Retinal Vascular Miniseries: ***Identify and Manage Retinal Vascular Tumors,*** *Page 62*

REVIEW® OF OPTOMETRY

May 15, 2017

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ONLINE REFRACTION:

A Prescription for Change?

Optometrists have the power to disrupt the disrupter and come out ahead. Here's how. *Page 34*

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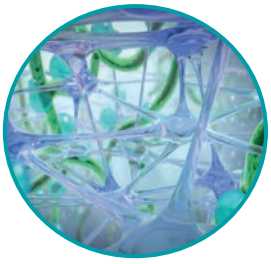

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‡ In a clinical trial, 97% of patients achieved a monocular VA 20/20 or better at the fitting visit with 100% achieving 20/25 or better.

1. Straker B, Hamada W, Sulley A, Olivares G. Fitting performance and efficiency with a low silicone hydrogel daily disposable toric contact lens. Poster presented at: GSLS Conference 2017.

ACUVUE® Brand Contact Lenses are indicated for vision correction. As with any contact lens, eye problems, including corneal ulcers, can develop. Some wearers may experience mild irritation, itching or discomfort. Lenses should not be prescribed if patients have any eye infection, or experience eye discomfort, excessive tearing, vision changes, redness or other eye problems. Consult the package insert for complete information. Complete information is also available by visiting acuvueprofessional.com, or by calling Johnson & Johnson Vision Care, Inc. at 1-800-843-2020.

VOL. 154 NO. 5 ■ MAY 15, 2017

IN THE NEWS

The FDA recently approved Genentech's **Lucentis (ranibizumab injection) for the monthly treatment of all forms of diabetic retinopathy (DR)**. Initially approved to treat DR specificlly in patients with diabetic macular edema (DME), The recent approval came after a Priority Review based on an analysis of the DRCR.net's Protocol S study. The study compared Lucentis treatment with panretinal laser photocoagulation in DR patients with and without DME, and found the Lucentis group experienced **improvements in retinopathy severity**.

Genentech. FDA approves Genentech's Lucentis (ranibizumab Injection) for diabetic retinopathy, the leading cause of blindness among working age adults in the United States. April 17, 2017.

A new study found the **microbial keratitis infection rate for contact lens wearers was higher than for those who had LASIK.** While contact lenses were traditionally thought to be safer than surgery, researchers found that soft contact lens wearers, after one year with daily disposables, had fewer cases of microbial keratitis than patients post-LASIK.

Masters J, Kocak M, Waite A. Risk for microbial keratitis: comparative metaanalysis of contact lens wearers and post-laser in situ keratomileusis patients. J Cataract Refract Surg. 2017;43(1):67.

A new National Institutes of Health (NIH) analysis suggests clinicians should **schedule eye exams for patients with Type 1 diabetes based on disease severity**, not a typical annual schedule. Adjusting the frequency based on the risk of complications would "result in **fewer eye exams at lower cost and quicker diagnosis and treatment** of advanced retinopathy," according to the NIH.

National Institutes of Health. Fewer exams and better eye health? Aye-aye, finds Type 1 diabetes study. April 19, 2017.

Unlocking the Genes Behind FECD

A new study may lead to improved screening tools for Fuchs' endothelial corneal dystrophy.

By Rebecca Hepp, Managing Editor

Researchers from 16 collaborating study sites compared data from more than 5,417 patients, 2,075 of whom were diagnosed with Fuchs' endothelial corneal dystrophy (FECD), and found new associations between three regions of genetic code, or loci, and the disorder: KANK4, LAMC1 and ATP1B1. They also confirmed the significance of TCF4, which earlier studies have linked to FECD.

To study the genes, investigators used corneal tissue from deceased patients, as well as the part of the cornea removed during the transplant procedure in living patients. Immunohistochemistry provided a look at protein expression in the tissue of the living patients.

Taken together, the four loci can predict the risk of FECD with an accuracy of roughly 78%, according to the study. Given no screening tools current exist for FECD, the findings may go a long way to helping clinicians one day better identify patients at risk.

One of the most significant findings, according to the investigators, is that variants of LAMC1 present a significantly higher risk of FECD among women, while TCF4 variants mean a greater risk in men.

These findings hold promise for both better diagnostics and therapeutics for FECD in the future, and ODs should keep an eye on where this research leads.

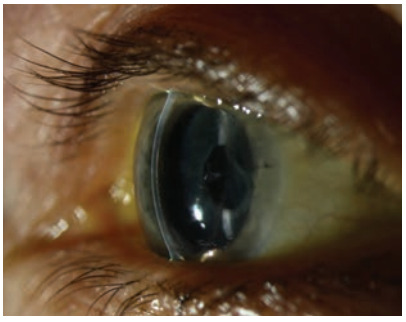

Photo: Christine W. Sindt, OD.

Posterior corneal changes in a patient with FECD and epithelial basement membrane dystrophy.

"While recent advances in transplantation have drastically improved surgical outcomes for Fuchs' dystrophy, by identifying a genetic basis for the condition, we are able to look toward preventative, rather than curative, management," says Stephanie Fromstein, OD, assistant professor at the Illinois College of Optometry. "We can move toward in-office testing for those at risk of the condition, as with other point-of-care tests for macular degeneration and Sjögren's. In-office genetic testing would allow us to identify those at risk much sooner and be more proactive—and successful—in managing their symptoms."

Afshari NA, Igo RP, Morris NJ, et al. Genome-wide association study identifies three novel loci in Fuchs endothelial corneal dystrophy. Nature Communications. 2017;8:14898.

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Evidence-Based Pediatric Practice Guidelines

Because eye and vision problems in children have become significant public health concerns, the American Optometric Association (AOA) released a new evidence-based guideline for pediatric eye care.

"An estimated one in five preschool children have vision problems and one in four school-age children wear corrective lenses in this country," says Andrea Thau, OD, president of the AOA. "Eye health and vision problems in children are significant public health concerns, which is why the new *Evidence-Based Clinical Practice Guideline: Comprehensive Pediatric Eye and Vision Examination* is so important for doctors of optometry and other health care professionals who treat children."

The new guideline is designed to increase awareness of the importance of checking children's eye health, at all ages.

"This provides the only set of evidence-based guidelines for children's vision care that completely follow the principles outlined in the National Academies of Sciences, Engineering and Medicine's report *Clinical Practice Guidelines We Can Trust*," according to Dr. Thau.

Photo: Kathleen F. Elliot, OD.

A new guideline can help clinicians succeed with pediatric care.

In addition, the guideline provides information to help clinicians:

- Recommend the best interval for in-person comprehensive eye and vision exams for patients from birth to age 18.
- Effectively conduct a full pediatric eye examination, including age-appropriate diagnostic testing procedures.
- Reduce the risk of adverse ocular effects in children.
- Educate patients and their caregivers about eye health and the importance of frequent exams.

The guideline includes new and expanded sections on trauma, myopia, ocular manifestations of child abuse/neglect, color vision deficiency and ultraviolet radiation and blue light protection. The new material highlights how far optometric practice has come since 2002, the AOA said in a press release.[1]

"What becomes critically important in children is the impact eye care and vision health can have on how well they function in their lives," says Diane Adamczyk, OD, chair of the AOA EBO Committee, which developed the guideline. "If this guideline heightens the awareness of getting children's eyes checked, we've accomplished our purpose."

American Optometric Association. AOA releases new evidence-based guideline for pediatric eye care. April 12, 2017. www.aoa.org/news/clinical-eye-care/aoa-releases-new-evidence-based-guideline-for-pediatric-eye-care?sso=y. Accessed April 21, 2017.

New Therapeutic Target for PDR Identified

A recent study from Massachusetts Eye and Ear found that a small-molecule drug initially developed for cancer therapy led to a significant reduction of abnormal blood vessels in tissue from patients with proliferative diabetic retinopathy (PDR).

"This is a very interesting finding demonstrating the important role of a relatively novel transcription factor—a protein facilitating the conversion of DNA into RNA—implicated in the development of neovascularization seen in several ischemic retinal-vascular diseases, including PDR, neovascular age-related macular degeneration, retinal vein occlusion and retinopathy of prematurity," explains A. Paul Chous, MA, OD, whose Tacoma, Wash., practice emphasizes diabetic eye care and education.

The first step to the new research was discovering the presence of the transcription factor RUNX1 in abnormal blood vessels, but not normal blood vessels, taken from patients diagnosed with PDR. "RUNX proteins are widely found in multiple species, and their production is exquisitely sensitive to hypoxia as seen in fetal tissue development and tumor growth," Dr. Chous adds.

From there, the investigators treated diseased tissue with the small-molecule RUNX1 inhibitor, leading to a 50% reduction of retinopathy in the preclinical models.

"The fact that a small molecule can hinder the RUNX1 protein is significant because larger molecules, such as those in anti-VEGF

(continued on page 9)

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Vitamin A Shows Promise in Retinal Disease

By adding a carbon ring to vitamin A, researchers can induce photoreceptor proteins such as rhodopsin to retain and recycle the designer chromophore molecule, without the help of the retinal pigment epithelial (RPE) cells, according to a new study published in the *Proceedings of the National Academy of Sciences*.[1] Researchers at Case Western Reserve University School of Medicine used the modified form of vitamin A, called locked retinal, to turn on the recycling mechanism and, additionally, activate an important G protein signaling molecule, called transducin, for a longer period of time than naturally occurs.

The revelation puts the biochemistry of vision into the spotlight. "The genesis of vision requires conversion of photons to electrical signals starting in the photoreceptors. In human, this process, known as the "visual cycle," involves alteration of chromophore 11-cis-retinal to the photoisomerized form known as all-trans-retinal," says Mohammad Rafieetary, OD, of Charles Retina Institute in Germantown, Tenn.

The reconversion or recycling of these visual pigments occurs in the RPE and depends on healthy RPE and a number of specific proteins. "This fascinating scientific discovery suggests that recycling of chromophores can take place in the photoreceptors themselves, bypassing the RPE and making sensory transduction less dependent on the health of the RPE, which is affected by a number of degenerative diseases," says Dr. Rafieetary.

RPE plays other significant roles, such as transmitting oxygen and nutrients to the photoreceptors and secreting anti-angiogenic factors to keep a balanced environment for the viability of rods and cones. Therefore, RPE will still remain an essential actor in the pathway. Nevertheless, the discovery may be a significant one for the future of retinal disease treatments.

The research team pioneered the use of another artificial chromophore, 9-cis-retinal, to treat Leber's congenital amaurosis (LCA), which currently is in Phase II/III of clinical trials, according to Sahil Gulati, a PhD candidate and first author of the current study. "One of the problems of using 9-cis-retinal for the treatment of LCA is the accumulation of spent chromophore that can cause retinal degeneration," Dr. Gulati says. "The detailed study of the biophysics and biochemisty of locked retinals in this most recent study offers more options to develop treatments for LCA."

"This study is a revelation that eye care providers need to keep a close eye on," says Dr. Raffieetary. "One facet we always have to be skeptical of is the development of any scientific discovery to a practical, clinically applied modality, one which has benefits that outweigh the risks."

While clinicians must be wary of new scientific discoveries, these findings may one day lead to a better way to intervene for debilitating disorders of the retina.

1. Gulati S, Jastrzebska B, Banerjee S, et al. Photocyclic behavior of rhodopsin induced by an atypical isomerization mechanism. PNAS. 2017;114(13):E2608. [Epub].

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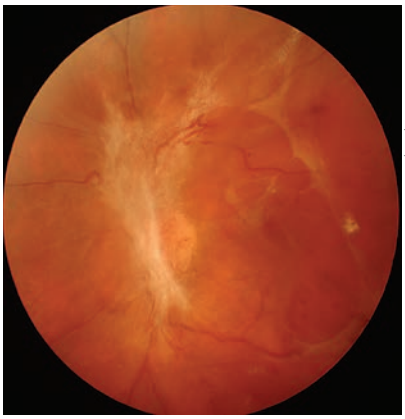

Photo: A. Paul Chous, MA, OD

A new therapy for proliferative diabetic retinopathy might be on the way, following new research findings.

agents, face physiologic barriers to absorption that limit their efficacy," says Dr. Chous. "This opens the possibility to not only topical or oral administration, rather than intravitreal injection, but improved treatment of disease with more targeted therapy and, perhaps, a lower probability of adverse systemic events."

Current therapies for PDR include laser treatments and anti-VEGF injections, both of which can be inconvenient for patients and come with the possibility, in rare instances, of adverse effects such as retinal hemorrhages, detachments or retinal atrophy, according to the study authors.

"This is the first study to show that blocking the RUNX1 protein is effective at reducing retinal angiogenesis, and it remains to be seen if this strategy is effective, safe and complementary to current anti-VEGF therapies in retinal disease," says Dr. Chous. ■

1. Lam JD, Oh DJ, Wong LL, et al. Identification of RUNX1 as a mediator of aberrant retinal angiogenesis. Diabetes. April 11, 2017;db161035. [Epub ahead of print].

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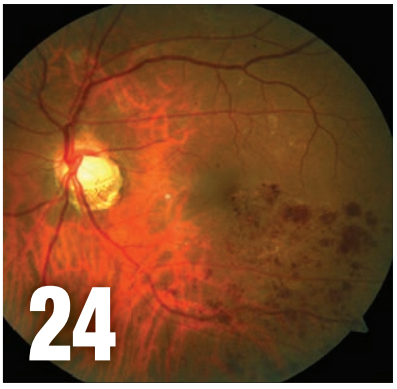

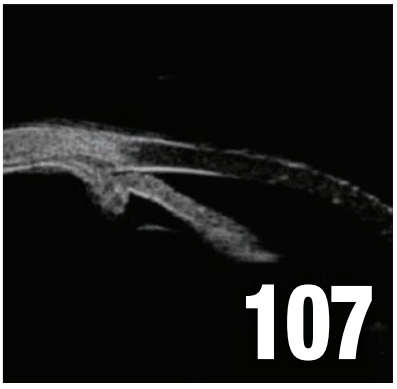

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Indication

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Important Safety Information

In clinical trials, the most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.

To avoid the potential for eye injury or contamination of the solution, patients should not touch the tip of the single-use container to their eye or to any surface.

Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

Safety and efficacy in pediatric patients below the age of 17 years have not been established.

For additional safety information, see accompanying Brief Summary of Safety Information and Full Prescribing Information on Xiidra-ECP.com.

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BRIEF SUMMARY:
Consult the Full Prescribing Information for complete product information.

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Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

DOSAGE AND ADMINISTRATION
Instill one drop of Xiidra twice daily (approximately 12 hours apart) into each eye using a single use container. Discard the single use container immediately after using in each eye. Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

ADVERSE REACTIONS
Clinical Trials Experience
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in clinical studies of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In five clinical studies of dry eye disease conducted with lifitegrast ophthalmic solution, 1401 patients received at least 1 dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had ≤3 months of treatment exposure. 170 patients were exposed to lifitegrast for approximately 12 months. The majority of the treated patients were female (77%). The most common adverse reactions reported in 5-25 % of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.

USE IN SPECIFIC POPULATIONS
Pregnancy
There are no available data on Xiidra use in pregnant women to inform any drug associated risks. Intravenous (IV) administration of lifitegrast to pregnant rats, from pre-mating through gestation day 17, did not produce teratogenicity at clinically relevant systemic exposures. Intravenous administration of lifitegrast to pregnant rabbits during organogenesis produced an increased incidence of omphalocele at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD], based on the area under the curve [AUC] level). Since human systemic exposure to lifitegrast following ocular administration of Xiidra at the RHOD is low, the applicability of animal findings to the risk of Xiidra use in humans during pregnancy is unclear.

Animal Data
Lifitegrast administered daily by intravenous (IV) injection to rats, from pre-mating through gestation day 17, caused an increase in mean preimplantation loss and an increased incidence of several minor skeletal anomalies at 30 mg /kg /day, representing 5,400-fold the human plasma exposure at the RHOD of Xiidra, based on AUC. No teratogenicity was observed in the rat at 10 mg /kg /day (460-fold the human plasma exposure at the RHOD, based on AUC). In the rabbit, an increased incidence of omphalocele was observed at the lowest dose tested, 3 mg /kg /day (400-fold the human plasma exposure at the RHOD, based on AUC), when administered by IV injection daily from gestation days 7 through 19. A fetal No Observed Adverse Effect Level (NOAEL) was not identified in the rabbit.

Lactation
There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lifitegrast from ocular administration is low. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Xiidra and any potential adverse effects on the breastfed child from Xiidra.

Pediatric Use
Safety and efficacy in pediatric patients below the age of 17 years have not been established.

Geriatric Use
No overall differences in safety or effectiveness have been observed between elderly and younger adult patients.

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis: Animal studies have not been conducted to determine the carcinogenic potential of lifitegrast. *Mutagenesis:* Lifitegrast was not mutagenic in the *in vitro* Ames assay. Lifitegrast was not clastogenic in the *in vivo* mouse micronucleus assay. In an *in vitro* chromosomal aberration assay using mammalian cells (Chinese hamster ovary cells), lifitegrast was positive at the highest concentration tested, without metabolic activation. *Impairment of fertility:* Lifitegrast administered at intravenous (IV) doses of up to 30 mg/kg/day (5400-fold the human plasma exposure at the recommended human ophthalmic dose (RHOD) of lifitegrast ophthalmic solution, 5%) had no effect on fertility and reproductive performance in male and female treated rats.

Manufactured for: Shire US Inc., 300 Shire Way, Lexington, MA 02421.

For more information, go to www.Xiidra.com or call 1-800-828-2088.

US Patents: 8367701; 9353088; 7314938; 7745460; 7790743; 7928122; 9216174; 8168655; 8084047; 8592450; 9085553; 8927574; 9447077; 9353088 and pending patent applications.
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Outlook

By Jack Persico, Editor-in-Chief

Zen and the Art of Dry Eye

A new definition stresses the need to achieve balance among the many forces at work on the ocular surface.

Get ready to hear a lot more about homeostasis. It's a key concept that has just been added to the definition of dry eye by the Tear Film and Ocular Surface Society (TFOS). "That was chosen to reflect the myriad of potential changes that can occur to the tear film and ocular surface" that might lead to "imbalance in the system," said Jennifer Craig, PhD, MSc, at the ARVO meeting earlier this month.

You, dear reader, will be called upon to restore that fragile balance.

At ARVO, TFOS previewed its forthcoming Dry Eye Workshop II (DEWS II) report. The mammoth volume (400-500 pages) will be published July 1st. The omnibus DEWS II is the culmination of an ambitious collaboration by 150 people in 23 countries, writing 10 separate reports.

The 90-minute ARVO session could only give highlights of such an all-encompassing work. Surely all 10 reports will be analyzed extensively, but Dr. Craig's talk on definitions is a good place to start, as it will be foundational to the entirety of DEWS II.

First, let's look at the 2007 definition from the original DEWS report:

Dry eye is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface.

And here's the new 2017 model:

Dry eye is a multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiological roles.

What changed? In addition to the homeostasis mention, "ocular symptoms remain still important but you'll notice it is more general this time," Dr. Craig said, as this "accommodates the differences in symptom reporting across the world."

For greater specificity—i.e., to help differentiate dry eye from other ocular surface diseases—the committee added a mention of etiology but stopped short of connecting causes with effects. "We have a range of the key etiological factors that are important uniquely in dry eye," she said, but the report "made sure to mention etiological *roles*" so they would not "be misrepresented as diagnostic criteria."

A new diagnostic algorithm included in DEWS II will help doctors follow these complex pathways a bit better. Dr. Craig summarized the impact of the definition and classification report in DEWS II as follows:

- It helps differentiate between dry eye and its mimickers.
- It recognizes that some patients experience signs without symptoms while others have just the opposite.
- It stresses that aqueous-deficient and evaporative dry eye aren't mutually exclusive. Be aware of mixed cases and tailor your therapy to suit.

TFOS gave itself a Herculean task in seeking to define the totality of dry eye, from pathophysiology to presentation to treatment targets, in a single sentence. Here, too, *balance* is the watchword: any more details would have undermined its universal appeal. ■

By Paul M. Karpecki, OD, Chief Clinical Editor

Which Trends are Our Friends?

Heightened dry eye awareness is definitely a friend to optometry, but the jury is still out about online refraction and our ultimate role in corneal crosslinking.

Change can be a double-edged sword, and nowhere is this more true than in today's optometric practice, where many things are in flux and not all of them look to benefit us. The latest gadgets are certainly revolutionizing how we care for our patients. But, in the wrong hands, advanced technology is also posing significant risk to our patients and our practices.

Fight the Online Threat

The first thing we must understand about online refraction is that this trend is firmly in place. It is no fad or flash in the pan. Hundreds of companies provide online or remote optical sales ranging from frames and spectacles to refraction. You can't knock one down without another popping up, so optometry needs a game plan.

Ultimately, we must always put our patients first. And an online or remote refraction is not in the patient's best interest. Many may perceive the availability of this service as a rationale for not pursuing an eye exam because they have a prescription in hand. But refraction is of course just a small part of a complete eye exam that has the potential to not only save a patient's eyes, but their life. We have all seen cases of a malignant choroidal melanoma in patients with 20/20 vision that would be missed with a remote refraction. Substituting an online refraction for a comprehensive exam would be the same as going to a drug store, using the automated blood pressure device and assuming you completed your cardiac health examination.

We must educate patients about the myriad systemic diseases detectable during an ocular exam, such as brain tumors, diabetes and hypercholesteremia, to name only a few. We cannot let the public put their vision, or even their lives, at risk assuming they can take an online or remote test that fails to assess ocular and systemic health.

Finally, the online refraction industry is fraught with companies that say they are working with optometry, but are setting up remote refraction systems to compete with optometry. We must keep an eye out for these masqueraders to protect our patients and our practice.

This trend may not be our friend, but we need to understand the patient needs and constraints it addresses, such as the lack of time and the desire for use of advanced technology. To acknowledge these needs in our own offices, we can invest in new technology that enhances the refraction experience and efficiency in office, including advanced automated refraction systems that outshine the rather simplistic methods used by online services. We truly can show the world that our care is demonstrably better.

Embrace Better Therapeutics

New technology isn't all bad, as it is improving our ability to provide medical eye care for conditions such as dry eye and keratoconus, both of which are featured this month. Before the FDA approval of the Avedro system for corneal collagen crosslinking, the lack of availability left a number of patients in need of a corneal transplant due to unfettered disease progression. In desperation, I have sent patients to Canada and study sites in the United States for this treatment. There is no question that the large majority of patients with keratoconus are seen in optometry practices, and the new treatment option is a welcome addition to the management plans for these patients.

Given the growing shortage of ophthalmologists (especially in rural areas), optometry is taking on more medical eye care to fill the void, and that includes minor procedures and lasers. Optometrists practicing in states that allow the use of UV light laser in optometric practice may one day have the opportunity to help slow or stop the progression of keratoconus, allowing patients to remain in their contact lenses if crosslinking is performed soon enough. More technologies are on the horizon involving contact lenses and crosslinking to help stabilize patients at the earliest diagnosis of keratoconus.

So, the trend is our friend—sometimes. When it isn't, we must follow it closely so we can properly educate patients about risks it may pose to their eyes and lives, and then work to ensure they are protected. In cases where the trend is our friend, those who embrace it will often thrive and enjoy the ride along the way. ■

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Watch Out for Those Gnats

I've got a good punctum story for y'all, if you stay with me.

By Montgomery Vickers, OD

It's been a while since I allowed my randomness to escape. Now is the time.

Research This!

I once posed this question to students at THE Ohio State University School of Optometry: "If they invented a pill that cures everything, would you be happy or sad?"

I know my answer. You?

Regardless, medical research marches on. I do see a tiny sparkle in the distance reassuring me deadly and health care system-sucking diseases are being studied by amazing minds. Life expectancies are lengthening, at least where people have access to health care. Charitable organizations and church-based missions are doing great work somewhere out there. Longer life = more needy presbyopes.

What about in our offices? When you hear about the latest ocular antihistamine or tear-enhancing eye drop, does that psyche you up as much as it psyches me up? Psyche! After 100 years of "use this drop every day," can't some billionaire geek decide we have enough eye lubricants and study something more critical, like a device that finds lost trial refracting lenses. I haven't seen my +0.50 since the first *Star Wars* movie.

Multifocals Schmultifocals

Once an aspiring young doctor asked me, "What do you say to patients who put on their multifocal contact lenses and tell you it makes distance vision blurrier?"

"Yes."

Now, I wear multifocal contact lenses because (a) I am 63 and (b) when I'm picking a hunk of steel out of a cornea using the slit lamp, I think it might be better if I have a wider field of view so I don't poke a hole through the patient's eye (or through my finger).

One time, I met with 10 researchers of a large contact lens company who had found a way to etch a microscopic mark on the lens that showed whether the lens was inside out before applying it to the eye. At the time, I had maybe two "successful" multifocal contact lens patients who were myopic enough to actually see a microscopic etching on a contact lens. Of course, my definition of "success" was they came in less than six times a year complaining about their vision. I brought that to the researchers' attention, and four of them said nothing and scribbled madly in their notepads. The other six texted one another about where they should have dinner.

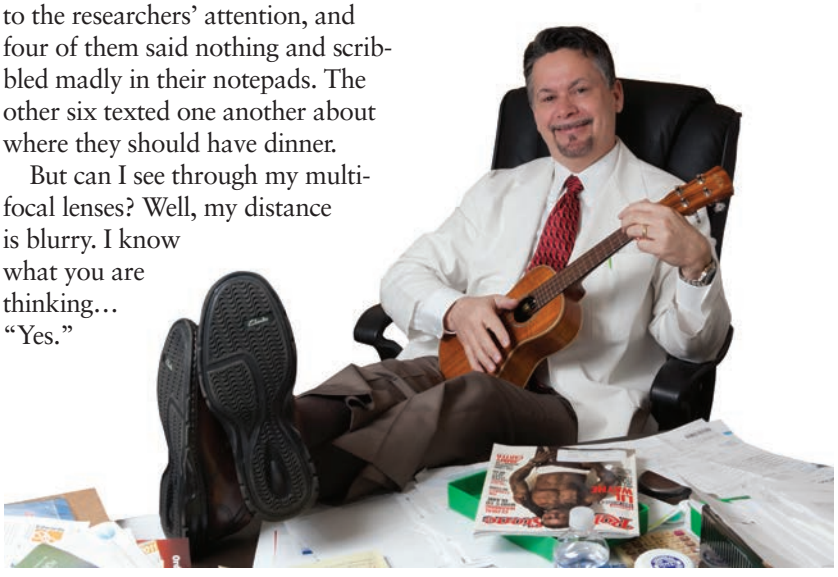
But can I see through my multifocal lenses? Well, my distance is blurry. I know what you are thinking…

"Yes."

Here's the Gnat You've Been Waiting For

Last week, I had a manicure. Quit laughing and keep reading, because the manicure is not the coolest part. Before I went to have my manicure, I applied coconut oil under my nose. Seriously, it's not funny; it was chafed from the allergies that are crazy in Texas right now. In Texas, if someone sweeps their porch in Juarez, Mexico, it lands on your porch in two days. I hope they make that wall out of HEPA filters.

Anyway, during my manicure, I thought I was having another vitreous detachment until I realized I had attracted a gnat with my coconut oil. Since both hands were in bags of hot wax, I decided to watch the gnat in vivo. He flew up my nose. Now here's the coolest part: I sneezed and he came out of my left inferior punctum. OK, now you can laugh. ■



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REFERENCES: 1. Data on file. Bausch & Lomb Incorporated. Rochester, NY. **2.** In vitro studies evaluated the rate of release of sodium hyaluronate (HA), a conditioning agent in the BPZ02 multi-purpose solution, from both conventional and silicone hydrogel contact lenses over a twenty-hour time period. HA was adsorbed on all traditional and silicone hydrogel contact lenses tested upon soaking in the solution overnight. HA is then released from the lenses throughout at least a twenty hour time period when rinsed with Hank's balanced salt solution at a rate mimicking tear secretions. The in-vitro performance of BPZ02 multi-purpose solution suggests that it will provide lens conditioning throughout a twenty hour time period.

*Highest household penetration among multi-purpose solutions; IRI Panel 52 weeks ending 12/25/16.

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A Spectre Over this Sector

Some cases of sector injection are not episcleritis, and you may have to jog your patient's memory to find the true cause. **Edited by Paul C. Ajamian, OD**

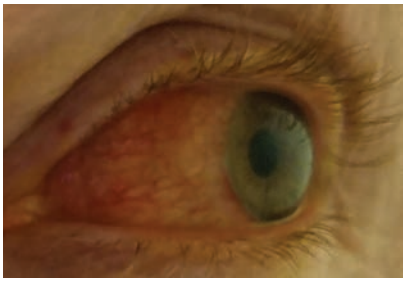
Q A 62-year-old male presented two weeks after cataract surgery in his left eye for surgery in his right eye. While the one-day and one-week post-op visits performed by his optometrist were perfect, with good vision and white, quiet eyes, my exam revealed sectoral injection nasally in the left eye. Could this be episcleritis, or something else related to surgery?

A "Sector injection almost always leads the clinician to a diagnosis of episcleritis," says Jessica Kenney, OD, an ocular disease resident at Omni Eye Services of Atlanta. While episcleritis is certainly high on your list of differentials for sector injection, she says, it should be entertained only after ruling out other entities, especially conjunctival abrasions. These are quite common, but often go undetected in the search for something more interesting, such as episcleritis, Dr. Kenney says.

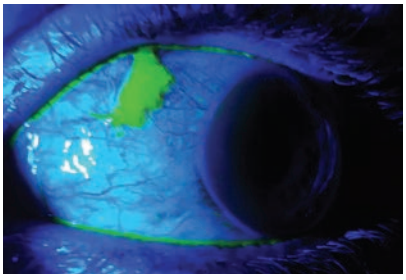
A patient with a conjunctival abrasion may present asymptomatically, as is the case with this patient, or with tearing, pain and general discomfort. Patients with episcleritis may also be asymptomatic, aside from noticing their eye is red. Pain is rare, but they may notice some irritation and watering as well. A detailed history is critical, and often patients' initial answers don't reveal the truth, so clinicians have to dig a little deeper.

Differentials

Always look at *Staph*. lid disease as a common cause of chronic injection, Dr. Kenney says, as it can mimic a number of other entities and can cause asymmetric patterns of injection. Other differentials for sector injection include inflamed pinguecula, pterygium, subconjunctival hemorrhage, lodged foreign body and scleritis, all with their own unique appearance and characteristics, according to Dr. Kenney. In this patient's case, clinicians can even consider a rebound iritis from the cataract surgery, although the injection is usually diffuse, not sectoral.



Sectoral injection after cataract surgery isn't always episcleritis.



Fluorescein revealed a conjunctival abrasion.

Often, when patients are not forthcoming with their history, objective findings outweigh the lack of confirmatory history. Dr. Kenney recommends clinicians make the proper treatment call based on the slit lamp exam, which will be grounded in the objective findings.

The Real Story

Dr. Kenney saw this patient prior to his right eye surgery, after the patient's wife mentioned the red left eye to a staff member. The examination revealed sectoral injection nasally in the left eye, with a clear cornea and no anterior chamber reaction. The patient reported an unremarkable history and "nothing out of the ordinary" around the time he noticed the redness.

But Dr. Kenney jogged his memory by inquiring about specific activities, such as working in the yard or other outdoor activities, and he recalled chasing after his dog into some brush when a branch hit his eye. "When I examined the nasal aspect of his eye, the conjunctiva had an elevated, clumped, milky appearance, which caused me to generously instill fluorescein into the eye," Dr. Kenney explains. "The area stained perfectly and revealed what was already suspected—a conjunctival abrasion."

