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REVIEW OF CORNEA & CONTACT LENSES
JANUARY/FEBRUARY 2021

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The Consequences of Corneal Endothelial Compromise

Optometrists must recognize the signs to ensure

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ALSO:

Unpacking the BLINK Study, ***Page 10***

A Rare Case of Megalocornea, ***Page 14***

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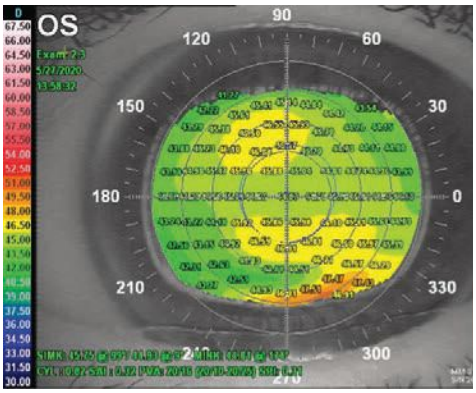

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IN BRIEF

■ **Women with polycystic ovarian syndrome (PCOS) may be at higher risk for dry eye, the severity of which appears to be tied to inflammation and hyperandrogenism levels**, a new study in *Eye & Contact Lens* suggests. In the PCOS group, Schirmer 1 scores and TBUT were significantly lower, while OSDI scores were markedly higher compared with controls. The investigators also found that lacrimal and meibomian glands seemed to be the target tissues in these individuals.

Asfuroğlu A, Kan O, Asfuroğlu M, et al. Association between dry eye and polycystic ovary syndrome: subclinical inflammation may be part of the process. Eye Contact Lens. 2021;47(1):27-31.

■ **Almost 25% of surveyed surgeons say they've had at least one case of persistent diplopia following lower blepharoplasty in children**, research finds. The inferior oblique muscle was involved in 61% of cases. Diplopia was paretic in 58% of patients and restrictive in 42%. The survey revealed that persistent diplopia in the primary position occurred in 8% of patients, and it occurred in other gaze positions in 19% of patients. **It resolved completely in 73% of patients**.

Becker BB. Diplopia following lower blepharoplasty. J Am Assoc Ped Ophthalmol Strab. November 24, 2020. [Epub ahead of print].

■ A study recently found no significant difference in the frequency of complications between multipurpose solutions and hydrogen peroxide. The researchers noted, however, that **hydrogen peroxide users were less likely to report discomfort**. The investigators reported that the most common complications were papillae (27.4%), hyperemia (21.3%) and discomfort (21.1%). They noted that 16 multipurpose solution users and nine hydrogen peroxide users experienced presumed microbial keratitis. As lens wearers who used multipurpose solutions were more likely to experience discomfort, "**hydrogen peroxide may be an appropriate recommendation by clinicians to proactively reduce the likelihood of a contact lens wearer experiencing discomfort**," the study authors concluded in their paper.

Tichenor AA, Cofield SS, Gann D, et al. Frequency of contact lens complications between contact lens wearers using multipurpose solutions versus hydrogen peroxide in the United States and Canada. Eye Contact Lens. December 7, 2020. [Epub ahead of print].

Delay of Final Contact Lens Rule Requested by Congress

Optometrists may get a temporary reprieve in gearing up for the requirements introduced by the Final Contact Lens Rule. The House of Representatives Committee on Appropriations recently requested that the FTC delay the effective date for the Rule until March 31, 2021.

In a report and accompanying bill, the committee states it is "disappointed that the FTC's final amendments to the Contact Lens Rule do not sufficiently address the patient safety concerns the Committee has repeatedly outlined in report language for the past four years. The Rule fails to sufficiently modernize the prescription verification process by eliminating the use of robocalls and imposes new burdensome paperwork requirements on providers and patients."

The delay by Congress is sensible and welcome, says Brian Chou, OD, of San Diego. "It gives ODs reasonable time to prepare when most are navigating business challenges due to COVID-19, including staffing disruptions. In addition, EHRs were caught flat-footed without forewarning to develop functionality and patient portals to help ODs comply with the FTC's requirements."

Updated EHRs are sorely needed to minimize new administrative burdens, Dr. Chou explains. "It takes time for software development and to push out new builds. Even March 31, 2021, is probably too soon to expect most EHRs to have robust functionality patterning the newly imposed workflows," Dr. Chou says.

"Congress's order is a step in the right direction, but it does not change the fact that the new Contact Lens Rule, as promulgated by the FTC, reflects bad public policy, which is also reflected in Congress' statement," says Clarke Newman, OD, of Dallas. "It is an example of regulatory overreach and does nothing to address the pressing health concerns created by seller abuses of the Act and the Rule. Congress is clearly not happy with this Rule, and the public should share Congress's dissatisfaction."

Under the Final Rule, prescribers will be required to do one of the following to confirm a patient received their prescription following a contact lens fitting:

- Ask the patient to acknowledge the receipt of the contact lens prescription by signing a separate confirmation statement.
- Ask the patient to sign a prescriber-retained copy of the prescription that contains a statement confirming the patient received it.

The prescriber can request the patient sign a prescriber-retained copy of the sales receipt for the exam that contains a statement confirming the patient received the prescription. The prescriber can also give the patient a digital copy of the prescription and retain evidence it was sent, received or made accessible, downloadable and printable.

Financial Services and General Government Appropriations Bill, 2021. US House of Representatives. appropriations.house.gov/sites/democrats.appropriations.house.gov/files/FSGG%20Report%20Full%20Print.PDF. Published 2021. Accessed January 19, 2021.

RCCL
REVIEW OF CORNEA & CONTACT LENSES

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PACK-CXL Relieves Treatment-Resistant Keratitis

The use of corneal collagen crosslinking (CXL) may extend beyond keratoconus management, a new study suggests. As an adjuvant therapy to standard antimicrobial treatment, researchers recently found that photoactivated chromophore for infectious keratitis (PACK)-CXL improves visual outcomes in patients with treatment-resistant corneal ulcers.

This observational cohort study evaluated 42 eyes of 41 patients with treatment-resistant infectious keratitis. All eyes underwent PACK-CXL treatment with the Dresden modified protocol in addition to standard antimicrobial therapy.

On the first day post-op, 16.67% of the eyes showed ulcer growth, while the remainder did not experience a change in size. At week one and months one and three, each of the ulcers either decreased in size (76.19%, 85.71%, 14.28%, respectively) or remained the same compared with the previous time point.

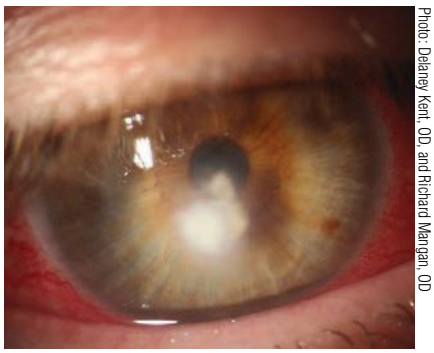

Photo: Delaney Kent, OD, and Richard Mangan, OD

The majority of corneal ulcers responded positively to PACK-CXL.

After three months post-op, the team reported a success rate of 90.5% and indicated that the treatment effect increased with time. Statistical analysis showed that PACK-CXL combined with standard antimicrobial therapy was able to significantly reduce overall corneal ulcer size.

"The healing rates obtained with PACK-CXL are unprecedented," the study authors wrote in their paper. They hope their findings prompt wider use of this procedure in cases unresponsive to standard therapy, especially taking into account the necessity of new lines of treatment as microbial resistance to antibiotics increases.

"PACK-CXL may be a promising new alternative, and its use is recommended due to the potential benefit obtained by controlling infection regardless of drug resistance, stopping the melting process, avoiding emergency keratoplasty and decreasing the possibility of performing lamellar grafts for visual rehabilitation," the investigators concluded. RCCL

Gulias-Cañizo R, Benatti A, De Wit-Carter G, et al. Photoactivated chromophore for keratitis-corneal collagen crosslinking (PACK-CXL) improves outcomes of treatment-resistant infectious keratitis. Clin Ophthalmol. 2020;14:4451-7.

EPI-ON CXL MAY BE SAFER

Researchers from Canada recently reported that while the efficacy of transepithelial, or "epi-on," CXL remains inferior to the standard epi-off approach for corneal ectasia, this technique is associated with fewer post-op complications. Still, investigators didn't find a significant difference between the two groups in uncorrected distance visual acuity or corrected distance visual acuity.

Nath S, Shen C, Koziarz A, et al. Transepithelial vs. epithelium-off corneal collagen cross-linking for corneal ectasia: protocol for a systematic review, meta-analysis and trial sequential analysis of randomised controlled trials. BMJ Open. 2019;9(5):e025728..

By Joseph P. Shovlin, OD

To Glove or Not to Glove?

Let's review hand hygiene in health care, as we continue to interact with high-risk patients.

Yes, it's another COVID-19-related editorial. At this point, I'm sure we're all running into pandemic fatigue. From seeing occasional high-risk patients (because we should in order to rule out sight-threatening eye pathology) to worrying about the asymptomatic spreaders, the ordeal has been draining. I encourage all of you to not yet drop your guard. Help certainly seems to be nearby, as more of us get vaccinated. As a front-line provider and part of a heavy exposure group, I hope that we take full advantage of the offer to getting the vaccine early.

A seemingly mundane but important topic of intense discussion is the decision to use gloves in your practice. For those of us who see contact lens patients, or even occasionally place a lens on an eye, such as a bandage lens, it's quite difficult to handle a lens with gloves on.

The use of gloves, as well as the frequency of removal and disinfection, has been a recent topic in our office and in online chat groups. We have 32 providers in our group and each of us is managing glove use a little differently. Some glove up throughout the day and replace their set after seeing each patient; others are handwashing between each patient and room.

What are you doing as a health care provider for hand hygiene? Are you wearing gloves throughout the day (changing between every patient and room)? Are you wearing the same pair of gloves during multiple patient encounters using gel sanitizer between patients? Are you washing your hands between patients and rooms?

Note that hand sanitizers over gloves may actually miss portions of the glove, and, after repeated application, the effectiveness may also be lost. Although the use of gloves can reduce skin irritation, it is not more effective than handwashing with soap for 20 seconds for routine patients and provides little additional protection for the user.[1]

KEEP SANITATION AT HAND

The Centers for Disease Control & Prevention (CDC) provides a helpful COVID-19 hand hygiene guidance document for health care providers (www.cdc.gov/coronavirus/2019-ncov/hcp/hand-hygiene.html).

The CDC continues to highlight the importance of hand hygiene in response to COVID-19. They recommend the use of alcohol-based hand rub gels and handwashing as effective measures in preventing the spread of infections and pathogens in health care settings. Handwashing mechanically removes pathogens, and alcohol-based gels (60% to 95%) can inactivate SARS-CoV-2.[1,2]

Supplies necessary for adherence to hand hygiene should be readily accessible in all areas of the office.[3] There is some evidence that suggests an alcohol-based hand rub is preferred over simply washing hands since there may be better compliance with the hand rub—and it may be even less irritating over time.[3]

Some providers will continue to use gloves. But, remember to change and remove them carefully between rooms and patients. You still need to also wash your hands carefully before you put on a new pair of gloves for added protection to ensure the gloves are not doing more harm than good. Review the proper way to don and doff gloves.[2] Using gel or any form of sanitization or disinfection on a used pair of gloves poses problems, so I'd strongly advise against this practice.

MY PERSONAL VERDICT

For me, I'll make the shift from gloves back to handwashing. However, I will also make sure to use hand moisturizers at the end of the morning and the end of the day to protect my hands from frequent handwashing. You can certainly use gloves when you need to protect your hands and especially if you are seeing a confirmed case of COVID-19 or if you have any open sores or lesions on your hands.

You may also want to assure your patients in some fashion before or during the exam that by not wearing gloves you really are not losing out on any measurable benefit if your hands are washed properly. Patients do have this false impression that gloves are universally better than handwashing or alcohol-based hand rub. That doesn't seem to be the case.

Here's wishing all of you a better 2021 and hoping you continue to stay safe! RCCL

1. CDC. Hand hygiene recommendations: guidance for healthcare providers about hand hygiene and COVID-19. www.cdc.gov/coronavirus/2019-ncov/hcp/hand-hygiene.html May 17, 2020. Accessed January 4, 2021.

2. CDC. Sequence for putting on personal protective equipment. (PPE). www.cdc.gov/hai/pdfs/ppe/ppe-sequence.pdf. Accessed January 4, 2021.

3. CDC. Hand hygiene in healthcare settings: show me the science. www.cdc.gov/handhygiene/science/index.html. Accessed January 4, 2021.

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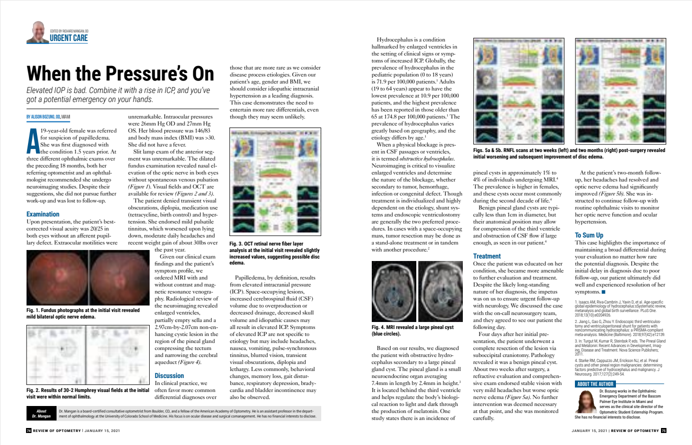

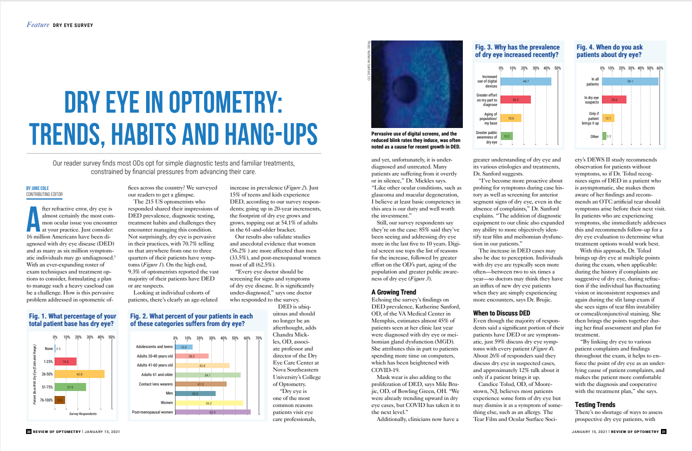

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Simplify and Move Forward

Commit and follow through with the change you want to see in your contact lens practice.

With the start of the new year comes new year's resolutions. Whether you make them in anticipation of breaking a bad habit or just for a general resetting of priorities, resolutions give us a chance to focus on what we wish to do better in the year ahead. For 2021, consider going back to the basics. What must we do well to fit GP lenses in the most efficient and accurate manner possible? How can we reduce the trials and tribulations of fitting and increase the happiness these lenses bring to our patients and practices? Here are some possible resolutions you can make (or break) this year.

