT, new software that analyzes the ocular surface—AOS (Advanced Ophthalmic Systems)—may be worth pursuing as a cheaper alternative. While validation between AS-OCT and AOS measurements is currently limited, this Windows-based technology can analyze and enhance any digital image, whether it originates from an anterior segment camera or a smartphone.

This software package has various clinical grading scales for conjunctival redness, vascular status, punctate epitheliopathy and more. It also includes a specialty lens-fitting module that measures scleral lens clearance. Additionally, this software indirectly assesses the peripheral lens fitting relationship by grading vasculatures within selected areas under the haptic zone, which may further aid clinicians in deciding whether to incorporate customizable features, such as a back-toric haptic (*Figure 2*).

2 PERFECT THE DESIGN

Even with a history of corneal GP non-adaptation, most patients can still comfortably wear modern hybrid lenses and scleral lenses. When patients present with a history of contact lens failure, clinicians

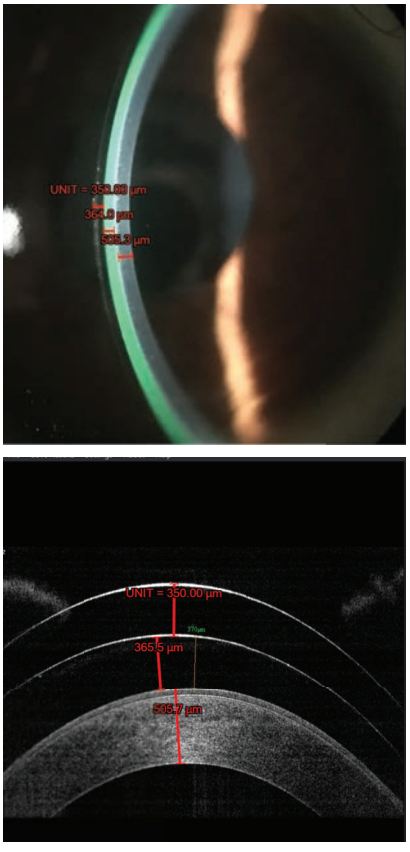


Image: John Gelles, OD

Fig. 2. The ruler function in the AOS software calibrates itself by using the known lens center thickness value (i.e., 350µm) and then calculates the corneal clearance and thickness as shown on the imported digital image (top). After an OCT image of the same patient is uploaded to the software, the calibrated ruler function yields nearly identical measurements for corneal clearance and thickness (bottom).

typically place more emphasis on lens comfort than sight. For example, a patient with severe keratoconus but relatively clear corneas and otherwise normal ocular findings may be conditioned by their doctor to be content with a visual outcome of 20/40, provided their lenses are comfortable. Fortunately, technologies are available to help give patients comfort *and* optimal vision.

Despite improved fitting success with today's hybrid lenses and sclerals, anatomical variations in the corneo-conjunctival junction angle and the scleral profile often affect the scleral lens fitting and visual outcome. As a result, scleral lenses may cause misalignment between the visual axis and the optical center, inducing lens instability and producing unintended higher-order aberrations (HOAs)—all of which can lead to unsatisfactory visual performances. Modern scleral lenses, however, have design-specific angular geometry built into the transition zone—new scleral lens designs tend to use a transition zone that assumes a tangential angular profile—which increase fitting stability because the scleral lens is able to better align with the anatomy of the corneo-conjunctival junction.

Recent studies show that scleral lenses become increasingly rotationally asymmetrical as the chord diameter on the ocular surface widens. Thus, incorporating back-toric in the haptic zone may improve both comfort and stability.[6,12] To make the process easier, some scleral lens technologies can develop different haptic angles for right and left eyes in diagnostic sets.

If the patient's vision remains below clinical expectations, even with enhanced centration and stability through the use of toric haptics, clinicians can perform a toric over-refraction to see if better visual acuity is attainable. If spherocylindrical over-refraction findings are clinically significant, incorporating front-toric optics into a lens with toric haptics will promote rotational stability, yielding a higher success rate.

Optical complexities can vary depending on individual case presentations, and some patients may continue to suffer from compromised visual function. A study suggests that the clinical benefits of modifying the front surface eccentricity of scleral lenses to 0.6 or 0.8 are analogous to adding wavefront-guided optics, whereby improvements in both high- and low-contrast visual acuity can be observed.[13] Thus, it is worth inquiring about this new customization feature with lab consultants.