The patient was put on a topical fluoroquinolone drop four times a day, and at the one-week follow-up visit, his referring optometrist reported that he was doing well, with resolution of the injection in his right eye and a quiet anterior segment. "If we had jumped to the first and seemingly most obvious diagnosis of episcleritis, we would have used a steroid that would most likely have delayed healing, not enhanced it," says Dr. Kenney. "Keep an open mind and get the big picture while running through all possible differentials on every patient." ■

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Behind RVO: Virchow's Triad

One simple concept can help you successfully treat retinal vein occlusions and prevent serious associated systemic conditions. **By Bisant A. Labib, OD**

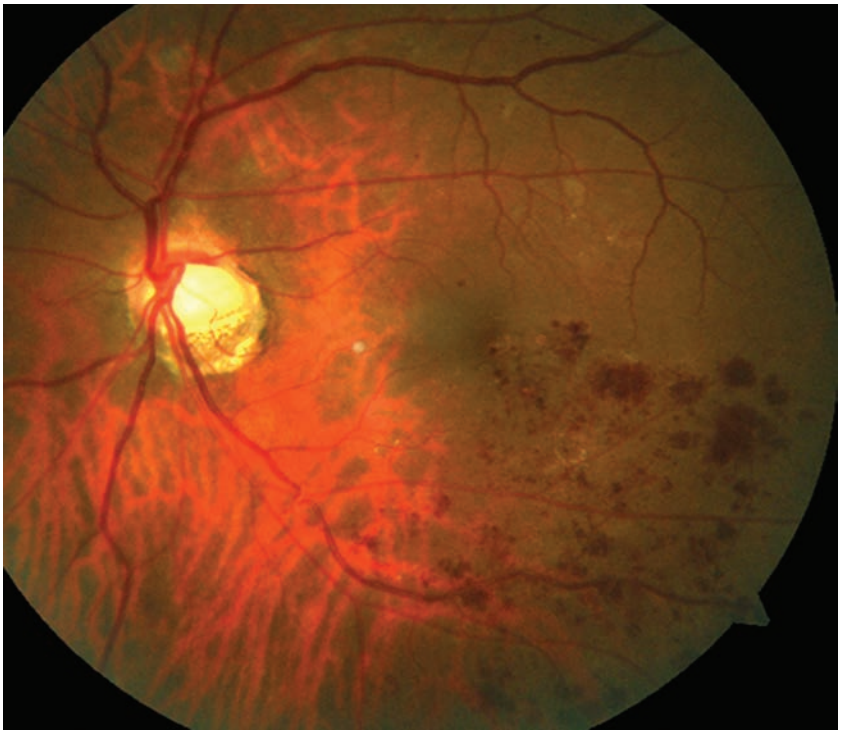
Retinal vein occlusion (RVO) is the second most common retinal vascular disease, exceeded only by diabetic retinopathy.[1] RVOs can be divided into two main subtypes: branch retinal vein occlusions (BRVO) and central retinal vein occlusions (CRVO).[1,2] These entities affect about 1% to 2% of all patients older than 40 and 16 million people worldwide, with BRVOs approximately five times more common than CRVOs.[1-3]

Despite the common presentation of RVOs, the pathogenesis is not well understood. Anatomically, the central retinal artery and vein are juxtaposed in the center of the optic nerve, enveloped in a common fibrous tissue. When this common tissue and the central retinal artery thickens and becomes sclerotic, the underlying vein is compressed. The resultant narrowing of the venous lumen creates the hemodynamic changes that lead to CRVO. In BRVO, degenerative blood vessel alterations and hemodynamic changes are caused by arteriovenous crossings and venous compression.[4]

Although the mechanism governing these occlusions is complicated and multifactorial, clinicians can better understand RVOs with Virchow's triad: stagnation of blood in the blood stream, endothelial cell injury and hemodynamic changes or blood hypercoagulability.[5]

Historical Perspective

In 1856, Rudolf Virchow first introduced the theory that a triad of physiological factors plays a significant role in the etiology of venous thrombosis.[6-8] Today, researchers still believe blood stagnation, endothelial cell injury and hypercoagulability—occurring separately or concurrently—increase a patient's risk for venous thrombosis.[6] The most recognized risk factors for RVO, besides advancing age, are systemic vascular disorders.[2] Several studies report systemic causes of hypercoagulability, as well as diseases that increase risk of endothelial damage are associated with RVOs.[1,4,5,9] Here is a closer look at the triad and the risk factors that may predispose a patient to developing RVO.



This photo ilustrates a BRVO along the inferior temporal arcade.

1. Hemostasis/abnormal blood flow. A 1976 study originally described the milder forms of CRVO as "venous stasis retinopathy," differing from the condition we often refer to today as the midperipheral retinal hemorrhages associated with early ocular ischemia secondary to carotid artery stenosis.[10-12] This sets the stage for the first component of Virchow's triad, stagnant blood flow. As blood viscosity is often raised at the time of occlusion, anything that contributes to blood viscosity may play a significant role in RVO. Research shows that hemostasis increases blood viscosity and platelet aggregation,

Down, Boy.

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Indication

LOTEMAX® GEL (loteprednol etabonate ophthalmic gel) 0.5% is indicated for the treatment of post-operative inflammation and pain following ocular surgery.

Important Safety Information about LOTEMAX® GEL

- LOTEMAX® GEL is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.
- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for 10 days or longer, IOP should be monitored.
- Use of corticosteroids may result in posterior subcapsular cataract formation.
- Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation and occurrence of perforations in those with diseases causing corneal and scleral thinning. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification, and where appropriate, fluorescein staining.
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infection. In acute purulent conditions, steroids may mask infection or enhance existing infection.
- Use of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and exacerbate the severity of many viral infections of the eye (including herpes simplex).
- Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use.
- Patients should not wear contact lenses when using LOTEMAX® GEL.
- The most common ocular adverse drug reactions reported were anterior chamber inflammation (5%), eye pain (2%) and foreign body sensation (2%).

Please see brief summary of Prescribing Information on adjacent page.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

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INDICATIONS AND USAGE

LOTEMAX is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once to fill tip before instilling drops.

Apply one to two drops of LOTEMAX into the conjunctival sac of the affected eye four times daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period.

CONTRAINDICATIONS

LOTEMAX, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.

WARNINGS AND PRECAUTIONS

Intraocular Pressure (IOP) Increase

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, intraocular pressure should be monitored.

Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

Delayed Healing

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

Bacterial Infections

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

Viral Infections

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

Fungal Infections

Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.

Contact Lens Wear

Patients should not wear contact lenses during their course of therapy with LOTEMAX.

ADVERSE REACTIONS

Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with infrequent optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, delayed wound healing and secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

The most common adverse drug reactions reported were anterior chamber inflammation (5%), eye pain (2%), and foreign body sensation (2%).

USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic Effects

Loteprednol etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic (increased incidence of meningocele, abnormal left common carotid artery, and limb flexures) when administered orally to rabbits during organogenesis at a dose of 3 mg/kg/day (35 times the maximum daily clinical dose), a dose which caused no maternal toxicity. The no-observed-effect-level (NOEL) for these effects was 0.5 mg/kg/day (6 times the maximum daily clinical dose). Oral treatment of rats during organogenesis resulted in teratogenicity (absent innominate artery at ≥5 mg/kg/day doses, and cleft palate and umbilical hernia at ≥50 mg/kg/day) and embryotoxicity (increased post-implantation losses at 100 mg/kg/day and decreased fetal body weight and skeletal ossification with ≥50 mg/kg/day). Treatment of rats with 0.5 mg/kg/day (6 times the maximum clinical dose) during organogenesis did not result in any reproductive toxicity. Loteprednol etabonate was maternally toxic (significantly reduced body weight gain during treatment) when administered to pregnant rats during organogenesis at doses of ≥5 mg/kg/day.

Oral exposure of female rats to 50 mg/kg/day of loteprednol etabonate from the start of the fetal period through the end of lactation, a maternally toxic treatment regimen (significantly decreased body weight gain), gave rise to decreased growth and survival, and retarded development in the offspring during lactation; the NOEL for these effects was 5 mg/kg/day. Loteprednol etabonate had no effect on the duration of gestation or parturition when administered orally to pregnant rats at doses up to 50 mg/kg/day during the fetal period.

There are no adequate and well controlled studies in pregnant women. LOTEMAX should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers

It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemic steroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when LOTEMAX is administered to a nursing woman.

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

No overall differences in safety and effectiveness have been observed between elderly and younger patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment Of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in a chromosome aberration test in human lymphocytes, or *in vivo* in the single dose mouse micronucleus assay. Treatment of male and female rats with up to 50 mg/kg/day and 25 mg/kg/day of loteprednol etabonate, respectively, (600 and 300 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender.

PATIENT COUNSELING INFORMATION

Administration

Invert closed bottle and shake once to fill tip before instilling drops.

Risk of Contamination

Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the gel.

Contact Lens Wear

Patients should be advised not to wear contact lenses when using LOTEMAX.

Risk of Secondary Infection

If pain develops, redness, itching or inflammation becomes aggravated, the patient should be advised to consult a physician.

Bausch + Lomb, a division of Valeant Pharmaceuticals North America LLC
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US Patent No. 5,800,807

LGX.0114.USA.16

Based on 9269101/9269201 Revised: 08/2016

Virchow's Triad	Systemic Associations
1. Hemostasis	• myeloproliferative disorders • sedentary lifestyle • pregnancy • oral contraceptives • systemic vasculidites
2. Hypercoagulability	• protein C and S deficiency • antithrombin III • factor V Leiden • hyperhomocysteinemia • thrombophilia • anticardiolipin antibodies
3. Damage to blood vessel wall	Arteriosclerosis secondary to: • hypertension • diabetes mellitus • hyperlipidemia

Here, the components of Virchow's triad are associated with systemic disorders that carry risks for the development of retinal vein occlusions.

highlighting its role in the pathogenesis of RVO.[5,9,10] Rarely, myeloproliferative disorders (cancers), pregnancy, use of oral contraceptives and systemic vasculitides that also result in blood hyperviscosity have been known to cause RVO, especially in younger individuals.[13]

2. Hypercoagulability. Research shows systemic causes of hypercoagulability significantly increase risk of CRVO.[3,9] These include: protein C and S deficiency, antithrombin III, factor V Leiden, hyperhomocysteinemia, thrombophilia and anticardiolipin antibodies.[3,9] However, these conditions are not as commonly linked to BRVO formation, which are often a result of the adjacent, compressive arteriolar changes.[9]

3. Degenerative changes to blood vessel wall. Researchers have extensively studied the histological changes in retinal blood vessel walls, especially at the site of arteriovenous crossing, and found hypertrophy of the intima media in 90% of BRVO cases.[5] These trophic changes are the initiation of RVOs, ultimately leading to thrombus formation. Hypertension, hyperlipidemia and diabetes mellitus are the main systemic risk factors of RVO, as patients with hypertension alone have an increased risk for BRVO—78% according to one study.[9] This is because these conditions cause or contribute to arteriosclerosis, resulting in the compression of adjacent retinal veins and venous stasis.[9]

In The Clinic

RVOs may cause profound visual deficits that require prompt recognition and treatment. However, it is just as, if not more, important to identify the various systemic risk factors and pathogenesis of thrombus formation to prevent serious consequences, including mortality. Understanding the several causes of RVOs, which is best summarized as Virchow's triad, will allow the clinician to develop a systematic approach for screening for the underlying pathogenesis. For patients with known metabolic syndrome or one of those components—diabetes mellitus, hypertension and hyperlipidemia—clinicians must stress the importance of tight control and treatment as preventative methods.[9] If metabolic syndrome is absent following initial laboratory work up (e.g., lipid panel, hemoglobin A1c and blood sugar testing), for example in a younger individual, evidence suggests further screening for hypercoagulable states and thrombophilia is warranted through additional blood tests (e.g., complete blood count).[13]

The multifactorial nature of RVO pathogenesis highlights the significance of a holistic approach.

Although the underpinnings of RVO are poorly understood, a historically grounded concept of the disease state can help clinicians diagnosis occlusion in the eye and, systemically, prevent serious risk associated with thrombus. ■

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Keeping Up With the Codes

Denying and rationalizing bad coding decisions are just putting your practice at risk.

By John Rumpakis, OD, MBA, Clinical Coding Editor

Billing and coding is a minefield of changes, and it's hard work to stay apprised of current information, rules and regulations. But when we get complacent and don't keep up, it often contributes to a lazy attitude about billing and coding. Rather than learn the rules or use technology to help keep the practice compliant, human nature—or optometric nature—often turns to rationalizing the behavior rather than changing it.

Worse yet, when challenged on coding habits or patterns, practitioners often get defensive and make excuses. "I heard about this from a friend," "I was told that if I used this code, I could get paid more" or "my sales rep told me to do it this way," are frequent reasons why a practitioner has been using a particular coding pattern. Keeping current with the torrent of change is a difficult task, and many get lulled into a state of complacency, just because they got paid.

Getting paid for a code is never a good defense for a particular coding or practice pattern. Your only defense is knowing that your medical record demonstrates the care delivered was the care required by the patient. Though, I must admit the stories are interesting.

You Can't Make This Up: Ignoring The Facts

Here is a situation that highlights just how easy it can be to rationalize a wrong coding behavior:

Dr. X: *How much do you charge extra for dilation?*

Coding expert: *Dilation is included in the definitions of both comprehensive ophthalmologic and EM codes. You can't charge extra.*

Dr. Y: *You can charge extra for a medical dilation.*

Coding expert: *There is no CPT code for a "medical dilation."*

Dr. X: *Yes, there is, 92225. Also, you can have them return and charge the dilation as a cycloplegic refraction since all dilating drops have cycloplegic action.*

Coding expert: *92225 is a separate procedure for extended evaluation of serious retinal conditions. It is not used to bill for dilation, which again is part of the medical office visit. Charging for a refraction that way is no different than charging for a photo when you really used a scanning laser. That is fraud.*

Dr. Y: *Totally wrong! We bill 92225 or 92226 in addition to every office visit during which we dilate. We have done it for years and always get paid.*

You Can't Make This Up: Fabricating The Facts

Each CPT code includes an entire set of characteristics that you must adhere to when providing the service. The medical record must explicitly explain the patient's chief complaint, your clinical assessment, your diagnosis, additional tests you ordered or performed (and why) and your recommendations for further testing or treatment.

A chief complaint (or reason for visit) is not inferred. If it is not recorded in the record, it is not there. You cannot say that a history of present illness is a chief complaint, or that the previous visit's instructions are the chief complaint, unless specifically written as such. Medical necessity must be explicitly stated for each and every additional procedure or test you perform. You cannot fabricate facts or rely upon patterns of practice to fulfill the factual elements required by the CPT.

An example: During one audit, the practitioner was flagged for excessive use of special ophthalmic procedures three to four standard deviations away from the mean used by his peers. He claimed he did every test on every patient to "do a thorough job"—how could he find every issue unless he tested? Fabrication of the facts like this is the first step of rationalization and puts you down the path toward complacency.

Health care today is dynamic, confusing and sometimes just too much information to process. But that's no justification for denying the rules exist or rationalizing that they don't apply to your situation. This not only makes you complacent in your approach to each patient, but also how you record encounters and code them for revenue generation.

It is a slippery slope that you don't want to be on. Provide every patient the care they require, and properly translate your record to reflect the true definition of the CPT codes you are using to bill for services provided. ■

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Reference: 1. Ngo W, Srinivasan S, Houtman D, Jones L. The relief of dry eye signs and symptoms using a combination of lubricants, lid hygiene and ocular nutraceuticals. *J Optom.* 2017 Jan-Mar;10(1):26-33.

HOW TO CONNECT WITH TODAY'S CATARACT PATIENT

*By David Geffen, OD**

Patient satisfaction with cataract surgery hinges on gathering accurate lifestyle information and matching it with clinically appropriate surgical options. Truly successful outcomes, as measured from the patient's perspective, simply cannot be achieved without knowing the patient's lifestyle and individual visual demands. For example, a truck driver and a seamstress will not likely benefit from the same type of lens since one demands distance and the other demands near.

Of course, this is an obvious example. Our responsibility as optometrists is to dig deeper and provide more information than can be conveyed in broad strokes. For instance, we know how our patients have responded to other vision correction modalities in the past. We know whether they were successful with monovision contact lenses, how closely they scrutinized the spectacles, and how motivated they are to see, look and feel their best. Indeed, our history and relationships with our patients are a tremendous advantage. In many cases, the rapport we've developed allows us not only to assess, but also to educate and support.

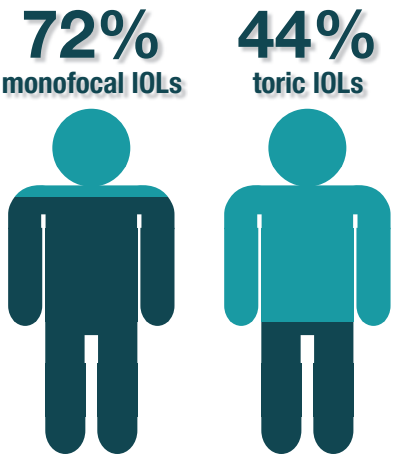
Fortunately, we've received significant assistance from Alcon in this regard. The company has commissioned extensive research on patients as well as on our colleagues' roles in seeing them along the way through their cataract journey. In addition, Alcon has worked to support our efforts to educate patients more effectively by launching a new consumer-facing campaign.

Relaying the options available at the time of cataract surgery not only leads to better educated patients; it also strengthens our relationships with patients along their correction journey. Cataract surgery is an important and memorable experience that we can be a part of. How well we connect will likely shape our shared future when our cataract patients return following surgery. The following is my personal recipe for success.

Take Nothing for Granted

Today's cataract patients are on the go. Many are still working and having good vision is essential to helping them stay active and involved. While it's true

Optometrists report discussing monofocal IOLs 72% of the time, but only educate patients on toric IOLs 44% of the time.[1]

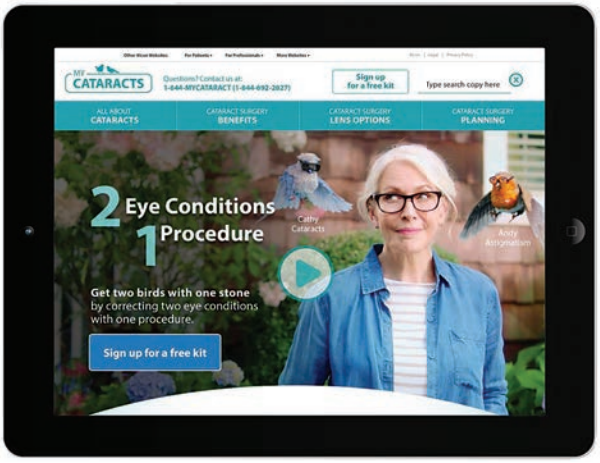


1. Survey responses from 573 United States-practicing OD attendees at 2016 educational presentations about cataract patient journey and cataract surgery options. This data is based on approximately 95% of the attendees before and after reporting.

How to Help Educate and Inform

Start the discussion. Educate patients on their condition and steps needed for cataract surgery. Alcon's campaign allows you to:

- Direct patients to the consumer website mycataracts.com.
- Refer patients to the cataract call center: 1-844-MYCATARACT
- Drive patients to the My Cataracts YouTube channel: youtube.com/mycataracts



Alcon has created an effective online experience at mycataracts.com. Significant search optimizations help drive patient awareness.

that many patients are also quite computer savvy, don't assume that their technical progress means they are well informed about surgical options. The average patient who comes into my office has just enough information to be more confused than they were before they began their investigation. For example, they assume that all lenses correct the vision for all distances and they do not realize they will still need readers if they choose a distance-only IOL.

Indeed, most of my patients have very little knowledge of the types of IOLs available to them. Patients often understand that they have astigmatism, and they know they'd like to get rid of it, but they don't know what their choices are.

52% of cataract patients with astigmatism are eligible for a toric IOL, yet only 7% of patients receive one.[2,3]

2. Hill W. Distribution of corneal astigmatism in normal adult population (n=6000). Keratometry database: http://www.doctor-hill.com/iol-main/astigmatism_chart.htm. Accessed May 17, 2013.
3. Alcon data on file, 2015.

I wish I could say that all of our optometric colleagues are making sure that their cataract patients don't leave their practices uninformed about their choices. However, this happens often. Market research shows that optometrists discuss monofocal IOLs 72% of the time, but only educate patients on toric IOLs 44% of the time.

How might this affect our patients' decisions or perceptions of their options when they arrive at the surgery center? Addressing astigmatism is a key aspect in providing a true refractive correction as part of the cataract procedure. Without complete and successful treatment of astigmatism, the goal of achieving excellent uncorrected distance vision and reducing spectacle dependence for distance vision cannot be met. Unfortunately, research reveals that 52% of cataract patients with astigmatism are eligible for a toric IOL, yet only 7% of patients receive one.

We need to engage patients early and often to ensure that we make a positive impact on the patient's final choice and enable them to feel prepared to make what is for the majority of people a once-in-a-lifetime decision.

Present the Opportunity

We need to do a better job helping patients understand that vision should be a big priority. Many

Understanding Lifestyle is Key

Knowledge of a patient's lifestyle and individual visual demands is key to achieving successful outcomes.

Help educate and inform patients by providing a free Alcon patient information kit.

patients will tell you sight is their most valued sense, yet we often take our vision for granted and don't consider the extent to which today's choices shape the future.

When I see that the cataract has matured and surgery is indicated, I go over the different surgical options and talk about the pros and cons of each. If my patient has corneal astigmatism greater than 1.00D, I talk about how a toric IOL can correct the distance acuity almost fully. Additionally, we have learned that at 0.50D of cylinder, there is clinically significant blur and a patient should be run through a modern day calculator to see if they are a candidate for a toric lens. To help patients with astigmatism understand the benefits, focus on the following key points:

- ***Toric IOLs correct two eye conditions, cataracts and astigmatism.***
- ***Toric IOLs deliver crisp, clearer distance vision and may reduce dependence on glasses to see at a distance.***

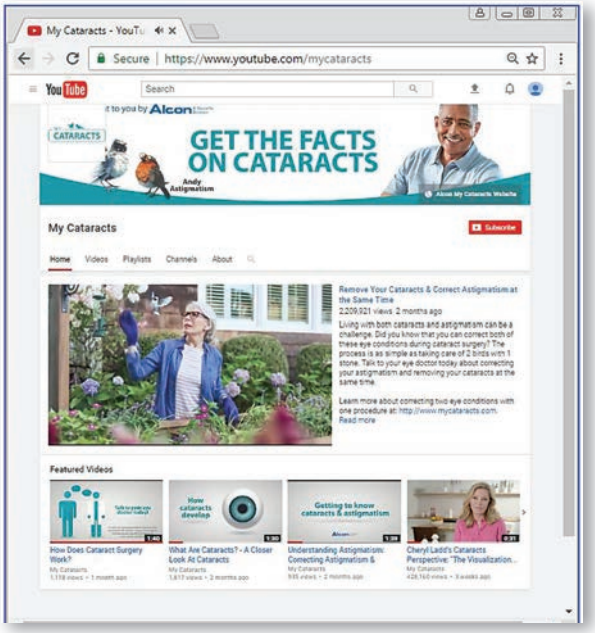
• ***Toric IOLs are proven to deliver the highest quality visual outcome versus a basic lens option.***

Next, I discuss the need for reading glasses and explain that we now have several multifocal IOLs that may help eliminate the need for near correction most of the time. I always tell the patient they may still need glasses on occasion to enhance their vision for certain tasks. If they were wearing monovision contact lenses I may talk to the patient about monovision IOLs, whereas if the patient was a successful multifocal contact lens wearer, I would explain multifocal IOL technology instead.

Provide Additional Resources

After you've provided information, invite patients to learn more about the possibilities that are most suitable. We send patients home with handouts and refer them to specific internet sites to learn more about cataract procedures. In particular, Alcon's new consumer facing campaign at mycataracts.com helps us explain the concept that correcting astigmatism at the time of cataract surgery is like getting two birds with one stone. The campaign also provides a patient support program that is tailored to each stage of a patient or caregiver's correction journey.

Alcon's "My Cataracts" YouTube channel also helps us meet the demand for online learning. The "Two Birds" educational video has already surpassed 1.6 million views. Another benefit is the new My Cataract call center (1-844-MYCATARACT), which allows patients to communicate on their terms. This patient call center is staffed with dedicated, trained cataract counselors and offers a best-in-class patient experience.



The MyCataracts YouTube channel helps meet the demand for online learning opportunities with more than 2.3 million views since the initiative launched in October 2016.

Reiterate to your patients to carefully consider the standard cataract lens option so they don't feel like they settled for something they didn't know enough about when they had the opportunity. It's our responsibility to help convey the long-term value of IOL selection. And, thanks to new tools, it's easier than ever to provide extra support and education.

**Dr. Geffen is director of optometric and refractive services at the Gordon Schanzlin New Vision - TLC in San Diego and is a paid consultant/advisor to Alcon.*

Be a Team Player

Communication between the OD and MD helps drive patient satisfaction and outcomes. We need to be able to convey to the surgeon why a particular type of correction may be in the patient's best interest. The primary care optometrist who has a history with the patient is well suited to review lifestyle, as well as pertinent clinical information, to the surgeon.

It's also important to note that communication ought to travel in both directions. Optometrists should know which IOLs the surgeon routinely uses so that we don't confuse patients by discussing options that the surgeon does not provide. The surgeon also needs to clearly communicate his or her preferences for post op care.

PEER • REVIEWED • PRA • ARTICLE

Disrupt the Disrupter: Keeping Patients in the Age of Online Refractions

By emphasizing expedience, these sites reveal their own shortcomings—and your strengths. **By Bill Kekevian, Senior Editor**

Market disrupters are having a moment. Disrupters—companies that subvert established business models, often using modern technology—purport to better serve the consumer. In some industries, they make a strong case. You can buy a quality mattress online without being hounded by commission-hungry salespeople. You can hail an affordable ride that arrives in minutes. You can stream a near-infinite collection of music and movies for a flat rate and never pay a late fee. Of course, the conveniences of this brave new world are predicated upon the losses of the traditional outlets for these services (for evidence: try to find your nearest record store; then, consider how close the nearest one was 15 years ago).

Harvard Business School professor Clayton Christensen defined the term "disrupter" in his 1997 book *The Innovator's Dilemma*. He says these companies anticipate the consumers' unstated, future needs.[1] In other words, they offer consumers something they didn't even know they wanted.

For example, Warby Parker launched in 2010 and, by 2014, *CNBC* had ranked it second on its list of top 50 disrupter companies for "taking on the Luxottica eyewear machine."[2] Giving the consumer a way around your optical shop—something they may have seen as a "middleman"—opened a market previously inaccessible to the average consumer.

Today's new threat is online refraction. These companies are crossing a barrier into patient care, according to many optometrists. The online refraction industry has the potential to create a system wherein patients obtain a refraction from the website (which

relies on prescriptions written by an ophthalmologist, since they can operate across state lines—optometrists can't) and use it to order frames or contact lenses from an online retailer. Notice anyone missing in that equation?

Optometrists have plenty of questions about the new modality's clinical validity and its impact on their brick and mortar practices. This article addresses those concerns, explains what these companies provide and how optometry is fighting back legislatively, individually and technologically.

Meet the Disrupters

You may have heard of one or two companies looking to become the "Netflix" of refraction, but even a cursory survey of the market shows there are many outlets available for patients to obtain their prescription online. The most visible company currently offering this service, Opternative—its name a portmanteau of "optometry" and "alternative"—provides a vision test patients can take at home, which is reviewed by an ophthalmologist. A short time later, the company delivers a lens prescription that can be used at any optical shop.

For its part, Opternative stresses that its refractive test is not an eye exam and that patients should still see their optometrist. In fact, the site says it "prohibits patients from taking an Opternative test more than four consecutive years without certifying that they have received a comprehensive eye health exam first."

Opternative has even partnered with another well-known disrupter, 1-800 Contacts. As part of the deal, 1-800 Contacts customers can take Opternative's refraction test and obtain a prescription on the 1-800 Contacts website.[3]

Their apparent hope, and many optometrists' fear, is that patients will take their refractive test online, order contacts from 1-800 Contacts (or frames from Warby Parker) and never visit the optometrist.

Another company, 2020Now, takes a different approach. Rather than an at-home exam, 2020Now provides an in-store exam, presumably at an optical shop, with an ophthalmologist who teleconferences in on an HD video.

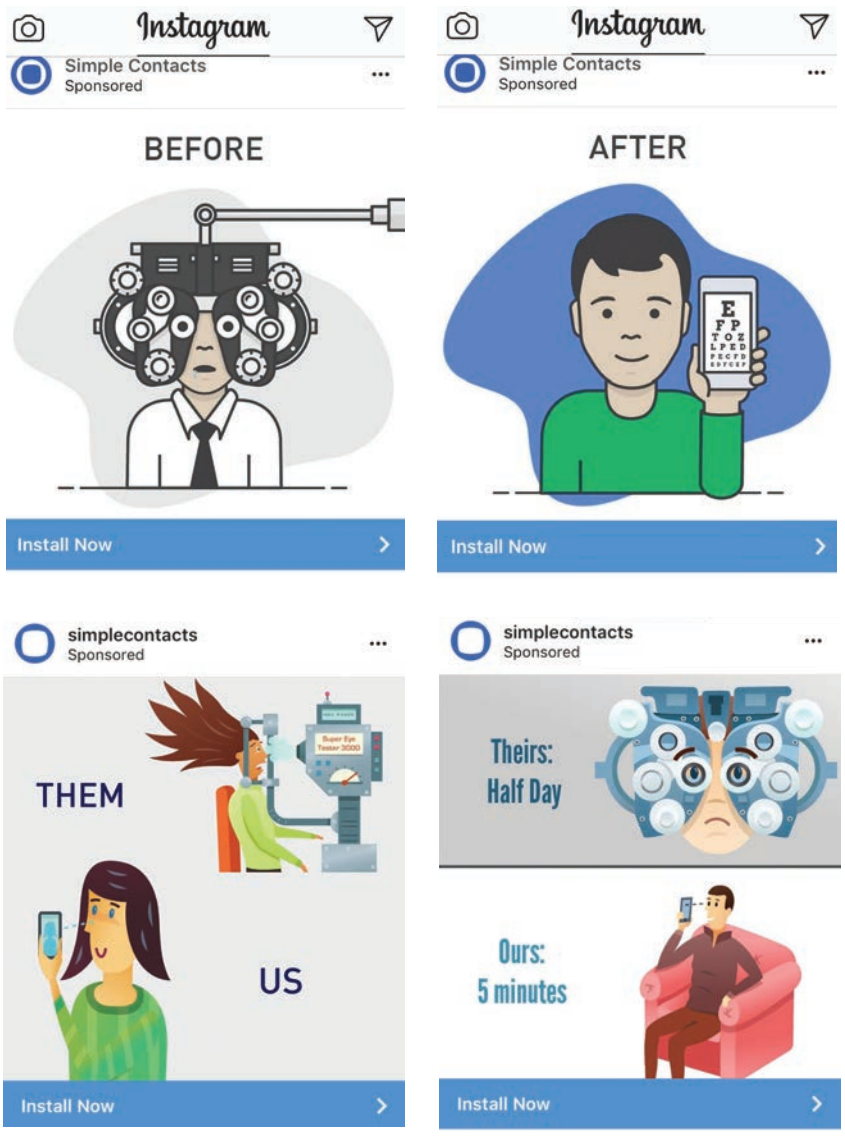
And that's not nearly the end of the list. Eyenetra, GlassesOn and Simple Contacts are making inroads, and each puts its own spin on the test. The entirely app-based Simple Contacts blatantly states in its advertisements: "Skip the office! Renew your prescription with an app."

Take it as a sign of the times. The disrupters have targeted eye care and they're convincing patients they want to avoid the optometrist. Your move.

LEGISLATION
Take Action

In the face of a disrupter, a *Harvard Business Review* article proposes traditional businesses evaluate three necessary points:

1. Identify the strengths of your disrupter's model.
2. Identify your own relative advantages.
3. Evaluate the conditions that would help or hinder the disrupter from co-opting your current advantages in the future.[4]



As these Simple Contacts advertisements—culled from popular-with-Millennials social networking platform Instagram—clearly show, online refraction testing casts visiting an optometrist as an unpleasant, time-consuming chore, as opposed to their convenient alternative. While organized optometry challenges that portrayal nationally, ODs can talk up visiting an in-person doctor with patients individually.

Online refraction companies' strengths are their convenience and novelty. Unless optometrists find a way to evaluate patients on demand and from the comfort of their homes, they're never going to beat the convenience of a website.

Naturally, optometry has a relative advantage—the ability to provide a comprehensive eye exam using both objective and subjective tests. But ODs have another powerful tool that can hinder the disrupter from co-opting its current advantages: organized optometry.

"When Opternative got together with 1-800 Contacts and started trying to deceive the public into thinking that they have a system that is standard of care, that's when I got involved," says Jeffrey Sonsino, OD, chair of the Contact Lens and Cornea Section of the American Optometric Association (AOA). In fact, he relates the story of a patient who presented to him with some irritation. The 30-year-old had ignored optometric evaluations and opted to simply reorder contacts for three years without seeking in-person care. The patient had a *Pseudomonas* ulcer caused by *Acanthamoeba* that ate through his intact cornea within 24 hours. "He had to get a corneal transplant that was 10.5mm in diameter," Dr. Sonsino explains. "Because of the size of the graft, for the rest of this guy's life he's going to have a repeat corneal transplant until, ultimately, he loses the eye."

"When they provide a service that is sub-standard of care, the public is invariably harmed," says Dr. Sonsino. "My position in the AOA is to protect the public."

He, along with the AOA, is certainly building the case against online refraction testing. To that end, they've provided an email address—stopillegalcls@aoa.org—where any optometrist can recount their horror stories of harm caused when patients opt for online tests over OD visits.

The AOA has also launched a campaign to educate the public about the risks of online exams. The group has talked to reporters for *Politico*, *Medscape Medical News* and published in *The Hill*.[5-7] State chapters, such as the California Optometric Association, have created YouTube videos for patients who like to do their own research.[8] The AOA has also partnered with the Vision Council to launch the site thinkaboutyoureyes.com, a resource to help patients and parents understand the value of an eye exam and put patients in touch with local ODs.