VERIFY DIAGNOSTIC LENSES

Prior to starting a new diagnostic fit, it's a good idea to verify the parameters of the diagnostic lens you will apply. This will not only ensure the lens is not chipped, cracked or damaged but also save you grief later. Signs your chosen lens might be incorrect include making a diagnostic lens change where the fit doesn't respond as anticipated or if your expected over-refraction doesn't pan out. Key parameters to verify include lens power (easily accomplished on a standard lensometer) and base curve (using a radiuscope). Less important is the lens diameter, though you could easily verify this in seconds using a 7x contact lens magnifier or a diameter gauge.

While you're at it, consider verifying your entire library of diagnostic lenses. Consider assigning a staff member to handle this task on a regular basis. This person will become an expert at lens verification, which is useful for other tasks, such as checking in ordered lenses or confirming a patient's habitual lenses.

Put your diagnostic GP lens in a non-neutralizing case filled with ophthalmic-grade hydrogen peroxide solution for disinfection.

If you're in the market to purchase a new diagnostic lens fitting set, ask your lab to manufacture a custom set for your practice that contains lenses in different material colors to hasten the verification process. Have all the brown lenses be of one design or all the green lenses take up one row in the diagnostic set. Make even-numbered base curves in clear material and odds are blue. Better yet, request that your diagnostic lenses come laser-marked with their parameters or an alternate code that you specify.

FOCUS ON DISINFECTION

I highly recommend disinfecting each of your diagnostic lens sets according to the latest standards and recommendations. More details on diagnostic lens disinfection can be found in my September/October 2020 column. A convenient flow chart is also available on the American Academy of Optometry website's "My COVID Hub" section. In short, after a GP lens is used on-eye, clean it, place it in a non-neutralizing case with 3% ophthalmic hydrogen peroxide solution, let it soak for three or more hours, rinse it with multipurpose solution, pat it dry, and then store it dry. Note that diagnostic hybrid and soft lenses follow an alternate protocol not outlined here and should undergo re-disinfection every 28 days.

Lenses that undergo disinfection should also be logged so that they can be tracked in case a subsequent infection is diagnosed that was present during fitting. For example, diagnostic lenses should be discarded (and not used again) in patients with hepatitis, HIV, prion disease, herpes ocular infection, adenovirus or *Acanthamoeba* keratitis.[1,2]

The information in the record can be used to contact patients later fit with the same diagnostic lens, to advise them of potential risk. If you do not currently have a standardized process for lens disinfection and logging in your office, now is the time to start. Assign a staff person to handle these tasks on a daily, weekly, or monthly basis as well.

OFFER TO PRESBYOPES

We know those with irregular corneas, high ametropia or moderate-to-high amounts of astigmatism are excellent candidates for GP lenses. Presbyopes who currently wear GP lenses are no-brainer candidates, too—but don't forget about neophyte wearers. You owe it to patients to discuss all potential options, and sometimes I'm surprised at the quick

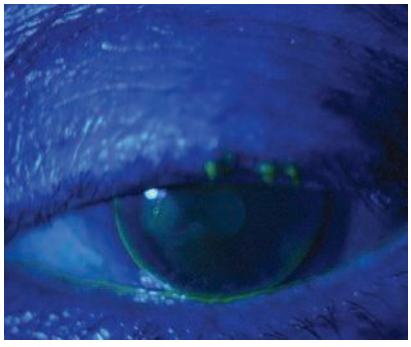
adaptation once they achieve freedom from reading glasses.

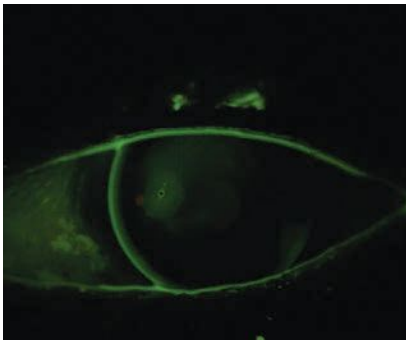
Depending on the degree of presbyopia, you may consider different designs. For emerging presbyopes, a simultaneous multifocal design can provide full correction in both eyes (as opposed to monovision, which does not). For mid-to-late presbyopes, both simultaneous and translating designs can provide sufficient near add. Within the multifocal fitting process, if you need additional plus, there are also fitting options to enhance distance or near (similar to modified monovision), or you can recommend top-up spectacles to provide additional plus. It's good practice to give the patient permission to wear spectacles over the lenses as needed for demanding near tasks.

COLLECT THOROUGH DATA

Remember the old saying, "garbage in, garbage out"? That's the case with empirical fits of GP lenses. If you don't gather good data on the front end, you won't have a successful empirical fit (or you'll leave your lab consultants confused on how to help you).

With any new fit, gather the appropriate data at the initial visit, including (at a bare minimum): keratometry readings, refraction, horizontal visible iris diameter and lid position. If you're fitting a multifocal, also gather the patient's near add power, pupil size and dominant eye and critically assess lid position and tone. A topography map can be useful, but is not required, and may help with habitual wearers than new wearers, where you can rule out conditions such as corneal warpage or molding. Of course, if you suspect ectasia, a tomography map is the key a problem-related diagnostic test. Assessment of tear quality and quantity, which may be reduced in the presbyopic age group, also warrants attention and associated treatment in the pre-fit phase.





The same lens is viewed with blue light (left) and then with a wratten filter (right). The filter highlights a small area of pooling with dimple veiling over a corneal scar in the temporal cornea.

ASSESS LENS COMPLETELY IN-OFFICE

When assessing lenses on dispense or follow-up, perform a complete evaluation. Referring to detailed notes can be useful later on, whether you are trying to verify a new finding or consulting with the laboratory on lens changes. When fitting GP lenses, record all aspects of the fit, including blinking (full or partial), lens position (lid attached, interpalpebral), centration (or direction of decentration), movement (in millimeters) and lens condition (note any surface scratches, debris, deposits or lens markings).

Instill sodium fluorescein and determine the fitting relationship using blue light. A Wratten filter can help quickly identify any subtle areas of touch or pooling.

ENSURE APPROPRIATE CARE

For new GP lens wearers, it is rather obvious that follow-up visits are necessary to ensure appropriate adaptation to lens wear. After-care visits also give us the opportunity to review proper practices for lens wear and care, including proper use of solutions. Through appropriate questioning, we can confirm the patient is happy with the outcome and answer any outstanding questions. Even in fits where the patient is a habitual GP lens wearer, if I make significant changes in base curve or edge design, I prefer a follow-up visit to confirm the eye is adapting well and the fit remains as expected at the end of the day.

Whether you love or hate resolutions, the new year gives you a chance to make changes in your contact lens practice. I wish you a year of happy fittings! RCCL

1. Sindt CW et al. Technical Report: Guidelines for Handling of Multipatient Contact Lenses in the Clinical Setting. Optom Vis Sci. 2020.

2. International Organization for Standardization. (2018). Ophthalmic optics—contact lenses—Hygienic management of multipatient use trial contact lenses. www.iso.org/standard/67859.html. March 2018. Accessed January 13, 2021.

UNPACKING THE BLINK STUDY

Finally, solid data shows us an approach to multifocal contact lens use in childhood myopia management.

By Maria K. Walker, OD, MS

The focus on myopia management in children has expanded tremendously over the past 10 years. In 2010, there were nearly two billion people—28.3% of the world's population—with myopia, yet at that time, treatment for myopic progression was rarely employed.[1]

In North America alone, a growth rate of 6.2% was observed between 2000 (28.3%) and 2010 (34.5%). The prevalence of myopia in this region is expected to further rise to a whopping 58.4% by 2050. Worldwide projections are at 49.8% for 2050, which means an estimated five billion people globally will be myopic and one billion will have high, or pathologic, myopia by that point.[1]

The consequences of high myopia extend beyond the standard burden of health care and workplace opportunity costs associated with low and moderate myopia, and include retinal detachment, glaucoma, cataracts, amblyopia, maculopathy and choroidal neovascularization.[2-4] In 2010, some 277 million people in the world (4%) were pathologically myopic, up from 163 million (2.7%) in 2000, with this number expected to rise to one billion people by 2050.[1] Needless to say, in 2020, the concerning magnitude of increasing myopic prevalence in children is fully realized, and eye care practitioners are increasingly prescribing interventions to reduce the rate of myopic progression.[5]

Genetics, environment, behavior and visual feedback are among the many factors associated with the risk of myopia development and progression. The strategies used in myopia management commonly target the most modifiable of these factors, such as visual feedback. The important role of the retinal image during myopia development is evidenced by years of animal models showing that peripheral hyperopic defocus is a stimulus for eye growth, and that myopic defocus stimulates a reduction in growth.[6] The retinal image focus in the central and peripheral retina has been found to be modifiable using different refractive techniques, and as such, the strategies for myopia management are predominated by refractive treatments.

Among the most effective and practical myopia control treatments currently available are contact lenses, with both orthokeratology and soft multifocal lenses aiming to create peripheral myopic defocus and presumably reduce the optical signal for eye growth.

The Bifocal Lenses in Nearsighted Kids (BLINK) study was completed in late 2019 and recently published in the *Journal of the American Medical Association* (*JAMA*). This study was the largest prospective randomized clinical trial to evaluate the efficacy of soft multifocal contact lens design in the management of myopic progression in children. This article summarizes and unpacks the study's findings and uses them as a guide toward practicing evidence-based clinical management of childhood myopia.

ABOUT THE AUTHOR

Dr. Walker, a NECO 2013 grad, is currently part-time faculty at the University of Houston College of Optometry while also completing her PhD, studying the effects of scleral lenses on the ocular surface.

THE BLINK STUDY

Doctors looking for clarity on the role of multifocal contact lens effects on myopia will find much to appreciate in this clinical trial.

Study design. The BLINK study was a three-year clinical trial that recruited 294 children from the Ohio State University and the University of Houston and fit them in spherical or bifocal soft contact lenses. The subjects were between the ages of seven and 11 with less than 5D of myopia and less than 1D of cylinder (*i.e.*, school-aged myopes without any signs of pathological myopia).

Over the course of the study period, subjects wore the contact lenses daily and underwent yearly comprehensive examinations that included refractive error, axial length, peripheral refractive error and axial length, accommodative lag and choroidal thickness measurements. Subjects were monitored closely for compliance and adverse events. Of the total subjects recruited, 287 completed the study. This extremely high retention rate is not only a testament to the tenacity of the investigators, but also to the motivation of families to receive this type of myopia management.

The contact lenses chosen for the study group were center-distance multifocal contact lenses with either a +1.50D add or a +2.50D add (Biofinity "D" multifocal lenses, CooperVision). A spherical design was picked for the controls (Biofinity spherical lenses, CooperVision). These commercially available lenses were selected because the center-distance and mid-peripheral add designs lend nicely to the myopia management optic needed to create peripheral myopic defocus in the retina. The two different-powered bifocal designs were selected to evaluate a potential dose-dependent effect, which would be seen if the +2.50D add provided a greater reduction in myopic progression than the +1.50D add.

BLINK validated an approach to myopia management using center-distance multifocal contact lenses, which slowed myopia progression by about a half-diopter over three years. Subjects were highly motivated; hence, the study's 97.6% retention rate.

The study participants were split equally between the three groups to wear either the single vision, +1.50D or +2.50D lenses. Lens powers for the subjects were selected based on the spherical equivalent manifest refraction. It should be noted that, on average, an additional -0.50D was incorporated into the sphere power of the lenses (beyond the predicted power based on the spherical equivalent after vertexing) to provide adequate vision.

Outcomes. The ultimate purpose of BLINK was to evaluate the effectiveness of these center-distance soft multifocal lens designs on slowing progression of myopia in children, and the primary outcome was the three-year change in spherical equivalent cycloplegic autorefraction as measured by an open-field autorefractor (Grand Seiko).

UNPACKING THE BLINK STUDY

The results showed that subjects in the high add treatment group progressed by -0.56D (95% CI: -0.70D to -0.41D) over three years, those in the medium add group progressed by -0.85D (95% CI: -0.99D to -0.70D) and those in the control group progressed by -1.01D (95% CI: -1.15D to -0.87D) over three years, which was -0.45D more than the high add treatment group. This signified a statistically and clinically significant treatment effect in the high add group, providing evidence that high add center-distance multifocal soft contact lenses are effective in reducing myopic progression in children.

As expected, axial length also increased the most in the control group (0.62mm; 95% CI: 0.56mm to 0.69mm) and the least in the high add group (0.39mm; 95% CI: 0.32mm to 0.46mm), with the medium add group falling in the middle (0.55mm; 95% CI: 0.49mm to 0.62mm). Again, these findings confirm the efficacy of the treatment in the high add group, which experienced less axial length growth than the control group by an average of 0.23mm over the three-year test period. These findings are comparable with the results of the MiSight three-year randomized clinical trial (0.32mm less axial elongation than the control group).[7]

In addition to measuring the efficacy of soft contact lens treatment for myopic progression, the BLINK study also collected data on adverse events in this pediatric population. These side effects will be more thoroughly assessed in a follow-up paper, but initial reports show that no serious adverse events occurred in the children in this study. Those that did occur were typically mild and included giant papillary conjunctivitis, infiltrative keratitis and ocular allergies.

BLINK study subjects were as young as seven years old and were not at a greater risk for contact lens complications than their older peers. Other studies, such as the Contact Lens Assessment in Youth (CLAY) study, have confirmed that the risk of serious adverse events is low with soft contact lens use in children.[8-10] However, it's worth emphasizing that many of the complications in these studies occur due to allergies, solution sensitivities and poor cleaning, which suggests that they could be reduced with the use of a daily disposable lens modality rather than the monthly lens used here. With the increasing availability of daily disposable multifocal lens options, it is perfectly reasonable to recommend daily disposable multifocal lenses when available. This could potentially reduce the mild, yet somewhat limiting, complications observed in this study.

The visual data collected from the BLINK study is also quite reassuring, as vision was optimal with the bifocal lenses, with subjects maintaining better than 20/20 vision in high-contrast visual acuity in both the treatment and control groups. Statistically, there was a slight reduction (two letters) in low-contrast acuity with the high add lenses compared with the controls, but this was not a clinically meaningful difference. These acuity findings should assuage some hesitant clinicians' fears that multifocal contact lens treatment may affect visual performance in the developmental years of a patient's life; the study's findings suggest that these kids are able to achieve visual success with these lenses.

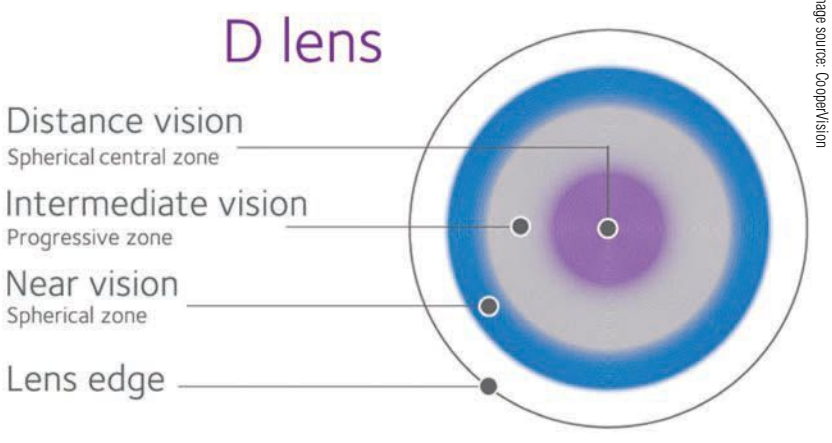


Image source: CooperVision

Schematic of the Biofinity "D" multifocal contact lens.