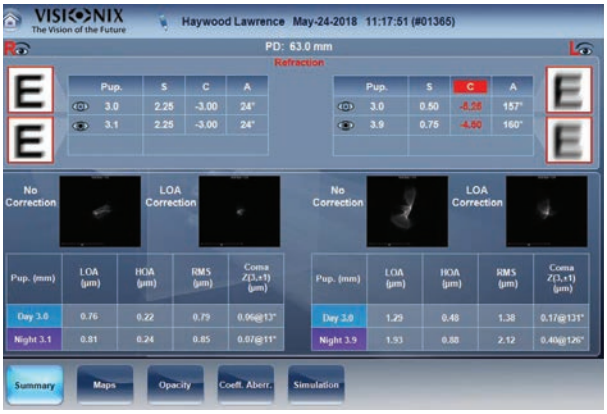


Fig. 3. In this wavefront over-refraction performed on a severe keratoconus patient who wears scleral lenses, the 3mm pupil measurement zone shows a -3.00D residual cylinder OD and a -5.25D residual cylinder OS.

3 FINESSE THE FIT

A recent study demonstrates that most eyes have some level of scleral asymmetry or irregularity.[6] Using a corneo-scleral topographer to scan ocular surfaces at 16mm diameters—a commonly used scleral lens diameter length—researchers found that only 5.7% and 28.6% of evaluated eyes had scleral profiles resembling spherical and regular toric shapes, respectively.[6] These findings imply that, when using a 16mm mini-scleral lens, haptic misalignment could potentially be observed in up to 71.4% of eyes even if a standard toric haptic design is used.

Misaligned scleral lens haptics may lead to discomfort, air bubble formation and debris trapped in the lens reservoir. Significant debris entrapment can result in visual fogging, which drastically decreases satisfaction. To combat this major barrier, clinicians must perfectly match scleral lens profiles, limbal transition angles and conjunctiva-sclera angles in all meridians.

This is where a corneo-scleral topographer comes in handy. It can capture circumferential ocular surface elevation data at a specified chord diameter and guide the manufacturing process to produce the appropriate amount of haptic toricity and the desired total lens sagittal depth. In addition, new software can compute the height and size of a lesion, such as a pinguecula, and create a focalized vaulting area under the scleral lens to best match the ocular surface profile.[14] This software can greatly reduce the chair time traditionally associated with designing a scleral lens notch.

4 SHARPEN THE OPTICS

The customization strategies discussed thus far help enhance specialty lens fitting outcomes. Some patients, however, will continue to experience reduced vision due to the presence of residual HOAs. Therefore, measuring these HOAs will assist you in finding ways to address continued visual challenges.

To account for the optical summation of both anterior and posterior

corneal profiles, diagnostic instruments capable of registering corneal data points beyond anterior corneal shape can further elucidate sources of visual disturbance. Scheimpflug imaging devices, such as the Pentacam (Oculus), can analyze anterior and posterior corneal profiles through a rotating mirror that travels in an arc around the eye and produces a 3D biometry of the eye.

Many will find that accounting for posterior corneal contributions is sufficient in obtaining desired clinical outcomes. However, using a wavefront aberrometer to precisely map HOAs will give you more data to consider when fine-tuning lens specs. Popular devices include the OPD-III (Nidek), KR-1W (Topcon) and iTrace (Tracey Technologies).

Some newer devices combine multiple diagnostic capacities to render a comprehensive analysis of the anterior segment. The VX130 (Visionix) is equipped with the functionalities of a Shack-Hartmann wavefront aberrometer, an autorefractor, a Scheimpflug-enabled corneal tomographer, an optical pachymeter and a non-contact tonometer. This single instrument allows clinicians to visualize the differential spatial arrangements between the anterior and posterior cornea and provides a wavefront over-refraction to help guide contact lens modifications (*Figure 3*).

In some cases, clinicians can compensate for residual HOA contributions with a spherocylindrical over-refraction, proving that wavefront aberrometry refraction over a specialty lens can be helpful during the initial fitting and subsequent follow-up. Nonetheless, depending on the magnitude of posterior optical complexities and the on-eye position of the lens, additional anti-aberration mechanisms could be required.

Researchers and manufacturers have already found success when incorporating wavefront-guided corrections into scleral lenses.[15,16] Thus, capturing HOA data will help guide the process of designing specialty contact lenses for your more challenging patients. As lab manufacturers further refine their own proprietary algorithms, patients will continue to benefit from the use of these advanced technologies.