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> *"When they provide a service that is substandard of care, the public is invariably harmed"—Jeff Sonsino, OD, chairman of the Contact Lens and Cornea Section of the American Optometric Association*

Organization

While outreach is important, the AOA's real power comes from its ability to educate legislators. The group filed a complaint with the FDA against the concept of online refraction testing.[9] "The entire claim—and the reason for the complaint that was filed—is that the standard of care is a face-to-face eye exam in which an eye health assessment and a refractive assessment are done at the same time," says Clarke Newman, OD, chair of the Federal Relations Committee at the AOA. "That being said, a refractive evaluation is still a face-to-face test that includes both objective and subjective testing." He says relying on blind subjective data alone—as online outlets do—often misses the refractive endpoint and delivers a flawed prescription. "We advocate across the board that the standard of care must be maintained and that all these conveniences are at the expense of the accuracy of the refraction and at the expense of eye health."

The complaint—filed April 4, 2016—also took issue with some of the claims sites have made concerning the efficacy of the technology.[9] "The self-administered nature of the test is uncontrolled, and that can lead to errors that significantly alter the prescriptions," he says.

"The FDA is looking at it and the FTC will look at it and see if the claims that they're making are valid and, if not, we have a deceptive trades claim," Dr. Newman says. "We're not advocating for these things to be made illegal; what we're saying is they shouldn't be available if they're not approved by the FDA. They shouldn't be exempt from going through the standards every other device does."

State-by-state efforts are taking effect, too. In Connecticut, for example, new legislation aims to prohibit prescribing contact lenses "using information obtained from a test using a 'remote refractive device' as the sole basis."[10]

While the AOA is taking on the online refractive threat legislatively, there's something you can do everyday to keep your patients where they belong: talk to them.

FACE TO FACE
Win Patients Back

The AOA's stance on these companies prompts the question: Does online refraction actually threaten optometry's model? Consider the lesson of Google Maps.[11] Google managed to topple the navigation device market (remember your Tom Tom GPS?) on four main selling points: price, quality, convenience and personalization. Improving on all four of these aspects disrupted the personal navigation device market forever.[10]

It may be worth discussing with patients whether online refraction companies can beat optometry in any of these selling points.

Price. No optometrist would provide a refraction separate from a comprehensive eye exam, explains John Rumpakis, OD, CEO of Practice Resource Management, Inc. However, since that's what these companies are doing, a hypothetical price-by-price comparison may be an appropriate point to discuss with patients. Opternative offers a glasses or contacts prescription for $40 ($60 for both). Although optometry offers a comprehensive exam at an average Medicare reimbursement of $120 to $150, the line-item for the refraction aspect of the exam averages between $20 and $25, says Dr. Rumpakis. Specifically, "The 2017 National Average Allowable from CMS for 92015 (Determination of Refractive State) is $20.13." In addition, while employer-based health insurance options often cover vision, no insurer currently covers online refraction tests.

Quality. Online services can offer subjective tests, but none are yet able to offer an objective measurement. Conversely, programs such as the VA TECS program—which employs an autorefractor and sends test results to an off-site ophthalmologist—uses only objective tests.[12] According to Dr. Newman, that's not nearly enough. "The face-to-face refraction using a confluence of both objective and subjective measurements is something that has developed organically over 200 years," he says.

Let's say a patient has an eye deviation that requires prismatic correction: They can't address that online. Even if they get the exact sphere and cylinder power, they can't get the prismatic power, Dr. Sonsino adds.

Another example is cyclorotation. "When some patients test themselves, their eyes rotate when they cover one eye," Dr. Sonsino says. "If you don't account for that, the axis will be off. There is an entire paradigm that accounts for what we do in an exam room when we're trying to control for things such as an accommodative spasm, cyclorotation and for prismatic induction. In the absence of those controls,

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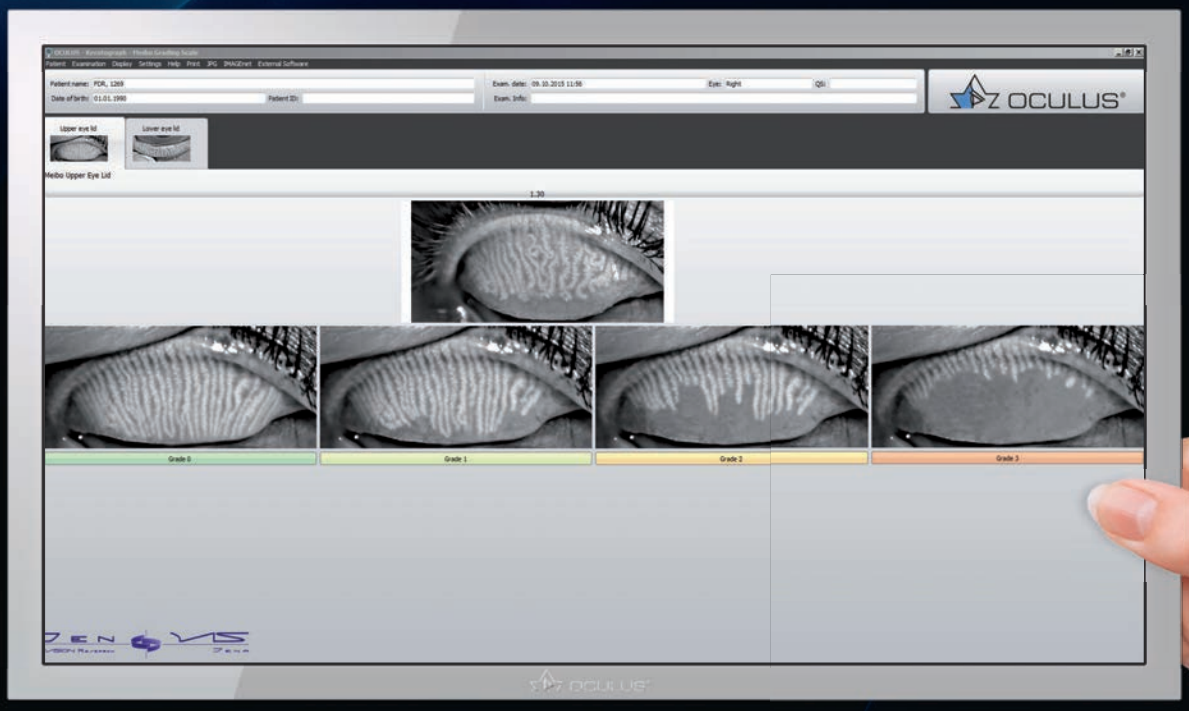

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patients end up with the wrong prescription."

Convenience. In a March 2016 interview with the podcast Tech in Chicago, Aaron Dallek, co-founder of Opternative, made a strong argument for the online convenience.[13] Mr. Dallek offers the scenario of a busy parent who believes they have a better chance of setting aside an hour for a new prescription once their kids are in bed and, since the patient won't have to leave the house, no babysitter is required.[13] Marc Taub, OD, a fellow with the College of Optometrists in Vision Development, understands that appeal, "It's ease of care and time. We all live very busy lives, and patients may think, 'Any way that I can get even a half an hour back, that'll be easier,'" he says. Convenient? Sure, so long as the patient is confident they don't have any indications of glaucoma, retinal disease or other syndromes a simple vision test won't detect. As Dr. Sonsino points out, catching those issues later in their development will naturally require a much lengthier time commitment and a greater cost to the patient's health as well as to their wallet.

Personalization. This is where the optometrist has a clear advantage. A visit to the OD provides a one-on-one interaction with a doctor. Patients just sit back and let the ODs and support staff do most of the work. For example, contact lens fitting and follow up is an essential aspect of patient care that a website could never provide. Dr. Sonsino's *Acanthamoeba* patient probably developed his disease from poor contact lens hygiene. "*Pseudomonas* ulcers are highly associated with contact lens wear," Dr. Sonsino says. "I can't tell you how many patients I have that I use that opportunity when they're in the chair to talk about the risks associated with contact lens wear and, in an evaluation, I'll find things on the surface of the eye that an iPhone can't find. It can only be done under high magnification under stereo vision. I'll find signs that tell me that we need to change the patient's contact lenses, maybe into something that provides more oxygen or a lens that fits the eye differently. That can only be done in person."

Putting it to the Test: My Take on Online Refraction

Every company's approach is a bit different, but for the purposes of this article, I took the Opternative test. Here's how it went:

In interviews, Mr. Dallek noted that the test begins by asking two questions: the patient's cell phone number and their shoe size. In fact, it starts with a few other questions that may not seem important to patients, but optometrists will recognize their value. First, patients are presented with a questionnaire to determine whether they have any systemic diseases, such as diabetes or hypertension (if you answer yes to any, you're not permitted to take the test. However, I had no problem going back to the start of the questionnaire and changing my answer until I was permitted). "They don't want to be on the hook for not doing a comprehensive eye health exam," according to Dr. Newman. The test also asks your home state, since online refraction is barred in 11 states. Interestingly, I had no issue using a banned-state billing address as long as I claimed to be from a state where online refractions are not barred.

After those disqualifiers (toothless though they may be) weed out some prospective customers, the test does ask for the patient's shoe size—to help them measure the distance they should step away from the computer—and cell phone number. The site essentially turns the patient's smartphone into a remote control the patient can use to respond to the test questions. Patients will require 10 feet of clearance. The test requires them to stand at varying distances and use a smartphone to answer, for instance, which way the "E" on the screen is facing. Opternative also uses a modified duochrome test to determine the sphere.

After the test, it asks patients to submit their previous prescriptions, provided by their own optometrists.

Results

Twenty-four hours after taking the test and submitting my old prescription, I received an email with a downloadable new prescription. It was convenient. I could take that prescription, signed by an ophthalmologist, and start shopping for new glasses online. But I wanted to be sure the new prescription was accurate. The online prescription was suspiciously similar to my 2015 Rx. In fact, the only change was in the axis of my astigmatic right eye, which the site measured 140 (in 2015, my OD measured it at 135).

So, I phoned my doctor, who agreed to participate in my experiment. After completing both objective and subjective tests, she noted that myopia had progressed, by a greater amount than the website detected. Instead of the website's recommendation of sticking with the -4.25 OD and -4.75 OS, my doctor measured my eyes at -4.75 OD and -5.00 OS. She also noticed astigmatism in my left eye for the first time (0.25x015) and a change in my right eye from 0.50x135 in 2015 to 1.00x155.

Sure, it's possible I could have gone to yet another optometrist and probably received a third prescription different than either the website or my doctor, but my doctor was able to do something a website can't. She used her phoropter to demonstrate my 2015 prescription, then she flipped to the website's recommendation and, finally, her recommendation. My choice was crystal clear. It wasn't as convenient, but I left the office with a significantly superior product, plus a dilated exam, visual fields test and IOP measurement, assured of my visual health.

Jack Schaeffer, OD, of Schaeffer Eye Center in Hoover, Ala., echoes that concern. "If you follow the research, the majority of complications in contact lenses are due to noncompliance by patients," he says. "Online sales can't do a proper contact lens evaluation."

An analogy that Dr. Sonsino shares with his patients: "It's like a timing belt in a car. If you fail to replace that timing belt as you should, you'll go along perfectly fine, until that timing belt breaks. When it breaks, you will be stuck on the side of the road. So, you can either choose to maintain your car or wait until something bad happens and address it then. The problem is, when you wait until something bad happens with your vision, a lot of times, there is no recovery."

It seems implicit that an online refraction test provides only an automated relationship that has no way of recreating the level of curation an optometrist can provide, and that curation can be the difference between healthy and unhealthy ocular habits.

Just to be sure, though, I took the test myself. See, *"Putting it to the Test: My Take on Online Refraction,"* p. 40.

INNOVATION
If You Can't Beat 'Em…

We're living in a do-it-yourself era. Consumers in a variety of fields are looking to dispose of barriers between them and the product they're after—and that extends to all branches of medicine. To wit, a consumer hearing loss group—The Hearing Loss Association of America—is pushing for over-the-counter hearing aides (there's a bill in Congress now).[14] Some ODs speculate that maybe trying to prevent patients from embracing these technologies is the wrong approach. Indeed, online refraction companies have their own consumer groups pushing legislation and attempting to control the narrative. Like the AOA, they're making their voices heard, and their characterization of optometry isn't pretty. The AOA is cast as "Big Eye" and optometrists as regulation-dependent "crony capitalists." One clickbait headline even reads, "How Eye Doctors Are Robbing Us Blind."[15-17]

Maybe, this is the time for optometry to develop a response to online refractions—to win back patients while maintaining the standard of care. "Imagine if patients could take an accurate refractive exam in the waiting area before even seeing the doctor, or if they could arrive with results in hand" from a home test, speculates Gary Gerber, OD, practice consultant with Power Practice in New Jersey. Dr. Gerber and others envision a future wherein the optometrist can redirect patients from today's bare-bones tests to a system monitored—not rubber stamped—by individual doctors. Rather than depend on the evaluation of a subjective test by an algorithm and an out-of-state ophthalmologist, patients would be able to more efficiently use that waiting time to take the subjective portion of their exam.

"At some point in time, there will be a sufficiently advanced technology," says Dr. Newman. "It's just not today."

Online refractions are, as Dr. Taub succinctly puts it, "not really eye care." But many of the outlets providing it are touting it as a way to avoid your optometrist. In that sense, the threat is real. It's going to require a keen analysis of your patient base to see if you, individually, are losing patients to this modality. And, perhaps, in a not too distant future, a salesman will appear in your office with a sufficiently advanced technology that you can add to your practice to offer an alternative to online refraction platforms. Until that day, patients need you to explain that they need an in-person doctor visit, because "there's a human aspect to putting all the data from a comprehensive eye exam together," says Dr. Taub. ■

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PEER • REVIEWED • PRA • ARTICLE

Corneal Crosslinking: Managing Keratoconus Beyond the Surface

This new treatment modality is changing the way we care for our irregular cornea patients. **By Clark Chang, OD, MSA, MSc, and Aaron Bronner, OD**

The standard of care for keratoconus (KCN) has changed very little over the years. Approximately 10% to 20% of patients will eventually require some form of keratoplasty due to the progressive nature of KCN.[1] In addition, most patients, whether before or after undergoing grafting surgery, will require gas permeable (GP) lenses to reduce optical aberrations and achieve adequate functional vision.

However, the status quo is undergoing revolutionary modifications due to the recent FDA approval of corneal collagen crosslinking (CXL). Currently indicated for treating progressive keratoconus and postsurgical ectasia, CXL represents the most significant treatment paradigm change for this population.

Current clinical data shows CXL is safe and highly efficacious in halting or slowing the progression of ectatic diseases—a clinical task that was previously thought to be impossible.[1-3] In addition, although KCN prevalence is often cited as around 1/2,000, recent epidemiological evidence shows it may be as high as 1/375 in certain populations.[4-5] As such, the impact of CXL may be more far-reaching than anticipated.

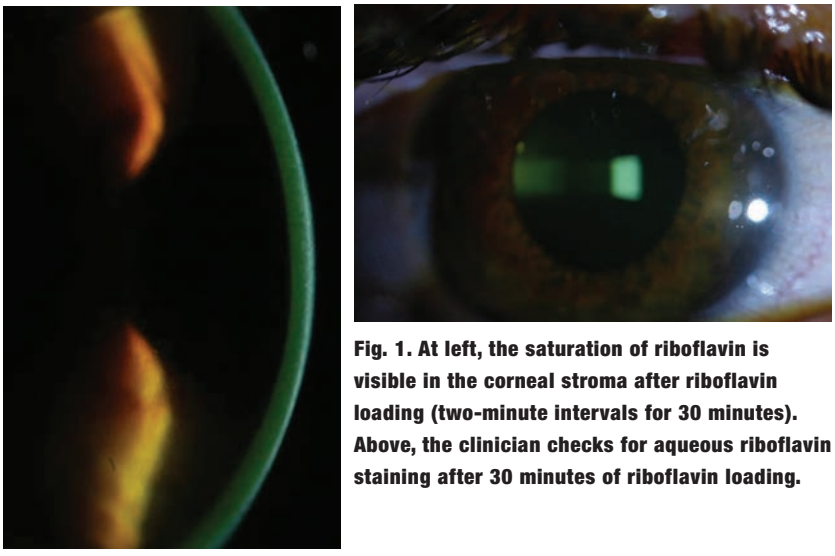


Fig. 1. At left, the saturation of riboflavin is visible in the corneal stroma after riboflavin loading (two-minute intervals for 30 minutes). Above, the clinician checks for aqueous riboflavin staining after 30 minutes of riboflavin loading.

This article discusses the benefits of corneal collagen crosslinking, candidacy selection, treatment techniques, potential complications and how we can best incorporate this innovative medical treatment into our care for keratectasia patients.

The Science Behind CXL

KCN typically presents during early puberty and progresses until the fourth decade of life.[6] The relative stability seen in most patients beyond this stage of life is possibly a byproduct of the cumulative aging-associated crosslinking observed in all connective tissues, including the cornea. Researchers have also noted a similar phenomenon of corneal stiffening in diabetic patients where additional tissue crosslinking is purported as a result of glycation.[7]

The principle of artificially accelerating formation of corneal crosslinks was first explored in Germany at the University of Dresden in the late 1990s. After epithelial removal, the researchers saturated corneal stroma with riboflavin (a photosensitizer) and then exposed the treatment zone to an ultraviolet-A light with wavelength of 365nm. This spectral emission was specifically selected since riboflavin absorption peaks at approximately 366nm. The photochemical reactions led to the production of singlet oxygen-free radicals and activation of the lysyl oxidase enzymatic pathway, which induce formation of new covalent bonds to sufficiently enhance tissue stiffness that slows down or arrests KCN advancement.[8]

During this initial investigation, the researchers observed corneal stability in 100% of the CXL-treated study eyes. They were also pleasantly surprised by a 2.01D of flattening with maximal keratotometry readings in 70% of patients enrolled in the study.[8] This discovery opened the door to a new era of ophthalmic CXL applications in keratoconus and ectasia patients and set the stage to explore various CXL techniques.

Approval and Implications

CXL received two treatment labels from the Food and Drug Administration (FDA) in 2016: progressive keratoconus and corneal ectasia following refractive surgery. The FDA's decision on CXL was unique in that its approval was granted as a specific drug-device combination, which includes the KXL UV system and Photrexa family of riboflavin solution (Avedro). This reflects the fact that the multicenter study data submitted for FDA review was derived solely from this single treatment platform using a traditional epithelium-off technique. Although Avedro also manufactures CXL platforms compatible with transpeithelial (or epithelium-on) CXL protocol, the current label is intended only for standard epithelium-off CXL technique.

The immediate implications of this FDA approval are twofold. First, if a health insurance carrier decides to offer CXL coverage to beneficiaries diagnosed with keratoconus or ectasia, only epithelium-off treatments performed as per FDA label will likely be accepted. Second, an eye care practice that offers CXL may only receive liability insurance protections if it uses the FDA-approved apparatus. For a practice to employ other CXL devices and techniques, such as transepithelial CXL (TE-CXL), it would have to submit a separate Investigational New Drug Application to the FDA, as well as proof of Institutional Review Board oversights to be fully FDA compliant and receive liability protections.

CXL Protocol

Epithelium-off CXL, similar to a photorefractive keratectomy (PRK), is performed under topical anesthesia to ensure patient comfort. Through standard aseptic technique, epithelium is removed from the central 9mm to facilitate faster and more homogeneous riboflavin saturation within the corneal stroma. Photrexa viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) is then instilled on the cornea in two-minute intervals for 30 minutes.[1]

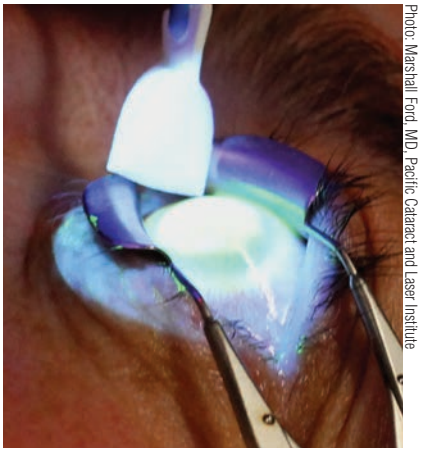


Photo: Marshall Ford, MD, Pacific Cataract and Laser Institute

Fig. 2. The clinician must tend to a patient's eye during the UV emission stage of CXL.

Since riboflavin serves dual functions as a photosensitizing agent to propagate CXL chemical reactions as well as a tissue protector by reducing UV transmittance beyond intended treatment depth, it is essential clinicians ensure full saturation within the corneal stroma prior to UV irradiation. This is done by checking for stromal and aqueous riboflavin staining in the slit lamp after the 30-minute riboflavin uptake phase (*Figure 1*).

A minimum of 400µm corneal thickness is required prior to the UV exposure phase, which is typically measured with an ultrasound pachymeter. Should pachymetry fail to show proper corneal thickness stipulated for treatment safety, hypotonic Photrexa riboflavin is administered every five to 10 seconds until the cornea is swollen to 400µm or greater.

Once clinicians have verified appropriate riboflavin saturation and pachymetry measurement, they

can program the KXL UV device for 30 minutes of continuous emission (3mW/cm^2) with a calibrated total energy dose of 5.4J/cm^2.[8] After UVA exposure is initiated, Photrexa viscous continues to be administered in two-minute intervals until the procedure is complete (*Figure 2*).

A bandage contact lens is maintained on the treated eye for three to five days or until epithelial closure. Although the exact ophthalmic medications may vary, patients are typically managed with topical antibiotic for one week and topical corticosteroid for two to three weeks.[1]

Candidates for CXL

The inclusion criteria set by the FDA for CXL includes a patient who: (1) is 14 years of age or older, (2) has a confirmed diagnosis of post-surgical ectasia or progressive KCN and (3) has a minimum stromal thickness of 400µm. However, disease severity and rate of progression tends to be worse in younger patients, stipulating a minimum age requirement of 14 excludes a large group of pediatric patients who may gain the most from CXL treatments.[9] Therefore, many clinicians offer off-label treatment to younger patients, provided they can ascertain 400µm of stromal thickness.

Given that post-surgical ectasia can occur at an older age than typically encountered for KCN, clinical consensus has not defined an age ceiling for these patients. Clinicians can recommend CXL in patients with post-surgical ectasia at any age based on documented progression and stromal thickness. For KCN, however, clinicians would be prudent to educate patients older than 40 years of age that CXL is a possible stabilization treatment option, but vigilantly monitor for evidence of progression prior to recommending CXL. Although we don't have a general agreement on what magnitude of changes and time frame constitute progression, an expert panel recently recommended that at least two of the following three criteria need to be present to establish clinical progression: (1) progressive steepening in anterior corneal curvature, (2) progressive steepening of posterior corneal curvature or (3) progressive thinning when comparing pachymetric distribution profile from periphery to thinnest point.[10]

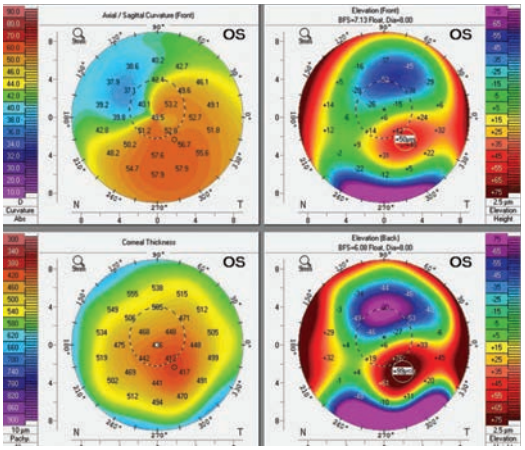
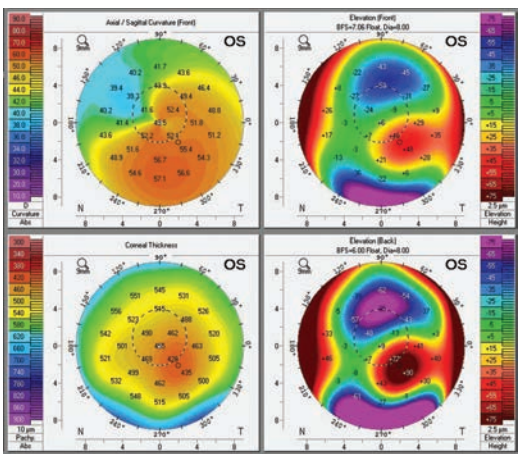


Fig. 3. Above is a patient's baseline tomography. Below, is the same patient's tomography 14 months after CXL treatment. It shows mild apical flattening on the axial map (upper left) and reduced elevations maps (anterior elevation, upper right; posterior elevation, bottom right).



The same group of experts also asserted that waiting for documented progression prior to CXL may not be necessary in younger KCN patients since the likelihood of progression is almost certain, and the best CXL outcome can be obtained with early treatment.[10]

Recovery Process

The recovery of epithelium-off CXL is much like the recovery with any corneal epithelial delamination procedure, such as PRK. Although a bandage contact lens will enhance patient comfort, many may still experience ocular discomfort or pain until the epithelial defect closes, which usually occurs in three to five days. After wound closure, vision is expected to slowly change as epithelial remodeling and subsequent CXL effects manifest over time.

During the recovery phase, visual acuity was generally observed to worsen during the first month compared with preoperative presentation and slowly returns to baseline by the three-month follow up. Patients may experience some improvement in visual acuity between month three and six or thereafter until a trend of stabilization emerges as the new baseline. Research also shows a similar pattern of recovery after standard CXL with keratometry, pachymetry and corneal haze measurements—further steepening, thinning and reduction in tissue transparency were initially observed during the first month with trend reversal expected at around the third month, which may persist until

stabilization (*Figure 3*). However, investigators found no clear associations between changes in corneal haze during the recovery phase and changes in other patient parameters such as best-corrected visual acuity (BCVA), maximum keratometry, mean keratometry and thinnest corneal point.[1,9]

Patients may misconstrue the worsening in these clinical parameters during the early postoperative period as CXL treatment failure; however, they need to be carefully monitored until at least month three or six when clinicians can assure a repeatable pattern prior to deciding if CXL treatment has taken effects.

Potential Benefits vs. Risks

Recent studies confirm the high level of efficacy with this standardized protocol—CXL with an epithelium removal technique—in halting keratoconus progression with a good safety profile. One meta-analysis on CXL demonstrated an average treatment success rate of 93.1%.[11]

In addition to slowing or arresting keratoconus progression, numerous reports suggest improved topographic, refractive and aberrometric parameters after standard CXL.[1,12,13] However, researchers have yet to discover specific preoperative patient variables that can reliably predict such postoperative improvements, so for now, patients should only be educated on corneal stabilization as the primary purpose of CXL rather than any potential refractive benefit.

Despite its good safety profile, CXL complications have been reported and should be part of our discussion with patients. Significant complications are rare and can include the common issues expected with any epithelial delamination process such as variable epithelial healing rate, eye pain, microbial keratitis and

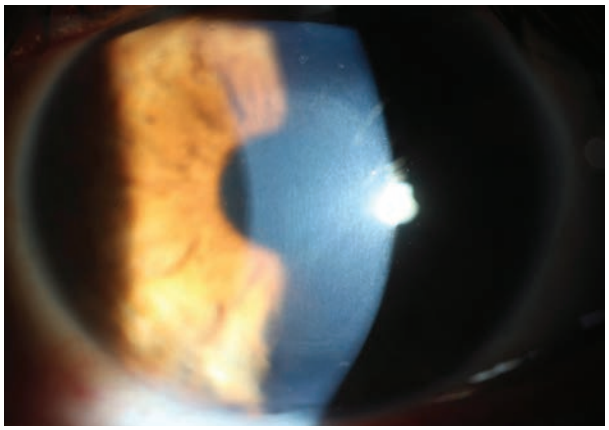


Fig. 4. Using a slit lamp, clinicians can see CXL-associated corneal haze distributed within the treatment zone.

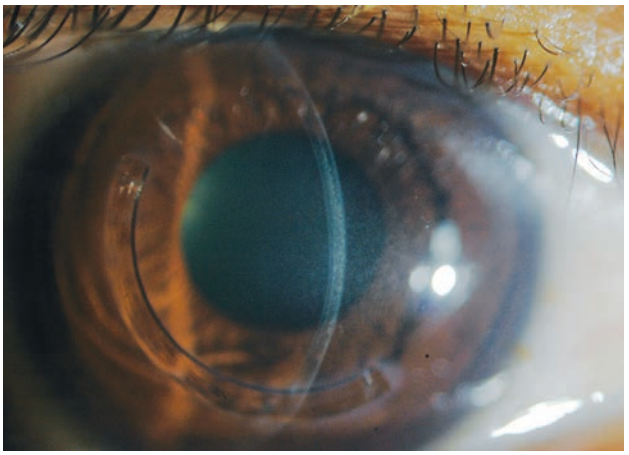


Fig 5. A slit beam shows the demarcation lines, which are a potential indicator of CXL treatment depth in a patient who received off-label treatment of CXL and an Intacs corneal implant (AJL Ophthalmic).

sterile infiltrates. Additionally, other CXL-related complications include corneal haze, persistent corneal edema/endothelial decompensation, unexplained loss of visual acuity and treatment failure. A closer look at these adverse events can help clinicians better manage patients should they arise.

Corneal haze. Unlike the rare event of PRK haze, CXL-associated corneal haze is common in the immediate post-CXL period (*Figure 4*); one study suggests it can be observed in up to 90% of patients after CXL, which significantly decreases on its own between three and 12 months.[12] The same study also found no correlations between corneal haze and other postoperative parameters such as BCVA and keratometry. Therefore, CXL-associated haze likely represents a different cellular event compared with PRK haze. At the very least, it does not appear to share the same clinical concern as haze after PRK.

Research suggests post-CXL haze, which occurs throughout the treatment zone in the anterior- and mid-stroma (as opposed to the reticular superficial scarring with PRK), is a result of increased density of extracellular matrix (ECM) with altered refractive indices in the treated tissue layers.[14] This finding is often used as a histological indicator of CXL effects and its penetration depth—the posterior limit of the treatment zone is also referred to as demarcation line (*Figure 5*).[1,14] Albeit uncommon, persistent and visually significant haze can occur, and some assert this may be more likely in patients with advanced KCN, highlighting yet another reason to attempt to diagnose the disease early in its course.[15]

Corneal endothelial decompensation. Part of the early development of CXL was to determine the endothelial cytotoxic threshold of UVA emissions. Investigators found the absence of cellular apoptosis if UV irradiance was below 0.35mW/cm^2. The standard UVA CXL treatment protocol described in this article was determined to reach only 50% of this cytotoxic threshold, assuming a stromal thickness of at least 400µm and that sufficient riboflavin bioavailability is present within the stroma. With that said, studies have reported a few cases of non-resolving corneal edema requiring penetrating keratoplasty.[15-17] Significant corneal thinning during the UV exposure phase may lead to such sequalae; thus, early CXL referral when ample corneal thickness is still present can help to prevent this rare complication.[18]

Loss of best spectacle-corrected visual acuity (BSCVA). Overwhelmingly, the majority of eyes either maintain the same or slightly improved BSCVA compared with baseline profile; however, studies reveal reduced BSCVA in a small group of eyes with no apparent link to other clinical parameters to explain such episodes.[1,19] Investigators estimate the risk for losing two lines or more in Snellen acuity after CXL treatment is between 1.4% and 3.5%.[1,19] Fortunately, this finding does not correlate with BCVA

The Benefits of Combined Procedures

By A. John Kanellopoulos, MD

Internationally, CXL is often combined with customized partial surface ablations, such as LASIK, to help patients become spectacle- or contact lens-independent. Known as the "Athens Protocol," the technique—extensively documented, even with 10 years of follow up—practiced globally as an option in lieu of CXL alone, with higher visual rehabilitation benefits. Now that both CXL and topography-guided ablations are approved in the United States, the actual clinical prevalence of the technique will soon be determined.[1-5]

Besides treating ectasia, researchers can perform smaller amounts of CXL, which is proven to aid as a biomechanical modulator (enhancer) in routine LASIK procedures in both myopia and hyperopia.[1-5]

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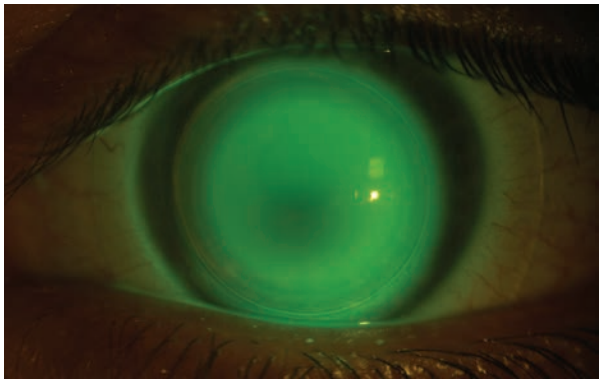

Fig. 6. This patient was successfully fit in a hybrid contact lens after standard epithelium-off CXL.

achieved with contact lenses when patients are ready for contact lens fitting after CXL.

Treatment failure or regression. Treatment failure is rare, as research shows approximately 2% to 8% of patients have continued worsening of ectatic disease after CXL.[1,12] However, such diagnosis may take time to formulate, given the expected keratometric steepening and corneal thinning during the first one to three months immediately after CXL. Nonetheless, researchers have observed long-term treatment regression from many clinical trials, with more reporting of this complication after TE-CXL and in the pediatric patient group (18 or younger).[20-22]

Epithelium-On or -Off?