TRANSLATING THE DATA INTO THE CLINIC

The primary clinical relevance of this study was to show that center-distance multifocal lenses can reduce the refractive progression and axial elongation in myopic children. This study strengthens the evidence for multifocal lens use and specifically recommends higher add powers (like the +2.50D add used here) for the maximum effect of the lenses to take hold.

Key clinical take-aways. Establishing a scientifically sound relationship is an important first step in curtailing myopia's advance. Translating science to practice is the next step. Consider the following:

1) Multifocal contact lenses work to slow myopic progression, and the response is dose-dependent. Higher adds should be recommended whenever possible. Keep in mind that higher add powers may require a greater amount of minus in the spherical power. We've found that approximately -0.50D added to the vertexed manifest power for a +2.50D add lens is necessary to achieve adequate vision. Clinicians need not be hesitant to add this power if it improves vision, as we have shown that even with this added minus power, treatment is efficacious and vision is adequate at distance and near.

The BLINK study and others have not yet evaluated the optimal amount of add power for maximum myopic management; it could be different for different eyes which have different prolate profiles.[11]

2) Age and severity play a role. The BLINK study and others that have proven the efficacy of multifocal contact lenses have primarily included children with relatively low levels of myopia. While the studies show promising results in these children, those with pathologic myopia at onset (i.e., >6D), those who develop myopia at a very young age (i.e., <5 years) and those with other predisposing risk factors should be counseled accordingly.

Be upfront with patients and their families about a potentially more severe diagnosis and the lack of clear evidence regarding their treatment options. Set appropriate expectations moving forward. More studies are needed in high-risk and high myopic groups to determine the outcomes of different myopia management approaches in these patient populations.

3) Thoroughly educate patients and their parents. We have work to do to increase public health awareness of myopia, but until then, it must be done thoroughly in the office. Educating patients and their parents on expectations for vision, treatment and adverse events is critical to success:

- ***Patients should be able to achieve good vision with the lenses.*** The BLINK study and others have shown that visual acuity at distance and at near are both comparable with single vision contact lenses. However, as we can see with presbyopic patients, some visual systems respond better to multifocal optics than others. It would be prudent to expect that about 5% to 10% of patients will struggle with subjective visual success in multifocal lenses, either due to the multifocal or uncorrected astigmatism. These patients may require a multifocal toric or another customized lens for success.
- ***Treatment for myopia is not able to halt progression.*** A 40% to 50% reduction in myopic progression is an appropriate goal, but this can be tricky to track on an individual basis. An optimistic goal is to aim for 0.15mm or less change per year in axial elongation, which would approximately line up with the average progression seen in the highest treatment group of the BLINK study. Realistic expectations, however, are vastly variable and depend on risk factors such as previous progression, level of myopia and age.
- ***Serious complications are rare, but specific education on compliance and contact lens care is obligatory.*** Children are a vulnerable population and must be followed carefully for the best outcomes.

WELL-POSITIONED FOR THE FUTURE

The conclusions the BLINK study arrived at can help practitioners feel more confident when recommending commercially available multifocal contact lenses for myopia management in children, especially seeing as high add multifocal contact lenses are a safe and effective strategy for reducing myopic progression in school-aged children.

The study has moved into the BLINK 2 phase, in which all subjects will wear the +2.50D add for the next two years and then single vision lenses for the final year of the study. Stay tuned, as this important study continues to provide information on how to best manage our children with contact lenses to reduce myopic progression. RCCL

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A RARE CASE OF MEGALOCORNEA

Here's how this patient's condition made for an extremely unique specialty contact lens fitting.

By Kenneth Chung, OD

Creating a specialty contact lens fit for a cornea with a significant amount of irregular astigmatism, scarring or advanced ectasia can be a daunting task for many practitioners. Fitting a scleral lens on a congenitally enlarged cornea, a condition otherwise known as megalocornea, may prove to be even more intimidating for some. Megalocornea is a rare, predominantly X-linked developmental condition characterized by a non-progressive bilateral enlargement of the cornea that is typically larger than 12.5mm in horizontal visible iris diameter (HVID).[1]

As these patients are generally at higher risk for more complex ocular complications, a successful scleral lens fit can be life-changing. By understanding the basic principles of an optimal scleral lens fit, being observant behind the slit lamp and becoming familiar with your scleral lens fitting set, fitting this modality on a megalocornea can be much more straightforward than most clinicians think. The following case report will show you where to start and walk you through the process.

THE BREAKDOWN

There are several conditions that present similarly to megalocornea but differ upon closer inspection. One is primary congenital glaucoma with buphthalmos, a term used to describe the enlargement of the eyeball detected at birth or soon after due to uncontrolled glaucoma in early infancy.[2]

When megalocornea is present at birth, the HVID is typically 13mm or larger in the newborn.[3] Unlike buphthalmos, megalocornea does not present with elevated intraocular pressure (IOP), corneal edema, opacification or Haab's striae, which are horizontal, curvilinear breaks in Descemet's membrane caused by elevated IOP.[4] Megalocornea is typically symmetric in appearance, whereas congenital glaucoma can display asymmetry.[5]

Another condition that presents similarly to megalocornea is keratoglobus, a non-inflammatory, progressive generalized thinning (or steepening) and global ectasia of the cornea. Unlike keratoglobus, though, megalocornea does not present with generalized peripheral thinning or steepening of the corneal structure and is found earlier in life.[6]

As over 90% of megalocornea cases are X-linked recessive, most affected individuals are male.[1,4] Myopia and with-the-rule astigmatism, but not amblyopia, have been associated with the condition in children. Those with the condition are also more susceptible to posterior vitreous and retinal detachments. When megalocornea is diagnosed, differentiation must be made between simple, or pure, megalocornea and megalophthalmus anterior.[4,5,7]

Simple megalocornea is known to have the following findings: bilateral HVIDs greater than 13mm, deep anterior chambers, normal IOP, normal central and peripheral corneal thicknesses, clear stromal tissue or central mosaic dystrophy,

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posterior positioning of the iris-lens diaphragm and a shortened vitreous cavity and body.[7]

Megalophthalmos anterior, on the other hand, combines all the signs of simple megalocornea with several additional abnormal findings, including iridodonesis, phacodonesis, ectopia lentis, early cataract and widened ciliary body band.[7] As this subtype involves movement of the iris and crystalline lens, these patients have a higher risk of developing pigment dispersion glaucoma (as opposed to congenital glaucoma in buphthalmos) due to Krukenberg spindles, trabecular meshwork hyperpigmentation and iris transillumination defects.[3,7]

Megalocornea often occurs as an isolated condition but can also be a presenting sign of a larger developmental disease, such as Alport syndrome, a rare, inherited disorder that damages the tiny blood vessels of the kidneys.[7-9] Marfan syndrome, the second most common inherited connective tissue disorder, is another condition that has been linked to megalocornea.[10,11]

Megalocornea is also associated with Down syndrome, or trisomy 21, one of the most common genetic diseases, which is marked by a characteristic facial appearance, short stature, intellectual disability and a host of developmental, ocular and cardiac abnormalities.[9,12] Ehlers-Danlos syndrome, a connective tissue disorder that affects the skin, bones, blood vessels and many other organs and tissues, may also be associated with this corneal condition.[13]

Osteogenesis imperfecta, otherwise known as brittle bone disease, develops from a defect in the gene that produces collagen and is linked to megalocornea. These patients have fragile bones that fracture from very minor trauma and signs associated with a blue sclera.[14,15] Finally, progressive facial hemiatrophy, renal carcinoma and mental handicap have also been documented in the literature as having a connection with megalocornea.[9]

THE CASE

A 57-year-old Caucasian male presented with constant blur in his left eye due to a recent spontaneous subluxation of an intraocular lens (IOL) without trauma. His medical history included migraines and chronic lower back pain, and his ocular history included megalocornea, metallic foreign body in his left eye and uneventful bilateral phacoemulsification during his late 40s.

Shortly after the lens subluxated, the patient saw a vitreoretinal surgeon who determined IOL removal would be the patient's best option without an iris-fixed IOL replacement. He was subsequently referred to a contact lens specialist prior to intraocular surgery.

Wearing his habitual spectacle correction, the patient's distance visual acuities were 20/20- OD and 20/400 that pinholed to 20/60- OS. There was no afferent pupillary defect noted, and IOPs were 10mm Hg OD and 11mm Hg OS. Manifest refraction yielded +1.00+0.75x055 with visual acuity of 20/20 OD and +7.25+0.75x120 with visual acuity of 20/20- OS.

Interestingly, during subjective refraction of the patient's left eye, the subluxated lens partially descended into the visual axis and caused him to have to tilt his head to reposition the lens out of the visual axis. Although manifest refraction may have shown a partial contributory effect of the subluxated IOL, there was no reduction in the patient's best-corrected visual acuity.

Slit lamp examination revealed bilateral enlarged corneas with moderately dense central mosaic dystrophy, diffuse pigmentation of the endothelium and a deep anterior chamber (*Figures 1 and 2*). Both corneas showed well-healed cataract incisional scars, and the left had a small subepithelial scar at 8 o'clock. The anterior chambers were quiet, and there were no signs of vitreous prolapse in the left eye. There was a well-centered posterior chamber IOL with a clear capsule in the right eye and a superonasally decentered posterior chamber IOL in the left.

Dilated fundus exam revealed syneresis of the vitreous in the right eye and a posterior vitreous detachment in the left. The optic cups were small with pink neuroretinal rims, the maculae were flat and intact with even pigmentation and the peripheral fundus was unremarkable bilaterally.

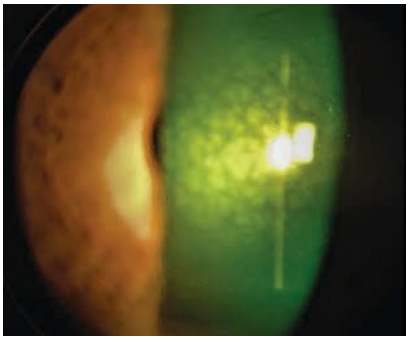

Fig. 1. This central mosaic dystrophy pattern is associated with megalocornea.

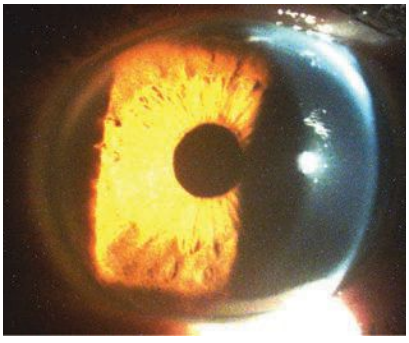

Fig. 2. A large HVID and deep anterior chamber are both characteristic signs of megalocornea.

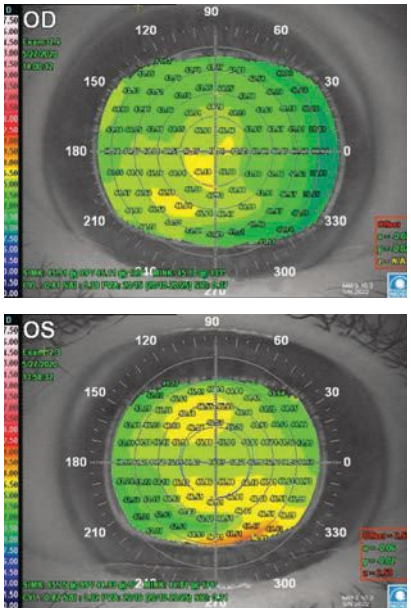

Fig. 3. These placido disc topographies of megalocornea have a generally uniform appearance OD (top) and mild peripheral inferior steepening OS (bottom).

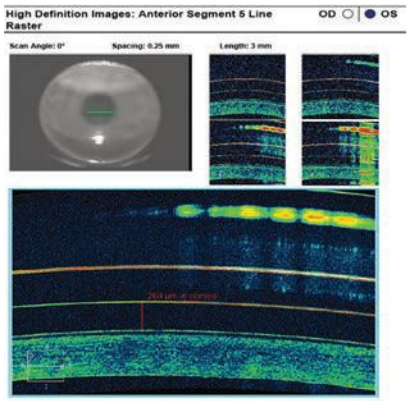

Fig. 4. AS-OCT of the 4300µm/38/44/8.4mm/16.0mm scleral lens reveals ideal apical tear film thickness after one hour of lens settling.

The topographical map of the patient's right eye showed an enlarged cornea with a uniform appearance without pathological steepening. The topographical map of his left eye also showed a generally uniform appearance with mild peripheral inferior steepening that was unable to be fully captured by topography (*Figure 3*). Simulated keratometer readings from the topographer were 45.11/45.91 at 039 and 44.93/45.75 at 099 of the right and left corneas, respectively. The HVIDs were 14.32mm OD and 14.56mm OS on topography.

Due to the high hyperopic prescription and the need for a contact lens with a larger diameter to vault the patient's megalocornea, the SynergEyes VS scleral lens was selected for the initial diagnostic fitting.

DIAGNOSTIC FITTING

The initial diagnostic lens used for the patient's left eye had parameters of 3600µm/36/42/8.4mm/16.0mm in the SynergEyes VS scleral design. This lens showed heavy edge lift of the scleral landing zone at both the flat and steep meridians. A cobalt blue penlight showed heavy central bearing. The patient immediately reported discomfort, so the lens was removed after a quick gross examination and slit lamp assessment.

The second diagnostic contact lens used had parameters of 4000µm/40/46/8.4mm/16.0mm in the same lens design. Once inserted, the lens immediately showed improved overall vault, although moderate central bearing persisted. The scleral landing zone showed improved scleral alignment as well, but there was still a decent amount of edge lift at both the flat and steep meridians. The patient noted dramatically improved comfort, but the foreign body sensation remained.

Although the tallest lens vault available in the SynergEyes VS diagnostic fitting set is 4000µm, the lens can be custom-ordered up to 4600µm.[16] I determined that the tallest vault of the fitting set did not achieve clearance and discussed transitioning to a trial-and-error approach with the patient. As luck would have it, I remembered that our clinic had a custom 4300µm/38/44/8.4mm/16.0mm lens with -0.75D of sphere power from a previous order that had never been dispensed.

Once inserted, this third lens immediately showed apical clearance to alignment and from the nasal to temporal limbus. Although there was moderate edge lift at the scleral landing zone at each hour of the clock, this was to be expected. The patient reported immediate comfort, and we allowed the lens to settle on his eye for an hour prior to further evaluation. AS-OCT images were then captured to fine-tune the fit. Apical tear film thickness showed an ideal value of 264µm (*Figure 4*). As expected, the scleral landing zone showed edge lift at both the nasal and temporal sclera (*Figure 5*). More importantly, limbal bearing was present at both quadrants, indicating this scleral lens was not large enough for the patient's corneal HVID and the base curve needed to be increased on the dispensing lens order.

With an overrefraction of +11.75+0.25x120 while wearing the most recent lens, the patient read 20/20-2 on the Snellen acuity chart. After vertexing the overrefraction, increasing the base curve to 8.8mm and incorporating the

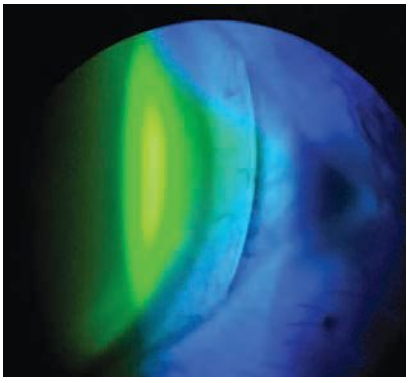

Fig. 6. The 4300µm/38/44/8.4mm/16.0mm scleral lens exhibits limbal bearing and mild edge lift of the scleral landing zone at the temporal sclera.