5 KEEP IN TOUCH

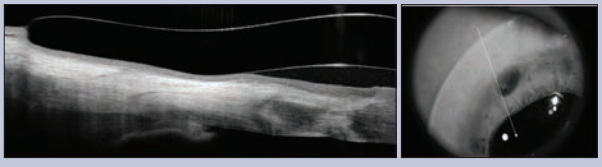
Constructing the perfect specialty lens for each patient requires a high level of clinical expertise, in addition to patient motivation and compliance. Although perhaps a controversial subject, telehealth applications can greatly benefit patient-doctor communication when used appropriately.

As is often the case with specialty contact lens evaluations, patients travel long distances to seek the expertise of clinicians who have a limited amount of time. Consequently, clinicians must identify ways to achieve the best clinical results within a limited number of office visits.

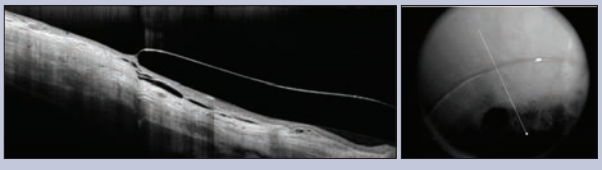
A LENS THAT FITS LIKE A GLOVE

When a patient's ocular, and especially scleral, anatomy is highly atypical (e.g., due to trauma, surgery or advanced disease), the best solution may be to abandon conventional fitting approaches. Rather than tinker with lens parameters in an attempt to approximate the scleral shape, mimic it.

EyePrint Prosthetics (EPP) introduced a manufacturing technology that aims to replicate the contours of a patient's ocular surface by using an ophthalmic-friendly molding material that captures the exact impression of the anterior ocular anatomy. The resultant impression is shipped to a manufacturing lab, where one to two million data points are scanned and converted into computer-aided design images, producing precise scleral lens geometry.



In this patient, the haptic is applying excessive pressure to an elevated glaucoma bleb. Patency is not seen on these OCT scans.



With EPP lenses, the haptic can easily be redesigned to reduce pressure over the bleb. Patency to the bleb is now seen on scans in the form of black spaces under the haptic.

Designing such a highly customized lens makes a wide range of clinical applications possible. EPP technology can accurately position itself on-eye, regardless of irregular conjunctiva-sclera angles or scleral elevations, such as pterygia, severe pingueculae and glaucoma blebs/shunts.

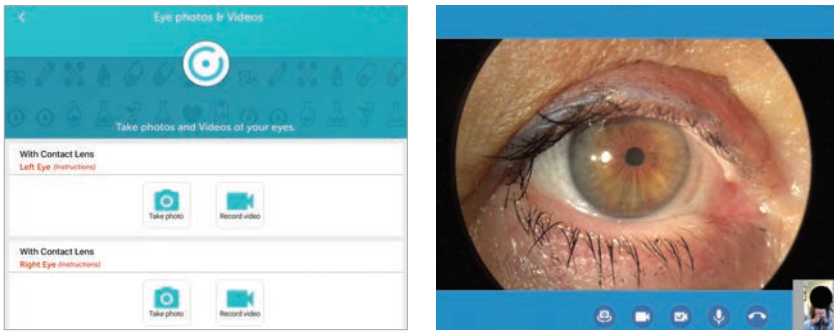


Fig. 4. Eyecare Live allows patients to send ocular images securely to their eye doctors via telemedicine. Before a follow-up, digital interactions with their doctor give patients the chance to ask questions and express concerns while adapting to their newly prescribed specialty lenses.

One solution may be a doctor-to-patient telehealth platform called Eyecare Live. The clinical objective is to use this platform to check in with specialty contact lens patients prior to their follow-up exams and complete non-office-related tasks online. From the comfort of their homes, patients can communicate questions and submit lens-related ocular images for analysis (*Figure 4*). This process aims to improve patient compliance and motivate patients to continue their lens adaptation efforts for a greater chance of fitting success.

A WIN-WIN SCENARIO

A specialty lens fitting can significantly improve a patient's quality of life if done successfully. However, selecting the most appropriate lens requires a high level of clinical expertise and the right pieces of equipment. Rather than focus on traditional specialty lens designs, clinicians should update their fitting strategies based on the most recent evidence-based data available, selectively adopting new diagnostic instruments and exploring alternate interfaces that can enhance clinical interactions and improve standards of care. As a result, clinicians and patients alike will have better experiences, feel more satisfied and see successful outcomes. RCCL

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Fungal Ulcers: Missed and Misunderstood

They may be less common, but they're also more severe.