Despite its proven efficacy and minimal invasiveness, investigators have raised clinical concerns over the epithelial removal technique, primarily due to its association with adverse events. While research shows fewer associated complications when the epithelium is left minimally disrupted, numerous reports also demonstrated lowered CXL efficacies with TE-CXL, which may necessitate more frequent retreatment with CXL across a patient's life time.[20-22] This may be because an intact epithelial barrier prevents riboflavin from gaining entry into stromal tissue as well as slow down stromal oxygen diffusion.

In addition, a patient noncompliant with follow up and with higher risk factors for progression may have more cumulative risks for progression between each CXL treatment. Given the primary purpose of CXL is stabilizing against progression, many investigators still favor the standard epithelium-off CXL technique due to its higher yield in treatment efficacy. Still, TE-CXL not only has fewer reports of associated adverse events, patients also experience a quicker recovery course;

hence, continual research efforts will likely bring about enhanced treatment effects in TE-CXL in the future.[11,22]

Contact Lenses After CXL

Despite findings of improved topographic, refractive and aberrometric characteristics post-CXL, most patients will still require contact lenses to achieve best visual outcome. With advancements in contact lens technologies, we now have myriad lens options to offer to our patients to accommodate their different disease severities and visual needs (*Figure 6*).

Patients' K values will flatten by two diopters, on average, in the first year after standard epithelium-off CXL, with most of that effect occurring in the first six months. Habitual lens wearers may resume lens wear as early as four weeks. In these cases, clinicians should instruct them to bring their habitual lenses during their one-month exam to ensure a reasonable fitting relationship with adequate visual function. If the previous lens modality provides a reasonable fitting relationship, adequate vision and good comfort, patients can continue wearing them throughout the initial six to 12 months to reduce the cost of frequent lens replacement within the first year after CXL. If needed, clinicians can refit a patient into a new lens as early as six months, as the majority of the topographical changes have already occurred and subsequent changes are expected to exert less impact on the patient's corneal elevation profile.

For non-contact lens wearers or if the previous lens modality exhibits a poor lens fitting relationship at the one-month visit, clinicians may fit patients earlier to provide necessary visual abilities to perform daily tasks. As long as patients understand the possibility of frequent lens replacements during the first year, clinicians can consider a refit or a new fit as early as four to six weeks after standard epithelium-off CXL.

Despite some evidence showing reduced treatment efficacy with TE-CXL protocols, patients do experience quicker visual recovery courses after such treatment.[11,20-22] Therefore, TE-CXL patients can often resume lens wear or be refit in to a new lens at one to two weeks after TE-CXL.

Take Home Message

CXL is an enormous change in the treatment algorithm of KCN and other keratectasias—it is now more crucial than ever to be mindful of early disease detection. Previously, clinicians had to tell patients their conditions would naturally worsen over time and that keratplasty might not be avoidable. But today, CXL

can help prevent these limitations, allowing patients to function at their absolute best.

Identifying these patients as early in the disease process as possible will allow them the option of earlier treatment to avoid the many barriers imposed by their ocular disorder across different stages of their lifespans. With the suspected higher disease prevalence and the positive impact we can make with early detection, proper keratoconic screening and timely referral for CXL will soon become the standard of care for our profession.[4-5]

Dr. Chang is director of cornea specialty lenses at Wills Eye Hospital–Cornea Service and director of clinical services at TLC Vision. Also, he is an advisory board member for the International Keratoconus Academy, the Gas Permeable Lens Institute and the Optometric Cornea, Cataract and Refractive Society.

Dr. Bronner is an attending optometrist at Pacific Cataract and Laser Institute in Boise, WA.

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Less is More: What You Need to Know About Dropless Cataract Surgery

Postoperative drops place a significant cost and compliance burden on our patients, but injectable medications can improve the experience. **By Mitch Ibach, OD**

In 2015 in the United States, 3.6 million cataract surgeries were performed, and more than 20 million are performed yearly worldwide.[1] Today's cataract surgery patients have access to new technologies that provide better preoperative and intraoperative surgical precision, which allow for unprecedented refractive outcomes. The rapid evolution in cataract surgery is nothing short of spectacular, and yet, a major drawback remains for our patients: the burden associated with instilling numerous postoperative eye drops.

While cataract surgery is safe, achieving and maintaining such high outcomes requires patients correctly instill eye drops after the procedure—for which no standard currently exists. The potential lack of adherence to the postoperative drop regimen can lead to complications, the most devastating being endophthalmitis.[2] Though a rare occurrence, it's dire enough to warrant consideration of every possible protection against it.

Intracameral ('into a chamber') or injectable medications after cataract surgery may be able to help patients overcome the hassle of post-op drops and avoid complications.[3-5] Here, you'll find essential details regarding patients who opt for dropless or reduced-drop cataract procedures and an overview of the OD's critical role in care.

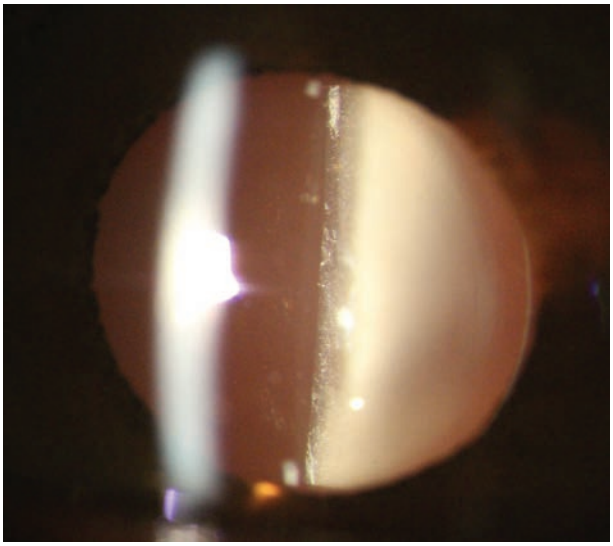

Fig. 1. Presentation one day after dropless cataract surgery using Tri-Moxi. Note the white "snowglobe" appearance in the anterior vitreous common after dropless surgery.

Injectables: Our Protocol

In our practice, we use Tri-Moxi (triamcinolone 15mg/mL + 1mg/mL moxifloxacin, Imprimis) injections for the majority of cataract surgery patients and a 'drop-a-day' regimen, which includes topical NSAIDs. Our surgeons have used both transzonular and intravitreal Tri-Moxi, and now primarily use the intravitreal route. Dex-Moxi (dexamethasone 0.1% + moxifloxacin hydrochloride 0.5%, Ocular Science) is another compounded intravitreal option that tends to be a clearer steroid, so likely creates less vitreous debris/haze; at the same time, dexamethasone has a higher likelihood of steroid response.

At the conclusion of cataract surgery, while the

patient is still under anesthesia, 0.15cc of Tri-Moxi is injected by intravitreal route. We maintain the importance of the betadine swab prophylactically before surgery. After the procedure, we start patients on a nonsteroidal anti-inflammatory (NSAID) drop once daily for one month. For patients with diabetes, epiretinal membranes with or without macular traction, or other pre-op risk factors for postoperative cystoid macular edema (CME), patients are kept on NSAIDs once daily for three months post procedure.

Fully dropless cataract surgery may work great for some patients, but in our practice we prefer a 'drop-a-day' regimen and the anti-inflammatory effects of topical NSAIDs compared with topical steroids. Research directly compares pseudophakic cystoid macular edema (PCME) in post-cataract surgery patients who were randomized to topical NSAIDs or topical steroids to mediate inflammation.[6] At one month, 25% of patients in the steroid alone arm had measurable PCME compared with less than 4% in the NSAID alone group.[6]

Set the Bar

For postoperative intracameral injections, setting expectations is a critical key to success, for both the patient and their clinician.

For the patient, clinicians must tackle the majority of education in the preoperative evaluation. In our practice, we educate patients on two categories of postoperative experiences: mild blurring or haziness of vision for three to four days, and increased floaters and vitreous debris for up to one month. Importantly, we over-emphasize what most patients will encounter. We also educate patients about the increased likelihood of a subconjunctival hemorrhage, especially in patients who take blood thinners, higher doses of aspirin or omega-3 fatty acid supplements.

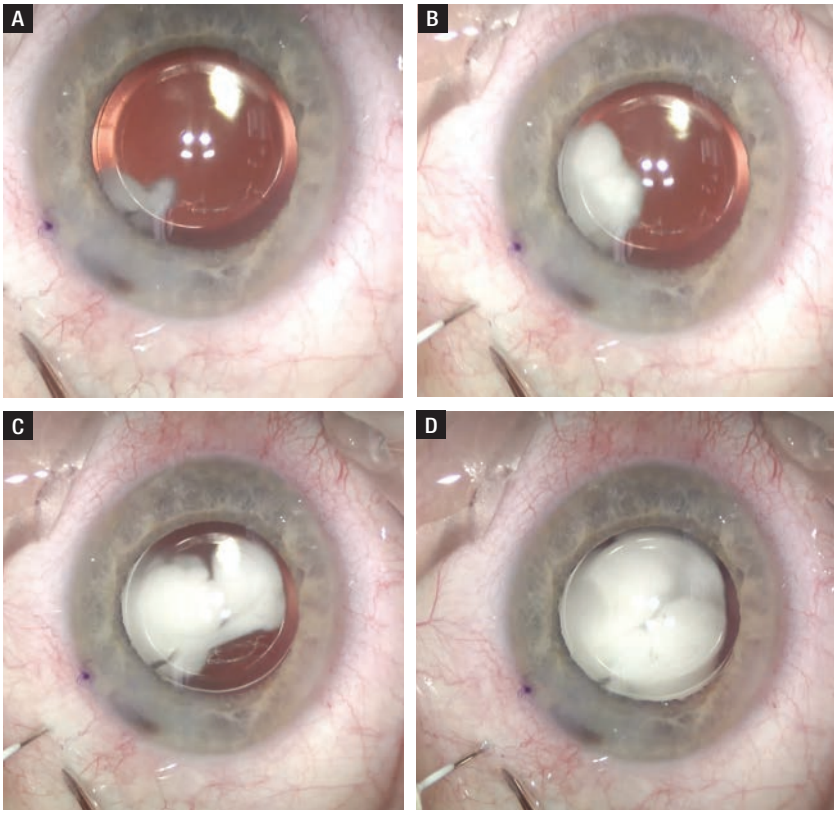

Fig. 2. Here, this time lapse shows an intravitreal injection of triamcinolone and moxifloxacin. The needle is routed posterior to the IOL and has a similar final destination to that of an anti-VEGF injection.

Clinicians should expect to see a white "snowglobe" appearance in the anterior vitreous hours after the procedure, and into the one-day post-op check *(Figure 1)*. On the one-day post-op, clinicians should expect to see visual acuity between 20/20 and 20/100, which should improve similarly to patients prescribed traditional postoperative drops. In our experience, corneal edema, if present, and anterior chamber inflammation both resolve much quicker with intracameral injections compared with a drop regimen. On dilated peripheral exam, the examiner will note a clumping, white material that generally rests in the inferior vitreous.

To see a narrated video of this procedure, visit www.reviewofoptometry.com, or scan this QR code.

Three Cs

The advantages of an intracameral injection over traditional drops can be summarized by the three Cs: compliance, cost and complications.

Compliance. Correctly and repeatedly instilling postoperative eye drops is a known difficulty for patients. A recent study shows only two-thirds of patients feel confident in instilling eye drops, and 42% believed they never missed their eye

on instillation.[7] More concerning, the same study's objective data shows less than 8% of patients properly instilled the drops per the study protocol, with the most common error being contamination of the bottle.[7]

Compliance with medications is almost always improved with decreased dosing. Traditional post-op drop regimens often require three bottles and up to 12 drops per day: an antibiotic four times daily for one week, an NSAID once daily for one month, and a steroid four times daily for one week, then tapered to twice daily for one week. Such protocols can be challenging for many patients, especially those with physical limitations such as Parkinson's disease and rheumatoid arthritis. If the practitioner substitutes this with a single injection of Tri-Moxi plus a once-daily NSAID, the patient's drop burden decreases by roughly 70 drops per eye.

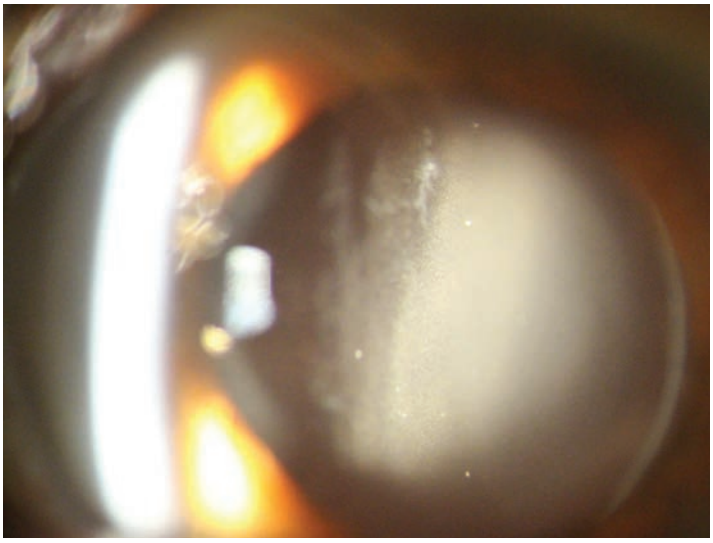

Fig. 3. Evidence of the white debris (medication) in the anterior vitreous one day after cataract surgery.

Cost. The traditional post-op regimen of topical antibiotic, steroid and NSAID can pose a significant cost burden to patients, even those with health insurance. An intracameral injection eliminates the need for the patient to purchase both a topical steroid and antibiotic.

According to one drug price comparison website, the price for one bottle of Vigamox (moxifloxacin HCl ophthalmic solution, Alcon) averages $160, while the same site has a mean price of about $60 for prednisolone acetate 1%.[8,9] Tri-Moxi, with an average price of $25 (no cost to patient), potentially saves a patient more than $400 for both eyes. With 1.82 million cataract surgeries performed in the Medicare population alone in 2011, the cost in postoperative antibiotics alone to Medicare would have been $136 million in 2011—and that's just using the conservative cost estimate of moxifloxacin at $75/bottle.

Currently, no billing code exists for post-surgical injections, so they aren't reimbursable by insurance. In our practice, we absorb the cost of Tri-Moxi for our patients because we see the immense value to both our patients and practice. Intravitreal/tranzonular medications have significant potential not only to lower the cost of medications for our patients, but also for private insurers and Medicare. We have found the small cost of Tri-Moxi to our organization is offset by less medication call backs from pharmacies, less prior authorizations side effect concerns.

Complications. While patients may benefit from dropless cataract surgery, use of injections after cataract surgery may help surgeons just as much, if not more, by minimizing the risk of postoperative complications, especially endophthalmitis.

Research has found endophthalmitis rates in the range of 0.04% to 0.2% after cataract surgery, and these numbers continue to decrease following a spike in reported cases during the late 1990s and early 2000s.[10] In 2006, the European Society of Cataract and Refractive Surgery published a landmark study comparing endophthalmitis rates post-cataract surgery in patients using drops versus intracameral antibiotics.[11] This study shows a fivefold decrease in endophthalmitis rates when intracameral cefuroxime is injected at the conclusion of surgery.[11]

One of the largest comparative studies on topical drops vs. injections, which looked at the result of more than16,000 cataract surgeries, concluded that intracameral cefuroxime with or without topical antibiotics decreased endophthalmitis rates 22-fold.[5]

The Risks

Although intravitreal and transzonular injections have moved the needle up in our practice, doing what is safest for our patients' eyes is paramount, and practitioners must be aware of the risks associated with their use.

A recent article reviewed outcomes with transzonular injections vs. topical post-op medications and provides important data, though it contained a small number of patients and a larger case series is warranted.[12] This contralateral eye study randomized patients to either cataract surgery with drops

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in one eye or cataract surgery with transzonular Tri-Moxi-Vanc (triamcinolone 15mg + moxifloxacin 1mg + vancomycin 10mg/mL, Imprimis) in the other eye. Here's what it concluded about the postoperative risks of injectable medications:

Cystoid macular edema. No statistically significant difference in macular thickness at one week and one month post-op existed between the study groups.[12]

Clinician's take: We have not observed increased CME rates using intravitreal injections, and we prescribe NSAIDs once daily for one month in routine cases.

IOP spikes. The study did not show statistical significance in IOP spikes or IOP readings between the two groups.[12]

Clinician's take: We have studied intravitreal injections vs. drops for IOP spikes in patients who undergo cataract surgery and the insertion of a trabecular microbypass stent (Glaukos). Our data, presented at the American Society of Cataract and Refractive Surgery (ASCRS) meeting in 2016, showed no statistically significant difference in IOP between the two groups.[12]

Post-op pain. The study found a statistically significant difference in pain post-surgery.[12] In this cohort, all patients had cell, flare or both in the anterior chamber on day one post-op, but this inflammation resolved over time near equally with patients who used the traditional post-op drop regimen.

Clinician's take: If corneal swelling is present, it resolves quicker with intravitreal medication, and the absence of anterior chamber cell resolves quicker with our injection patients.

Hemorrhagic occlusive retinal vasculitis (HORV). While not studied in the contralateral eye study, this is a severe ischemic hemorrhaging of retinal blood vessels research shows can happen after cataract surgery or intracameral injections. This rare but devastating pathology can cause bilateral no light perception vision. A retrospective case series report by the American Academy of Ophthalmology linked all cases of HORV to intraocular vancomycin.[13]

Clinician's take: We no longer use intravitreal vancomycin, and the popularity of intracameral moxifloxacin continues to grow. We've managed hundreds of cataract patients with post-op intravitreal injections, and have not had one case of HORV.

Retinal detachment. Anecdotally, clinicians were concerned of increased retinal tears and detachments with intracameral meds.

Clinician's take: Unfortunately, retinal tears and detachments are an inherent risk with any cataract surgery, but in our practice we have not seen an uptick in these complications with the near total adoption of intravitreal Tri-Moxi.

Conclusion

Intravitreal and transzonular medications are improving patient compliance, reducing pharmacologic cost and increasing the post-op drop convenience—and these all positively affect patient satisfaction. In one study, patients show a statistically significant preference for injectable medications over postoperative drops.[14] Optometrists are referring more patients for cataract surgery, and the option of offering fewer drops continues to gain steam with patients.[14] According to the 2014 ASCRS Endophthalmitis Survey, 47% of American surgeons are using some type of intracameral injection after cataract surgery, and this number is up 20% from the data reported in 2007.[15]

In our practice, a common question from patients at the conclusion of a cataract evaluation is, "Can I do that injection so I don't have to use so many drops?" The drop-a-day cataract surgical option with intravitreal post-op medications has elevated both our patients' experience and their satisfaction. ■

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Going Old School: A Refresher on Retinoscopy

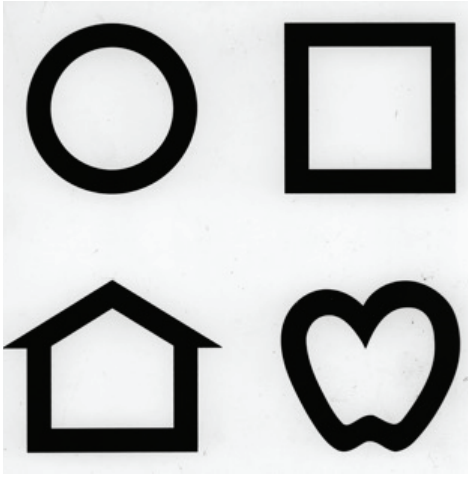
Refracting without an autorefractor or a phoropter has its advantages for some patients. Brush up on your skills with these case examples.

By Mark E. Wilkinson, OD, and Khadija S. Shahid, OD, MPH

Retinoscopy began to be used on a regular basis approximately 100 years ago.[1] In the past decade or so, for many practitioners an autorefractor has replaced the use of the retinoscope to objectively determine a patient's refractive error. However, there are still a variety of patients who are better served by an evaluation using something other than an autorefractor or a phoropter.

Patients who cannot or should not be refracted using an autorefractor or phoropter include those who are physically unable to sit up to an autorefractor or sit behind a phoropter.

Additionally, some individuals have pathology that prevents them from getting an accurate autorefraction or prevents an accurate refraction with a phoropter. Examples of individuals who are better served by retinoscopy, a trial frame refraction or both include those who are physically incapable of raising their head due to spinal degeneration, patients with nystagmus or reduced central vision who need to use eccentric fixation to achieve their best acuity, babies, some patients with special needs as well as patients in wheelchairs and some individuals who have to use sign language or a communication device.



Lea symbols are a must for patients unable to read a traditional visual acuity chart.

Practitioners will be at a loss on how to accurately determine whether these individuals can benefit from a spectacle correction or a spectacle correction change—unless they are savvy with retinoscopy and trial frame refraction.

Where to Begin

As practitioners decide between using a phoropter vs. a trial frame, they should consider some of the disadvantages of a phoropter:

- The light reflex for retinoscopy is poorer in a phoropter compared with loose lenses.
- Using multiple lenses in the phoropter decreases light transmission.
- Eccentric viewing by the patient is difficult to impossible with a phoropter.
- Patient with nystagmus struggle to use their null point when looking through a phoropter.
- It is difficult to use just noticeable difference (JND) refraction techniques with a phoropter.

For patients with ocular diseases or physical limitations, using a trial frame will make subjective refractions not only possible, but accurate. The primary advantage of trial frames is that refractions are easier and more natural than with a phoropter for patients who are difficult to refract or those who are visually impaired.

Just Noticeable Difference Refraction Techniques

Clinicians must remember that standard refraction techniques are employed when performing a trial frame refraction on an individual with normal sight. JND refraction techniques are used for those who are visually impaired.[2] When in doubt, use the trial frame.

Just noticeable difference is the amount of lens power needed to elicit an appreciable change in clarity or blur. The poorer the visual acuity, the larger the JND.

JND power is determined by taking the denominator of the 20ft Snellen acuity and dividing it by 100. For example, for a patient with 20/200 acuity: 200/100 = 2.00D. Therefore, you would start your subjective refraction with +/-1.00D.

When practitioners use JND refraction techniques, they are better able to do an accurate refraction at any acuity level. JND refracting techniques apply to both sphere and cylinder corrections. Most importantly, JND elicits reliable answers from the patient.

JND Spherical Power Refraction Determination

A patient presents with uncorrected VA of 20/400. There are no old spectacles and the practitioner is unable to do retinoscopy due to significant band keratopathy. To determine JND sphere power, divide 400/100 = 4.00D, and start with +/-2.00D.

If the patient states +2.00D is clearer, put +4.00D in the trial frame. With +4.00D in the trial frame, again asked the patient to compare +2.00D/-2.00D. If the patient still prefers +2.00D, replace the +4.00D lens in the trial frame with a +8.00D lens. With +8.00D in the trial frame, again asked the patient to compare +2.00D/-2.00D. If the patient now prefers -2.00D, replace the +8.00D lens in the trial frame with a +6.00D lens. Check VA, which is now 20/200, making the JND lens +/-1.00. Now the practitioner can refine with +1.00D/-1.00D bracketing lenses. If the patient's acuity continues to improve, you will eventually fine tune with +0.50D/-0.50D.

JND Cylinder Power and Axis

Finding the best cylinder axis and power requires the same JND technique described above, now using a Jackson cross cylinder (JCC).

- For 20/50 or better vision, use a +/-0.25D JCC
- For 20/63 to 20/100, use a +/-0.50D JCC
- For 20/125 to 20/160, use a +/-0.75D JCC
- For 20/200 or less, use a +/-1.00D JCC

For patients who cannot read, Lea paddles can help clinicians test visual acuity.

JND Cylinder Power and Axis

After establishing the patient's spherical power as describe above, VA is 20/200; 200/100 = 2.00D, so start with a +/-1.00 JCC.

With the JCC oriented for power at 90/180 degrees, ask the patient which is clearer. If the patient states that -1.00D axis 180 is clearer, put a -2.00D axis 180-cylinder lens in the trial frame. Remember to adjust the sphere power by adding +1.00D to maintain the circle of least confusion on the retina. Now, with a -2.00D axis 180-cylinder lens in the trial frame, again ask the patient to compare +1.00D to -1.00D axis 180. If the patient still prefers -1.00D axis 180, replace the -2.00D axis 180-cylinder lens in the trial frame with a -4.00D axis 180-cylinder lens.

With the -4.00D axis 180-cylinder lens in the trial frame, add an additional +1.00D sphere in the trial frame. Again ask the patient to compare +1.00D to -1.00D axis 180. If the patient now prefers +1.00D axis 180, replace the -4.00D axis 180-cylinder lens in the trial frame with a -3.00D axis 180-cylinder lens and adjust the sphere power by adding -0.50D sphere power. If the patient's VA has improved to 20/100, refine with a +0.50D/-0.50D JCC. Once the cylinder power is determined, repeat the process to determine the cylinder axis using the standard technique of 15 degree interval change in axis until reversal, then five to seven degree interval change in axis if the patient's VA allows for this discrimination.[3] Remember to recheck the cylinder power with any significant change in the cylinder axis.

A closer look at several cases will help illustrate the benefits of refracting with a retinoscope and trial frame. These cases will also highlight nonconventional VA testing techniques used to aid the subjective refraction.

Case 1: Significant Pathology

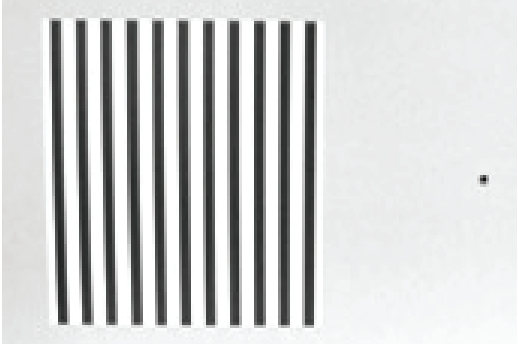
An 81-year-old Ethiopian who is unable to read and does not speak English presents with a history of reduced vision. Through an interpreter, we learn that he has not been able to see for any near vision tasks for nine to 10 years. He states he was told he had macular degeneration and cataracts and was informed to not consider cataract surgery due to his macular degeneration because it would limit his potential for improved vision.

Because this patient is unable to read, VA testing was accomplished via matching with Lea symbols. Uncorrected acuity measured 1/100 (20/2000) OD, 0.5/1000 (20/4000) OS and 1/100 (20/2000) OU. Near acuity measured 30M @ 1' (1M is equivalent in size to newsprint).

The patient states he would like better walking around vision, which could not be enhanced with a spectacle correction. Additionally, there was no improvement possible with his near vision using optical or electronic magnification devices. In addition to the cataracts and macular degeneration, the clinical examination revealed climatic droplet keratopathy and pseudoexfoliation with normal pressures.

In an effort to enhance this patient's overall visual functioning and quality of life, cataract surgery was performed with the placement of an IOL followed by penetrating keratoplasty to address the climatic droplet keratopathy for the right eye. Uncorrected VA improved in the right eye following these procedures to 1/80 (20/1600).

The next step was to refract the patient for best-corrected vision.



When matching visual acuity is not possible to quantify entrance visual acuity, clinicians can use Teller cards.

A trial frame set is a must when working with patients who don't do well with a phoropter.

Because the patient could not fixate for an accurate autorefraction assessment, we used retinoscopy to find he was plano -5.00 x 083 with resultant acuity of 2/63 (20/630) and 6.4M @ 6". This was a 3x improvement in distance vision compared with his pre-cataract surgery vision. No improvement was found in near vision with any powered reading correction. However, the patient was very happy with the improved walking around vision he had when he received his single vision spectacles, which was his primary goal.

Case 2: Low Vision

A 48-year-old non-verbal male presented for evaluation with a history of autism and high myopia, as well as a retinal detachment in his right eye 20 years ago. He had cataract surgery with an IOL 15 years ago, which dislocated 10 years later, leaving him functionally aphakic in his right eye. The left eye is anophthalmic and the patient has no spectacles. He was referred for an evaluation by his care facility to determine current level of visual abilities for programming and appropriate expectations.

Because matching VA was not possible to quantify entrance visual acuity, we used Teller preferential viewing acuity. Teller acuity found the patient able to preferentially view down to the 0.86 cycles per centimeter card at a 50cm working distance. This is equivalent to a Snellen acuity of 20/800. With this level of acuity, he was not able to view the fixation target in the autorefractor. Retinoscopy found +6.75D sphere. This improved acuity by Teller to 1.6 cycles per centimeter (~20/400). The patient was prescribed a single vision Rx to see if it would help him with his activities of daily living, including his ability to see sign language and with social interactions. A month after the patient

recieved his new glasses, his care facility reported that he was wear them daily. They noted he was more visually aware of his environment and now no longer needed to use hand-over-hand sign language.

Case 3: Post-surgery

A 58-year-old male was referred by his cornea specialist for a refraction following a penetrating corneal transplant. Severely irregular astigmatism was noted by keratometry and autorefraction results were inconsistent. Uncorrected acuity was 10/160-2. Retinoscopy found +3.50 -9.75 x 162. Manifest refraction found +3.75 - 10.25 x 161, which improved distance vision to 20/50-2+1. Based on his excellent visual potential with high cylinder, his remaining interrupted sutures were removed. Follow-up refractive assessment one month later found +0.50D sphere with resultant acuity of 20/40-2+2.

Clinicians should use standard refraction techniques when performing a trial frame refraction on an patient with normal sight.

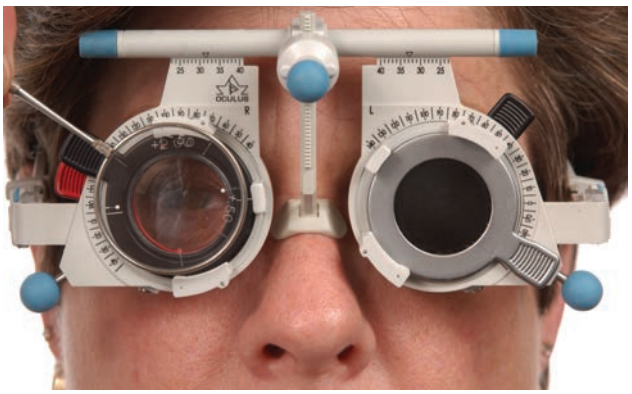
Case 4: Physical Limitations

A 67-year-old female with severe scoliosis presents with a chief complaint of an inability to read with her recently prescribed bifocals. She is wheelchair bound and cannot raise her head without assistance due to her spinal curve. Corrected visual acuity was 20/25 OD and 20/20 OS. Near acuity through her current spectacle correction was 2.5M continuous text print at 18". Because this patient could only look down, it was clear she was not able to use the bifocal portion of her spectacles. With her reading correction in a trial frame, she was able to easily read 0.5M continuous text print and the newspaper. Given her physical limitations, she was switched from a bifocal to two single vision Rxs, one for distance and one for near. With a single vision reading Rx, she was able to resume reading with ease.

Case 5: Mental Limitations

A 76-year-old female with Alzheimer's disease presented for evaluation following the loss of her spectacles at her care facility. Initially, it was felt that because of her lower functioning secondary to the Alzheimer's disease, she didn't need spectacles. However, it was noted that, functionally, she was doing much worse with ambulation since losing her spectacles. Additionally, she was having more difficulty seeing to eat.

These observations prompted her referral for an evaluation to see if there was a beneficial prescription. Throughout her visit, she was inattentive, singing children's songs and did not respond to any form of subjective or objective visual acuity testing. Autorefraction was not possible because the patient would not hold steady for Rx determination. With this in mind, retinoscopy was performed to determine a tentative Rx. Retinoscopy was done a second time over this Rx in a trial frame to refine sphere, cylinder and axis. The final prescribed Rx was for significant hyperopia and astigmatism and, of course, presbyopia. Follow up found her back to baseline for ambulation and the ability to see when eating with the new spectacles.



Using a Jackson cross cylinder, clinicians can find a patient's best cylinder axis and power during trial framing.

Case 6: Congenital Complications

A 22-year-old male with a history of reduced vision secondary to oculocutaneous albinism type II with resultant nystagmus presented with a complaint of distance and near vision blur. He had refused spectacles in the past, but recently noted poor vision with work-related tasks. For example, he complained of difficulty identifying distant objects, and he stated he was unable to read for more than a few minutes without significant asthenopia. Uncorrected distance VAs were 20/250 OD, 20/125-2 OS and 20/125-1 OU. At near, he was able to read

0.63M continuous text print at 4". This patient had a significant anomalous head position with left head tilt and chin-down position. Both the phoropter and autorefraction were challenging secondary to increased nystagmus when he had to position his head in primary position. Trial frame refraction found +1.00 -2.50 x 035 OD with vision improved to 20/125 and +1.00 -2.00 x105 with vision improved to 20/100 OS. Using a 4.00D add, the patient could read 0.50M continuous text for extended periods of time, comfortably and efficiently.