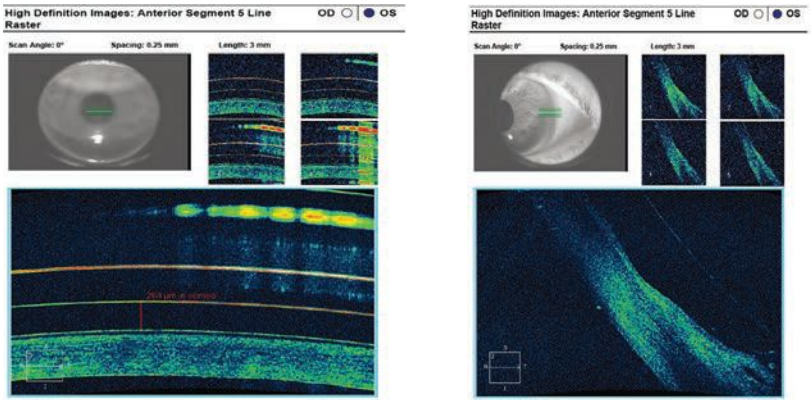

Fig. 5. AS-OCT reveals moderate edge lift at both the nasal (left) and temporal (right) sclera of the 4300µm/38/44/8.4mm/16.0mm scleral lens and mucosal debris in the tear layer. There is insufficient clearance at the limbus, indicating the scleral lens diameter and base curve are too small for this corneal HVID.

diagnostic lens power, the final lens power came out to +15.50D of sphere. During slit lamp evaluation, the lens showed apical alignment with mid-peripheral clearance. There was moderate bearing at the limbus at all hours of the clock and moderate edge lift at both the flat and steep scleral landing zones (*Figure 6*). The patient reported foreign body sensation but not pain or major discomfort. We ordered a new lens with parameters of 4300µm/42/48/8.8mm/17.5mm and +15.50D of sphere power with Menicon Z material to promote high oxygen permeability due to the extremely high plus power of the lens.

LENS DISPENSING

The patient returned for his first follow-up two months after the initial diagnostic fitting. He had seen a retina surgeon a month prior and undergone uneventful IOL removal. The patient was given clearance to wear sclerals about a month after the procedure.

The patient immediately noted a significant improvement in his vision with the new lens. On gross examination, the lens appeared to vault most of the megalocornea but showed signs of light bearing from 3 o'clock to 7 o'clock at the inferior limbus. AS-OCT images were captured after allowing the lens to settle for 60 minutes. Apical vault showed a thin but sufficient tear film thickness of 112µm after lens settling (*Figure 7*). Despite increasing the scleral landing zone by four points at both the flat and steep meridians of the diagnostic lens, it continued to show moderate edge lift at both quadrants over the sclera (*Figure 8*). Surprisingly, the patient reported the lens was very comfortable and did not note any foreign body sensation.

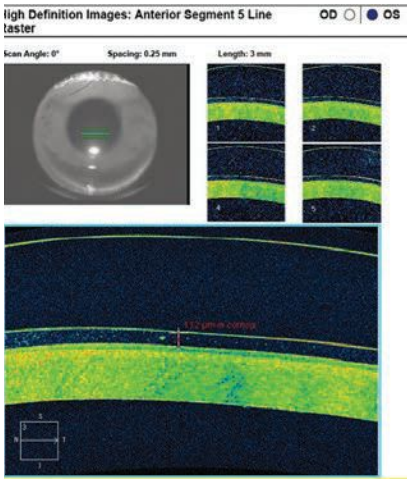

Fig. 7. AS-OCT of the 4300µm/42/48/8.8mm/17.5mm scleral lens shows a very high center thickness and apical tear film thickness of 114µm that is thin but acceptable after 60 minutes of lens settling.

During visual acuity testing, the patient read a slow 20/40 line on the Snellen chart and accepted +1.25D of sphere power from an overrefraction that improved his visual acuity to 20/20-1. Although the patient was very satisfied with both the comfort and vision offered by the most current lens, I knew we could do even better with one more revision and placed an order with the following parameters: 4400µm/44/50/9.0mm/17.5mm

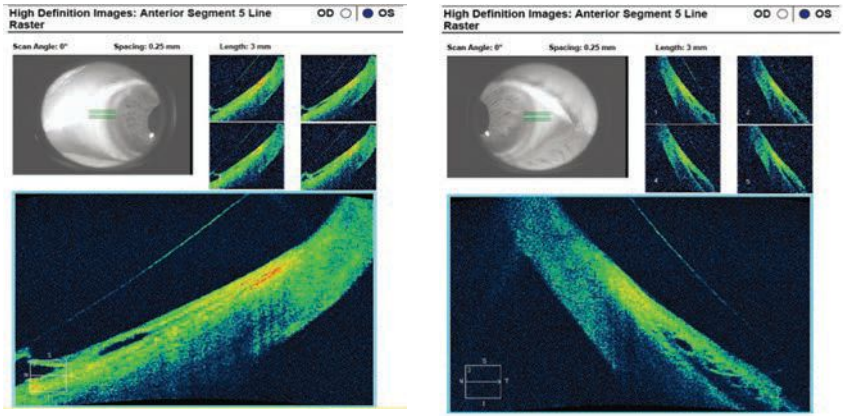

Fig. 8. The nasal (left) and temporal (right) scleral landing zone indicate moderate edge lift of the 4300µm/42/48/8.8mm/17.5mm scleral lens on AS-OCT.

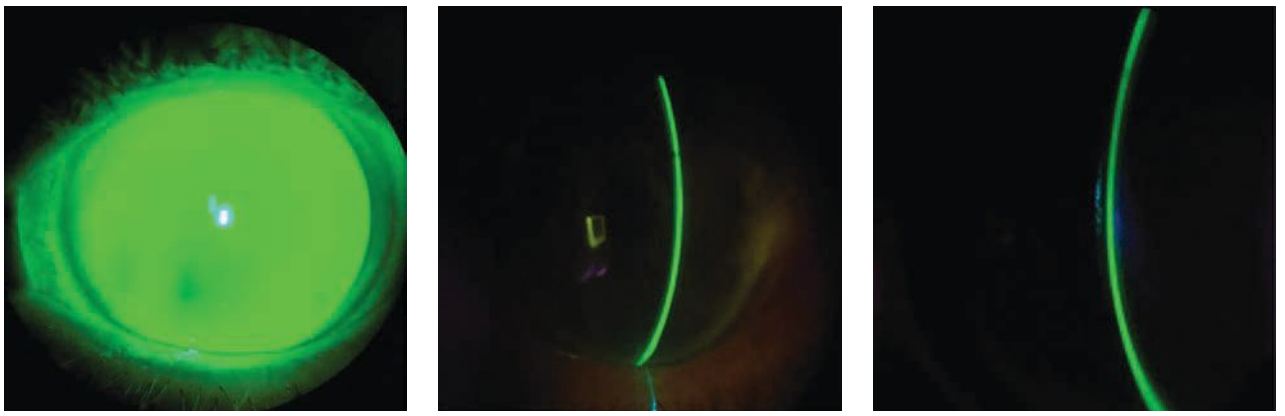

Fig. 9. The diffuse beam (left) and optic sections (center and right) on slit lamp examination of a scleral lens filled with preservative-free 0.9% NaCl solution and fluorescein dye show apical alignment with peripheral clearance from limbus to limbus.

with +17.75D of sphere power in the Menicon Z material.

FOLLOW-UP

After a little over a month, the patient returned for his second follow-up. He reported he had been able to wear the lens comfortably for over 12 hours a day and had no issues with lens removal in the evening. After inserting the newest lens, the patient immediately reported great comfort and vision. There was adequate lens vault on broad beam and optic section from limbus to limbus (*Figure 9*). AS-OCT images were taken after 60 minutes of lens settling.

AS-OCT showed an ideal tear film thickness of 180µm at the apex after lens settling (*Figure 10*). Both the nasal and temporal scleral landing zones showed mild edge lift on slit lamp examination and AS-OCT (*Figures 11 and 12*). On visual acuity testing, the patient read 20/20-2 on the Snellen chart and did not accept an overrefraction. NaFl evaluation on the slit lamp showed apical alignment, midperipheral clearance and minimal touch at the limbus.

As the patient expressed great satisfaction, comfort and vision, we dispensed the lens to him. We reminded him to continue with his current contact lens hygiene regimen of Clear Care (Alcon) peroxide cleaner for lens disinfection and 0.9% preservative-free NaCl solution for lens insertion with a vented DMV inserter and to immediately discontinue scleral lens wear should

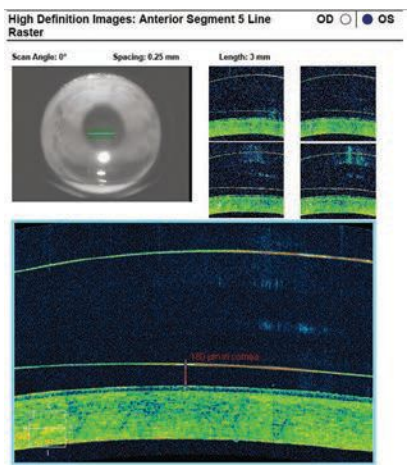

Fig. 10. AS-OCT revealed an ideal tear film thickness of 180µm at the apex after lens settling with the 4400µm/44/50/9.0mm/17.5mm scleral lens.

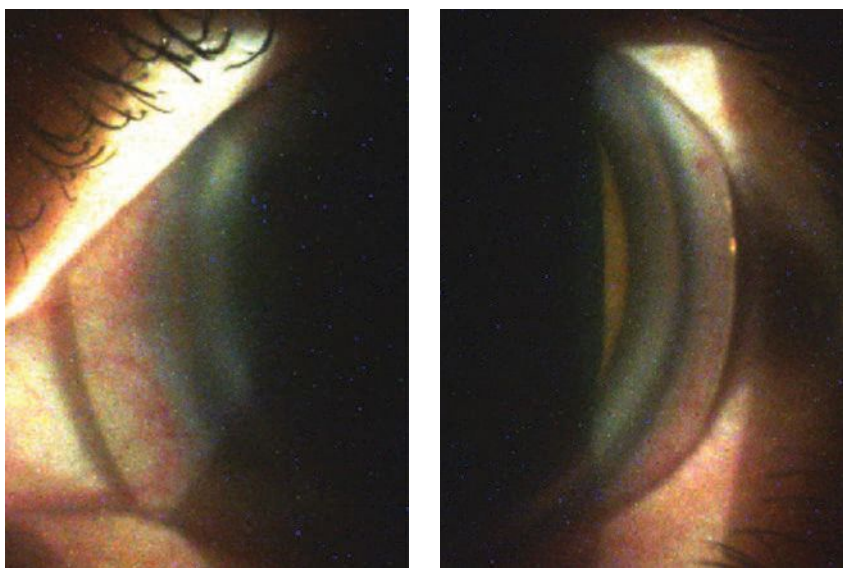

Fig. 11. Despite the nasal (left) and temporal (right) edge lift findings of the 4400µm/44/50/9.0mm/17.5mm scleral lens on slit lamp examination, the patient reported excellent comfort with wear.

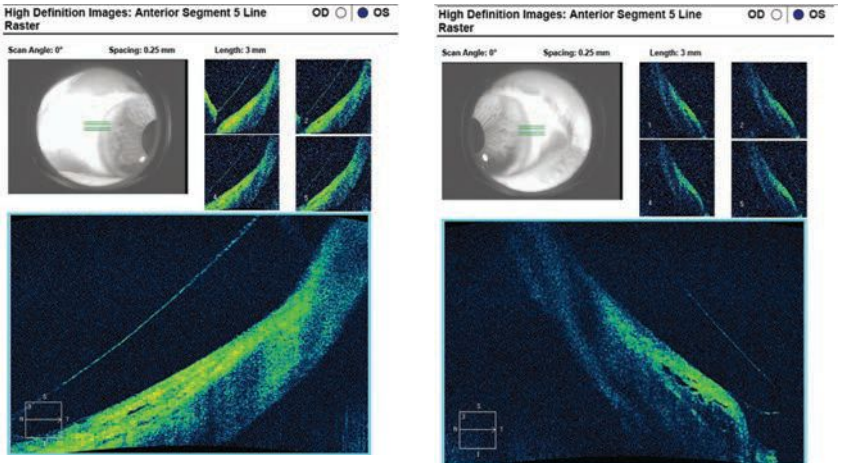

Fig. 12. With modified SynergEyes VS scleral lens parameters, the scleral landing zone showed ideal alignment at the nasal quadrant (left) and mild edge lift on the temporal sclera (right) on AS-OCT.

he experience any ocular hyperemia with associated pain, discomfort or hazy or decreased vision.

DISCUSSION

When initially diagnosed, megalocornea is a condition that necessitates further testing from both an ocular and systemic standpoint. From an ocular standpoint, the diagnosis must be further differentiated between simple megalocornea and megalophthalmos anterior. If the latter is suspected, further testing must be performed routinely to monitor for pigment dispersion glaucoma, ectopia lentis and early cataract.

In addition, extra precaution must be taken if phacoemulsification is to be performed on these corneas due to the enlarged capsular bag and weakened zonules. Anterior or posterior iris-fixed IOLs may be necessary, as the enlarged anterior chamber, enlarged capsular bag and weakened zonules all pose a challenge to standard IOL placement.

From a systemic standpoint, the optometrist may have to consider referral to a nephrologist, rheumatologist, orthopedist or cardiologist if any underlying associated systemic conditions are suspected. A megalocornea diagnosis in a young patient should automatically trigger a developmental evaluation by a pediatrician. Overall, the prognosis of simple megalocornea is good.

As for the case study, the correct diagnosis for this patient is megalophthalmos anterior without pigment dispersion glaucoma and systemic involvement.

This scleral contact lens fitting was unique in several ways. First, the patient's megalocornea required an extremely tall lens vault despite having average-to-steep keratometry readings on the topographer. Second, as the patient is aphakic, he required a scleral lens that is available in a very high plus power and a hyper-dK material to promote oxygen permeability. In addition, the patient's scleral profile required a very steep scleral landing zone at both the scleral flat and steep meridians. In fact, the patient's scleral profile was so steep that there was residual edge lift at the steep meridian despite having maxed out the scleral landing zone parameter in the manufacturer's guidelines.[16]

The SynergEyes VS scleral lens was selected for this fitting because it offered desirable qualities and customizable parameters for this patient's unique corneal condition and aphakic status. RCCL

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LESSONS FROM THE LABS:
GP PROS SHARE THEIR BEST TIPS

Learn what consultants *wished* they got from doctors when they order specialty lenses.

By Heidi Miller, OD, and Robert Ensley, OD

Fitting a customized contact lens can be a rewarding experience. By combining empirical data and clinical expertise, specialty lenses can be designed for nearly any refractive state or ocular condition. However, the fitting process is not without challenges. Fortunately, contact lens manufacturers are armed with highly trained consultation teams available to offer their assistance when needed.

We reached out to consultants from multiple gas permeable (GP) lens manufacturers to seek their advice and perspectives on how to cultivate a relationship and maximize their expertise. We have also assembled a consensus of their suggestions for how to best streamline the contact lens fitting process.