Though familiar corneal pathogens, such as *Staphylococcus epidermidis* and *aureus* and *Pseudomonas aeruginosa*, cause the majority of ulcers clinicians see, a small percentage are caused by protozoan and fungal etiologies. Of these atypical microbial keratitis sources, fungal origins are encountered most frequently and have a worse prognosis than many other corneal infection sources. A number of fungal species that cause corneal infection only cause one disease—keratitis—and haven't been documented to cause infection anywhere else in the body.[1] This illustrates how the cornea is perfect for incubating fungal infections; it's a warm, damp environment isolated from the immune response—a fungal infection trifecta. This column will review this group of pathogens and the challenges they present.

A GLOOMY FORECAST

The incidence of fungal keratitis varies based on geographic location. In the northern temperate and southwestern desert parts of North America, the incidence is relatively low, accounting for 6% to 10% of all ulcers encountered, whereas in tropical parts of the continent, the incidence approximately doubles.[2-5]

The prognosis of fungal keratitis is startling; 43% of emergent keratoplasties performed out of Bascom Palmer are fungal keratitis surgeries, though the incidence is about 20% in Southern Florida—meaning that fungal keratitis is more than twice as likely as bacterial keratitis to lead to emergent transplant.[5,6]

Many reasons for this negative prognosis exist, including limited, poorly penetrating ophthalmic preparations of antifungal medication. Perhaps more important is the missed opportunity for early recognition of fungal keratitis due to a lack of knowledge about the infection's risk factors.

LOOK AT THE BIG PICTURE

Fungal keratitis is widely associated with organic trauma—the most frequent risk factor for fungal disease across the globe.[1] Unfortunately, the index of suspicion drops when the historic risk of trauma is absent. Organic trauma, however, is not the only cause, and clinicians should consider other risk factors when weighing the likelihood of a fungal ulcer. One study found that while 25% of fungal ulcers were associated with trauma, 37% were associated with contact lens use and 29% with opportunistic infections in patients with ocular surface disease (OSD).[7] Though the study notes the percentage of cases associated with contact lens use dropped after an offending cleaner was pulled from the market, lens use is still associated with approximately as many cases of fungal keratitis as trauma.[7,8]

More perplexing is the association with OSD. While clinicians are often more concerned about members of the normal ocular flora and less about atypical etiologies, they should also remember that fungal elements can be components of the normal flora and cause opportunistic corneal infection in patients with OSD.[7,8] In fact, yeast sources of fungal keratitis predominate in cases related to OSD, exposure and ophthalmic surgery.[7,8]

KEEP YOUR EYES OPEN

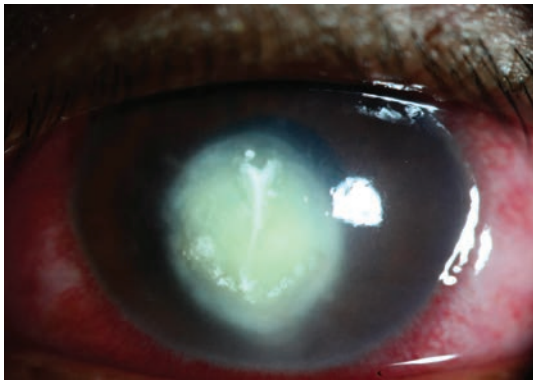
Clinicians may also assume fungal ulcers can be differentiated by their clinical appearance. Fungal ulcers are known to have a number of supposed "classic findings," such as feathery margins, satellite infiltrates, pigmented infiltrates and endothelial plaques, that doctors can lean on to achieve a timely diagnosis. Unfortunately, nearly 60% of fungal ulcers do not have any classic clinical features related to fungal keratitis. When a lack of findings characteristic of fungal keratitis is paired with mundane risk factors, such as contact lens use and OSD, it is no wonder fungal keratitis is frequently misdiagnosed and wrongly managed as bacterial keratitis. One study suggests that nearly 90% of the fungal ulcers reviewed were originally being treated for bacterial keratitis.[9] Given this finding, it is important to understand how to develop appropriate clinical suspicion regarding fungal keratitis.