For individuals with nystagmus, remember to fog the non-tested eye by adding plus to decrease vision by two to three lines in that eye. This is a better alternative to occlusion because covering one eye can significantly increase nystagmus amplitude, frequency or both. Additionally, research shows correcting refractive error, especially when significant, can be one of the most effective treatments for vision impairment secondary to nystagmus.[4] A careful and accurate refraction has the potential to improve the visual function of patients with both acquired and congenital nystagmus more than other therapeutic interventions, including surgery, medication and prism.[4]

For patients who present with conditions that make determining refractive error by autorefraction or with a phoropter challenging, clinicians can turn to tried-and-true retinoscopy. Thus, maintaining your retinoscopy and trial frame refraction skills can make the difference in your ability to help all of your patients see their best.

Use trial frame refraction when visual acuity is 20/50 or worse, or if regular refraction techniques are not successful. For many patients with vision problems, the only intervention needed to enhance their visual functioning is the prescription of appropriate spectacles. ■

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Identify and Manage Retinal Vascular Tumors

This rare presentation can lead to a larger systemic diagnosis, if you know what to look for.

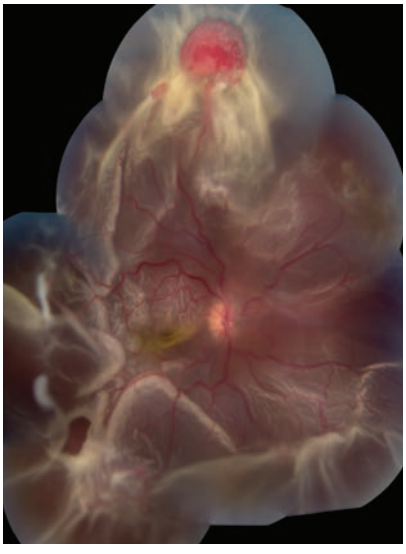
By Elliott Brafman, OD, Leslie Small, OD, and Mark T. Dunbar, OD

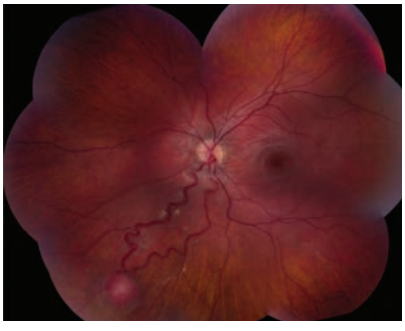
Ocular vascular tumors are rare, and you may have few opportunities to diagnose one. However, when present, they may be the initial finding of one or more serious systemic deficits, which will require you to mobilize and perhaps even lead a multidisciplinary team to provide collaborative patient care.

In the posterior segment of the eye, tumors are classified by their location: retinal or choroidal. Retinal vascular tumors are categorized into one of four main types; *retinal capillary hemangiomas*, *retinal vasoproliferative tumors*, *cavernous hemangiomas* and *racemose hemangiomatosis* (Wyburn-Mason syndrome). Choroidal vascular tumors are categorized as either circumscribed or diffuse.

This article, last in our four-part miniseries on the retinal vasculature, reviews how to clinically distinguish these tumors and discusses their associations.

To read the other installments in this special series, visit www.reviewofoptometry.com.



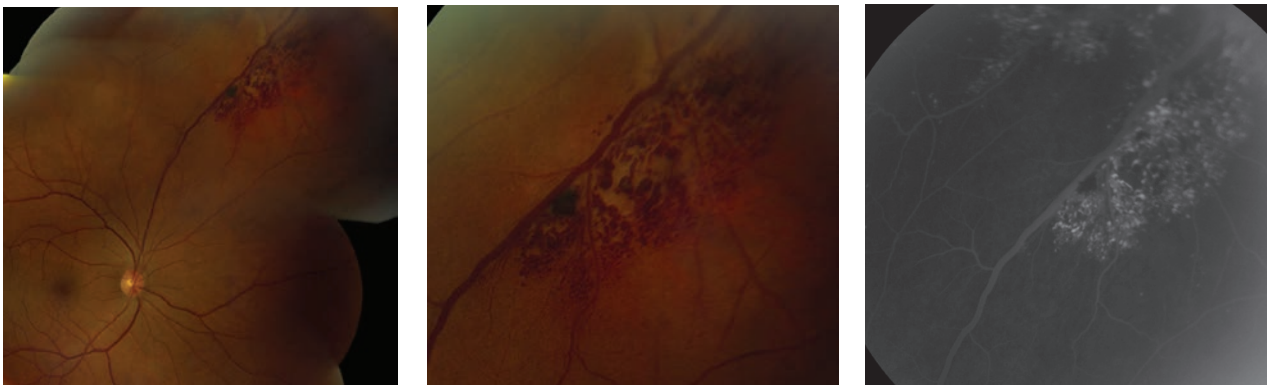


At left, extensive circumferential retinal detachment is secondary to a retinal capillary hemagioma in Von Hippel-Lindau disease. Above, peripheral retinal capillary hemangioma is located inferior-nasally with dilated, tortuous vasculature in Von Hippel-Lindau disease.

Retinal Capillary Hemangiomas

Retinal capillary hemangiomas (RCH) are highly vascularized tumors that typically present as a red, round, circumscribed mass, more commonly in the midperiphery (85%) or less commonly juxtapapillary (15%).[1,2] When peripheral, they are often in the superotemporal or inferotemporal quadrants and can easily be found by following their feeder vessel extending from the optic nerve.[1] The majority of RCHs are solitary (66%) but they can also present as multiple lesions (33%).[2-4] They demonstrate no sex, racial or laterality predilection.[1]

While RCHs are most commonly endophytic in presentation and portray the classic round mass in the inner retina, they may also be exophytic or sessile, varying



This cavernous hemangioma demonstrates the classic "cluster of grapes" distribution. At right, the corresponding fluorescein angiography demonstrates the persistent hyperfluorescence in the late phase.

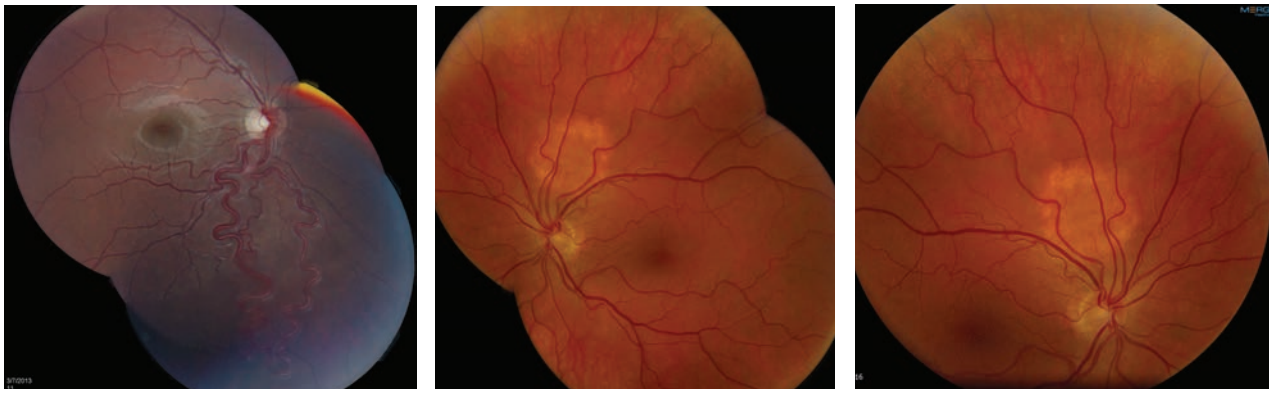
in appearance.[3,4] Juxtapapillary exophytic lesions are sometimes misdiagnosed as optic disc edema as they may blur the disc margin.[4] Most RCHs are asymptomatic and are, therefore, commonly diagnosed incidentally between the ages of one and 40 years, with a mean age of 25.[1-3] However, their secondary effects may elicit symptoms. Secondary complications include intraretinal and subretinal exudation in the vicinity of the hemangioma, uncommonly a macular star (a circular distribution of exudates around the macula) and rarely retinal or vitreous hemorrhage (less than 3%).[3] Advanced cases may present with tractional or exudative retinal detachment.[1,3,4] Symptoms in these instances may include loss of vision, flashes, floaters, photopsias and metamorphopsias.[1-3]

Although patients can have RCHs alone, RCHs are also associated with Von Hippel-Lindau (VHL) disease.[3,4] RCHs are the most common, and often earliest, presentation of VHL.[3-5] Twenty to 58% of patients with RCHs have VHL disease as the underlying cause.[3] VHL is an inherited autosomal dominant syndrome that has age-dependent penetrance.[3,5] The onset is classically between the first to fourth decade of life.[3] VHL manifests in a range of benign and malignant tumors, including hemangiomas of the retina and central nervous system (CNS), renal cell carcinoma, pheochromocytomas, pancreatic carcinoma and cysts in the liver, kidneys and pancreas.[2,5]

VHL is caused by a mutation in a tumor suppressor gene called VHL gene, resulting in the upregulation of angiogenic factors, including vascular endothelial growth factor (VEGF). One study found an increased incidence of retinal neovascularization similar to that found in diabetic retinopathy.[6] VHL gene may also present with additional rare retinal manifestations that include atypical retinal vascular hamartomas and twin blood vessels, paired artery and veins that are separated by less than one venual width for the extent of one disc diameter.[3,7,8] Associated CNS hemangiomas may involve the visual pathway, resulting in optic nerve compression and chiasmal syndrome.[3]

The average life expectancy of patients with VHL is less than 50 years, with morbidity most commonly due to renal cell carcinoma.[1,3,5] Early detection of affected gene carriers can play a critical role in improved prognosis. Today, commercially available genetic testing for VHL yields exceptionally high detection rates (99%). Therefore, this testing is indicated in all patients with RCHs.[2] Primary eye care providers may have a vital role in the early screening and diagnosis of VHL in relatives of those already diagnosed.[5,9]

While RCH is largely a clinical diagnosis, ancillary testing can help monitor regression, growth or the production of intraretinal or subretinal fluid.[1,2] Due to the vascular nature of RCHs, fluorescein angiography (FA) tends to be the most revealing test.[1,4] On FA, the tumor displays fine capillary filling that rapidly becomes homogenous and demonstrates late leakage.[3,4] While OCT does not contribute to the diagnosis of RCHs, it can help monitor success of treatment, such as tracking resolution of subretinal fluid.[2] On A-scan ultrasonography, the initial spike is followed by high internal reflectivity due to blood flow, and on B-scan there is a well-demarcated retinal lesion without choroidal involvement.[3] While thin orbital sections on magnetic resonance imaging (MRI) can detect retinal capillary hemangiomas greater than 2mm thick, MRI is most beneficial for detecting associated CNS hemangiomas using



At left, an engorged artery and vein in an arterial-venous malformation extends from the optic disc to the inferior peripheral retina in a patient with Wyburn-Mason syndrome. At middle and right are choroidal hemangiomas.

gadolinium enhancement.[3] In addition, enhanced CT scanning can detect other organ involvement.[3]

Treatment for RCH is dependent on size, location and associated findings such as exudation (25%) or retinal detachment (16%).[1,3,4] If the tumor is less than 500µm without exudation or subretinal fluid, the lesion may simply be observed.[1,2,4] However, if the patient's visual acuity becomes affected or threatened, anti-VEGF injections, laser photocoagulation, cryotherapy, photodynamic therapy (PDT), radiotherapy or other vitreoretinal procedures may be indicated.[1,2,4]

Similarly, visual prognosis is dependent on number, size, location and degree of exudation or traction.[2] Severe visual impairment in affected eyes is more likely with increased age, juxtapapillary location of lesion and increased number of peripheral lesions.[1] Overall, there is a guarded prognosis with more than 25% of eyes developing permanent vision loss and 20% having a visual acuity worse than 20/100 in at least one eye.[1,2]

Racemose Hemangiomatosis

This congenital form of arterial-venous malformation (AVM) classically presents as dilated tortuous retinal vessels spanning from the optic disc to the periphery.[2] The clinical appearance is categorized into three groups:[1,2,7]

- *Group I* has an abnormal capillary network
- *Group II* lacks any capillary network
- *Group III* presents with dilated tortuous vessels that make it difficult to differentiate arteries and veins.[1,2,10]

Distinguishing features of AVMs include the absence of one or more feeder vessels and the absence of exudation or subretinal fluid.[1] Patients are typically asymptomatic and the malformations are usually incidental findings.[1] Some visual disturbances may occur depending on the size and location of the retinal AVM. Additionally, vessel occlusions may result due to turbulent blood flow, damage to vessel walls and thrombosis formation.[10] Retinal vessel occlusions can cause direct vision loss themselves or secondary vision loss from macular edema or if neovascular glaucoma (NVG) develops.[2,10]

Retinal AVMs can be associated with the rare phakomatosis, Wyburn-Mason syndrome (WMS), also known as congenital unilateral retinocephalic vascular malformation syndrome.[10] Phakomatoses, more descriptively known as neuro-oculocutaneous syndromes, are a group of conditions that result in hamartomas, which are benign tumors that arise from normally existing tissue. WMS, however, is not commonly characterized by cutaneous involvement as with other phakomatoses.[2]

WMS is a congenital, non-hereditary sporadic disorder with no sex or ethnic predilection.[1,2] The syndrome may involve other tissues including skin, bones, kidneys, muscles, GI and the brain, resulting in a variety of systemic symptoms.[2] Cerebral vascular changes in the brainstem and subarachnoid hemorrhage may elicit nystagmus or affect ocular motility, causing diplopia.[10] Uncommonly, there may be optic disc atrophy or edema and visual field defects due to cerebral AVMs affecting the visual pathway.[10] Unilateral proptosis is indicative of orbital involvement and is secondary to AVMs involving the orbit or intracranial vessels.[10]

These patients may also present with dilated conjunctival vessels, similar to the presentation of a cavernous-carotid fistula.[10] The most critical systemic manifestation occurs when intracranial AVMs hemorrhage, which may result in mortality.[2] While the incidence of

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co-existing intracranial AVMs with retinal AVMs is 30%, only 8% of patients with intracranial AVMs have retinal AVMs.[2] The current recommendation is for all patients with retinal AVMs to undergo brain and orbital neuroimaging to rule out cerebral AVMs.[10]

Due to their distinct clinical appearance, retinal AVMs are a clinical diagnosis; however, for confirmation and staging of the condition, fluorescein angiography demonstrates the anomalous arteriovenous communication and the lack or presence of capillaries.[2] Of note, there will be no leakage on FA and, on OCT, there will be no subretinal fluid.[1] In group III retinal AVMs, FA cannot distinguish arteries from veins. For detecting associated intracranial AVMs, MRI is currently the imaging of choice to determine the size and extent of the AVM as well as its impact on surrounding neurogical tissue. On the other hand, conventional angiography is still the standard for characterizing the AVM due to its ability to visualize the angio-architecture of the lesion.[2,11,12]

Retinal AVMs are typically not amenable to treatment.[1] Treatment is, therefore, targeted towards resulting comorbidities such as retinal ischemia and NVG.[1,2] Clinicians can consider several treatment strategies, including anti-VEGF injection, panretinal photocoagulation, glaucoma surgery or glaucoma medication.[1,2,10] The prognosis is guarded, as there is high risk for functional vision loss due to retinal ischemia or NVG.[1,2,10] Unlike brain AVMs, retinal AVMs rarely hemorrhage.[2]

Cluster of Grapes

Retina cavernous hemangionas are rare benign, thin-walled intraretinal vascular tumors.[7,13] They manifest as multiple venous aneurysms along one or more veins, and less often appear on the optic nerve head.[13] From their configuration and purple color, their appearance is commonly described as a "cluster" or "bunch of grapes in the retina."[9] These lesions tend to be unilateral and solitary, and usually are non-progressive.[13] Their sizes are variable, and the larger ones are at a higher risk of leading to complications such as vitreous hemorrhages, preretinal fibrosis and traction, hyphema and secondary glaucoma.[13]

Retinal cavernous hemangiomas are usually isolated; however, they can be autosomal dominant, which can have associated central nervous system, hepatic and cutaneous vascular anomalies. In these instances, they are considered phakomatoses.[14-16] Investigators estimate that about 5% of retinal cavernous hemangiomas have associated cerebral cavernous malformations.[14] There is a strong expression of cerebral cavernous malformation genes in both the brain and the retina, which code for proteins important in endothelial cell structure and function.[14]

Fluorescein angiography is beneficial in clinching the diagnosis. Early hypofluorescence is seen in the vascular filling phase with persistent hyperfluorescence in the recirculation phase due to the slow-flow nature of the lesions.[13,16] Stagnant erythrocytes layer inferiorly in the saccules (hypofluorescent), leaving the plasma superiorly within each aneurysm (hyperfluorescent fluorescein capping).[13-16] In addition, due to an intact endothelium, there is no extravascular leakage, which is a key differentiator from retinal telangiectasias.[13-16]

These lesions possess a good visual prognosis.[17] Testing should be done to rule out similarly presenting lesions, including capillary hemangiomas, Coats' disease and Leber's miliary aneurysms.[14] If there are recurrent vitreous hemorrhages, particularly from larger lesions, possible treatments include focal photocoagulation, cryotherapy, vitrectomy or diathermy in an effort to sclerose leaky tumor vessels.[17] With treatment, however, there is an increased risk of vitreous hemorrhage as well as secondary tractional membrane and retinal detachment.[17]

Tomato-Ketchup Fundus

Choroidal hemangionas are rare hamartomas that are highly vascular, yet benign in nature.[1,18] They are composed of vascular channels lined with endothelium.[1] Despite their intrinsic vascularity, they lack any feeder vessels but can have nearby dilated choroidal vasculature.[1,19] More than 90% of the time they are found in Caucasians, but do not have a sex predilection.[18,19] They range in shape from round to oval; in color, from orange-red to pink to yellow to amelanotic; and are variable in size.[1,18,19] They are typically unilateral solitary lesions that are non-proliferative; if they do enlarge, it is not due to cell proliferation but rather from venous congestion.[18,19] Choroidal hemangiomas are separated into two categories: circumscribed and diffuse.

Circumscribed choroidal hemangiomas, also known as discrete choroidal hemangiomas, represent about 50% of cases.[11] While possibly congenital, these typically are not discovered until adulthood, since the symptoms are rare. If they are not congenital they arise later in life, between

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the third and sixth decades.[1,18-20] Symptoms include blurred vision from a hyperopic shift, and metamorphopsia (if in the macula), photopsia and visual field defects secondary to serous retinal detachments and subsequent RPE and outer retinal degenerative changes.[1,18,19] These tumors are mainly located posterior to the equator. They may often be found in the peripapillary region and adjacent to the macula.[1,18,20]

Despite their location, these lesions can often be missed due to indistinct margins and color that blends into the surrounding choroid.[1,20] Specific features will help with lesion identification, such as the appearance of a brown ring around the tumor margin secondary to tumor compression of the surrounding choroid, and yellow-white surface foci secondary to lipofuscin deposition from macrophage activity.[19,20] Typically, these lesions average 7mm in diameter with a broad range of 3mm to 18mm, and 3mm in thickness with a range of 1mm to 7mm.[1,20]

Diffuse choroidal hemangiomas represent the other 50% of choroidal hemangiomas. Unlike circumscribed tumors, these have a syndromic association with Sturge-Weber.[18] They are present at birth and involve a large portion of the choroid.[1,20] They appear as a diffuse, orange choroidal thickening, creating the "tomato-ketchup fundus."[1] It is estimated that about 50% of Sturge-Weber syndrome patients have choroidal hemangiomas, which are mostly ipsilateral to their characteristic birthmark known as a "port-wine stain" or facial nevus flammeus.[1,20]

Fluorescein angiography may not be entirely revealing in these cases.[18] ICG readily highlights the intrinsic vascular pattern within 30 seconds of injection (much earlier compared with other choroidal tumors).[1,19] In the later stages, there is a "wash out" phenomenon, which represents loss of dye from the tumor.[1] On B-scan there is a characteristic dome-shaped, acoustically solid lesion with regular structure and smooth contour. Upon A-scan, there is a high internal reflectivity between 50% and 100% from the multiple vascular channels but an absence of spontaneous vascular movements.[1,18,19]

Choroidal hemangiomas are typically observed as long as the patient is asymptomatic and the tumor location is not vision-threatening.[20] However, given the similarity in appearance to amelanotic choroidal melanomas, aforementioned ancillary testing should be done to confirm the diagnosis.[20]

If symptoms do arise, treatment should be initiated to induce tumor atrophy and regression of subretinal fluid.[1] Treatments include photocoagulation, photodynamic therapy, radiotherapy and transpupillary thermotherapy (TTT).[1] While photocoagulation has been a staple, it is often ineffective at inducing tumor atrophy and has a 40% chance of failing to irradiate subretinal fluid.[1,18] Both radiotherapy and TTT have demonstrated effectivness at tumor and fluid regression, but radiation increases the risk of optic neuropathy and radiation retinopathy with the added complications of cystoid macular edema, preretinal fibrosis formation and retinal vein occlusion.[1,18] ■

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Orbital Mucormycosis On the Attack

Not all cellulitis cases are what they seem. Know when you may be facing this rare but ravaging pathogen before it's too late.

By Nicholas Karbach and Andrew Gurwood, OD

Chances are, you're never going to see a patient with mucormycosis. The rare fungal infection's incidence is approximately 1.7 cases per million inhabitants per year.[1] Still, you can never say never. We saw a case at The Eye Institute at Salus University that nearly evaded us. The propensity of the disease to mimic more common orbital conditions, such as bacterial orbital cellulitis, can result in a delayed diagnosis, which can significantly worsen the outcome. And that worsened outcome can mean some serious consequences for the patient, such as losing vision, the eye itself or even their life.

This article will guide you to a better understanding of this condition and discuss the tools necessary to recognize when an atypical orbital cellulitis includes underlying risk factors of mucormycosis.

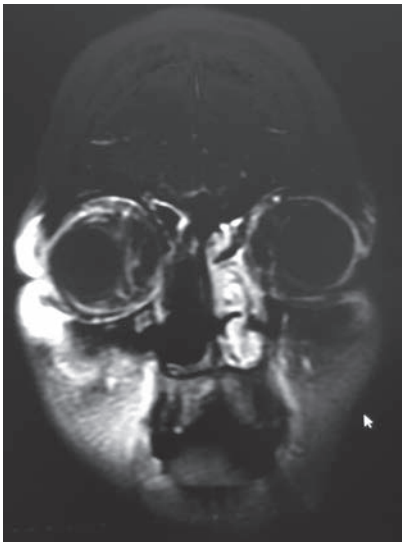
Case Report

A 22-year-old female was referred from the emergency department with a chief complaint of vision loss and eyelid swelling of two days' duration. The patient reported she was also suffering from mental status changes presumed secondary to chronic substance abuse (heroin injection and inhalation). She reported no vision, but pain, in her right eye and a headache. She had no history of previous ocular injuries or trauma but reported having insulin-dependent diabetes mellitus, for which she was properly medicated, with both metformin and insulin, but noncompliant. She denied having allergies of any kind.

Her best-corrected visual acuities were no light perception OD and 20/50 OS. Her left eye exhibited normal motilities while the right eye exhibited complete ophthalmoplegia. She had an obvious right afferent pupil defect. Using biomicroscopy, we found an injected, boggy and edematous conjunctiva in her eye.

Her intraocular pressures (IOPs) were 24mm Hg OD and 13mm Hg OS. The dilated fundus examination demonstrated an ophthalmic artery occlusion with papillitis in her right eye and normal structures with no posterior pathology in the left.

Additional testing at the patient's bedside included retropulsion of the globe to determine the level of orbital congestion, forced duction testing to establish mechanical resistance to eye movement, Luedde exophthalmometry to record the amount of proptosis and first aid for retinal artery occlusion, which consisted of lowering IOP to increase perfusion along with aggressive ocular pulsed pressure therapy. Additionally, we ordered neuroimaging studies in conjunction



This coronal MRI shows our 22-year-old patient's orbital inflammation status, post nasal sinus tissue resection.

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Ultimately, we diagnosed this patient with complete ophthalmoplegia secondary to orbital swelling (orbital cellulitis) induced by mucormycosis infection of the right ethmoid sinus with concurrent ophthalmic artery occlusion.

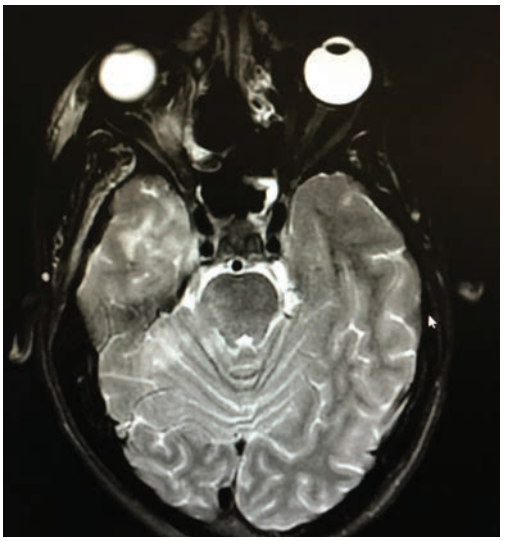
The Basics

Mucormycosis is a rare, fulminant fungal infection caused by a mold of the order Mucorales.[2-5] It is most frequently found as an infection of the nasal and maxillary sinuses that spreads to adjacent structures and causes a condition known as rhino-orbital-cerebral mucormycosis (ROCM).[2-4] Though rare, ROCM is the third most common fungal infection behind *Candida* and *Aspergillus*, with its incidence continuing to rise most likely due to increased diagnostic accuracy.[4]

Researchers have identified several significant risk factors for onset of ROCM, including: uncontrolled diabetes, immunosuppression, excess serum iron levels and ketoacidosis.[2,3,6-9] Often, some form of breakdown of the physical barriers of the immune system are present in mucormycosis patients; for example burns, surgical wounds or compromise of the mucocutaneous barrier.[9] Uncontrolled diabetes is documented as the most prominent risk factor, accounting for 36% of total infections.[10] These risk factors, caused by increased blood glucose and iron levels along with neutropenia, create a microenvironment that is favorable for the growth of mucorales.[8]

Disease Proliferation

Mucormycosis grows and spreads via two primary mechanisms: soft tissue invasion and angioinvasion.[2,3,6,11] These two processes create a devastating effect on local tissue as the mucor invades the lumen of blood vessels and adheres to the internal elastic lamina.[2,3,6,11] Its broad, nonseptate hyphae block the lumen and interrupt perfusion, causing thrombosis, infarction and rapid tissue necrosis accelerated by various fungal proteases, lipases and mycotoxins.[2,3,6,11] Histopathological examination of specimens and neuroimaging recently established a third mechanism, perineural invasion.[11] It is thought that this mechanism accounts for the spread of infection that can occur further away from the primary site of infection, such as through the trigeminal ganglion.[11] The most common site of mucormycosis infection is in the sinuses, accounting for 39% of all mucormycosis infections (while pulmonary and cutaneous infections account for 24% and 19%, respectively).[2,11] In ROCM, the infection typically starts in the nasal or maxillary sinus and spreads to the sphenoid or ethmoid sinus.



Our patient's axial MRI shows residual orbital congestion and inflammation post extensive sinus tissue resection.

From there, it can invade the orbit, either through the ethmoid foramina or nasolacrimal duct or via dehiscence of the lamina papyracea.[2,3,11] Upon invasion, the fungus can affect the medial rectus muscle, optic nerve and orbital apex structures, causing ocular discomfort and acute conjunctival chemosis and eventually proptosis, ophthalmoplegia and diplopia.[2-4,6,7,12,13] Due to the angioinvasive properties of the fungus, it can also invade the central retinal artery or ophthalmic artery, possibly leading to a central retinal artery occlusion (CRAO) or ophthalmic artery occlusions (OAO).[3]

Once inside the orbit, the infection can also spread to the brain via the orbital apex or orbital veins, which drain into the cavernous sinus and can cause cavernous sinus thrombosis, carotid cavernous sinus fistula, local multiple occlusive strokes or carotid artery thrombosis.[7] Unfortunately, once brain involvement occurs, the death of the patient is almost invariably the result.[13]

Identification

Initial suspicion of fungal infection may be aroused via a case of orbital cellulitis that does not respond to conventional antimicrobial therapy or the presence of orbital apex syndrome (proptosis in the case of ophthalmoplegia) with associated sinus involvement.[4] Roughly 20% to 40% of patients show signs of a necrotic eschar if the initial infection involves the external nasal or maxillary sinuses.[2] Presence of major risk factors, such as diabetes and immunosuppression, should raise the index of suspicion considerably, though it should be known that mucormycosis can also occur in the absence of underlying conditions.[10]

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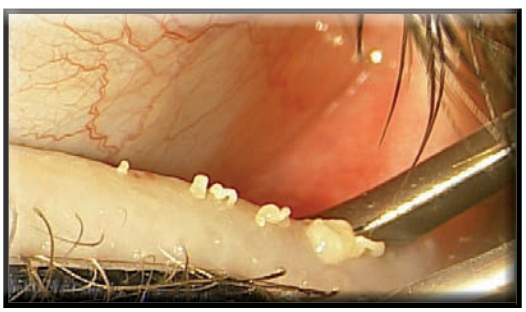

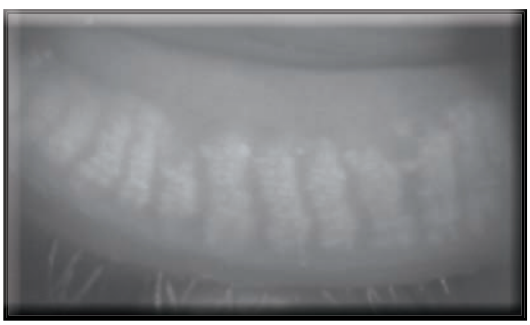

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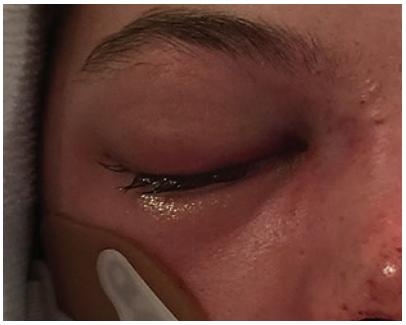

Our patient displays external orbital chemosis.