SAME OLD STORY

When polling the labs regarding their interactions with optometric practices, many had similar responses. Below we have included some commonly asked questions, along with answers provided by various consultants from different lens manufacturers.

What do ODs ask labs about the most about and how do the design consultants help them?

• ***Advice on selecting designs and materials.*** "What designs work best for a particular disease? Lid anatomy, topography, the patient's lens history and motivations are very helpful before making a suggestion. Wearing habits, occupational visual needs and patient history can also be very valuable. Knowing the problem helps design lenses that will work the best. However, ECPs also need to understand that there is no single lens design that will magically provide the optimum outcome for every situation."

• ***How to handle limbal zone changes.*** "They usually need to increase the limbal clearance in some areas without getting excessive limbal clearance in other areas. With quadrant-specific designs, this allows us to design and customize lenses accordingly. Also, incorporating oval optic zones into the lens design to accommodate for the asymmetrical nature of the limbal zones has provided great improvement."

What are common problems labs face when they don't get good feedback from an OD?

• ***Lack of and/or low quality information.*** "Many times consultants only receive Ks and refraction—not enough information to design a specialty lens. Having complete and accurate information will allow consultants to design the best lenses for the patient."

• ***Note locating lens marking.*** "When doctors place an order and need adjustments in

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some areas, they often forget. We either must guess it or, in some cases, they must get the patient back in the office for an accurate assessment."

• ***Only relying on one diagnostic modality.*** "They can rely too much on optical coherence tomography (OCT) alone and fail to assess the lens under a slit lamp."

• ***Not having good quality mappings.*** "Better and more complete maps give us the information needed to make an educated decision on what design will work best for the patient and what parameters are appropriate."

What would lab design consultants like ODs to know when they put in an order?

• ***The more information we have, the better the lenses will fit.*** "Previous orders, K reading, maps, photos, trial lenses—all can help us to design a better lens for their patient."

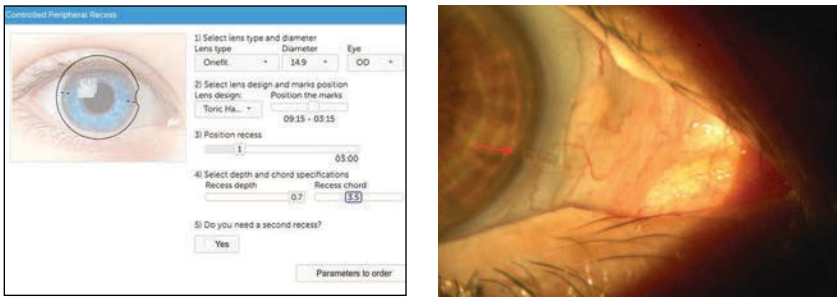
• ***Take time and navigate through the trial set if the first lens did not work well.*** "The other trial lenses might have the perfect fit or might have been a much better starting point if they had only tried them on."

When ODs are doing their initial design, what do labs emphasize not to forget?

• ***Lens parameters.*** NaFl patterns, horizontal visible iris diameter (HVID) or any pertinent information that is available.

• ***The location of any laser markings on the lens.*** "Toric markings are important for haptic changes and astigmatism correction and helps the consultant make changes to the lens's fit and power."

• ***Trial lens.*** "Document which trial lens was used to assess the fit."



Blanchard's CPR tool helps visualize the lens and can be used to populate lens parameters (left). At right, the ordered lens displays toric markings, which are important to note prior to making any haptic changes.

What can ODs do so that the lab can ensure adequate fit and eliminate as many initial issues from their end?

• ***Manipulate the lens on the patient eye with their thumb.*** "Scleral lenses tend to decenter down and out, and if the OD is able to move the lens and center it better, that will be important information to give to the consultant in order to suggest the proper change."

• ***Submit a comprehensive list of items with order.*** This should include:

- Accurate K readings and refraction
- Topographies, when available
- Patient history, *e.g.*, Is the patient post-surgery? Do they have an IOL?
- Previous lens history
- Patient expectations
- Slit lamp photos, when available
- OCT images, when available

OPEN COMMUNICATION

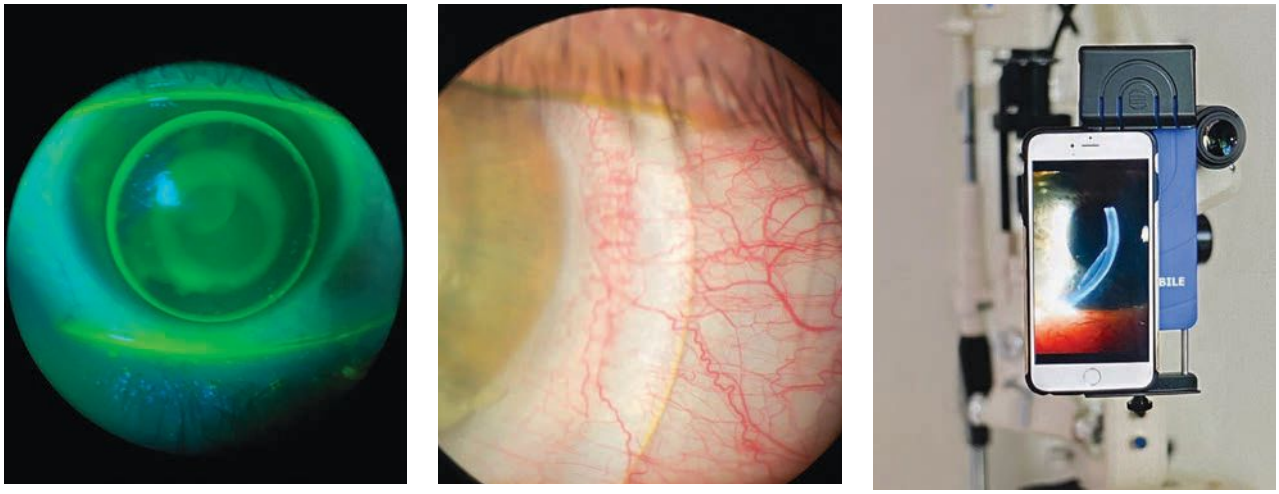
Whether you are a recent graduate or a seasoned contact lens fitter, there should be no hesitation to reach out to the laboratories when necessary. Besides the traditional fax and phone options, many laboratories now have online portals and encourage the use of email communication. This allows for greater flexibility to work around clinic and office hours.

When no assistance is required, online portals are simple and convenient enough for either the practitioner or trained staff to input lens data or upload files. In other cases, the lab's feedback may be desired, and an email may be more appropriate. If possible, reach out to a specific consultant with whom you have a comfortable working relationship.

When emailing, we highly encourage providing account numbers, previous invoice numbers and shipping information to save time. Laboratories aren't responsible for your record-keeping; rather, it's incumbent upon you to maintain a careful log of your previous orders to help prevent any ordering errors.

Concise, consistent communication makes it easier for consultants to determine what is needed. If ordering for both eyes, start with the right eye and provide the pertinent information before moving to the left eye. A lens evaluation is welcomed, but terms like "tight" or "loose" may lack context. For example, describe a "tight" scleral lens by detailing where the conjunctival compression is located and if there is heel or toe blanching.

Units of measurement can be helpful, but keep them consistent along with the formatting for providing lens parameters. For



An iPhone and adapter at the slit lamp (right) is an option when taking images of troubleshooting issues. This is an easy way for doctors to send photos and videos to consultants directly.

instance, describing a lens's sagittal depth as "good" and limbal clearance as "adequate" is not as useful as stating there is 200µm of apical clearance and 50µm of limbal clearance.

Of course there's no such thing as too much information when it comes to providing data to the laboratory. Corneal topographies provide more information regarding corneal curvature and condition than Ks alone. Pictures or video of the lenses on the eye can help as well.

If you don't have an imaging system at hand, most phone cameras have high enough resolution to take quality photos for the lab with the aid of an adapter. These options allow the consultant to remotely view the lens even while the patient is in the chair. Anterior segment OCT can also supplement a lens evaluation, showing both the sagittal depth of the lens as well as the lens edge in order to provide a better visual of just how much or how little change is required.

GATHERING DATA

As one lab consultant told us, "ODs need to treat the patient as an individual and gather both clinical and lifestyle information as well as the patient's expectations in order for consultants to be able to effectively assist in optimizing the design process."

Before ordering any specialty contact lenses, learning more about the patient and their objectives is a critical factor for success. What are their needs and goals? Are there any lifestyle considerations? How often will they wear them? Do they need to be wearing them for their job? Do they have any history of contact lens wear that was either successful or a failure?

For example, if a patient desires crisp, stable optics at both distance and near but has not had success with an aspheric GP multifocal, it makes sense to consider a translating design. Although these lenses may be best fit diagnostically, empirical fitting is possible. However, sending only keratometry measurements and refraction to the laboratory will result in guesswork during lens design. Clarifying lens design as well as providing data such as pupil size, HVID), aperture size and eyelid position are pertinent for initial lens design.

Of course, careful evaluation of the ocular anatomy is also important when considering different lens designs. For GP lenses, upper eyelid position is a primary consideration for choosing lens diameter. If lid attachment is not possible, then consider a smaller interpalpebral fit. Similarly, lower eyelid position is critical for the success of translating GP multifocals.

When considering larger design lenses, like sclerals, evaluate aperture size and eyelid laxity. Small aperture or tight eyelids might make application and removal difficult. Tight or heavy eyelids can also contribute to lens decentration. Conjunctival abnormalities like cysts or pterygia can make scleral lens fitting more complex, often requiring higher levels of peripheral customization. Knowing the availability and limits of the design options for your scleral lens of choice is essential before starting a fitting.

Topographical analysis, especially for irregular corneas, can be used to understand size and shape of the cornea. Although not its primary use, most topography systems measure HVID, which plays a role in determining scleral

lens diameter and hybrid lens skirt curves. Identifying the steepest and flattest points on the cornea will help you choose between prolate or oblate design lenses. Location of the steepest point of an ectatic cornea can also help you choose lens designs and diameters. Corneas with large elevation differences may also be difficult to fit with corneal GPs and require a scleral lens.

When sending refractive data for especially higher-powered lens orders, make sure it is clearly known if the power has already been vertexed. If a spherocylindrical over-refraction is found, lens flexure must be ruled out, and the decision to incorporate front surface toric power may be dependent on lens stability. In these cases, noting the lens markings at every visit is mandatory to ensure the lens is stabilized prior to incorporating the power in the lenses. Discussing subjective quality of vision at all working distances can help determine if zone size or centration should be modified.

TIPS FOR TROUBLESHOOTING

Once a lens is ordered, there may be challenges that arise related to vision, lens fit or comfort. When attempting to troubleshoot a concern, it is important that the practitioner helps the lab consultant clearly understand the issue or objective. When describing a lens fit to a consultant, be more descriptive with the exact location of the issue and lens markings.

The capability to easily pass along photos and videos of the lens's on-eye performance has greatly assisted our troubleshooting efforts. Videos tend to be more helpful than a single image since the movement of the lens is important as well as the lens position. OCT images don't necessarily show us where there might be blanching.

In some cases, the OCT image of the landing looks ideal, but upon slit lamp examination, we might see mild blanching or redness. In other cases, the edge appears to be digging in, and we might assume there is blanching, but then slit lamp evaluation reveals that the patient has redundant conjunctiva and blanching is not present. This does not mean the landing won't be altered; it simply means that it might be altered in a different way. Another example is that when a single OCT cross-section is taken along the 180° meridian, it can completely miss the elevated area of a cone in a patient with keratoconus or other ectasia. We recommend, if possible, taking both a 0° to 180° cross-section along with a 270° to 90° cross-section.

Lid structure could be the culprit of poor contact lens performance. Always make sure to retract the eyelids at the microscope to evaluate how a lens is sitting on the cornea in the absence of lid involvement. Verify if the fit is related to the lens or if the lid is creating a difference in lens alignment. Maybe the lens sits central in the absence of eyelid interaction, but interacting with the eyelid pushes the lens or causes it to ride high. Some ways to adjust for this could be changing the center thickness of the lens and modifying the edge profile. A floppy lid might need an increase in lens edge in order to grab the lens upon blinking. You can avoid making excessive parameter changes if you determine that the lid is manipulating lens alignment.

A patient's description of what they feel is happening can help guide any changes, especially when everything might objectively look great. Comments like, "I feel the lens over here," "I tip my head up to see better," "It feels like a pressure or tightness" and "It's like looking through a tunnel," all detail the lens fit or the optics of the lens. If a patient reports vision changing with blinking, this could indicate either poor lens alignment or a wetting issue with the lens material. If you look at the lens surface behind the slit lamp and notice the material is not wetting well, tell the lab consultant so they can consider a different lens material with a different wetting angle or add a coating such as Tangible Hydra-PEG for increased lubricity.

Custom specialty contact lenses are a fantastic service to provide for our patients. Using the expertise of consultants from various lens manufacturers is both beneficial and can help streamline the contact lens fitting process. Patient history and thorough data collection is critical during a contact lens exam. So are capturing images and recording videos whenever possible.

Consider setting up a weekly time to discuss patient cases and lens orders with your consultant. Depending on your contact lens volume, setting up a standing appointment for a weekly or biweekly meeting with your laboratory consultant may be beneficial whether it be by phone or video call. Whichever method you choose, ultimately, clear communication is key. RCCL

Thank you to our consultants from ABB Optical Group, Valley Contax, Alden Optical, BostonSight, Blanchard, Art Optical and TruForm Optics for contributing to this article and providing valuable insight on how to improve the GP lens ordering experience.

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The Consequences of Corneal Endothelial Compromise

Optometrists must recognize the signs to ensure proper diagnosis and treatment.

By Bhawan Minhas, OD

The simple yet sophisticated organization of the corneal layers—the epithelium, Bowman's membrane, stroma, Descemet's membrane and endothelium—results in transparency, allowing visual rays to reach the retina. The corneal endothelium, the most posterior layer, is also the most fragile. This hexagonal, non-replicating monolayer of tissue is able to maintain balanced corneal hydration through the help of ion channels that enable fluid transport.[1]

This intricate balance can be disrupted by a variety of factors including age, injury or trauma, genetic dystrophies and secondary degenerations. A precise understanding of normal anatomy and physiology, as well as the application of various examination techniques, can aid the clinician in the evaluation of this thin but mighty corneal layer.