IS IT FUNGAL OR BACTERIAL?

An article on *Acanthamoeba* keratitis (AK) notes that the initial step in diagnosing AK is to suspect it.[10] This mindset holds true when dealing with fungal keratitis as well; a more varied set of risk factors and a vaguer clinical appearance than classic cases leads to delays in diagnosis and treatment for a condition that already has a greater risk of surgical treatment. Keeping a fungal etiology somewhere on your differential until you achieve treatment success or receive culture results is critical to prevent further delays in diagnosis.

While culturing is important in the diagnosis of fungal keratitis,

it isn't always timely; fungal cultures can take nearly a month to produce a definitively negative result, thus, it is important to consider the possibility that you may be dealing with a fungal pathology when treating a microbial keratitis, even without a positive culture. This doesn't mean that clinicians should start each patient who has a corneal ulcer on an antifungal, but until a positive response to therapy is observed or a culture result is obtained, clinicians need to at least consider the possibility that they may be dealing with a fungal ulcer, especially if the ulcer worsens after initial treatment.



Despite the absence of classic clinical findings, this severe corneal ulcer is fungal in nature.

This further illustrates the importance of aggressively treating infections with modern, broad-spectrum or fortified agents as initial therapy. If an unspecified ulcer is treated with a dated antibiotic QID and doesn't respond, no clinically relevant conclusion can be drawn from that treatment failure. However, if initial treatment with a modern, broad-spectrum agent fails, fungal keratitis suddenly becomes a more reasonable etiology to suspect. Your initial treatment should be valuable, even if it eventually fails.

GOING THE DISTANCE

When starting therapy for a fungal ulcer, there is only one commercially available topical antifungal, Natacyn (natamycin 5%, Novartis), that exists—all others must be compounded. The medication has reasonable efficacy against filamentous fungal pathogens but doesn't perform as well against yeasts. In these cases, clinicians can use fortified AmBisome 1.5mg/ml (amphotericin B, Gilead Sciences) or fortified Vfend (voriconazole 1%, Pfizer). All topical antifungals can be paired with oral agents, particularly in cases of deep keratitis where penetration of the topical agent is a concern, but tolerance can be an issue with systemic antifungals.

Fungal ulcers are generally typified by a lower grade of inflammation than their bacterial counterparts, the clinical manifestation of which is the ulcer's ability to deepen despite the epithelium healing over the ulcer bed. In most microbial keratitis cases, stromal inflammation precludes epithelial healing, which is why most of these ulcers have epithelial defects equal in size to their infiltrates. Stromal inflammation in fungal keratitis, however, can be mild enough that the epithelium may heal despite the active underlying infection. This further lowers stromal concentrations of antifungals and subsequently reduces their effectiveness, making it necessary to debride fungal ulcers to make topical medications more successful.

Fungal sources are also characterized by an indolent course. While the slow metabolic rate typical of fungal organisms reduces the rate of proliferation and spread, it also causes a slow response to therapy; full recovery may take several months, with the final treatment in a disproportionately high number of cases being therapeutic keratoplasty.

Given the varied risk factors and clinical appearances of fungal keratitis, diagnosis can be very difficult. Therefore, it is critical that a clinician keeps fungal keratitis in the back of their mind until they receive culture results or a patient responds positively to treatment. Doctors who are uncomfortable caring for true or suspected cases of fungal keratitis should promptly refer these patients to a cornea service. RCCL

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By Mile Brujic, OD, and David Kading, OD

Multifocals: A Roadmap to Success

A good presbyopic contact lens fit starts with communication—and ends with a well-informed patient.

Clinicians have been fitting presbyopic contact lenses for almost as long as contact lens wearers have been struggling with the loss of accommodation that comes with age. This uphill battle often culminates in patients choosing to stop wearing their lenses. Nonetheless, contact lens wear *is* attainable, especially with today's lens improvements and patient education strategies.

Photo: Stephanie L. Woo, OD

With today's advances, soft multifocal lenses present many benefits to patients.

An eye care provider's success rate depends on their ability to educate patients about both presbyopia and contact lenses. Patients who have been properly informed about the condition and the advantages and disadvantages of the available correction options walk into the multifocal fitting process far more prepared and come out far more successful. These tips can help you become a better multifocal contact lens fitter, boosting your practice in the process.