Neuroimaging via magnetic resonance imaging (MRI) or computed axial tomography (CT) with contrast can aid in diagnosis by revealing an invasion of the sinuses; however, definitive diagnosis is only achieved via histopathological study.[2-4,6,11] Positive analysis typically reveals large, nonseptate hyphae branching at right angles.[2,3,6,11]

The differential diagnosis for mucormycosis should include other infectious etiologies, such as bacterial orbital cellulitis, MRSA orbital cellulitis and orbital aspergillosis, as well as certain inflammatory and neoplastic conditions such as orbital pseudotumor, mucocele invasion, thyroid eye disease and orbital or lacrimal gland tumors, any of which may present acutely. Most of these can be ruled out with case history or clinical examination, but some may depend on histopathological diagnosis for differentiation.[15]

Neuroimaging is also helpful to determine the extent of invasion and to provide clues as to the nature of the lesion.[15,16] CT scanning, though sensitive to determining the extent of invasion and the presence of abscesses, usually gives nonspecific information regarding the type and nature of the lesion. Both T1 or T2 weighted MRI images and diffusion-weighted imaging are more helpful in showing the nature of orbital lesions.[16,17]

Finding the Culprit

Bacterial infections comprise the vast majority of orbital cellulitis in adults with 60% to 80% arising from spread of paranasal sinusitis.[18-20] The most common causative organisms are *Staphylococcus aureus, Streptococcus* and *Haemophilus influenzae* type B.[19] A lack of response to conventional therapy warrants further work-up including orbital biopsy to rule out fungal or MRSA infections, inflammatory masses or neoplasms.[19] Local rates of MRSA infections and antibiotic response profiles should be obtained in consultation with infectious disease. MRSA orbital cellulitis has an atypical presentation, and frequently lacks any of upper respiratory illness, paranasal sinusitis or eyelid trauma which typically precede bacterial infections of the orbit.[21] Aspergillosis, like other infectious etiologies, can invade along a rhino-orbital-cerebral pathway but usually lacks the aggressive clinical course of mucormycosis.[22,23]

Non-infectious conditions that can mimic mucormycosis include orbital pseudotumor, mucocele invasion, thyroid eye disease and even neoplasms and vascular masses (capillary hemangioma, orbital varix) though these are typically ruled out in the case of an acute presentation.[15] Orbital pseudotumor is an idiopathic inflammatory disorder of the orbit and can present with acute pain, ptosis, proptosis, ophthalmoplegia and vision loss.[24] It is typically found in the absence of sinusitis and is sometimes associated with chronic systemic inflammation, such as autoimmune disease.[24] Though neuroimaging is helpful, an orbital biopsy is needed to confirm or rule out this diagnosis.[24]

Mucocele, although slow growing in nature, can have an acute onset of symptoms with the patient exhibiting exophthalmos, ptosis, diplopia and pain. However, 60% to 89% of mucoceles arise from the frontal sinuses, an unusual site for mucor involvement, according to investigators.[25] Thyroid eye disease can also present with pain, diplopia, chemosis, and pressure sensation behind the eyes. However, it typically is bilateral and causes eyelid retraction in contradistinction to ptosis.[15,26] Lacrimal gland neoplasms also present with ptosis, exophthalmos, and diplopia but can be ruled out with imaging and biopsy.[15]

Treating the Patient

Timely diagnosis is critical due to the rapid progression and potentially fatal complications of the disease. Though some variation in the pace of progression exists, a one-week window between orbital involvement in which the condition can be diagnosed and CNS involvement in which it proves fatal is fairly typical.[2,13]

Conventional treatments consist of a combination of IV amphotericin B (3mg/kg to 5mg/kg administered daily) and surgical resection of the infected tissues.[3-7,10] Different combinations of these approaches can be used, including repeated debridement of necrotic tissue, irrigation of resected tissue with amphotericin B and application of amphotericin B-soaked gauze to areas of surgical removal.[2,7,14] Note: renal function should be monitored in patients taking amphotericin B due to its nephrotoxicity; for this reason, liposomal amphotericin B is sometimes used in place as a first-line treatment due to its lower incidence of nephrotoxicity.[2,4]

Hyperbaric oxygen therapy has also been incorporated to treat mucormycosis due to the fungicidal and angiogenic effects of oxygen.[2,4] Oral posaconazole can be used as



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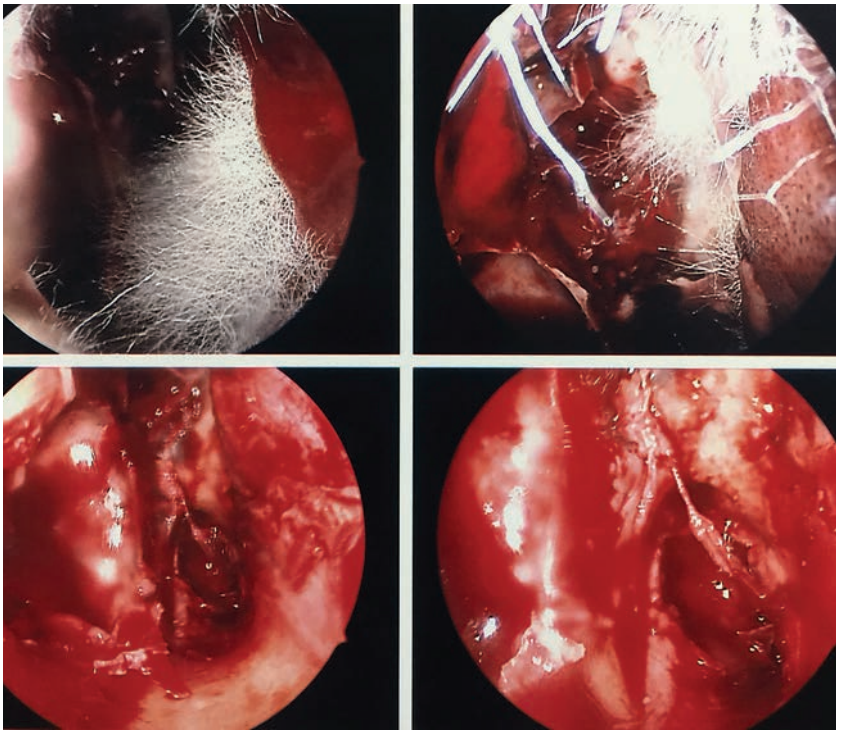

These nasal sinus endoscopy images show *mucorales hyphae*.

an alternative treatment if nephrotoxicity or amphotericin B resistance develops.[2,4] Lastly, due to its multisystem involvement, management of ROCM should occur in a tertiary interdisciplinary setting with practitioners from intensive care; ear, nose and throat; ophthalmology; infectious disease; internal medicine and neurosurgery all playing a role in patient management.[2]

Prognosis is directly related to how early diagnosis is made and treatment is initiated. Patients can expect full recovery of ocular motility and lid function within 10 months with successful treatment and eradication of the infection; however, visual loss due to CRAO/OAO or optic nerve compression is permanent.[4] Additionally, even with a prompt diagnosis and aggressive treatment, mortality rates for the condition remain between 30% to 35%.[2,10]

Mucormycosis can mimic common bacterial infections of the sinuses and orbit until its advanced stages—a dangerous trait, as resulting delays in diagnosis and treatment can mean catastrophic outcomes.

Orbital cellulitis that does not improve with antimicrobial therapy or orbital apex syndrome with sinus involvement should undergo investigation for mucormycosis, especially when the patient exhibits primary risk factors including uncontrolled diabetes, ketoacidosis or immunosuppression.[2,4,6]

Despite heroic measures of early diagnosis and proper treatment, our patient ultimately required an orbital exteneration and eventually a hemiface-ectomy. Currently, the patient remains in a complicated long-term recovery situation. ■

Nicholas Karbach is an OD candidate at the of Pennsylvania College of Optometry at Salus University. He will begin his primary care/ocular disease residency at The Eye Institute in July. His interests include primary care optometry and neuro-ophthalmic disease.

Dr. Gurwood is a professor at Salus University.

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From Alpha to Omega: How Fatty Acids Fight Dry Eye

A better understanding of the mechanisms of action can help you prescribe these supplements—and educate patients. **By Julie Poteet, OD**

Omega fatty acid supplements are some of the most widely used nonvitamin, nonmineral products on the market today. According to one study, 7.8% of adults and 1.1% of children ages four to 17—nearly 20 million people in all— have used a fish oil supplement in the previous 30 days.[1,2] Researchers defined the supplement as either a fish oil, omega-3, docosahexaenoic acid (DHA) or eicosapentaenoic acid (EPA) fatty acid.

Research shows fish oil supplementation can reduce blood pressure and inflammation, increase brain blood flow and provide structural strength for neurons.[3-7] As the compounds are a natural and expected component of our bodies and diets, they have a wide margin of safety.[8] Although humans evolved consuming a diet with roughly equal amounts omega-3 and omega-6 essential fatty acids, in today's western diet the ratio of omega-6 to omega-3 fatty acids ranges from approximately 20-30:1, and the amounts of saturated and trans fatty acids, all of which are inflammatory, have increased sharply.[8]

Because omega-3 fatty acids decrease inflammation and promote health, they can provide significant benefits for patients with dry eye—a disease inflammatory in nature.[9] A closer look at omega fatty acids will help you better understand their use in dry eye and give you the tools necessary to educate your patients on their benefits.

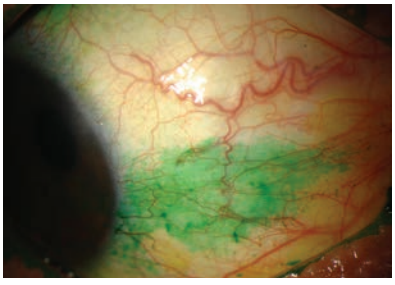

Photo: Michelle Hessen, OD

Conjunctival staining with lissamine green in a dry eye patient.

Inflammation Modulation

Omega-3 and omega-6 fatty acids, both dietary polyunsaturated fatty acids (PUFAs), are essential nutrients—they cannot be synthesized in the body and must be obtained from the diet. Omega-3s are incorporated into cell membranes in all tissues of the body.[13] Diet-induced changes in the polyunsaturated fatty acid composition of a cell membrane have an impact on the cell's function, partly because these fatty acids represent a reservoir of molecules that perform important signaling or communication roles within and between cells.[13] Further, omega-3s compete with omega-6s for incorporation into all cell membranes, which depends on dietary intake.[10,11]

Arguably, arachidonic acid (ARA), an omega-6, is most important. When cells are activated by external stimuli, ARA is released from cell membranes and transformed into proinflammatory cellular mediators such as thromboxanes, prostaglandins and leukotrienes.[12] Arachidonic acid metabolism is the target of nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and celecoxib, and leukotriene antagonists (e.g., montelukast). Dietary omega-3s displace ARA from membranes and compete with it for the enzymes that catalyze the biosynthesis of thromboxanes, prostaglandins and leukotrienes.[9] This is considered to be one of the main mechanisms of their anti-inflammatory effects.[13] Thus, omega-3s limit cells such as monocytes, neutrophils and eosinophils from synthesizing the arachidonic acid-derived mediators of inflammation.[13]

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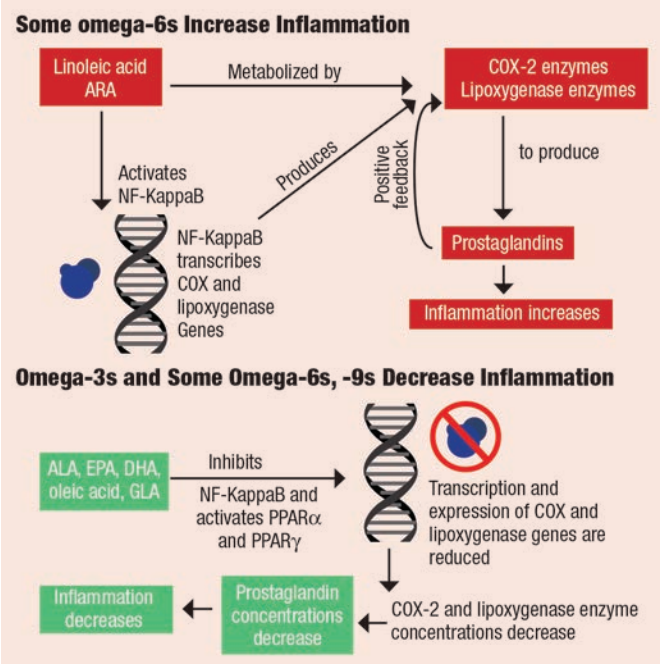
In addition, enriching membranes with omega-3s can modulate cellular signaling events, membrane protein function and gene expression.[13] Research shows alpha-linolenic acid (ALA) dramatically reduces prostaglandin formation, probably by downregulating the transcription of genes coding for proinflammatory mediators such as c-reactive protein and IL-6.[9,14] EPA exerts much of its anti-inflammatory benefit by suppressing NF-KappaB activation, a protein complex that controls transcription and cytokine production, which reduces the elaboration of proinflammatory mediators.[15]

DHA and EPA are the precursors to docosatrienes and resolvins, which downregulate proinflammatory IL-1 gene expression, inhibit TNFα and reduce neutrophil entry to sites of inflammation.[9,16] EPA and DHA can be synthesized from ALA (and are more potent), but this process does not reliably or efficiently occur in humans.[13,17] Dietary oils rich in ALA, although having beneficial effects of their own, usually do not reproduce the biological activity associated with dietary fish oils.[13]



In omega-6s, transcription factor NF-KappaB (blue) is activated by linoleic acid and ARA. NF-KappaB binds to the genes' promoter regions that code for cyclooxygenase and lipoxygenase, responsible for forming prostaglandins. Formation of prostaglandins activates the inflammatory cascade. In omega-3s and some omega-6s and -9s, fatty acids ALA, EPA, DHA, oleic acid and GLA NF-KappaB activity and activate peroxisome proliferator-activated receptors (PPARα and PPARγ) in the nucleus of cells. This decreases concentrations of COX-2 and lipoxygenase proteins, which decreases the concentration of prostaglandins and, ultimately, decreases inflammation.

GLA and DGLA

Not all omega-6s are proinflammatory. Gamma-linolenic acid (GLA) is known as the most powerful health-promoting omega-6, and is found in evening primrose oil, borage seed oil, hemp oil and black currant seed oil.[9] GLA is elongated to form the biologically activated dihomo-γ-linolenic acid (DGLA), which goes on to either form the anti-inflammatory prostaglandin E1 or it forms anti-inflammatory ARA.[9]

Research shows GLA can be beneficial in dry eye therapy, but it should not be given without EPA/DHA. Only one enzymatic step is necessary to convert the anti-inflammatory DGLA to proinflammatory ARA, and EPA competes against DGLA to ARA conversion, ensuring DGLA forms prostaglandin E1.[9,27]

Fatty Acids & Dry Eye

Since supplementing with healthy fatty acids causes competition and displacement of proinflammatory fatty acids from the cell membranes, a strong case has been made for proper fatty acid supplementation in inflammatory diseases such as dry eye. Fatty acids affect gene expression by multiple complex mechanisms.[9] In an animal model, resolvins and protectins reverse corneal epithelial damage associated with dry eye, increase tear flow, promote healthy epithelia and decrease cyclooxygenase-2 (COX-2) expression and the infiltration of macrophages.[18]

Research also shows omega-3s inhibit the inflammatory properties established in moderate to severe dry eye disease such as: increased T-cell infiltration, increased tear inflammatory cytokines, increased ocular surface human leukocyte antigen (HLA)-DR and increased intercellular adhesion molecule expression.[19-21]

Investigators find the anti-inflammatory effect of omega-3s on dry eye disease is similar to that of cyclosporine. In a 2011 study, dry eye participants were given a combination of omega-3s and the omega-6 GLA, which was shown to improve tear film break-up time (TBUT) and relieve patient symptoms; however, the addition of topical cyclosporine did not convey any statistically significant improvement in TBUT beyond that achieved by the supplement alone.[22]

In a recent study, researchers studied the relationship between lipid profiles in human tears and dry eye symptoms and signs, and found that both omega-3 and omega-6 lipid pathways are activated in the

human tear film.[23] Results show the ratio of omega-6 to omega-3 tear lipids is elevated in dry eye patients in proportion to the degree of tear film dysfunction and corneal staining.[23] They also found a significant correlation between the tear film omega-6 to omega-3 ratio and tear volume (Schirmer score), as well as tear stability and corneal staining.[23] These findings are consistent with prior studies that show how changes in tear volume correlate with dietary omega-3 intake, and improvements of dry eye signs occur with omega-3 supplementation.[24-26]

Prescribing Essentials

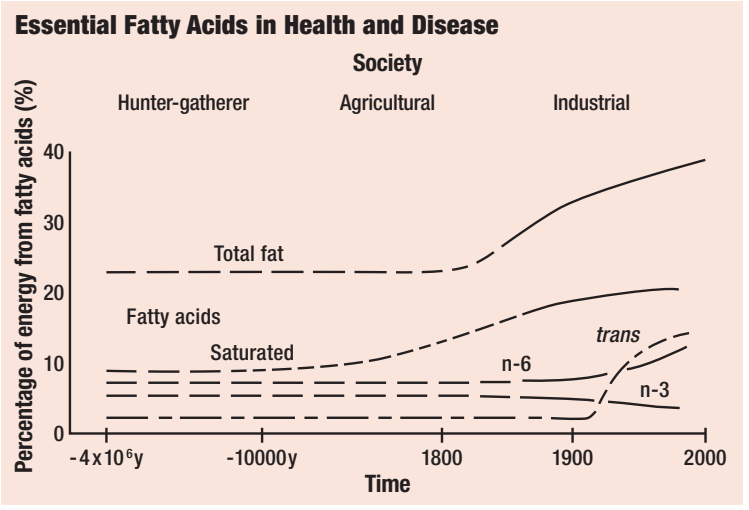
While data show the benefits of fatty acids—for instance, meta-analyses show omega-3s improve TBUT and Schirmer scores—no consensus exists on the dose, composition, length of treatment or form used of omega-3s or omega-6s for dry eye therapy.[23,27-29] Consider the following when deciding on a treatment:

Not all studies are the same. Clinicians should take into consideration the results and methodologies of well-designed studies. For instance, many studies use olive oil—oleic acid—as a placebo to study the effects of omega-3 therapy. Olive oil is not a biologically inert substance, as it provides anti-inflammatory benefits itself.[30] While some study results look promising, the methodology may influence expectations.

Triglyceride vs. ethyl ester omega-3s. Omega-3s occur naturally in the triglyceride (Tg) form. For purification and concentration, manufacturers create fatty acid ethyl esters (EEs) by replacing the glycerol backbone of a Tg and substituting it with ethanol. The resulting EEs allow manufacturers to perform fractional distillation to concentrate the long-chain fatty acids at lower temperatures. Most commercially available over-the-counter fatty acid supplements, as well as the prescription-only Lovaza (omega-3-acid ethyl esters, GlaxoSmithKline), are in the EE form. Research shows pancreatic lipase enzymes break down EE to a lesser extent than Tg, explaining the poorer absorption of EE forms.[31] Studies also show that if the EE form is taken with food, particularly a meal high in fat, its absorption increases significantly.[32] Finally, studies show differences in the stability of EE vs. Tg forms, with

EE breaking down and oxidizing more quickly than the Tg form.[33,34]

Some manufacturers convert the EE form back to the natural Tg form using food-grade enzymes. This process, called glycerolysis, removes the ethanol molecule and re-esterifies the EPA and DHA fatty acids to a glycerol backbone, forming a re-esterified Tg. This step adds to the cost, but it creates a better tolerated and more easily absorbed product.[31]



Saturated and trans fat intake has increased substantially in recent history.

Dosage. The ideal omega-6 to omega-3 ratio in the diet should be less than 4:1.[8] Since western diets have a much higher ratio, higher doses of omega-3 supplementation are usually safe. No consensus in the literature exists regarding the optimal dose for dry eye therapy. For adults with coronary disease, the American Heart Association (AHA) recommends a daily omega-3 fatty acid supplement of 1g EPA and DHA.[35] For adults with high cholesterol, the AHA recommends a daily supplementation of 2g to 4g of EPA and DHA.[35]

In a recent study, 105 participants were given either 2,240mg of re-esterified omega-3s daily or a placebo of safflower oil. The treatment group showed statistically significant improvement in tear osmolarity, omega-3 index levels, TBUT, Matrix metallopeptidase 9 (MMP-9) and ocular surface disease index (OSDI) symptom scores.[36] Based on the wide margin of safety of the fatty acids and dosages used in the literature, a reasonable starting dose is between 1,000mg and 2,250mg of a combination of EPA and DHA daily.[36-39]

Contraindications and precautions. The biological effects of omega-3 and omega-6 fatty acids may pose some risks to patients:

- *GI tract.* High doses of fish oil may cause loose stool, diarrhea, "fishy burps" and other gastrointestinal side effects, but these are more common with the more difficult to digest EE form.
- *Bleeding.* EPA and DHA therapeutic doses usually start at 1,000mg per day, but more than 3g per day may increase the risk of bleeding.[35] Therefore, take into context the patient's overall procoagulant vs. anticoagulant balance before prescribing. Ask patients if they are on blood thinners or taking supplements known to have an anticoagulant effect such as garlic, ginkgo or saw palmetto.
- *Immunosuppression.* While suppressing inflammatory responses with omega-3s benefits those with inflammatory or autoimmune diseases, it may decrease the immune system's ability to destroy pathogens.[40] One study comparing immune cell function *ex vivo* at baseline and after supplementing with omega-3s (mainly EPA and DHA) demonstrated immunosuppressive effects.[40] While it's unclear if these findings translate to impaired immune function *in vivo*, exercise caution should in individuals with compromised immune systems.

Label. The two most important numbers on a fatty acid supplement label are the actual omega-3 content, expressed in milligrams of EPA and DHA, and the number of pills in a serving size. Also, fatty acids are no different than any other poorly regulated dietary supplement category and are prone to inaccurate label claims and contamination. Several independent labs conduct periodic reviews of commercially available supplements to audit their omega-3 content and assess their purity.

Combination therapy. Since fatty acids compete for space in cell membranes, supplementation with a single fatty acid can exacerbate depletion of other fatty acids. For instance, supplementation with EPA and DHA reduces DGLA.[41] Therefore, GLA should also be supplemented in addition to EPA and DHA. An adequate dose of GLA would be 500mg per day. [9]

Research continues to highlight health benefits of fatty acid therapy's. While more research is needed to set specific dosing guidelines in dry eye, supplementing with reliable brands offers patients relief from dry eyes and other health benefits beyond the ocular surface. ■

Dr. Poteet is a certified nutrition specialist, fellow and vice president of the Ocular Nutrition Society. She has a special interest in autism research.

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PEER • REVIEWED • PRA • ARTICLE •

Slay Severe Dry Eye

When a patient's ocular surface disease is particularly nasty, ODs need to rethink the approach. **By Maria Walker, OD**

Dry eye disease (DED) is a common ocular surface condition with multiple and sometimes overlapping etiologies.[1-4] When the disease becomes severe, it can cause major disruptions in a patient's quality of life. Fortunately, they need look no further than their optometrist to bring these symptoms under control and get back to reading, driving and sleeping comfortably.

Even for patients with a severe case, the optometrist can take a lead role in identifying the underlying etiology and use a multifactorial approach to manage this disease state and its associated symptoms.

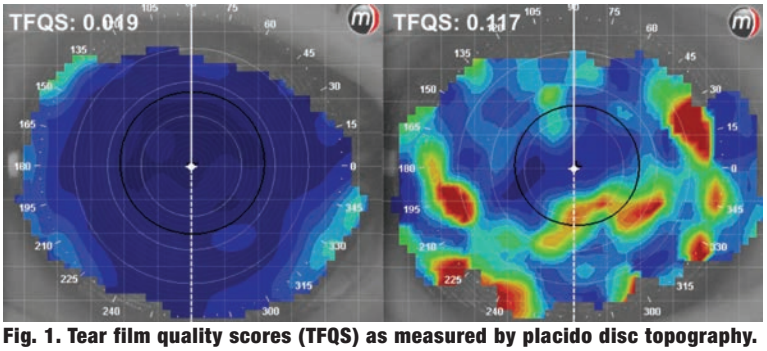


Fig. 1. Tear film quality scores (TFQS) as measured by placido disc topography. A low score (left) indicates better tear film quality than a higher score (right).

Identify the Etiology

Severe dry eye is often catalyzed by a primary etiology.[2] That primary etiology is frequently inflammatory based and is either systemic (e.g., Sjögren's, sarcoidosis, graft-vs.-host disease), or it is due to direct, localized inflammation of the patient's ocular surface structures.[2-9]

However, researchers are also studying the corneal nerve as a potential instigator of severe dry eye.[5-8] The densely innervated pain receptors in the cornea can respond to mechanical, chemical or temperature stimuli. These nociceptor terminals transmit signals along a complex neurological pathway, and the perception of pain can be:

(a) due to true exposure of the nerve endings;

(b) influenced by neural injury from chronic diseases that affect the density, size and tortuosity, and;

(c) a function of the nerves, or even representative of a central nervous system dysfunction.[10-14]

Although the role of these corneal nerves is complex, understanding it may help ODs manage DED.[10-14]

Diagnosis and Management

Severity of dry eye can be measured subjectively, through the assessment of patient comfort and visual quality, and also using diagnostic techniques such as tear break-up time (TBUT), surface staining and meibomian gland patency. One of the challenges of dry eye diagnostics is that the severity is often mismatched between the subjective and objective modes of evaluation.[9] While clinicians may see a disparity between objective and subjective tests, they only need one positive outcome to begin treating aggressively.

If the patient is reporting drastic reduction in their quality of life or, conversely, if their ocular surface appears to be at high risk for long-term damage, a diagnosis of severe dry eye is warranted.

Subjective severity is best quantified using a validated ocular surface disease survey, such as the Ocular Surface Disease Index (OSDI).[10] After subjective testing, the ocular surface can be evaluated to determine the objective severity and, ultimately, the most effective approach to managing the patient.

When objectively evaluating the severity of dry eye, clinicians should carefully evaluate and grade each component of the ocular surface system to help direct their treatment. But they must also identify and capitalize on any features of the system that may be able to promote rehabilitation of the ocular surface and reduce symptoms of the condition. Here are the ocular surface systems that may be affected in the disease, the various methods of diagnostic evaluation and the acute and chronic treatment strategies for each component.

Meibomian Glands

Diagnostics: Clinicians should evaluate the MG comprehensively, from the orifice to the glandular structure. The orifices are best evaluated without stain (for capping and for lid margin telengectasias) and then with lissamine green (for devitalization and keratinization of the MG opening). The integrity of the glands themselves can be imaged using quantitative meibomography, which also allows quantitative monitoring over time. Commercially available diagnostic systems can image the area of the gland using infrared light and allow clinicians to observe the length, width and tortuosity of the glands (*Figure 1*). The images are grades from one to six to measure the level of MG atrophy.

Treatment and management: The first step to maximize treatment efficacy in patients with an MG deficient component to their dry eye is to use a cotton-tipped applicator or spud to debride devitalized cells and coagulated meibum from the MG orifices, which research shows, improves symptoms and MG function.[11] For this technique, anesthesia isn't necessary, and clinicians should use gentle motion and pressure of the spud to avoid debridement of healthy underlying tissue.[11] Once the MG opening is visible, gland expression can be done manually or using advanced thermodynamic treatment systems (e.g., Lipiflow, TearScience; MiBoFlow, MiBo Medical). For patients whose glands have atrophied—which they often do in severe cases of dry eye—thermo-treatment is controversial.[12] However, some experts believe these systems can be helpful even when there is extensive gland atrophy. Regardless, it is important to consider the atrophic state of the glands when deciding on treatment and to understand that the success of these systems may be limited by the stage of meibomian gland atrophy. Clinicians should focus on appropriate supplementation of the lipid layer if they're unable to salvage the health of the glands (i.e., preservative-free artificial tears). When successful, repeated thermo-treatments every six to 12 months may be necessary to maintain meibum flow.[12]

For severe dry eye, low dose antibiotics and steroids are often necessary to acutely reduce inflammation and enhance potential recovery of the glands (*Table 1*). They are also often used to manage dryness. Lid hygiene and maintenance gland expression treatments should be recommended as needed; dietary supplementation (omega-3) may help reduce inflammation.[8]

Tear Film

Diagnostics: To evaluate the status of the tear film itself, apply sodium

Table 1. Severe Dry Eye Therapeutics

Medication	Mechanism of Action	Indication	Dosage	Trade Name
Doxycycline	Anti-inflammatory (reduce cytokines)[17] and antibiotic (inhibits RNA synthesis)	Reduces inflammation, reduces lid bacteria	100mg taken QD or BID for two to three months[18]	generic
Minocycline	Anti-inflammatory (reduce cytokines)[19] and antibiotic (inhibits RNA synthesis)	Reduces inflammation, reduces lid bacteria	50mg taken QD or BID for two to three months[20]	generic
Oral azithromycin	Anti-inflammatory (reduced prostaglandin production)[21] and antibiotic (inhibits RNA synthesis)	Reduces inflammation, reduces lid bacteria, increases MG secretions[22]	500mg QD for one day, 250mg QD for five days	Z-pak (Pfizer), generic
Topical azithromycin	Anti-inflammatory (reduced prostaglandin production)[21] and antibiotic (inhibits RNA synthesis)	Improves MG secretions and reduces inflammation	Variable (example: BID for two days, then qd for 12 days)[23]	Azasite (azithromycin, Merck)
Cyclosporine	Inhibits T-cell transcription[24]	Reduces inflammation	0.05% taken BID	Restasis (Allergan)
Lifitegrast	Inhibits T-cell migration[25]	Reduces inflammation	5% taken BID	Xiidra (Shire)
Omega-3	Increases lipid production[26]	Improves MG secretions[27] and reduces inflammation[28]	Variable: 1,000mg to 3,000mg daily	several
FML	Steroid, reduces prostaglandin production	Reduces inflammation	0.1% with variable dosing	generic
Loteprednol etabonate	Steroid, reduces prostaglandin production	Reduces inflammation	0.5%, 0.2% with variable dosing	Lotemax (0.5%, Bausch + Lomb), Alrex (0.2%, Bausch + Lomb), generic
Autologous serum	Presence of growth factors, neuropeptides, vitamins[29]	Rehabilitates and nourishes tissues	Approx. 20% serum, QD to BID	n/a

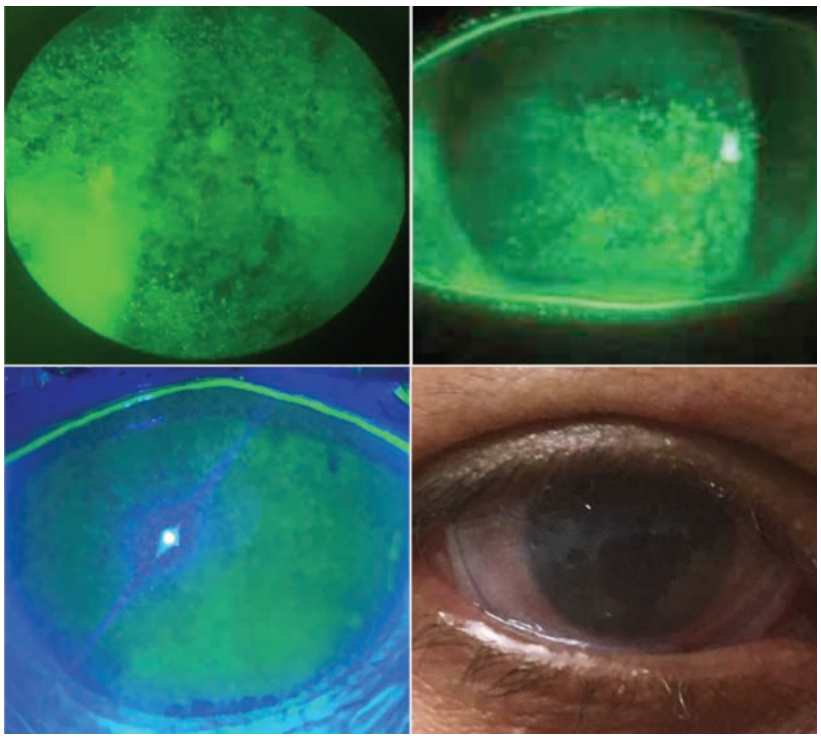
fluorescein (NaFl) to the ocular surface to measure the TBUT. Additionally, advancements in corneal topography instruments now allow clinicians to evaluate the tear film non-invasively (without the use of NaFl, which disrupts the natural tear layer), and obtain sensitive objective data about the tear film through programs that measure its quality using placido disc technology. In addition, other instruments, such as the LipiView, offer a quantitative measure of tear film, and, specifically, lipid layer thickness. If available, using these systems prior to NaFl application will allow for a sensitive evaluation of tear characteristics that can be objectively monitored.

Whether non-invasive testing is available or not, NaFl should be applied to further evaluate the tear stability on the ocular surface, and assess the efficiency and apposition of the puncta.

Osmolarity testing, which is commonly performed in research, has become an essential modern diagnostic technique. It is a strong tool to asses the severity of dry eye, and has been shown to be more predictive of severity of the disease than several other tests, including MG grading, OSDI index, TBUT and staining.[23] The published osmolarity threshold scores for grading severity of DED are variable, but an approximate threshold for severe dry eye is 320mOsm/mL.[24] While this testing can be quite helpful, it is important to consider the effect of reflex tearing (diluting the tears and artificially lowering the osmolarity), and also on the diurnal fluxuations in osmolarity, which vary on average by approximately 20mOsm/L in dry eye patients.[24] Measurement of inflammatory components in the tear film is also becoming a target for diagnostic technology.

Treatment and management: Replenishing the surface tear film with preservative-free artificial tears (PFAT) is always a part of dry eye treatment, continuous instillation of often indicated in severe dry eye patients. These not only act to supplement the natural tear film, but can also dilute the tear film and reduce the osmolarity, which can precipitate ocular surface damage.

Excessive tear drainage can be reduced by punctal occlusion with either plugs or cauterization. Remember to carefully evaluate the tears and ocular surface of a severe dry eye patient before recommending this treatment, and confirm the likelihood that the severe dry eye is exacerbated by excessive tear drainage. If the drainage system is not



Photos: Amber Gaume-Giannoni, OD and Sheila Morrison, OD

Fig. 2. These epithelial staining examples all merit the use of an amniotic membrane (bottom right).

contributory to the severe dryness, punctal occlusion may do more harm than good. For example, if excessive inflammatory mediators are seen on the ocular surface, it would be more effective to mitigate those mediators using therapeutic intervention than potentially create stagnation on the ocular surface.

The Corneal Epithelium and Conjunctiva

Diagnostics: Ocular surface staining with NaFl is the traditional approach to evaluate the integrity of the cornea and conjunctiva. NaFl will stain irregularities in tear film apposition, but lissamine green should also be used in dry eye patients to specifically stain dead or devitalized cells on the ocular surface. Additionally, confocal microscopy can help evaluate the anterior cornea at the cellular level. Although the most severe involvement of the cornea in dry eye patients occurs at the level of the epithelium, the evaluation of epithelium via confocal microscopy is less validated than the more commonly used stromal evaluation. While the confocal microscopy technique is relatively novel in clinical practice, it is becoming more readily used in research and some clinical settings.