THE PUMP-LEAK PROCESS

The dimensions of an average corneal endothelial cell are 18µm to 20µm wide, 4µm to 6µm thick and 7µm in diameter with a six-sided shape comprising the majority of cells.[4,5] These cells are not known to undergo mitosis *in-vivo*; on the contrary, they gradually undergo apoptosis during their lifetime, with a critical mass of approximately 400 to 700 cells per mm^2 that is necessary to maintain tissue transparency in normal individuals with average intraocular pressure (IOP).[6,7] Due to this natural, progressive decline, the surface of the remaining cells may morph to compensate the subsequent changes to the monolayer. It is well documented that the average adult endothelium maintains a cell density of approximately 2,500 to 3,000 cells per mm^2.[8]

The endothelium contributes to visual clarity and corneal deturgescence using a specialized pump-leak system. The "pump" aspect pertains to active transport properties of membrane-bound channels and the intercellular junctional complexes. These compensate for stromal swelling that occurs as a result of the "leak" created to maintain corneal hydration and nutrition via hydrostatic pressure of the aqueous and the oncotic pressure of the cornea.[6]

Active transport mechanisms of the endothelium are primarily achieved by the Na+, K+, HCO3- and Cl- ions along with carbonic anhydrase.[9] Active exchange of these substances gives rise to an ionic gradient between the stroma and aqueous humor, which allows for the extraction of water from the cornea. The pumping process is further facilitated by lateral interdigitations, gap junctions and tight junctions on the lateral borders of adjacent cells.[9]

As discussed above, though normal throughout the course of life, endothelial cell death potentiates a problem in maintaining endothelial cell clarity where the pump function is compromised. Centripetal migration and stretching to compensate for lost cells in the absence of regeneration naturally causes changes in cell size and shape that then correlate with pump dysfunction. Specifically, polymegethism (increase in cell size) and pleomorphism (change in cell shape) are both related to a reduction in the ability of the endothelium to dehydrate the cornea.[10]

ENDOTHELIAL EVALUATION

Comprehensive evaluation of the corneal endothelium is crucial to ensure proper diagnosis and care. The various ways to conduct this evaluation are discussed below.

Specular and confocal microscopy. While most clinicians do not have access to these tools, these visualization instruments are important, revealing that the endothelium is quite complex and maintains a three-dimensional shape that counterparts its multifarious role. Specular and confocal microscopy allows for quantitative evaluation of the endothelium for diagnostic purposes, monitoring for progression and assessing response to treatment in endothelial cell pathology (*Figure 1*).

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Dr. Minhas is director of on-campus residency programs and an assistant professor at Salus University/Pennsylvania College of Optometry.

The Cornea Close Up

The complex balance of the five recognized layers of the cornea is fundamental to maintaining visual integrity. Although Dua's layer has been detected and reported as a discrete pre-Descemet's entity, its relevance has been limited to visualization during corneal graft procedures, namely deep anterior lamellar keratoplasties.[2,3]

Generally, the corneal epithelium functions as a barrier to invaders from the external world, the stroma maintains adequate corneal thickness and shape in order to provide refractive power and the endothelium maintains hydration of the stroma and nutrition of cells.

With the exception of oxygen, corneal nutrients are extracted primarily from the aqueous humor. This necessitates the use of both passive diffusion and active transport of molecules through various enzymatic transport systems on the apical and basolateral flanks of the endothelial layer.[4]

The honeycomb-like mosaic of the endothelium is best evaluated through a specular microscope. This hexagonal shape, however, is only visible on the apical surface of the cell, which is in contact with the anterior chamber.[5]

As it pertains to the remaining surfaces, three-dimensional confocal microscopy has enabled researchers to categorize and map the lateral and basilar aspects of endothelial cells. Lateral membrane expansions with multiple membrane folds on the lateral aspects indicate a complex network of cellular interdigitations.[5] Additionally, these membrane expansions have been shown to increase in number and length as they move from the apex to the basilar surface.[5]

Interestingly, a smartphone-based microscopy system using an iPhone has shown initial promise in visualizing the endothelium in a sub-cellular resolution as a possible alternative in rural settings.[11] Though many preliminary studies have revealed the qualitative and quantitative abilities of smartphone specular microscopy in analyzing the most posterior corneal layer, further refinement to standardize light sources and automate analysis is needed before this can become commercially available.[12]

More widely used and readily available methods to examine the corneal endothelium in the routine clinical setting can be distinguished into three strategies: slit lamp biomicroscopy techniques, indirect measures of adjacent stromal thickness and anterior segment optical coherence tomography (AS-OCT).

Slit lamp biomicroscopy. This is often the workhorse of visualizing corneal health and monitoring for pathology of the endothelium. Many times, it is one of the only visualization tools a clinician may have access to. This tool can be infinitely useful for perceptive clinicians if used appropriately. Initial analysis of

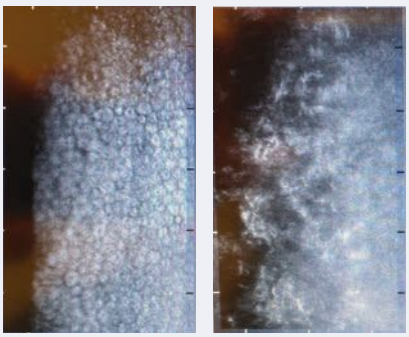

Fig. 1. Non-contact specular microscopy of a normal corneal endothelium (left) and of a patient with Fuchs' dystrophy (right).

observed corneal pathology is performed through the use of an optic section. This cross-sectional observation technique aids in determining anterior to posterior depth and specific corneal location of an abnormality. Additional lighting techniques, such as specular reflection, direct and indirect lighting and retroillumination may then be employed.

As a primary means of visualizing the endothelium in a focal location, specular reflection of the endothelium at a high magnification allows direct visualize of a discrete number of cells. Best practices include keeping the area of illumination small, reducing extraneous reflected light, utilizing the highest possible magnification and attempting to view monocularly. In this method, individual cells appear as a hexagonal mosaic and guttae; droplet-like accumulations of collagen will appear as dark, non-re-

Release Date: February 15, 2021
Expiration Date: February 15, 2024
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Educational Objectives: *After completing this activity, the participant should be better able to:*

- Describe the pathophysiology of endothelial diseases.
- Identify and monitor the common warning signs of endothelial compromise.
- Diagnose endothelial diseases.
- Evaluate patients when a specular microscope is unavailable.

Target Audience: This activity is intended for optometrists engaged in primary care of the anterior segment of the eye.

Accreditation Statement: In support of improving patient care, this activity has been planned and implemented by the Postgraduate Institute for Medicine and Review Education Group. Postgraduate Institute for Medicine is jointly accredited by the Accreditation Council for Continuing Medical Education, the Accreditation Council for Pharmacy Education, and the American Nurses Credentialing Center, to provide continuing education for the healthcare team. Postgraduate Institute for Medicine is accredited by COPE to provide continuing education to optometrists.

Faculty/Editorial Board: Bhawan Minhas, OD, FAAO, Salus University/ Pennsylvania College of Optometry.

Credit Statement: This course is COPE approved for 2 hours of CE credit. Course ID is **70780-AS**. Check with your local state licensing board to see if this counts toward your CE requirement for relicensure.

Disclosure Statements:
Dr. Minhas has no financial disclosures. *Managers and Editorial Staff:* The PIM planners and managers have nothing to disclose. The Review Education Group planners, managers and editorial staff have nothing to disclose.

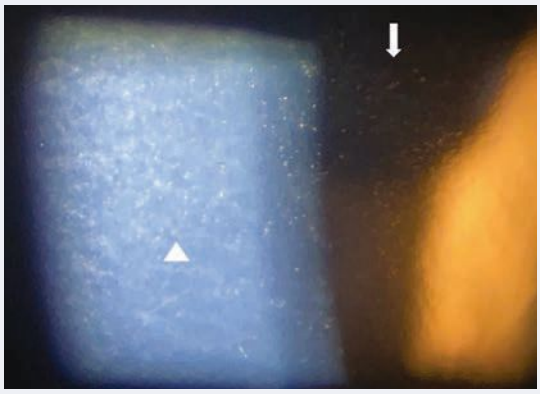

Fig. 2. Slit lamp imaging through an iPhone X of pigmented corneal guttata in a patient with Fuchs' endothelial dystrophy with lesions viewed in high magnification in direct (triangle) and indirect (arrow) illumination.

flective areas. Additionally, both direct and indirect illuminations are helpful, especially under high-powered magnification, in viewing pigmented abnormalities of the endothelium (*Figure 2*). Sclerotic scatter is best used to visualize even subtle stromal edema that may result from endothelial dysfunction.[1] Finally, retroillumination in the setting of a dilated pupil can help determine the extent and severity of endothelial pathology (*Figure 3*).

Indirect measurement of stromal thickness. Due to the endothelium's role in maintaining stromal clarity, an indirect measure of endothelial pump integrity can be ascertained through the measurement of corneal thickness. As the pump-leak process breaks down, such as in Fuchs' endothelial dystrophy, the cornea has the propensity to thicken as a result of edema within the stromal layer. Even in cases where the edema is not readily observed through clinical exam, studies have demonstrated that there is still an increase in measurement of central corneal thickness in all grades of Fuchs'.[13] Thus, it can be extrapolated that central corneal thickness can be used as an indirect, quantitative parameter to help monitor progression of endothelial loss in pathology.[13] It is important to note that this relationship has been established in endothelial diseases, but not in relation to the natural, age-related degradation of endothelial cells.[14,15]

Pachymeters measure corneal thickness. The most common type of ultrasound pachymetry is a handheld portable device. While this device is fairly cost-effective, it is particularly dependent on the proper positioning of the probe perpendicularly to the corneal surface.

More modern devices that include pachymetry measurements are able to take accurate measurements without contact but come with a higher price tag. Optical devices include AS-OCT such as Visante (Zeiss), slit-scanning corneal topography such as Orbscan (Bausch + Lomb) and Scheimpflug systems such as the Pentacam (Oculus) and Galilei (Ziemer). Scheimpflug devices demonstrate a higher repeatability of thickness measurements in advanced corneal pathology vs. slit-scanning devices.[16] Additionally, the latter devices allow clinicians to obtain pachymetry measurements of the entire corneal surface and monitor for variations as opposed to a single, central locale as seen in ultrasonic devices.

AS-OCT. This high-resolution cross-sectional modality is used for a vast array of anterior segment pathologies and can be used for postoperative monitoring and management of endothelial keratoplasties, such as Descemet's stripping endothelial keratoplasty (DSEK) and Descemet's membrane endothelial keratoplasty (DMEK).[17] It can also be used to visualize *in vivo* biomarkers for various corneal diseases in a noninvasive fashion. Altered reflectivity patterns within Descemet's can be visualized in Fuchs' endothelial dystrophy.[18] Furthermore, AS-OCT can be used to directly image endothelial disruptions, the presence of inflammatory cells or keratic precipitates, and stromal edema or opacities with more detail and accuracy.[19]

WARNING SIGNS

The endothelium lies adjacent to Descemet's layer and relies on a healthy and intact basement membrane and, subsequently, the production of the extracellular matrix.[20] Although the endothelium is not in direct contact with the stroma, should it fail in maintaining optimal hydration, the uniform spacing of the stromal fibers that is typically coordinated by glycosaminoglycans collapses, causing increased scattering of incident light due to non-uniform spacing and loss of transparency.

Early warning signs of endothelial dysfunction can include pleomorphism, polymegethism and guttae, but these can also be present in normal eyes. Thus, the most diagnostic sign of corneal decompensation is typically edema and, in more advanced stages, bullae formation. An affected patient may initially report blur, discomfort and even severe pain as conditions worsen. In chronic cases, permanent scarring may occur.

PATHOPHYSIOLOGY

To ensure timely and proper diagnosis, optometrists should be aware of the various factors that can disrupt the corneal endothelium.

Age. The natural and gradual reduction in endothelial cell density occurs at a rate of 0.56% to 0.60% per year.[21,22] On the contrary, Descemet's is known to steadily increase throughout life due to the continuous secretion of the basement membrane. It is important to distinguish the rate of change due to normal aging from that which is more prominent in pathology.

Injury/trauma. Corneal endothelial injuries from trauma are clinically observed as a "snail-track" or winding gray lines. A relatively common example of this is found in the incisional scar following extracapsular cataract extraction. Rapid focal distortion of the endothelium is often the culprit behind the linear opacities and is similar to the injury received during large-incision surgeries from excessive corneal bending.[9]

The endothelium responds to injury in three stages: (1) initial coverage of the wound via migration of adjacent cells, (2) re-establishment of tight junctions and return to normal corneal thickness and (3) remodeling of endothelial cells into regular hexagonal shape.[9] The initial stage compensates for the markedly reduced number of tight junctions and ability to carry out optimal pumping and maintain transparency. The subsequent stages compensate by increasing the quantity of tight junctions and endothelial remodeling, a process that takes place over several months.[9,23] Further, in the case of more significant trauma during large-incision anterior segment surgery that may cause a Descemet's break, deposition of a new basement membrane also follows immediate endothelial cell migration, which can take more time, especially if the split edges are not in close proximity.[9,24]

Intraocular surgeries, especially involving phaco, can lead to endothelial cell damage and corneal edema, occurring in 4% to 25% of cases.[25] One study concluded that, three months post-cataract surgery, average cell loss was 6.9%.[26] Additionally, after initial decline, endothelial cell density continues to decrease at an annual rate of 2.5% for at least 10 years, with or without lens implant.[27] Though the exact mechanism behind the increased rate of loss is unknown, theories include decreased nutrition from the aqueous humor, reduced innervation, subclinical inflammation and exposure to vitreous humor.[22]

Shallow anterior chamber depth, especially in the context of dense cataracts, is correlated with increased endothelial cell loss following phacoemulsification.[28] Due to the confinement of space within a narrow chamber, surgeons must be cognizant of cataract density, surgery and phaco time, and ultrasound power to ensure post-op success.

During the procedure itself, it is imperative to additionally monitor for intraocular lens (IOL) contact, instrument-related trauma, incision size, irrigation solution turbulence, IOL type and ophthalmic viscoelastic substance to decrease the risk of resultant corneal edema.[28,29] Endothelial cell density and morphology has been demonstrated to decrease more so with anterior chamber than posterior chamber IOLs.[30] Finally, angle-supported anterior chamber intraocular lens designs can increase the risk of bullous keratopathy up to 10%, which is thought to be due to chronic inflammation from lens-endothelial cell contact at the corneal periphery.[31]

Loss of endothelial cell density of donor corneas has been observed following penetrating keratoplasty, which is strongly dependent upon duration of donor corneal storage and surgical trauma.[22] A three-year post-op analysis indicated that cell density reaches 53% of the pre-op level.[22] To cover the area of the wound, endothelial cells migrate from the recipient to the donor and from the donor to the recipient cornea.[22] Finally, greater morphological abnormalities and a longer recovery time has been noted in diabetic corneas as they are considered more vulnerable to stress and trauma after cataract surgery compared with non-diabetic corneas.[32]

Endothelial dystrophies. Optometrists should consider the following endothelial corneal dystrophies: Fuchs' dystrophy, posterior polymorphous dystrophy (PPD) and congenital hereditary endothelial dystrophy (CHED), with Fuchs' being the most common.[22] Fuchs' is a bilateral disease that typically manifests in middle age or later and is marked by the presence of guttae. Although decreased cell density, polymegethism and pleomorphism are all part of both normal aging and the pathophysiology of Fuchs', the enlarged endothelial cells in Fuchs' secrete an excess of Descemet's membrane in the form of banded collagen, which is not seen in senescence.[22] This abnormal deposition is clinically witnessed as mushroom-like projections on the posterior surface of Descemet's membrane; guttae can also be seen on AS-OCT and ultra-high resolution AS-OCT as distinct hyperreflective entities projecting into the aqueous.[18]

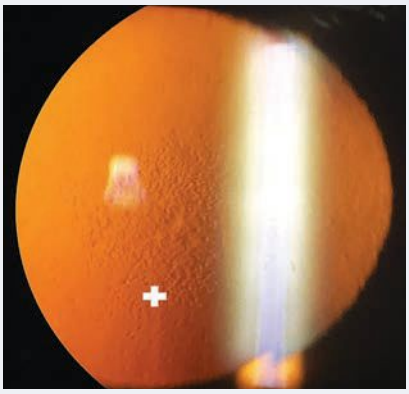

Fig. 3. Slit lamp imaging using an iPhone X of central guttata in a patient with Fuchs' endothelial dystrophy with lesions viewed in retroillumination (plus sign).