COMMUNICATION IS KEY

Many presbyopic patients do not understand why they are struggling or why their vision continues to worsen, let alone what the root of the problem is, and may falsely assume that their eyes are getting worse because of the lenses or glasses they wear. To correct this misconception, a clinician's first step has nothing to do with multifocal lenses; it is having a conversation with patients about presbyopia as an identifiable condition.

Only after the patient understands presbyopia should methods of correction be discussed, even with patients who have worn contact lenses for years and have already tried multifocals. Letting patients know that their vision will likely never return to what it was when they were 30 sets the foundation for the discussion about lens options. While possibly the most important step, this is also the one that is most often skipped. Ensuring that the patient and the provider are on the same page by setting realistic expectations is critical for success.

When discussing the available corrective options, it is vital to a patient's lens-wear success that a clinician covers both the advantages and disadvantages of multifocal contact lens wear. Despite the negative perception toward multifocal lenses in the past, they allow patients the opportunity to gain independence from glasses and acquire a full range of vision in all fields of gaze. In addition, prescription lenses have a non-glare coating that helps reduce visual problems patients often have while driving at night, looking at computer screens and using digital devices. Clinicians should also inform the patient that, while they have advantages, progressive and bifocal glasses also have limitations. Knowing alternative options present challenges as well helps patients realize they are gaining something by wearing lenses over glasses.

LENS OPTIONS

The key to successfully fitting multifocal contact lenses is to follow the fitting guide. Even though it might be tempting for providers to take the fitting process into their own hands, the guide lays out exactly what to do if the initial lens fit is not successful. Following the fitting guide can help clinicians reach at least a 90% success rate with the second and third lens.

While most commercially available lenses are limited in that they do not correct for astigmatism, soft lens companies continue to innovate with new materials and designs, and spherical multifocal lenses usually help the vast majority of patients. The following lens options may be available for presbyopic patients depending on their circumstances:

Toric soft multifocal lenses. A substantial percentage of our practice's patients has astigmatism and can only be fit with custom-ordered lenses. It is important to inform these patients that the fitting and their lenses will both cost more to accommodate the astigmatism. If a patient chooses to continue with the fitting process, clinicians should then provide their custom soft lens manufacturer with the patient's sphere, toric, add power, keratometry readings, horizontal visible iris

diameter and pupil size in photopic and scotopic lighting to ensure the most effective lens is created.

Hybrid lenses. These lenses consist of a gas permeable center and a soft skirt and are designed for spherical and toric patients. To produce the best fit and calculate power measurements, clinicians should use a fitting set and do an over-refraction. If a provider has not fit a hybrid lens in the last couple of years, they should contact a colleague, attend a workshop at a conference or reach out to SynergEyes—the only manufacturer of hybrid contact lenses in the United States—to discuss the process and learn how to produce the best results.

Gas permeable lenses. These are usually successfully fit because clinicians are able to modify the lenses until a patient's vision is maximized.

Scleral lenses. Although they have grown more popular over the last five years, some consider scleral lenses overkill for patients with normal corneas because of the larger size and increased cost of the lenses. Regardless, scleral lenses are fantastic options for presbyopic and toric patients.

FITTING CHALLENGES

For some patients with adequate pupil size who are fit in the right lens design, multifocal lenses provide a suitable depth-of-focus. For others, the combination of limited lens options and their anatomy and lifestyle may reduce their chance of success with lenses alone. In this case, clinicians often elect to prescribe over-glasses for either distance or near. Over-glasses can be presented as an alternate choice for completing specific visual tasks. Most patients do not need them, but those who do usually find them to be a great option for the times they could use a boost in their distance or near vision.

Patients fit with multifocal contact lenses may face different obstacles depending on their add power, cylinder amount, pupil size and visual demand. Because a patient with multifocal lenses looks through distance and near correction at all times, they will notice a difference in their vision.

A patient's initial lens experience is usually the most uncomfortable and unnatural because cortical adaptation needs to take place. Once the patient's brain realizes what to focus on, it will likely ignore areas of vision that are not as important for visual tasks. While clinicians should work diligently to reduce the shadows and glare patients sometimes experience, they must also realize they may not be able to get rid of either entirely, even with careful lens selection.

Presbyopic contact lenses should account for a majority of the lenses clinicians fit because all patients who wear contact lenses age, and the vast majority want to continue wearing their lenses. By having detailed conversations before lens fittings, understanding the various lens designs and being prepared to troubleshoot when patients struggle with adaptation and anatomical or lifestyle challenges, clinicians can help their patients find satisfaction through presbyopia correction. RCCL

By Christine W. Sindt, OD

Shape Shifter

If you see a 'squiggle' on the endothelium, what's your first suspicion?