Treatment and management: To regenerate the epithelium in patients with severe dry eye, autologous serum is often part of the treatment regimen. In the most severe cases, an amniotic membrane should be applied prior to autologous serum implementation to give the surface a strong boost of growth factors and nutrients prior to the chronic treatment plan (*Figure 2*). Patients with severe dry eye often have severe, consistent breakdown of the ocular surface, so chronic treatments such as autologous serum and

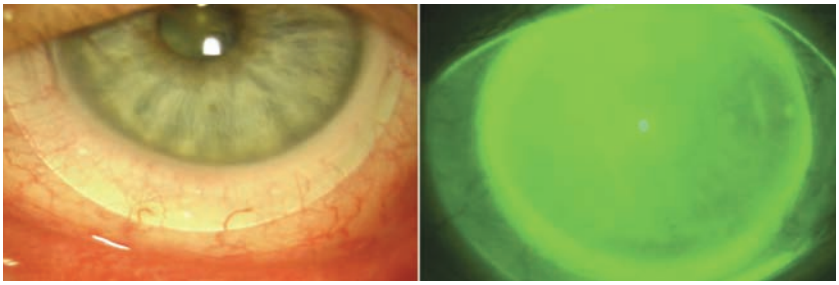


Fig. 3. At left, a scleral lens allows full coverage of the cornea and variable conjunctival coverage with a 100µm to 200µm tear layer between the lens and the corneal surface. At right, the same eye with NaFl instilled to visualize the tear layer.

anti-inflammatory drugs are necessary. Scleral contact lenses have also become strongly indicated to protect the surface from environmental insult, which prevents a cycle of tissue stress, or further tissue breakdown that worsens the disease.

Inflammatory Mediators in the Tear Film and Ocular Tissues

Diagnostics: Some patients will exhibit classic and strong signs of clinical inflammation (redness, edema), which can be evaluated using a slit lamp; however, clinicians do not generally test for subtle upregulation of inflammatory mediators that may contribute to the dry eye inflammatory state.

The most specific and clinic-friendly diagnostic test for measuring inflammation is the Inflammadry (Rapid Pathogen Screening), which measures the level of matrix metalloproteinase (MMP-9) in the tear film. Values greater than 40ng/ml will show a positive result (indicating increased inflammation).[25]

Treatment and management: In patients with severe dry eye, a therapeutic eyedrop that specifically targets inflammation should be prescribed, and many of the modern therapeutics for severe dry eye are centered on targeting inflammatory mediators on the ocular surface. Restasis (cyclosporine, Allergan) and Xiidra (lifitegrast, Shire) are two of the most common therapeutics, both developed to target T-cell activity and subsequent cytokine production. Cyclosporine interferes with T-cell transcription, and lifitegrast inhibits an integral protein complex (LFA-1/ICAM-1) that allows for T-cell migration.[19,26]

Autologous serum is also an appropriate adjunctive choice to target inflammation on the ocular surface, and there is potential for additional anti-inflammatory serum-derived treatments, as well as targeted mediation of inflammatory cytokine interleukin-1.[27-29]

Corneal Nerves

Diagnostics: Few advanced diagnostic techniques are available for evaluating the corneal nerves. Esthesiometry can quantify the level of pain, and help to locate any focal areas of extreme corneal sensitivity, and confocal microscopy is available to evaluate the cornea on a cellular level and allow visualization of the density, length and tortuosity of the corneal nerves.[30]

Treatment and management: Autologous serum drops contain several pro-epithelial and neural growth factors and are the strongest therapy recommended for corneal pain due to damage to the corneal nerve terminals.[29] If the corneal pain is associated with dysfunction at a higher cognitive level than the peripheral nerve terminals, further neural evaluation may be needed to elicit the exact cause.

Scleral Lenses

Scleral lens treatment for dry eye can be extremely beneficial for patients, the primary advantage being that they cover and protect the anterior ocular surface (*Figure 3*). However, it is important to remember that scleral lenses are not intended to be a standalone treatment for dry eye. They are devices indicated for severe dry eye patients, and should be used as part of the treatment regimen to heal and protect the ocular surface while the adjunctive therapies can treat the targeted molecular level.

Large-diameter scleral lenses (>18mm) may be the most appropriate to use when treating DED due to their more complete coverage of the ocular surface, especially if the clinical signs show damage that extends far beyond the limbus on the conjunctiva. One of the benefits of these lenses is that they offer the opportunity to deliver co-therapies to the cornea, since preservative-free medications can be put into the bowl of the scleral lens prior to application for prolonged apposition to the ocular surface. Sterile saline is the most common application solution used with scleral lenses, although individuals with DED may benefit from the use of a non-preserved artificial tear. In addition, these patients could be prescribed off-label formations, depending on what preservative-free systems works best for each individual disease state.

The following are two agents to consider using in an application solution for patients:

1. Autologous serum drops (one vial per lens, or split a vial between each).

2. Preservative-free artificial tears (to top off the autologous serum drop, or exclusively).

Patient Education

Optometrists should offer patients solutions for ocular surface disease that also promote the greatest quality of life and least inconvenience, as possible. While major advancements in the therapeutics and medical devices available for dry eye exist, a truly multifactorial approach to management of severe dry eye must be the standard of care. In severe cases, one of the most important aspects of treatment is education. The primary educational topics are:

1. The multifactorial and individualized treatment strategies, and the importance of careful compliance to each regimen.

2. The effect of exposure to elements (wind, dust, sun), and the effects of digital device fatigue and other external lifestyle influences.

3. The role of nutrition (e.g., omega-3 and omega-6 imbalance), hormones and overall systemic health (e.g., autoimmune diseases) in the success of their dry eye treatment.[31]

DED management has become an increasingly important role for the optometrist, especially as more information about the specific etiologies of the disease and the mediators involved come to light. As awareness grows, it is important to specifically identify etiologies and risk factors on a personalized level and customize our treatment plans. ■

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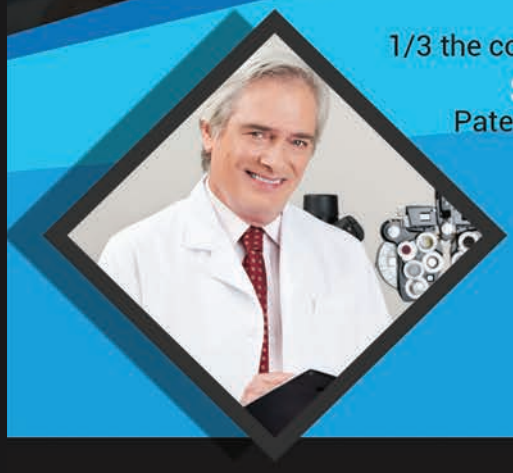

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18TH ANNUAL DRY EYE REPORT | TREATMENT

A Comprehensive Look at Dry Eye Therapy

With such a robust dry eye toolbox, knowing the best approach can be tricky. This run-down of options will help clarify the treatment strategies at your disposal.

By Justin Kwan, OD

As a multifaceted disease, dry eye demands an equally diverse treatment approach with every patient. Clinicians have myriad treatment avenues to explore until they find the best solution—even for those who present with two or more conditions at play. New diagnostic technology complements new treatment modalities, creating the opportunity to not only diagnose the condition better, but also treat it more effectively than ever before. Let's take a comprehensive look at the latest tools and treatments that have revolutionized dry eye management—and the mainstays that still play a crucial role.

Diagnosis is Key

The best way to start treating, even if it's first-line therapy, is to identify those patients who don't even know they have a problem. Revamping the health history form and including the SPEED or OSDI questionnaire can be the best time spent by the patient and becomes an educational tool. Patients may be surprised to find that their symptom scores land them in a moderate or severe classification. The case history then becomes more focused, and clinicians can dig deeper to understand the underlying cause of the patient's symptoms.

Meibomian gland dysfunction (MGD) may be the leading cause of dry eye disease (DED), and one study found 86% of patients with DED demonstrated signs of MGD.[1,2] But just as importantly, 42% of those patients had both MGD and aqueous deficient dry eye (ADDE).[1] Even more specifically, the MGD Workshop and other studies suggest meibomian gland obstruction may be the most common form of MGD and a major cause of evaporative dry eye.[3,4] Thus, a gentle press on the eyelid margin to evaluate the quality and expressibility of the meibum is vitally important during the initial dry eye workup.

Demodex is also a common cause of dry eye symptoms, and classic

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Goal Statement: Because dry eye is a multifaceted diagnosis, optometrists need to stay current with rapid advances that change current treatments and how optometrists manage dry eye patients. This article discusses the keys to diagnosing dry eye and the myriad treatment options available to help patients manage their specific form of dry eye, whether it's meibomian gland dysfunction, aqueous deficient dry eye or caused by an outside irritant such as cosmetics or *Demodex*.

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signs include cylindrical dandruff and distention of the eyelash base (*Figure 1*). End-stage *Demodex* presents as chronically inflamed eyelids, madarosis and severe itchiness (*Figure 2*).

Because symptoms of *Demodex*, allergic conjunctivitis, MGD and ADDE often overlap, these four conditions should always be at the forefront when a patient presents with a complaint of dry eye.

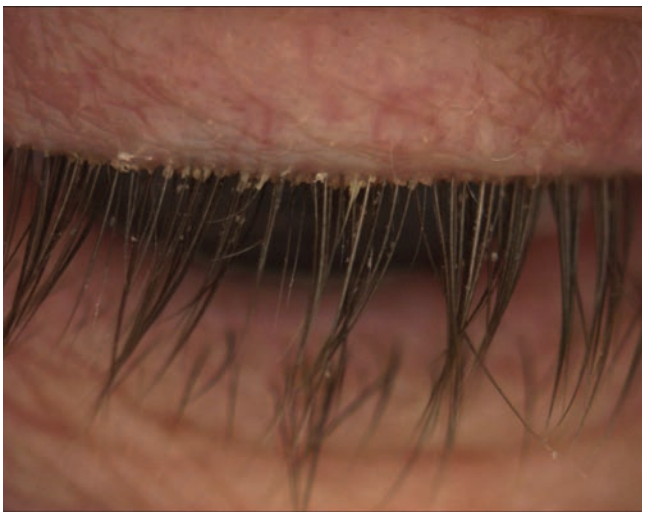

Fig. 1. Pervasive cylindrical dandruff and thinning eyelashes are signs of a *Demodex* infestation.

Another important factor in dry eye that is recently gaining attention is cosmetics and makeup removal. The environmental working group surveyed 2,300 people and found that the average woman uses 12 products around, and inadvertently in, their eyes.[5] For example, some patients apply eyeliner not only to the outer lash line but also the inner water line, directly over the meibomian gland orifices. Cosmetics are largely unregulated, and offending agents such as parabens and isopropyl cloprostenate promote inflammation and dry eye.[6] Questioning a patient's cosmetic use can often help clinicians better diagnose even the simplest cause behind dry eye.

Dry Eye Imaging

Educating patients with pictures of their own eyelids, meibomian glands, tear meniscus height and ocular surface staining often helps them better understand the underlying mechanisms of their specific form of dry eye—not to mention providing incentive to be more compliant with treatment. With meibography, both patients and doctors can view the structural integrity of the meibomian glands, which is especially helpful for patients with MGD (*Figure 3*). However, the degree of atrophy doesn't consistently correlate with symptoms, tear break-up time (TBUT) or Schirmer.[7]

Structure is one thing, but function is another, and imaging can only go so far in guiding treatment. Ultimately, clinical acumen will help uncover the specific needs of the patient. For example, sometimes all the glands will appear intact, but gentle fingertip expression will yield nothing. Regardless of the imaging, this patient would benefit from a targeted management strategy to clear the glands.

Tried-and-True Treatments

For most patients with DED, the first treatment is artificial tears—and at the end of the day, we know many patients self-prescribe. Practitioners must be familiar with the eye drop aisle—90% of which serves ADDE, not MGD. Clinicians should recommend patients use preservative-free formulations whenever possible, considering preservatives such as benzalkonium chloride (BAK) are cytotoxic to ocular surface epithelia.

Emulsions with liquid lipids, which may better stabilize and support the lipid layer of the tear film, can be either charged or uncharged microemulsions and liposomes. Charged microemulsions, such as Retaine MGD (carboxymethylcellulose sodium 0.5%, Ocusoft) and Systane Balance (propylene glycol 0.6% ophthalmic solution, Alcon), show improvements in symptoms and corneal staining when compared with aqueous eye drops.[8,9] Uncharged microemulsions such as Refresh Optive Advanced (carboxymethylcellulose sodium 0.5%, glycerin 1.0%, polysorbate 80 0.5%, Allergan) may also improve a patient's symptoms, OSDI score and TBUT.[10]

But artificial tears simply won't cut it for MGD or any number of other DED manifestations. Warm compresses and lid hygiene continue to be the main two treatments when MGD and blepharitis are the cause of the dry eye symptoms. The ideal temperature must be at least 40°C for the heat to reach the meibomian glands.[11] Clinicians can prescribe a warm compress—such as a Bruder mask, ThermoEyes (Ocusoft), TheraPearls (Bausch + Lomb) or TranquilEyes (Eye Eco)— that can be microwaved for 10 to 25 seconds and sustain dry or moist heat for more than five minutes. Because the goal is to melt viscous or hardened meibum, the ideal time to use a warm compress is morning and mid-day, as most patients wake up with their eyes feeling very dry due to the lack of blinking during sleep.

Lid hygiene is particularly important for patients with dry eye stemming from an overgrowth of eyelid

and eyelash bacteria and build up of cosmetics. With cosmetics, the first step to treatment is often education on proper and daily removal. Baby shampoo can be a cost-effective option to clean the lid margin, although all-natural alternatives such as jojoba, coconut or olive oil would be ideal for general and waterproof makeup removal, as they contain antibacterial and anti-inflammatory properties that can soothe irritated skin.[12] Commercially available lid scrub wipes and foam cleansers are another option for makeup removal and lid hygiene in general.

When treating *Demodex*, using lid scrubs with tea tree oil is the common approach, as it provides anti-inflammatory, antimicrobial and antifungal properties.[13-15] Mild cases can be treated at-home with Cliradex (Bio-Tissue), SteriLid (TheraTears), Blephadex (Lunovus) or Ocusoft scrubs BID. More stubborn cases of *Demodex* may warrant a higher concentration solution for use in-office.

Hypochlorous acid—such as Avenova with Neutrox 0.01% HOCL (NovaBay) or over-the-counter Hypochlor gel 0.02% HOCL (Ocusoft)—is another treatment option, as it can normalize the eyelid and eyelash environment without a laundry list of ingredients.[16]

In-office Tools

In-office procedures also help differentiate your dry eye management. Lipiflow (TearScience) heats the meibomian glands from the inside out and evacuates the meibum with an air bladder, while the MiBo-Flo (Mibo Medical Group) heats the glands from the outside in. For practices without these treatment units, two simple handheld instruments—golf club spud and Mastrota paddle (Ocusoft)—can really make a difference. Research shows the technique of eyelid margin debridement scaling, when done on the lower eyelid margin, improves the number of meibomian glands yielding liquid secretion and improves symptoms per the SPEED questionnaire.[17] The process of debriding the material, nasal to temporal, of each lower eyelid using the golf club spud takes less than 10 seconds per eye and doesn't require anesthetic. After the procedure, clinicians can use the Mastrota paddle for a therapeutic expression and evacuation of the stagnated meibum. These two procedures work in tandem, as debridement opens up some of keratinized epithelium, making the gland expression that much more effective. The BlephEx (Rysurg) device can also help clinicians perform eyelid margin debridement while also cleaning the eyelashes.

The occasional capped gland may appear on lower or upper eyelids. Using a cotton-tipped applicator moistened with contact lens multipurpose solution, clinicians can gently scrub until the cap is removed. However, spotting the orifice metaplasia even before the capped glands form is critical, as these are more easily expressed (*Figure 4*).

The goal of in-office treatments is to do for the patient what they cannot consistently or effectively do themselves, which is valuable to keep them on the path of relief.

Contact Lenses

For some, contact lenses can help alleviate symptoms associated with dry eye.[18-20] Research shows patients with dry eye can find improved comfort after switching to a daily disposable, or from hydrogel to silicone hydrogel lenses.[18-20] Also, a premium daily disposable soft contact lens may protect a patient's sensitive cornea and help them overcome extreme light sensitivity that may make it difficult for them to keep their eyes open both indoors and outdoors. This approach is most often used for post-refractive surgery cases such as PRK, LASEK and corneal collagen crosslinking.[21]

Scleral lenses are also a viable treatment option for severe dry eye.[22] They create a tear reservoir that lubricates the corneal surface while maintaining the oxygen supply, not to mention they can mask surface irregularities that may contribute to visual issues.

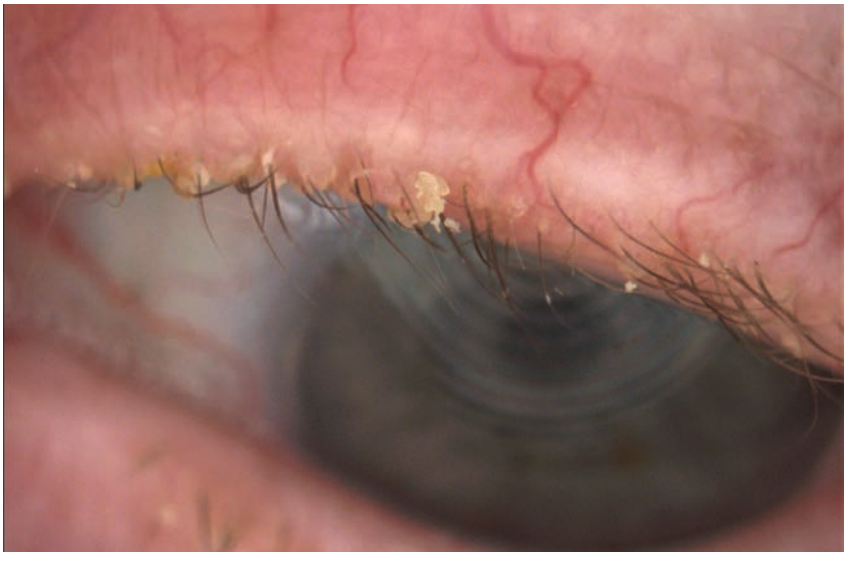

Fig. 2. This patient has end-stage *Demodex* with madarosis.

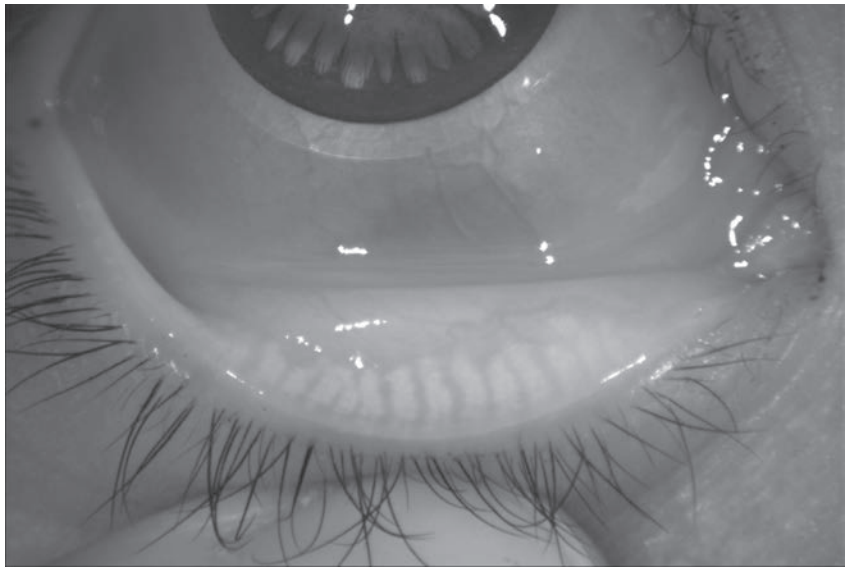

Fig. 3. Meibography shows more than 50% meibomian gland atrophy of the lower lid.

Amniotic Membranes

Research shows using an amniotic membrane for treating persistent corneal epithelial defects due to severe dry eye can hydrate and oxygenate the corneal tissue, promote epithelial healing and reduce inflammation.[23] However, although an amniotic membrane makes sense to accelerate healing, repeated use for recalcitrant cases is not a long-term solution secondary to cost and inconvenience.

Oral Meds

Oral antibiotics such as minocycline, doxycycline and azithromycin can work to reduce inflammation and growth of lid bacteria by various mechanisms, one of which is to decrease MMP-9 expression, a known biomarker produced by inflamed epithelial cells.[24] Because azithromycin's stimulatory effects are unique and not the same as the tetracycline family, a patient can respond to one and not the other if there are no contraindications.[25] These oral medications should only be reached for once a year to minimize bacterial resistance. From there, Restasis (cyclosporine, Allergan) or Xiidra (lifitegrast, Shire), along with triglyceride omega-3 fish oils, can build on the groundwork done by the oral antibiotics. These can be started concurrently for the severely symptomatic patient.

One study that looked at the use of re-esterified omega-3 fish oil at baseline, six weeks and 12 weeks found many dry eye parameters improved by six weeks.[26] However, a clinically significant improvement in symptoms didn't occur until the 12-week mark.[26] The delayed effect could be due to the time it takes for the eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) to saturate in the red blood cells and then reach the meibomian glands. After starting patients on any therapy that takes time to ramp up, clinicians should schedule the first follow up two months from the initial visit. In addition, new research suggests oral supplementation with omega-3 and -6 stimulates the accumulation of small neutral lipid-containing vesicles in the meibomian glands.[27]

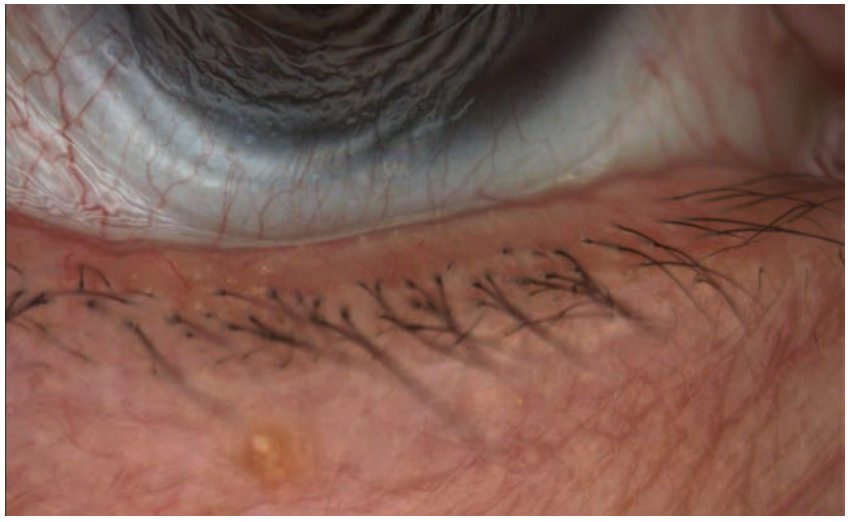

Fig. 4. Orifice metaplasia and irregularity in the eyelid margin, as seen here, are key indicators of the underlying meibomian gland structure and function.

Topical Options

When it comes to topical prescription options for DED, most clinicians start with Restasis. Research shows cyclosporine reduces inflammation by inhibiting T-cell activation and downregulating inflammatory cytokines in the conjunctiva and lacrimal gland, thus enhancing tear production.[27,28] Xiidra is a new class of drugs known as lymphocyte function-associated antigen-1 (LFA-1) antagonists, which inhibits T-cell recruitment and activation associated with DED inflammation.[29,30] Clinical trials showed participants using Xiidra had a statistically

significant clinical improvement in corneal staining and eye dryness compared with placebo.[31]

But for some patients, more than one topical treatment is necessary. In these cases, topical nonsteroidal anti-inflammatory drugs (NSAIDs) and corticosteroids may help.

NSAIDs inhibit different forms of the cyclooxygenase enzyme, thus reducing prostaglandin production and treating inflammation.[32] While useful in the short-term, clinicians should use NSAIDs cautiously, as they have been known to reduce corneal sensitivity, increasing the risk of additional insult to the epithelium.[33] BromSite (Sun Ophthalmics) was recently approved to treat pain after cataract surgery. It contains the NSAID bromfenac 0.075% and has the DuraSite vehicle that turns into a gel to coat the ocular surface and increase retention time and delivery of the drug to target tissues. NSAIDs for pulse treatment of dry eye is off label but can really help dry eye patients who experience ocular pain in the short term.

Corticosteroids, such as Lotemax (loteprednol etabonate, Bausch + Lomb), are more potent than NSAIDs and reduce ocular inflammation.[34] For one, research suggests topical administration of methylprednisolone 1% ophthalmic solution for several weeks provides moderate, or even complete, relief of dry eye symptoms.[35] Clinicians should monitor patients treated with topical corticosteroids closely for known risks such as cataract formation, glaucoma, corneal thinning and infectious keratitis.[36] Lotemax gel in particular provides a consistent concentration of 0.5% loteprednol etabonate without having to shake the bottle.

Autologous serum, as a dry eye treatment and for ocular surface healing, is the most natural, compatible component that can be added to the eye since it's derived from blood plasma. It contains anti-inflammatory factors that ultimately inhibit the ocular surface inflammatory cascade responsible for dry eye.[37] While some studies show autologous serum drops improve ocular irritation symptoms, a recent Cochrane Review did not find conclusive evidence of its benefits compared with artificial tears.[38-40]

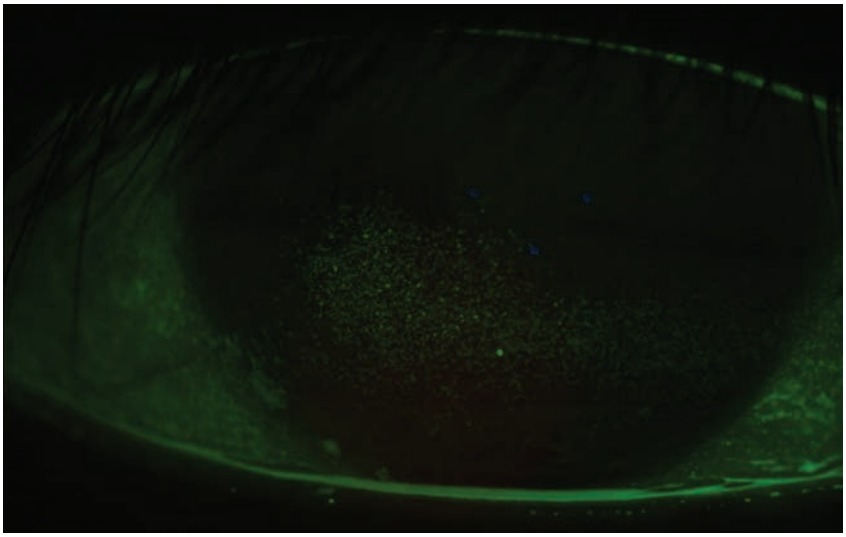

Fig. 5. Coalesced corneal staining is common with post-LASIK dry eye in the first one to four weeks postoperatively.

Punctal Plugs

For patients with ADDE, punctal plugs work wonderfully. Patients should be prepared for delayed gratification, however, as research shows patients did not see a dramatic improvement in symptoms, Schirmer's and tear break-up time until six months post-insertion of permanent punctal plugs.[41]

Many patients have post-LASIK dry eye, and micro and macro punctate staining is often seen in the first one to four weeks postoperatively (*Figure 5*). Ninety or 180-day dissolvable collagen punctal plugs work well during this time to hold more aqueous tears on the ocular surface while the corneal nerves regrow and the lacrimal gland is signaled to produce aqueous at a normal level again. Post-LASIK

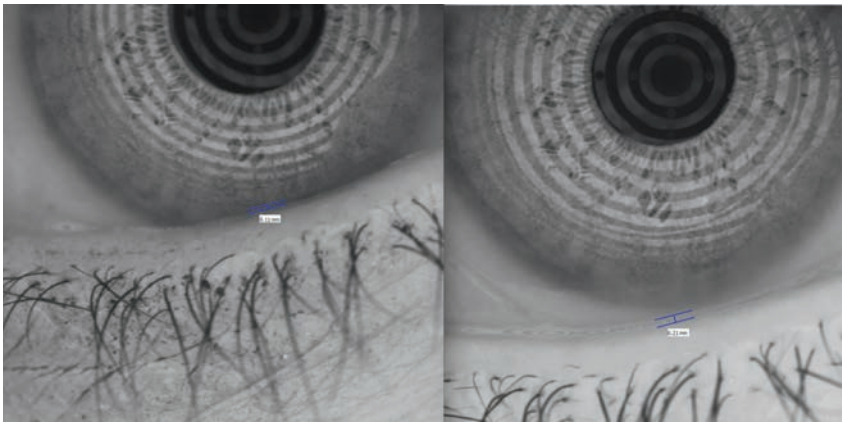

Fig. 6. Punctal plugs can double the tear meniscus height, as seen here.

patients are also dumping significant amounts of BAK onto the ocular surface with the prophylactic antibiotic eye drops and corticosteroid eye drops that first week, possibly adding to the epithelial irritation.

Many contact lens wearers struggle with dry eye, and punctal plugs can help. In one case, permanent punctal plugs helped elevate the tear meniscus height of a 49-year-old female by almost double, even while wearing a soft contact lens during both measurements (*Figure 6*). The first sign of dryness can be intermittent or constant blurry vision, mainly because the prelens tear film is thin and breaks down easily.[42] Research shows a lipid-based artificial tear can be a beneficial rewetting drop to extend comfortable contact lens wearing time and reduce lid wiper epitheliopathy, as well as corneal staining.[43]

Prescribe a Lifestyle Change

Getting to know the patient's work environment and how they view their computer monitor(s) can be a key component to dry eye therapy. Too many computer users continue to look straight or upwards at their monitors on stands. The preferred slight down gaze reduces the palpebral aperture size and keeps the tear film more stable.[44] It also reduces the muscle strain caused by keeping the upper eyelid in a higher position than necessary. Encouraging patients to raise their chairs, lower their monitors and blink more often are simple first steps to minimizing dry eye related to close computer work.

Research shows digital device use affects blink rate and completeness, thereby affecting tear film stability.[45,46] A free computer application called EyeLeo encourages blinking and other short, seven-second exercises every 10 to 15 minutes and suggests a longer break once an hour. While the frequency may seem excessive, the patient can begin to understand that blinking ensures the flow of meibum and keeps the eyes from becoming excessively strained or tired. In addition, an occupational computer lens specific to the workstation set up and accommodative demand would be a necessary tandem prescription.

Dry eye therapies, on their own, can be simple in mild cases; however, once patients begin to use more than a few all-natural treatments and still don't find relief, short courses of prescription medications are necessary. Knowing mechanisms of action and anticipating the time it takes to feel an effect are essential to proper management. Working with a team approach with other optometrists and ophthalmologists, particularly when scleral lenses are indicated, can greatly improve a dry eye patient's quality of life.

The overall goal of dry eye therapy is to be preventative and promote long-term wellness, not just prescribe a palliative artificial tear. Too many interventions at once could affect the patient's compliance and may mask what is, and is not, working. Luckily, clinicians see dry eye patients regularly, providing an opportunity to build a long-lasting relationship. If we can meet patients where they are and understand their struggles, we provide compassionate care that's highly customized. In the end, it's rewarding for both patients and practitioners alike. ■

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1. According to some research, what percentage of dry eyes demonstrate signs of meibomian gland dysfunction?
a. 43%.
b. 56%.
c. 65%.
d. 86%.

2. Which of these is a telltale sign of *Demodex*?
a. Flakes.
b. Crust.
c. Cylindrical dandruff.
d. Collarettes.

3. What is the newest NSAID used off-label for the treatment of inflammatory dry eye?
a. Nevanac.
b. Ilevro.
c. Prolensa.
d. BromSite.

4. What is the mechanism of action when using oral doxycycline for dry eye?
a. Anti-MMP-9.
b. Anti-interferon gamma.
c. Increasing aqueous production.
d. Inhibiting cyclooxygenase pathway.

5. How should patients look at their computer monitors to minimize tear film evaporation?
a. In up gaze.
b. In down gaze.
c. In straight ahead gaze.
d. It doesn't matter.

6. What type of contact lenses can be used to treat severe dry eye?
a. Soft contact lenses.
b. Corneal gas permeable (GP) lenses.
c. Scleral GP lenses.
d. Hybrid lenses.

7. Which of these inhibits T-cell activation?
a. Restasis.
b. Xiidra.
c. Lotemax.
d. All of the above.

8. Amniotic membranes help treat dry eye by:
a. Healing persistent epithelial defects.
b. Hydrating the ocular surface.
c. Reducing inflammation.
d. All of the above.

9. Post-LASIK dry eye is mainly due to:
a. Meibomian gland dysfunction.
b. Temporary reduction in aqueous production.
c. Epithelial trauma during flap creation.
d. Perioperative topical medications.

10. What is the ideal warm compress temperature to effectively melt meibum?
a. 32°C.
b. 38°C.
c. 40°C.
d. 47°C.

11. Autologous serum works mainly by:
a. Washing away tear debris.
b. Protecting the cornea from the external environment.
c. Delivering anti-inflammatory factors from the blood plasma.
d. Hydrating the ocular surface.

12. Which instrument is used for eyelid margin debridement scaling?
a. Forceps.
b. Golf club spud.
c. Mastrota paddle.
d. Cotton-tipped applicator.