Guttae are not pathognomonic for Fuchs'. When they are found peripherally, they are defined as involutional Hassall-Henle bodies. In the case of Fuchs', the guttae are found centrally. Along with guttae, folds in Descemet's, stromal edema and microcystic epithelial edema can be seen in advanced disease.[1] As the disease progresses, the natural ability of the endothelium to maintain appropriate corneal hydration is compromised,

exacerbating symptoms of blur and glare upon awakening.[1] Ultimately, this may necessitate keratoplasty. Interestingly, the micron-scale dimensions of guttae can affect the migratory behavior of endothelial cells.[20]

PPD is along the spectrum of inherited bilateral endothelial disorders in which the majority of patients have subtle clinical signs and unaffected vision. Histologically, the endothelium takes on epithelium-like characteristics. Should these cells infiltrate the trabecular meshwork, IOP may rise.[1,22] Features of PPD can include vesicular, curvilinear and placoid irregularities on slit lamp exam, similar to those seen on the epithelium in basement membrane dystrophy. Rounded, dark areas with central cell detail appearing as a doughnut-like pattern on specular microscopy can also occur. In visually significant cases, the reduction is often due to edema.[1]

Whereas Fuchs' and PPD typically arise beyond the fifth decade of life, CHED is present at birth, appearing as bilateral corneal clouding.[22] It often requires keratoplasty, as corneal thickness can be two to three times higher than normal, and up to 1mm centrally. However, in contrast with iridocorneal endothelial syndrome, corneal diameter and IOP are within normal ranges.[1] Other features of CHED can include discrete white dots in the stroma, pigskin-like roughness to the epithelial surface and peau d'orange appearance to Descemet's.[1]

Contact lens-induced endotheliopathy. A metabolic source of stress, such as hypoxia from contact lens wear, can also affect the endothelium. In order for this to happen, the inciting agent must typically occur over a large span of time. Hypoxic stress can cause morphological changes to cell size and shape, alteration of microanatomy and dysfunction of the endothelium.[5,22]

Glaucoma-induced epitheliopathy. Changes to corneal endothelial cell density have been documented in primary open-angle glaucoma (POAG). Studies have shown patients with POAG have significantly lower endothelial cell density than age-matched controls.[33] The mechanism of damage is thought to be from high IOP hindering normal metabolic function and damaging the physical barrier function of endothelial cells, similar to damage of the retinal nerve fibers in the posterior segment.[33] Another theory is benzalkonium chloride preservative toxicity to the endothelium from topical hypotensive agents often used in glaucoma.[33] These adverse effects to the cells appear to be dose- and time-dependent.[34]

Carbonic anhydrase inhibitors. Given that carbonic anhydrase is one of the key components of endothelial pumps, it has been postulated that the use of carbonic anhydrase inhibitors (CAIs) may cause disequilibrium of this system. However, studies indicate that topical use of a CAI, such as brinzolamide, has no influence on endothelial cell characteristics as examined with specular microscopy.[35] Others have suggested that use of dorzolamide, for example, in patients with pre-existing endothelial cell pathology caused a 12µm increase in size. This change, however, is not considered clinically relevant.[36]

INTERVENTIONS

The current standard of care for advanced endothelial compromise is surgery, typically DSEK (or the automated version, Descemet's stripping automated endothelial keratoplasty—DSAEK) and DMEK. While DSEK/DSAEK and DMEK both provide a reprieve for endothelial decompensation, DSEK/DSAEK involve descemetorhexis of the host's cornea and grafting with donor tissue that consists of endothelium, Descemet's and some stromal tissue (*Figure 4*). By contrast, DMEK has a thinner donor graft by eliminating stromal tissue completely. Penetrating keratoplasty is often reserved for patients with severe end-stage edema or deep scarring of the stroma, in which a full-thickness graft is necessary.[31]

DMEK is growing in popularity compared with DSEK, providing rapid, predictable and efficacious visual rehabilitation for endothelial decompensation with minimal changes to refractive error.[31] Though descemetorhexis without grafting is also an option, it is no the standard of care for all endothelial compromise as it requires careful patient selection, limiting research potential in large-scale studies.

Though keratoplasties are the standard surgical treatment for corneal decompensation, donor corneas can be difficult to come by. Alternative ways to improve vision and decrease pain/discomfort include topical osmotic solutions, bandage contact lenses (alone or in combination with hypertonics), amniotic membranes, stromal puncture or phototherapeutic keratectomy for advanced cases of epithelial compromise from persistent edema or a Gundersen conjunctival flap to reduce pain in severe cases of bullous keratopathy.[31]

There is excitement in the research community over approaches that may preclude or delay surgery. This includes collagen crosslinking or topical rho-associated kinase (ROCK) inhibitors. Although crosslinking is traditionally seen as a treatment for strengthening stromal collagen fibers in ectasia, transendothelial inflow and stromal imbibition pressure have been shown to decrease. This leads to resolution of bullae and improved vision and symptoms following the procedure; however, it remains experimental to date.[37] ROCK inhibitors promote endothelial cell proliferation, enhance cell adhesion and suppress apoptosis on endothelial cells

in vitro.[38] ROCK inhibitors applied topically to edematous corneas after cataract surgery have proven beneficial in improving corneal clarity.[39] As such, both *in vivo* and *ex vivo* use of ROCK inhibitors that proliferate cultured cells may be useful for endothelial compromise.[31]

The future of corneal endothelial management may lie in the use of culturing and proliferating endothelial cells, as well as pluripotent or multipotent stem cells, to produce additional endothelial cells in bioengineering corneal endothelium.[40] Regeneration of healthy corneal endothelium via the use of transplanting cultured endothelial cells has been established with culture protocols and transplantation techniques that are currently under investigation.[41] Various techniques that may even aim for multiple cells from a single donor cornea to be used in hundreds of patients are also under investigation.[40] Finally, many pathologies of the endothelium leave the peripheral tissue unaffected. Given the migratory potential of endothelial cells, investigation of regeneration in the absence of implantation of donor tissue is also being considered.[40] RCCL

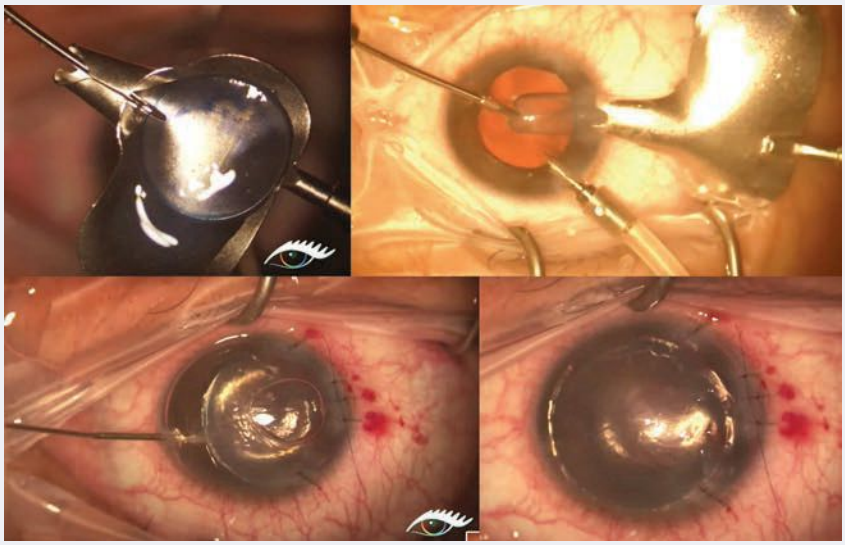

Photo: James Lewis, MD

Fig. 4. *Top left:* A 9.0mm donor graft is loaded into the plate of the glide with the endothelium side up. *Top right:* The donor tissue is folded up like a taco and pulled through the funnel-shaped portion of the glide, then pulled through the temporal incision. *Bottom left:* After the graft has been successfully inserted into the anterior chamber, it is unfolded in the recipient anterior chamber with balanced saline solution and/or an air bubble. *Bottom right:* The donor button maintains apposition with the host cornea through use of an air bubble, giving time for the endothelial pumps to aid in donor-host tissue binding.

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1. Which corneal layer maintains corneal shape to provide refractive power?
a. Epithelium.
b. Stroma.
c. Descemet's membrane.
d. Endothelium.

2. Which of these corneal nutrients is not predominantly supplied by the aqueous humor?
a. Oxygen.
b. Ascorbic acid.
c. Glucose.
d. Amino acids.

3. What border of an endothelial cell contains junctional complexes to maintain the pump-leak system?
a. Apical.
b. Lateral.
c. Basal.
d. Both B and C.

4. Which of the following ions is not a part of the active or passive transport mechanisms of the endothelium to maintain corneal clarity?
a. Na+.
b. K+.
c. HCO3-.
d. Ca2+.

5. Which of these statements about endothelial cell behavior is false?
a. Polymegethism is the increase in cell size.
b. Pleomorphism is the change in cell shape.
c. Endothelial cells will undergo mitosis to help with wound healing.
d. Endothelial cells migrate in a centripetal fashion as part of wound healing.

6. On which surface of the endothelium is the hexagonal shape of cells present?
a. Apical.
b. Lateral.
c. Basal.
d. All surfaces.

7. Which of these lighting strategies on a slit lamp allows visualization of the distribution of guttae?
a. Specular reflection.
b. Wide angle direct light.
c. Sclerotic scatter.
d. Retroillumination.

8. Which of the following pachymetry methods use ultrasound in order to determine corneal thickness?
a. iPac Handheld.
b. AS-OCT.
c. Orbscan.
d. Pentacam.

9. Which of the following is the last step in resurfacing of the endothelium after injury?
a. Reestablishment of tight junctions.
b. Return to normal corneal thickness.
c. Coverage of wound by migrated nearby cells.
d. Remodeling into hexagonal shape.

10. Remodeling of the corneal endothelial cells into their normal hexagonal shape may take several _____ to be restored after an injury.
a. Days.
b. Weeks.
c. Months.
d. Years.

11. Which of the following is not a risk factor for endothelial cell loss during cataract surgery?
a. Deep anterior chamber.
b. High cataract density.
c. Increased surgery time.
d. Increased phacoemulsification power.

12. Which of the following risk factors increases the loss of endothelial cell density of a donor cornea after penetrating keratoplasty?
a. Duration of donor corneal storage.
b. Trauma during surgery.
c. Irrigation solution use.
d. Both A and B.

13. Which of these physiological changes noted in Fuchs' endothelial dystrophy is not also seen in natural aging?
a. Guttae formation.
b. Deposition of banded collagen.
c. Increased thickness of Descemet's membrane.
d. Decreased cell density.

14. What is the mechanism behind contact lens-related endothelial dysfunction?
a. Mechanical loss.
b. Change in pH.
c. Decreased tear exchange.
d. Hypoxic stress.

15. Topical carbonic anhydrase inhibitors can change the endothelial physiology in which manner?
a. Decrease cell density.
b. Increase polymegethism.
c. Increase pleomorphism.
d. Topical CAIs have no influence.

16. Which of the following therapies would not be beneficial in corneal decompensation due to endothelial disease?
a. Topical antibiotic.
b. Topical hyperosmotic agents.
c. Amniotic membrane.
d. Gundersen flap.

17. Which of the following surgical procedures is noted to resolve bullae and improve vision and symptoms?
a. Phototherapeutic keratectomy.
b. LASIK.
c. Collagen crosslinking.
d. Penetrating keratoplasty.

18. Which of the following effects of ROCK inhibitors has not been noted on the behavior of endothelial cells?
a. Promotion of proliferation.
b. Improved carbonic anhydrase activity.
c. Enhanced cell adhesion.
d. Suppression of apoptosis.

19. In a DSEK procedure, which technique is used to maintain donor-button-to-host-cornea apposition postoperatively?
a. Gravity.
b. Air bubble.
c. Silicone bubble.
d. Irrigation solution.

20. What is the difference between a DSEK and DSAEK procedure?
a. The former is used in mild cases of edema while the latter is used in moderate to severe ones.
b. The donor corneal dissection is performed in an automated fashion in DSAEK.
c. The recipient corneal dissection is performed in an automated fashion in DSEK.
d. They are the same procedure, but DSAEK happens in the UK.

Examination Answer Sheet

The Consequences of Corneal Endothelial Compromise

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1. Ⓐ Ⓑ Ⓒ Ⓓ
2. Ⓐ Ⓑ Ⓒ Ⓓ
3. Ⓐ Ⓑ Ⓒ Ⓓ
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19. Ⓐ Ⓑ Ⓒ Ⓓ
20. Ⓐ Ⓑ Ⓒ Ⓓ

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

21. Describe the pathophysiology of endothelial diseases ① ② ③ ④ ⑤
22. Identify and monitor the common warning signs of endothelial compromise. ① ② ③ ④ ⑤
23. Diagnose endothelial diseases. ① ② ③ ④ ⑤
24. Evaluate patients when a specular microscope is unavailable. ① ② ③ ④ ⑤
25. Based upon your participation in this activity, do you intend to change your practice behavior? (choose only one)
    - Ⓐ I do plan to implement changes in my practice based on the information presented.
    - Ⓑ My current practice has been reinforced by the information presented.
    - Ⓒ I need more information before I will change my practice.
26. Thinking about how your participation in this activity will influence your patient care, how many of your patients are likely to benefit? (please use a number): ☐
27. If you plan to change your practice behavior, what type of changes do you plan to implement? (check all that apply)
    ⓐ Apply latest guidelines ⓑ Change in pharmaceutical therapy ⓒ Choice of treatment/management approach
    ⓓ Change in current practice for referral ⓔ Change in non-pharmaceutical therapy ⓕ Change in differential diagnosis
    ⓖ Change in diagnostic testing ⓗ Other, please specify: _____
28. How confident are you that you will be able to make your intended changes?
    ⓐ Very confident ⓑ Somewhat confident ⓒ Unsure ⓓ Not confident
29. Which of the following do you anticipate will be the primary barrier to implementing these changes?
    - ⓐ Formulary restrictions
    - ⓑ Time constraints
    - ⓒ System constraints
    - ⓓ Insurance/financial issues
    - ⓔ Lack of interprofessional team support
    - ⓕ Treatment related adverse events
    - ⓖ Patient adherence/compliance
    - ⓗ Other, please specify: _____
30. Additional comments on this course: _____

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

31. The content was evidence-based.
    ① ② ③ ④ ⑤
32. The content was balanced and free of bias.
    ① ② ③ ④ ⑤
33. The presentation was clear and effective.
    ① ② ③ ④ ⑤

By submitting this answer sheet, I certify that I have read the lesson in its entirety and completed the self-assessment exam personally based on the material presented. I have not obtained the answers to this exam by any fraudulent or improper means.

Signature _____ Date _____

Lesson 120920, RO-RCCL-0221

By Aaron Bronner, OD, and Alison Bozung, OD

ROCK the Boat of Corneal Care

Originally intended to treat glaucoma, rho-associated kinase inhibitors may offer an alternative to transplantation.

While many optometrists may think that anterior diseases such as keratoconus and corneal scarring are the chief indicators for corneal transplantation, endothelial decompensation is actually the primary indication. This broad condition, which includes Fuchs' endothelial corneal dystrophy (FECD), pseudophakic and aphakic corneal edema and failed corneal transplantation, accounted for 60% of the 51,000 corneal grafts performed in the US in 2019.[1] In all of these cases, surgery was the only option available to successfully restore vision.