A 14-year-old boy presented with bilateral decreased vision. Ocular examination showed gray linear deposits on the posterior central cornea but no edema. The patient was refractable to 20/40 OD, 20/30 OS. Gonioscopy did not reveal anterior synechiae. His intraocular pressures (IOPs) were 16mm Hg OD and 17mm Hg OS.

The patient was given his refractive correction and counseled about posterior polymorphous dystrophy (PPMD), a rare autosomal-dominant dystrophy that causes abnormal developmental differentiation of endothelial cells. It can present in early childhood, but symptoms generally appear in the second or third decade.[1]

While corneal dystrophy is, by definition, a bilateral condition, PPMD may be asymmetric or unilateral.[1]

PPMD is best viewed at the slit lamp by retroillumination with a widely dilated pupil. It appears as gray collagenous tissue at the level of Descemet's membrane and can form various shapes, including isolated dots, diffuse clusters or linear lesions.

Lesions range from small (0.1mm to 1mm) vesicles to bands anywhere from 2mm to 10mm in length. These are differentiated from tapered, smooth-edged Descemet's tears seen in congenital glaucoma, trauma and hydrops by the presence of parallel scalloped edges; they also do not taper toward the ends. Numerous other dystrophies are in the differential.

PPMD generally does not progress and can remain unchanged for many years. However, patients should be monitored for endothelial decompensation. It is rarely extensive enough to cause visual impairment; however, band keratopathy or stromal clouding can develop. There can be peripheral iridocorneal adhesions in about 25% of cases. IOP should be monitored, as it will be elevated in about 15% of cases.[1]

While asymptomatic cases do not require treatment, patients with corneal edema, vision decrease or increased IOP require intervention. Mild corneal edema can be managed with sodium chloride 5% drops and ointment, a soft bandage contact lens for ruptured bullae, and stromal micropuncture for areas of localized swelling and poor endothelial adherence.[2] Severe cases may require surgical intervention, such as some form of corneal transplantation or glaucoma surgery. The presence of anterior synechiae signifies a poor visual prognosis. RCCL

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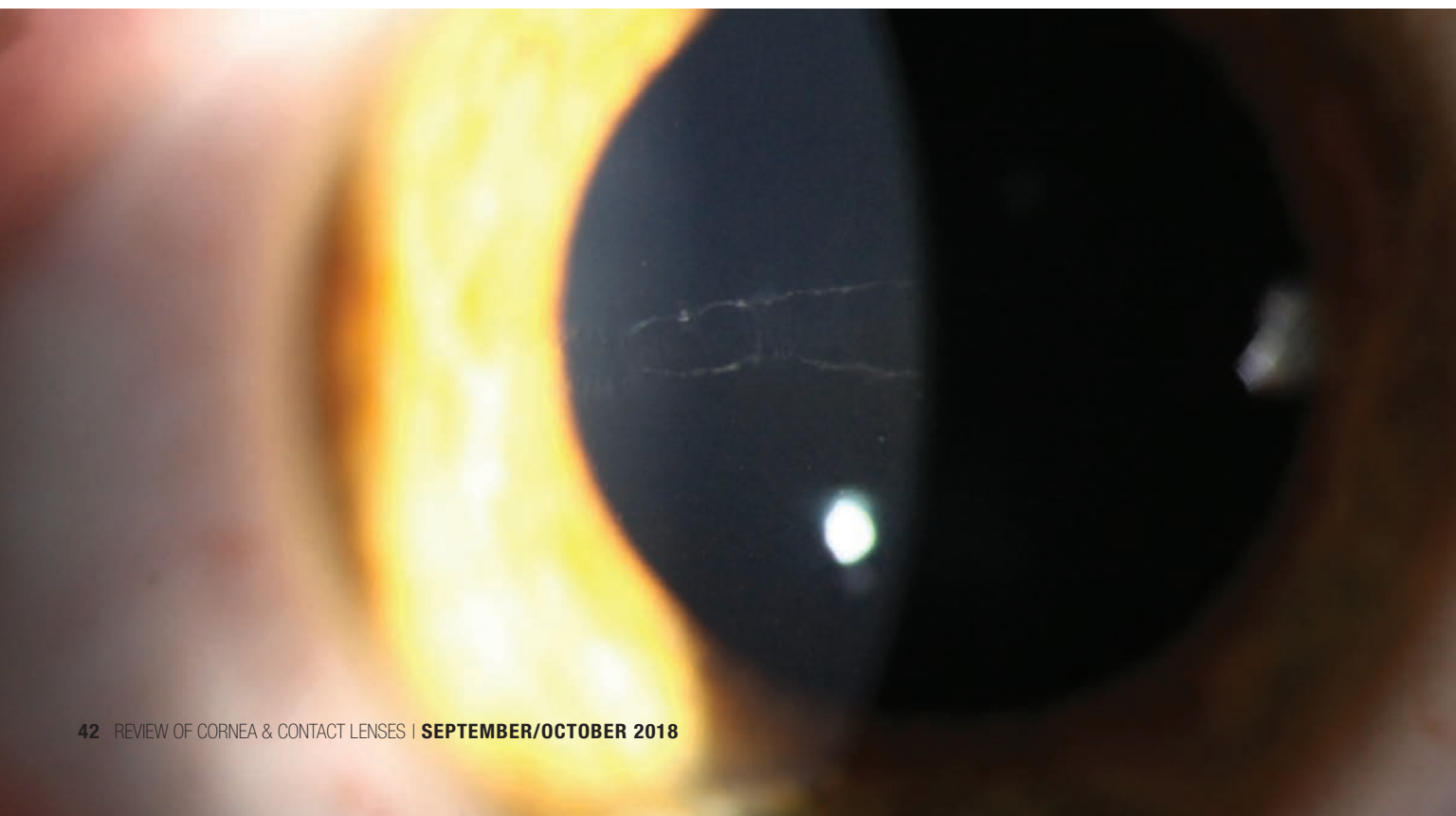

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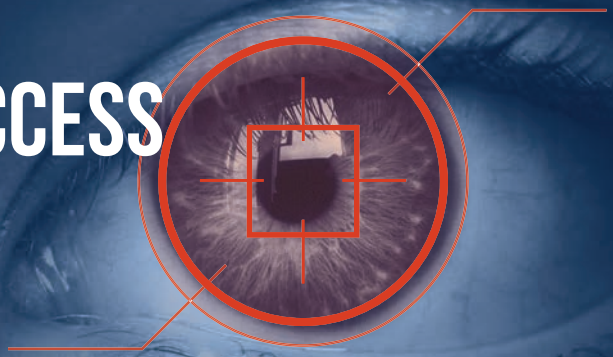

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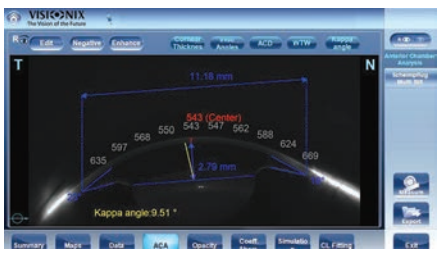

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- Assess corneal ectasia and edema
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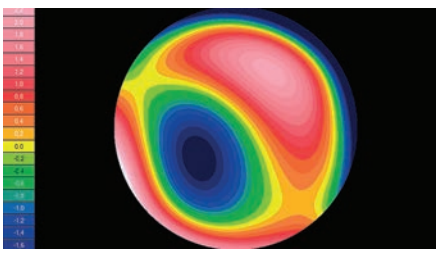

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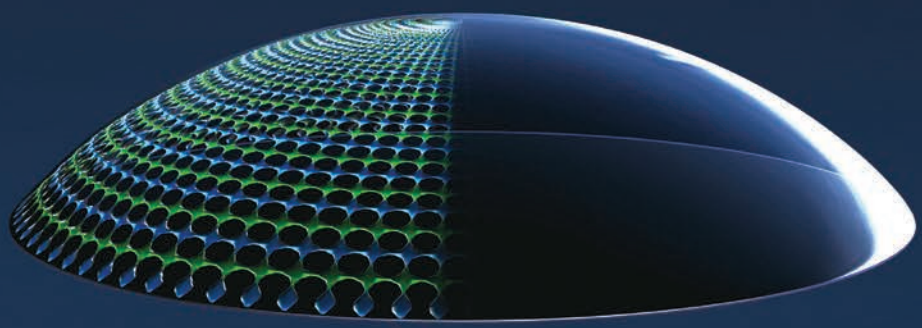

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