Modern endothelial transplant surgeries, such as Descemet's membrane endothelial keratoplasty (DMEK), Descemet's stripping automated endothelial keratoplasty (DSAEK) and Descemet's stripping only (DSO)—also known as descemetorhexis without endothelial keratoplasty (DWEK)—are associated with a substantially improved course, recovery and complication rate compared with penetrating keratoplasty. However, the post-op period can be complicated by detachment of the transplant requiring rebubbling, failure of the transplant and patient positioning restrictions, which are all problems that come up rather frequently, even among the most experienced surgeons.

Given the limitations of surgery and recovery, a medical approach to managing corneal edema would be beneficial to patients, optometrists and cornea specialists alike. Interestingly, we may already have access to something of a similar nature.

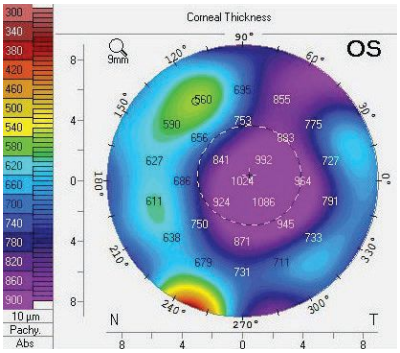
BACKGROUND

Rho-associated kinase (ROCK) inhibitors were recently introduced for the management of glaucoma. In 2017, Rhopressa (netarsudil, Aerie) became the first widely available ROCK-inhibiting agent on the market.[2] This family of molecules produces an IOP-lowering effect via its impact on the cellular cytoskeletons and actin filaments, which creates an anatomical shift in the architecture of the trabecular meshwork. This shift reduces resistance to outflow, thereby lowering IOP.

Interestingly, but perhaps unsurprisingly, the potential of ROCK inhibitors seems to extend beyond the management of glaucoma. The ROCK pathway was identified as a potential target of intravitreal therapy in diabetic retinopathy as far back as 2010, and trials are ongoing.[3] It is possibly within corneal disease, however, that these molecules may alter the management paradigm of disease the most dramatically.

In 2013, a group out of Japan found that the ROCK inhibitor Y-27632 was able to restore corneal clarity and endothelial cell density (ECD) after a short course of treatment in a primate model following transcorneal freezing (to kill endothelial cells). The treated animals had twice the ECD of controls by six weeks post-injury.[4]

The same team published a case report shortly after, in which a patient with FECD treated with the same ROCK inhibitor went from a pre-treatment central corneal thickness (CCT) of 757µm and peripheral ECD of 757c/mm^2 to a CCT of 568µm and ECC of 1,549c/mm^2 post-treatment. The researchers also pointed out that the structure of post-treatment corneas did not exhibit the polymegethism and pleomorphism often seen on specular microscopy after endothelial injury, and instead had a shape and size consistent with a healthy endothelium. They speculated that in addition to impacting cellular adhesion and migration of the endothelium, these results also suggest that treatment with this particular ROCK inhibitor may increase proliferation of the endothelium.[5] As the endothelium is generally considered non-miotic and arrested in the cell cycle, the ability to produce short bouts of endothelial replication and migration has enormous potential in the management of corneal pathology.



Pachymetry following a DSO supported by Rhopressa shows profound central edema.

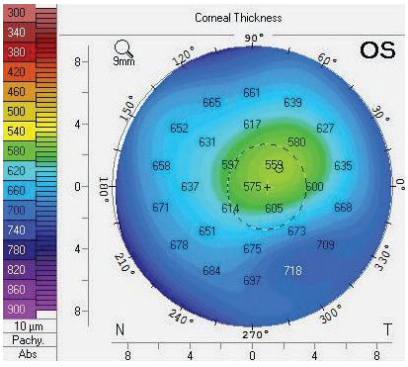
Since that time, ROCK inhibitors have been used as adjunctive therapy for DSO, a procedure for patients with localized, central FECD, during which the central endothelium is removed and not replaced with a transplant. The goal is to remove the light-scattering influence of guttata and allow the normal endothelium to fill in this gap. The addition

of ROCK inhibitors is thought to facilitate a more rapid clearing of postoperative edema and potentially improve ECD.

Recently, the Massachusetts Eye and Ear Infirmary published a cases series on patients who received Rhopressa in an attempt to facilitate the clearing of corneal edema that would likely otherwise lead to transplantation. A patient with iridocorneal endothelial (ICE) syndrome-induced corneal edema, a patient with early corneal graft failure resulting in corneal edema and a patient with chronic corneal graft failure resulting in corneal edema all responded to once-daily dosing with netarsudil. This effect was measureable by one month and was maintained even after discontinuation of the drop (the ICE patient continued with the regimen for glaucoma control). Of note, the series also contains one case of pseudophakic bullous keratopathy that did not respond to therapy.[6]

The study points out that it is difficult to predict who will respond to netarsudil and won't. It notes that, regardless of ultimate response, all cases of corneal edema treated with netarsudil will develop prominent honeycomb/macrocystic corneal edema, which will either clear as corneal deturgescence takes place with the drop or remain in unresponsive cases and clear on discontinuation of netarsudil. This series is unique in that, with the exception of the Japanese research group's findings in 2013, there have been no further reports of the purely medical treatment of corneal edema with ROCK inhibitors.

The variety of pathologies treated in the series is important, as it suggests the exact source of endothelial



Pachymetry of the same eye three months later shows dramatic clearing of central edema with continued use of Rhopressa. It's unclear whether the DSO, Rhopressa or a combination had the most profound impact.

dysfunction is unimportant when it comes to efficacy. That's not to say you should treat herpes simplex virus endotheliitis or acute corneal graft rejection with netarsudil alone. You still need to treat underlying inflammatory or infectious pathology accordingly. It does appear, however, that some cases of corneal decompensation may respond to netarsudil, regardless of the etiology.

Finally, given the impact of guttata on corneal optics, a patient with FECD may still have reduced vision due to guttata alone even if they successfully respond to netarsudil therapy. Consider, though, that the FECD patient from the Japanese case report described earlier had VA of 20/20 following treatment with the alternate ROCK inhibitor Y-27632.[4]

CONCLUSION

The small case series out of Massachusetts lends support to the use of netarsudil in the management of non-clearing corneal edema. While a randomized, double-blind interventional study on the corneal effects of netarsudil would be more telling, there is no such research currently available. Although this would take an off-label approach—and so the medication would likely not be covered by insurance—beyond cost, there appears to be little harm in a one-month trial of once-daily netarsudil. Common side effects of the medicine used in this capacity include redness, verticillata and honeycomb/macrocystic edema, but all should clear with cessation of the drug. While medical risks associated with this therapy are slight, the potential benefit of avoiding or delaying a corneal transplant may be profound.

In my (Dr. Bronner) opinion, the pros of using Rhopressa in non-clearing corneal edema tend to outweigh the cons. In the absense of research to the contrary, I fully intend to use this approach prior to considering DSAEK and DMEK. If you decide to do the same, again, understand that it is off-label, educate the patient on the resultant expected cost of therapy, take pre- and post-treatment pachymetries at similar times of the day and, if using ultrasound pachymetry, measure the same part of the cornea to ensure you are comparing equivalent measurements. RCCL

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By Christine W. Sindt, OD

A Flaky Patient

Signs of pseudoexfoliation should raise suspicion for glaucoma.

A 69-year-old white female with a history of keratoconus, hypertension and early cataract presented for her yearly exam, which revealed fibrillar material deposited around her pupil and on the crystalline lens of the left eye. Pressures were 14mm Hg OD and 13mm Hg OS. She was diagnosed with unilateral pseudoexfoliation and scheduled for a glaucoma work-up. Her primary care doctor, managing her hypertension, was informed of the diagnosis.

Pseudoexfoliation syndrome (PXF) is an age-related systemic disease where abnormal crosslinked fibrils progressively accumulate in various organs but primarily the anterior eye. Ocular manifestations present bilaterally but often asymmetrically and may result in cataract or glaucoma. Prevalence ranges from 6% to 10%, more so in women with increasing age. It is associated with a mutation in the LOX1 gene, which codes for elastic fiber components of extracellular matrix, and also with increased ultraviolet light exposure and caffeine intake. PXF is different than true exfoliation from heat or infrared damage to the anterior capsule.

PXF presents as white fibrillary material on the anterior lens surface and has a classic three-zone presentation: a central disc corresponding to pupil size, peripheral deposits and a clear zone separating the two. There may be pigment loss from the iris sphincter, transillumination defects, loss of pupillary ruff, pigment dispersion after dilation, pigment deposition on the iris surface and increased trabecular meshwork pigmentation.

The endothelium may show exfoliative material and reduced cell count. Nuclear cataract, phacodonesis and cataract surgery complications (e.g., capsular rupture, zonular dehiscence, vitreous loss) are all more common.

The greatest risk with PXF is development of glaucoma, with a highly significant correlation between elevated IOP and the degree of pigmentation and fibrillary obstruction of the trabecular meshwork. IOP may rise after dilation due to the release of pigment; therefore, be sure to check post-dilation IOP. Beyond the eye, people with PXF also have a threefold increased risk for hypertension, angina, myocardial infarct or stroke. RCCL

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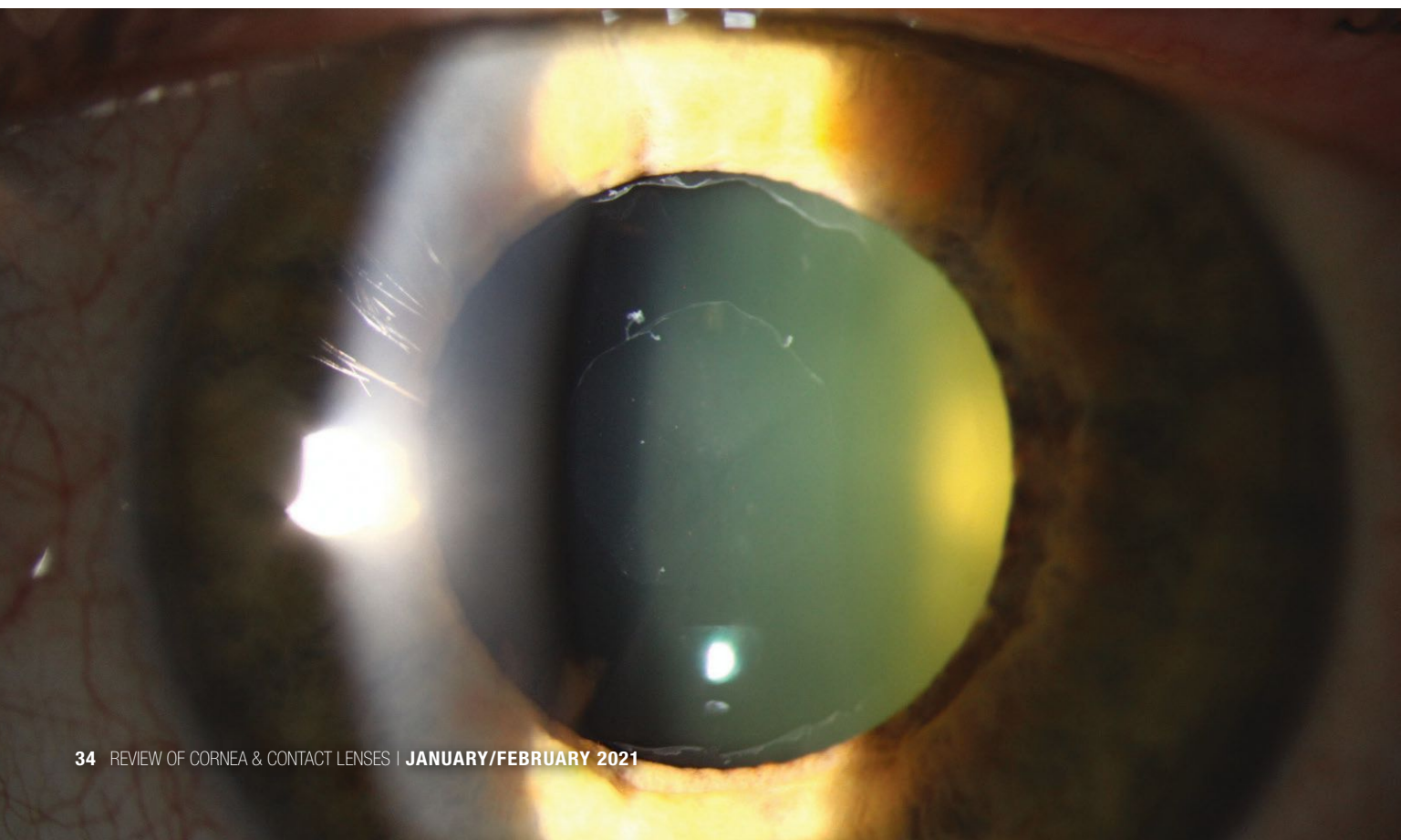

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Douglas P. Benoit, OD, FAAO
Executive Director,
Professional Services for VTI

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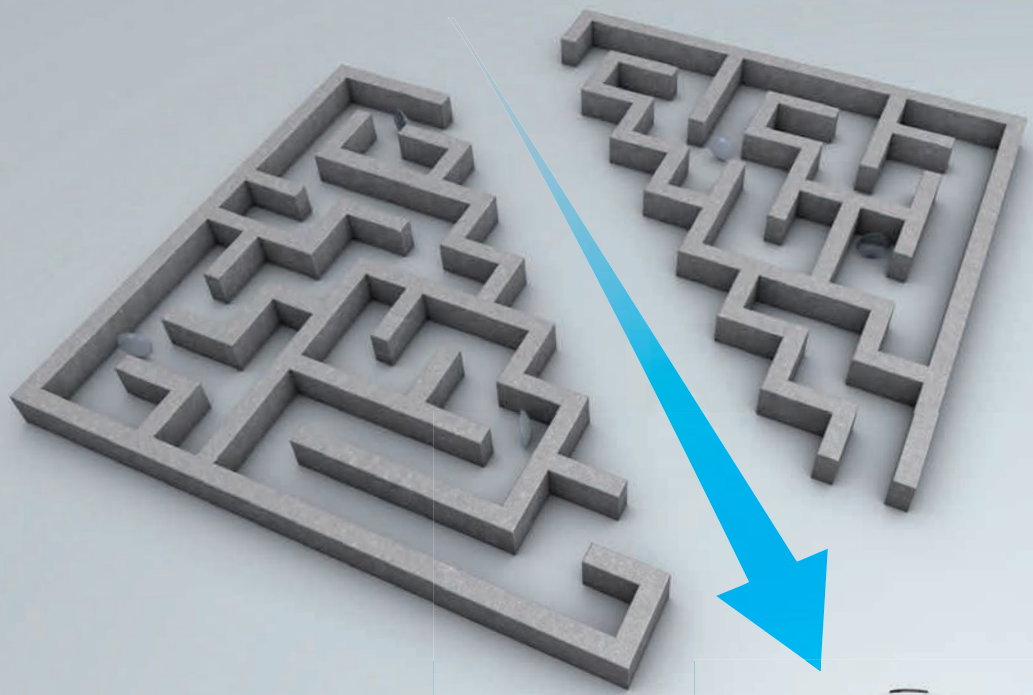

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