13. In the omega-3 fish oil study, how long did it take for patients to see a clinically significant improvement in symptoms?
a. Two weeks.
b. Four weeks.
c. Six weeks.
d. 12 weeks.

OSC QUIZ

14. According to research, meibomian gland loss does not consistently correlate with:
a. Schirmer's.
b. Symptoms.
c. Tear break-up time.
d. All of the above.

15. What is the most common corticosteroid used to treat inflammatory dry eye?
a. Pred Forte.
b. Durezol.
c. Lotemax gel.
d. Medrol (Pfizer).

16. What is most effective *Demodex* treatment?
a. Baby shampoo.
b. BlephEx.
c. Hypochlorous acid.
d. Tea tree oil.

17. Which of the following is not a lipid-based artificial tear?
a. Blink Tears.
b. Retaine MGD.
c. Systane Balance.
d. Refresh Optive Advanced.

18. On average, how many cosmetic products do most women use?
a. Four.
b. Eight.
c. 12.
d. 16.

19. Which of the following is important in diagnosing meibomian gland dysfunction?
a. Meibum expressibility.
b. Meibum quality.
c. Meibomian gland structure.
d. All of the above.

20. Which of the following is *false* about the importance of blinking for patients with dry eye?
a. Blinking ensures the flow of meibum.
b. Digital device use affects blink rate and completeness, thereby affecting tear film stability.
c. Blinking triggers Bell's phenomenon.
d. The lack of blinking during sleep can make dry eye symptoms worse in the morning.

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2. Ⓐ Ⓑ Ⓒ Ⓓ
3. Ⓐ Ⓑ Ⓒ Ⓓ
4. Ⓐ Ⓑ Ⓒ Ⓓ
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14. Ⓐ Ⓑ Ⓒ Ⓓ
15. Ⓐ Ⓑ Ⓒ Ⓓ
16. Ⓐ Ⓑ Ⓒ Ⓓ
17. Ⓐ Ⓑ Ⓒ Ⓓ
18. Ⓐ Ⓑ Ⓒ Ⓓ
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. Improve my clinical ability to diagnose dry eye disease. ① ② ③ ④ ⑤
22. Become familiar with the rapid advances that have changed current treatments in dry eye. ① ② ③ ④ ⑤
23. Increase my skill in choosing the right treatment plan for patients with dry eye. ① ② ③ ④ ⑤
24. Better understand the possible underlying etiologies of dry eye disease. ① ② ③ ④ ⑤
25. Increase my knowledge of tools available to aid in diagnosing dry eye. ① ② ③ ④ ⑤
26. Improve my ability to communicate with patients about the nature of their dry eye and any treatment needed. ① ② ③ ④ ⑤

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

27. The content was evidence-based. ① ② ③ ④ ⑤
28. The content was balanced and free of bias. ① ② ③ ④ ⑤
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Canalicular Rolling Stones

Stop this rare infection while time is on your side.

By Alan G. Kabat, OD, and Joseph W. Sowka, OD

A 63-year-old Caucasian male presented for consultation with complaints of a chronically red and watering right eye. He said the condition had persisted for at least six months, intermittently improving, but gradually worsening overall. He claimed that his eye really was not terribly uncomfortable, but that the tearing was problematic and interfering with his ability to drive and read. His medical history was positive for controlled hypertension (nebivolol 5mg once daily). A dermatologist diagnosed him with rosacea, but he was not currently treating it.

Upon examination, his right eye showed moderate conjunctival injection and epiphora. The upper and lower lids were grossly normal, but inspection of the inferior nasal region showed distinct swelling with punctal occlusion. When pressure was applied, a small amount of pus regurgitated through the punctum, along with two small yellowish concretions. The nasolacrimal sac area did not appear hyperemic, and was not tender to the touch. The remainder of the ocular surface and anterior segment structures appeared normal. Based upon the history, symptoms and examination, the patient was diagnosed with chronic canaliculitis.

To see a narrated video of this procedure, visit www.reviewofoptometry.com, or scan this QR code.

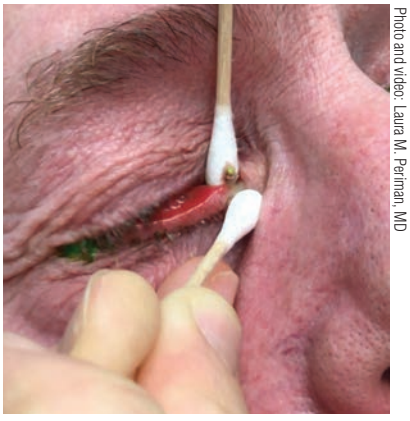

Photo and video: Laura M. Perlman, MD

Expressing the canaliculus firmly on either side with cotton-tipped applicators should help "roll" these dacryoliths stones through the punctum, affording medications greater access.

A Red, Red Eye

Canaliculitis is an uncommon infection of the lacrimal system, yet it remains grossly underdiagnosed in clinical practice. The hallmark symptoms include a chronic, recalcitrant red eye with focal swelling and variable tenderness of the medial canthus. Epiphora, or excessive lacrimation to the point of overflow, is also characteristic. Ocular discharge may range from simple tearing to full-blown mucopurulence. In many cases, the patient will report previous therapy with topical antibiotics, but to no avail.

Low-grade infections can sometimes persist for a long time because the clinician simply fails to observe the subtle signs. Studies suggest that the average duration before a correct diagnosis is made may be up to 36 months.[1,2]

The classic biomicroscopic sign of canaliculitis is said to be a "pouting punctum."[1-10] This term describes the red, swollen and outwardly turned punctal orifice, which tends to resemble a pair of pouting lips. In actuality, however, the most common (and most important) sign is the presence of discharge and concretions upon canalicular compression.[11] These dacryoliths, a term which literally translates as "tear stones," are another hallmark of this disease. According to a recent study, 90% of patients will have dacryoliths that are observable with expression.[4] Other important signs include erythema and swelling of the lid and adnexal tissue, and a conjunctivitis that is more pronounced inferiorly and nasally.[8] Canaliculitis is typically encountered in older adults, with a mean age of 59 years.[2] Women are affected up to five times more often than men.[4,6] Most cases are unilateral, though bilateral phenomena have been documented.[12,13]

Discussion

Canaliculitis is essentially an infection (and subsequent inflammation) of the lacrimal outflow system, at the level of the canaliculus.[4] While a great many pathogens have been associated with this condition, the most widely reported organism is a gram-positive, anaerobic bacterium called *Actinomyces israelii*.[4,9] In canaliculitis, infection by *Actinomyces* (or similar pathogens) helps to produce the aforementioned dacryoliths, which harbor the microbes and

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create small intervening "pockets" in the canaliculus. This physical blockade by the dacryoliths allows the pathogens to flourish undisturbed, invulnerable to the natural antimicrobial properties of the tear film or even to topically administered antibiotics.[4]

Canaliculitis can also occur secondarily as a complication of lacrimal occlusion, either from migrated punctal or intracanalicular plugs.[4,5] These plugs can function as artificial dacryoliths, harboring potentially pathogenic bacteria and providing an environment in which they can thrive. In some cases, concretions can form around or adjacent to retained plugs.[14] Secondary canaliculitis has seen its greatest incidence with use of the SmartPlug (Medennium) device, a thermoacrylic polymer designed for lacrimal occlusion therapy in patients with dry eye.[12-16]

Treatment Options

Conservative measures such as warm compresses, digital massage, topical antibiotics and even oral antibiotics are generally insufficient to overcome canaliculitis infections, although they may provide temporary improvement and symptomatic relief.[4,11,17] Much greater overall success can be achieved by first removing the obstructing dacryoliths. Simply expressing the canaliculus firmly on either side with cotton-tipped applicators should help to "roll" these stones out through the punctum, affording greater access to medications that can help overcome the infection. A study employing this technique, followed by canalicular irrigation with fortified cefazolin (50mg/ml) and the use of topical antibiotics for several weeks resulted in a success rate of 100%, although most subjects required multiple irrigations.[17]

Should these less invasive efforts for canaliculitis fail to achieve resolution, surgical intervention may be required. Classically, canaliculotomy (surgical excavation of the canaliculus) with canalicular curettage (surgical removal of the dacryoliths and other obstructions of the canaliculus) is considered the treatment of choice.[3-7,17] This technique is performed under local anesthesia and involves a horizontal incision through the conjunctiva into the canaliculus, dissecting the nasal lid from the punctal orifice down to the level of the common canaliculus (approximately 10mm). Next, a small chalazion curette is used to remove the dacryoliths and other debris, and canalicular irrigation with antibiotic solution (aqueous penicillin G) or povidone-iodine may be subsequently performed. Performing smears, cultures, or both, of the retrieved material may be helpful in determining the correct pharmacologic

course, as postoperative antimicrobial therapy is generally indicated.[1]

Medical Intervention

In cases of *Actinomyces* canaliculitis, oral penicillin or ampicillin is commonly prescribed for several weeks following surgical recovery.[1,4] The use of topical, broad-spectrum antibiotics (e.g., ciprofloxacin 0.3% solution QID or bacitracin zinc/polymyxin B ointment BID) may be employed as an adjunct to systemic therapy.[6]

The prognosis for recovery is dependent upon how quickly the correct diagnosis is made, as well as the level of therapeutic invasiveness. With prolonged infections or in cases that require radical surgical intervention, the nasolacrimal system may become scarred and permanently occluded. In such instances, dacryocystorhinostomy may be required to successfully reestablish lacrimal outflow. This surgical technique essentially creates a new channel to bypass the canaliculus and drain tears from the punctum directly into the superior nasal cavity.

Remember, canaliculitis does not come around often, but when it does we need to recognize its calling card: a chronic red eye with persistent tearing in an older patient, who often has not responded to conventional therapy with topical antibiotics. Inspect the punctum and, if it appears swollen or occluded, always check to see if any material can be expressed. Take note of any little stones that come rolling your way, and you'll know exactly how to proceed. ■

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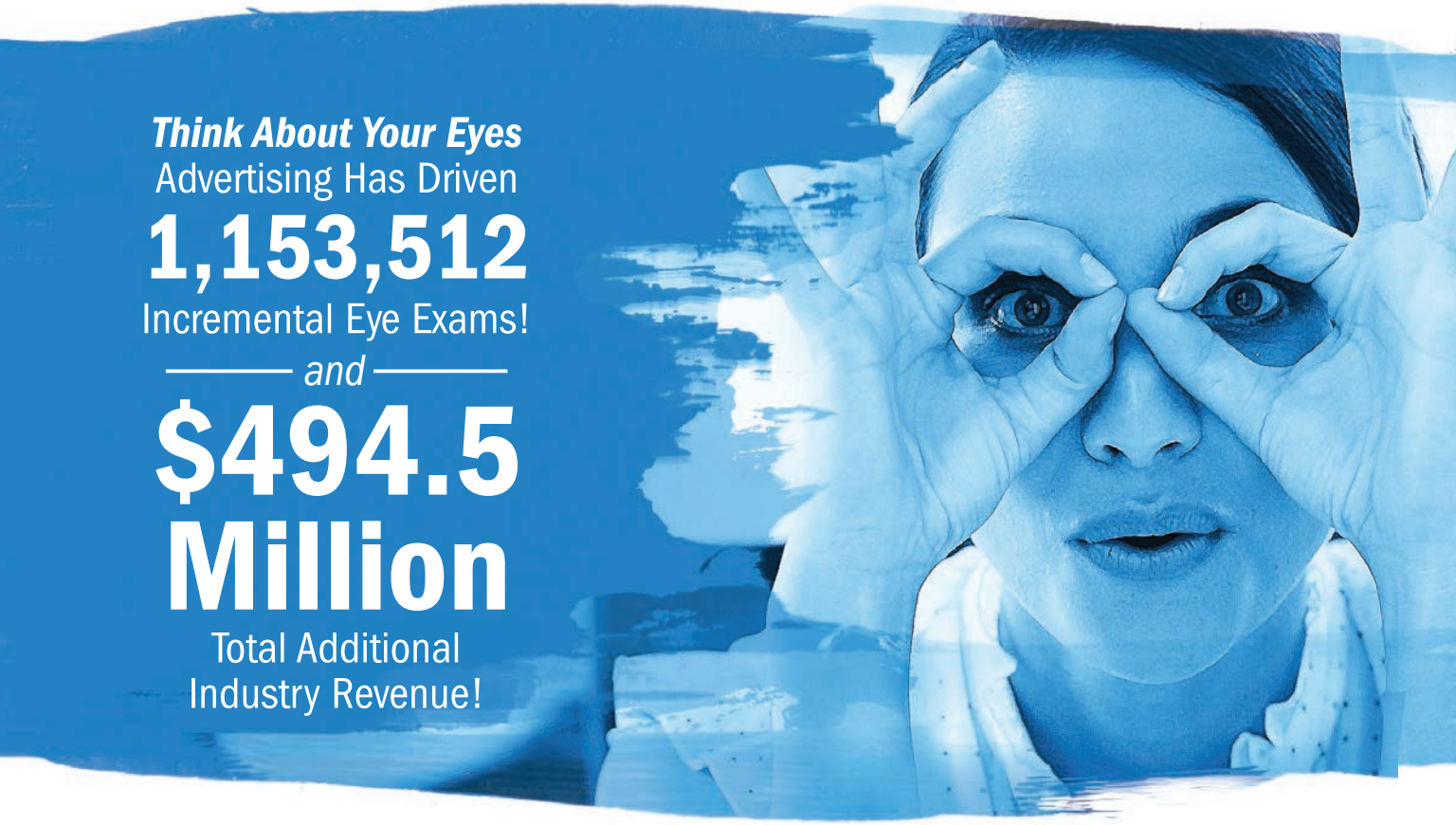

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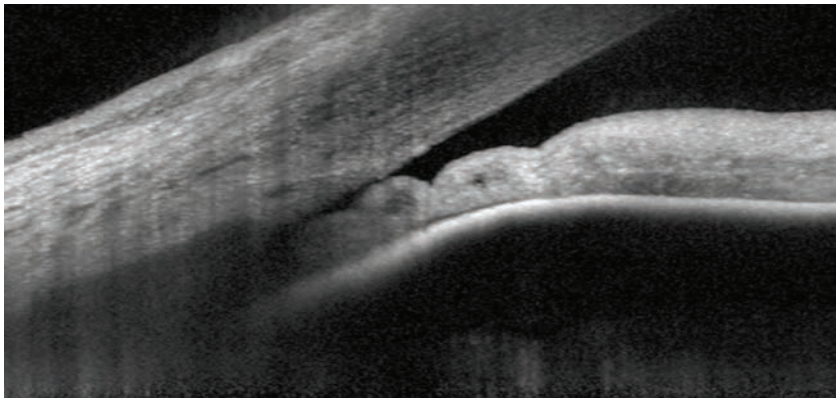
A Confounding Corner of the Eye

A 71-year-old glaucoma patient presents for a scheduled follow-up—and is headed to the OR for cataract surgery. **By James L. Fanelli, OD**

A long-standing glaucoma patient presented in March for her regularly scheduled follow-up visit. We scheduled her for anterior segment OCT, gonioscopy, and ultrasound biomicroscopy (UBM), as well as the standard intraocular pressure (IOP) check and nerve evaluation. She is a 71-year-old Caucasian woman who has seen me for many years. She has glaucoma in her right eye and is a glaucoma suspect for her left eye. Current glaucoma medications include Travatan Z HS (Travoprost, Novartis) OD, for which she reports good compliance. Her only other systemic medication is lisinopril and she reports no known allergies to medications.

History

We initially saw her in 2003, when we diagnosed her as a glaucoma suspect based on asymmetric optic nerve cupping. At that time, her threshold visual fields were normal, with no evidence of early field loss, applanation tensions averaged 19mm Hg OD and OS, and cup-to-disc ratios were estimated to be 0.5 x 0.6 OD and 0.3 x 0.35 OS. Her central corneal thicknesses were 588µm OD and 567µm OS when initially obtained. She was hyperopic and initially presented with opened, but slightly narrowed, angles. Over the next several years, she began to develop age-related nuclear cataracts. With time, her angles narrowed a bit, but always remained open and non-occludable. Post dilation IOPs did not alter from predilation IOPs. She remained stable until 2014, at which time she demonstrated manifest changes to her neuroretinal rim in her right eye and subtle visual field deficits corresponding to the rim changes. That's when we started her on Travatan Z.



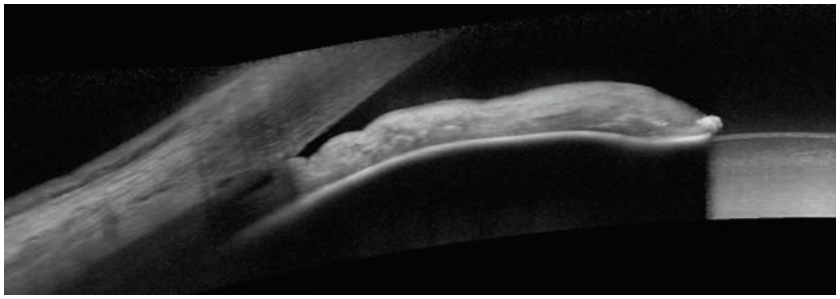


Fig. 1. At top, our 74-year-old patient's anterior segment OCT image from 2015 shows narrowing of the temporal angle.

Fig. 2. Below, two years later, the narrowing of the temporal angle has progressed.

At the 2017 visit, her applanation pressures measured at 14mm Hg OD and 16mm Hg OS. Her visual fields were stable when evaluated five months earlier. Cup-to-disc ratios were also stable when evaluated then and were judged to be 0.6 x 0.65 OD and 0.3 x 0.35 OS. Heidelberg Retina Tomograph (HRT 3) imaging and optical coherence tomography (OCT) imaging of the RNFL and macular ganglion cell layers were stable. Visual acuity was 20/30- OD, 20/30+ OS and 20/25- OU. Her cataracts at this point were estimated to be grade 1 anterior and posterior cortical, as well as grade 1 nuclear in configuration.

A slit lamp examination of her anterior segments was unremarkable except for narrowing of the anterior chamber angles by Von Herick, with the narrowest angles

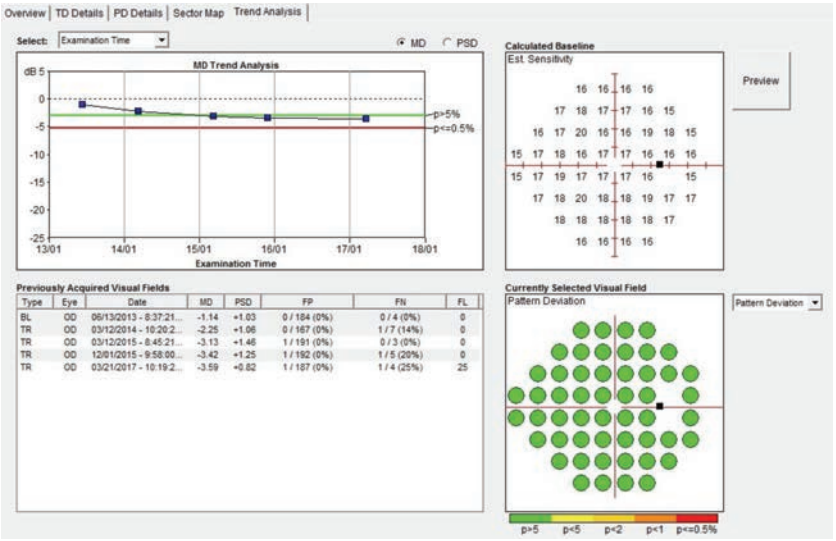


Fig. 3. Although we could see the patient had narrow angles, the visual fields over a four-year period remained stable.

seen nasally and temporally in both eyes, followed by the superior angle, with the widest angles being inferiorly OU. The posterior segment was characterized by bilateral PVDs of several years' duration, fine RPE granulation in the central maculae and normal retinal vasculature. Previous dilated fundus examinations demonstrated intact peripheral retina.

The focus of this visit was to evaluate her angles, in particular their gradual narrowing over the past few years as her cataracts developed. Anterior segment OCT, UBM and gonioscopy were all performed.

Discussion

Optometrists have a couple options for dealing with patients such as this one. A prophylactic laser peripheral iridotomy (LPI) procedure, for instance, can create a communication channel between the anterior chamber and the posterior chamber, which is extremely important when pupillary block is a possibility. Another option is to monitor these patients closely for signs or symptoms associated with subtle episodes of angle closure, as we've done in this instance.

The key to managing these patients is to obtain a good perspective of the angle as seen gonioscopically, and other relevant angle structures, such as the iris and the position of the ciliary body in reference to the iris and the angle. These last two perspectives are best given by anterior segment OCT imaging and UBM imaging.

Reading the Images

In our patient's anterior segment OCT image, taken in 2015, we were able to see a magnified view of the temporal angle in the right eye (*Figure 1*). You can easily see the close proximity of the peripheral iris to the trabecular meshwork, as well as some adjacent collecting channels. Not surprisingly, with the structures positioned in this image, gonioscopic examination of the angle would show a narrowed angle, with obscuration of the trabecular meshwork, consistent with the appearance of an anatomically narrowed angle. The angle configuration varies somewhat throughout the 360 degree structure, but at its narrowest, other OCT positions are similar to the image shown.

In a 2017 image of the same sector of angle, the angle structures demonstrate even further narrowing, even to the point of obstruction of the trabecular meshwork (*Figure 2*). While the patient's optic nerves and fields have remained stable, the angle is progressively narrowing (*Figure 3*). But what is not readily visible in these images is the ciliary body. This is where UBM imaging comes into play (*Figure 4*).

The current UBM finding is consistent with UBMs previously performed on this patient, and her

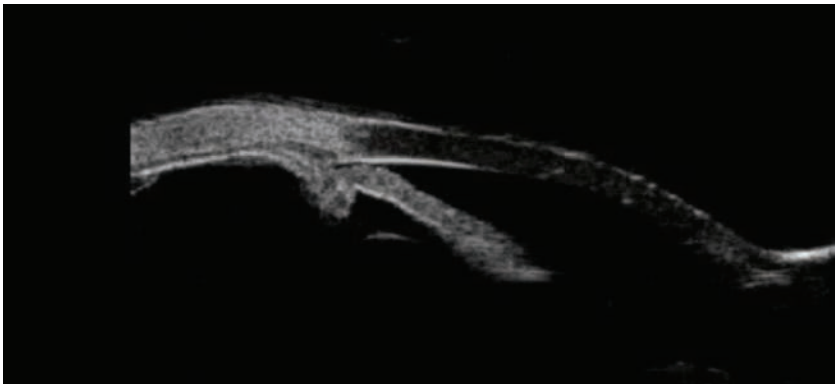


Fig. 4. This UBM scan shows the patient's plateau iris configuration and anterior positioning of the ciliary body.

plateau iris configuration has remained unchanged. But the important point here is that, from a slit lamp perspective, from a gonioscopic perspective and from an anterior segment OCT perspective, this patient appears to have a straightforward presentation of anatomically narrow angles, perhaps worsening by the increasing axial length of the cataractous lens.

Interpreting the Data

LPIs have little effect on plateau iris induced narrow angles. However, in many patients with plateau iris configurations, not all quadrants demonstrate a plateau iris configuration, as is the case for this patient. Narrow angles are complex, dynamic structures that can change over time. In most cases, angle closure is due to pupillary block and is amenable to peripheral iridotomy. But, optometrists are tasked with considering all potential causes of narrow angles, including plateau iris, lens vault and increased thickness of the lens with cataract progression, scleral buckles, malignant glaucoma and even changing iris thickness.[1-3]

To find the applicable cause or causes, obtain all the imaging you can. Gonioscopy, anterior segment OCT and UBM technology are all in the mix. The classification that we use to describe narrow angles is not uniform, and often there are multiple mechanisms in place with each individual.[4,5] Any angle that is not closed is by definition open, and they can have many faces and many degrees of openness. But an angle that is narrow, while technically still open, may eventually close. Gathering as much information as possible to fully assess the narrow angle is the best way to ascertain the risk of closure.

The patient in this case—though her cataracts were not visually debilitating—was best served now with cataract extraction and IOL implantation, especially in light of research that shows cataract extraction's effect on lowering IOP are greatest in patients with angle closure.[6] ■

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Good Walls Make Good Patients

Can these images help explain this patient's blurry vision?

By Angela Diamantakos, OD, and Mark T. Dunbar, OD

An 80-year-old Hispanic female presented complaining of blurry vision—in the right eye more than the left—at distance and near over the last year. Her ocular history was remarkable for cataract surgery in both eyes and her medical history was significant for hypertension, hyperlipidemia and asthma.

Examination

Her best-corrected visual acuity was 20/70 in the right eye and 20/40 in the left eye. Pupils were equal, round and reactive to light without afferent pupillary defect. Ocular motility was full in both eyes. Confrontation visual fields were full to finger count in each eye. Her intraocular pressures were 12mm Hg OD and 13mm Hg OS.

Anterior segment examination revealed mild meibomian gland dysfunction and dry eye, but was otherwise unremarkable. There was a posterior chamber intraocular lens in each eye with no posterior capsular opacification. Dilated fundus examination of the right eye revealed clear vitreous and a healthy optic nerve.

There were some notable findings within the macula and along the superior temporal arcade (*Figure 1*). There was mild attenuation of the retinal vasculature. An optical coherence tomography (OCT) of the macula was taken (*Figure 2*) as well as a fundus autofluorescence photo (*Figure 3*). Dilated fundus examination of the left eye was significant for macular drusen and mild attenuation of the retinal vasculature.

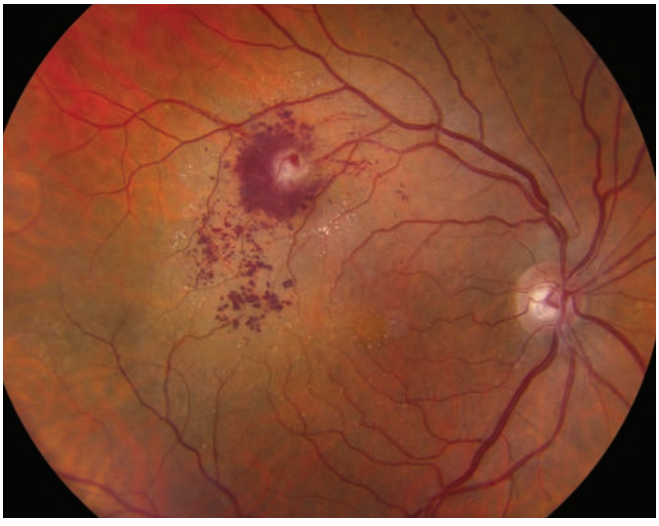

Fig. 1. Fundus photo of the right eye showing areas of intraretinal and subretinal hemorrhages along the superotemporal arcade surrounding a macroaneurysm.

Take the Retina Quiz

1. What additional test would be helpful to confirm the diagnosis?
a. Fluorescein angiography.
b. Fundus autofluorescence.
c. SD-OCT.
d. All of the above.

2. How could this patient be managed?
a. Observation.
b. Anti-VEGF injection.
c. Focal laser photocoagulation.

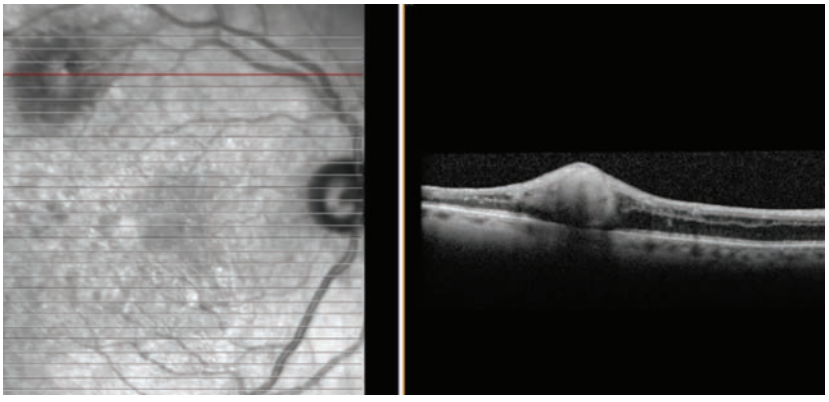

Fig. 2. OCT of the right eye showing a hyperreflective wall in the area of the marcoaneurysm as well as intraretinal edema with no choroidal abnormality.

d. Both b and c.

3. What is the most common systemic condition associated with this ocular condition?
a. Diabetes mellitus.
b. Hypertension.
c. Hyperlipidemia.
d. Thyroid disease.

4. What other ocular conditions are commonly associated with this diagnosis?
a. Retinal artery occlusion.
b. Retinal detachment.
c. Retinal vein occlusion.
d. Both a and c.

5. In which patients does this condition typically occur?
a. Young males.
b. Elderly males.
c. Young females.
d. Elderly females.

Diagnosis

Based on the clinical appearance, as well as the medical history, we diagnosed the patient with retinal artery macroaneurysm (RAM). As you follow the superior temporal artery, a large aneurysmal dilation of the artery can be seen with surrounding retinal hemorrhage and exudate. Spectral domain OCT (SD-OCT) showed an adequate amount of intraretinal fluid and a small pocket of subretinal fluid. The patient was educated on the importance of strict blood pressure control and a referral was made to her primary care doctor for further blood pressure management. The patient was scheduled for a retina consultation within one week.

RAMs result from a focal weakness in the arterial wall, which is believed to be the combined result of aging and atherosclerosis. It is thought that arteriosclerosis leads to vessel wall fibrosis. The resulting decrease in wall elasticity, combined with elevated luminal pressure results in aneurysmal dilation.[1] Because the arteries are high flow vessels, when the aneurysm ruptures, it does so under significant pressure, pushing blood into many retinal layers.[1] Often the macroaneurysm can have spontaneous pulsations.

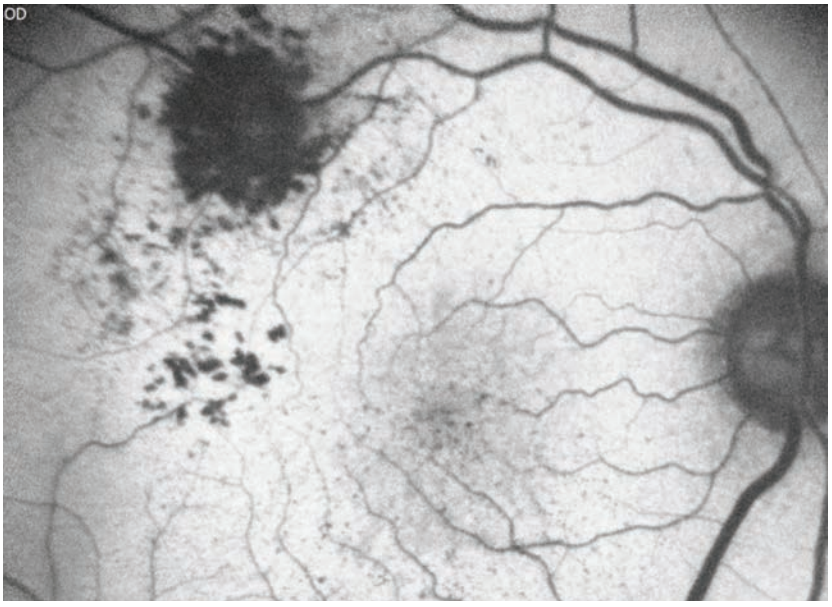

Fig. 3. Fundus autofluorescence reveals hypofluorescence corresponding to the areas of the hemorrhage seen clinically.

RAMs typically occur in women after the sixth decade of life. They are usually unilateral and most commonly associated with systemic hypertension. They may remain unchanged for a period of time, but most will spontaneously resolve.

On fundus examination, there will be aneurysmal dilation of an arteriole, usually superotemporally, at an arteriovenous crossing. The presence of blood at multiple layers, including the preretinal, intraretinal, subretinal and sub-ILM spaces and the vitreous, is a classic finding. Exudation may also be present, usually seen in a circinate pattern surrounding the aneurysm. However, exudation may also be found in the macular region. Macroaneurysms are frequently associated with other ocular conditions including retinal vascular occlusions and retinal emboli.[2]

Fluorescein angiography can help visualize macroaneurysms, which typically fill in the early arterial phase, and staining of the vessel walls with possible leakage may be found in later phases. In cases where hemorrhage blocks

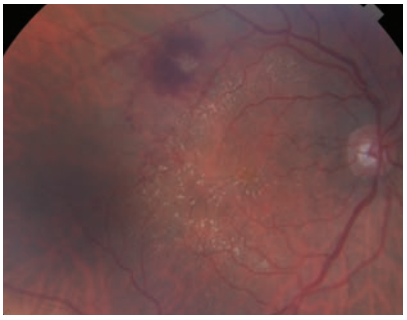

Fig. 4. Fundus photo of the right eye showing improvement in retinal hemorrhaging but increased exudation.

visualization of the aneurysm and imaging with fluorescein angiography is inconclusive, indocyanine green (ICG) may be more useful.[1] OCT is beneficial to diagnose and monitor associated retinal edema that may be present.

Management

Many treatments exist for RAM, yet no established treatment protocol has been determined. Treatment of this condition is dependent upon macular involvement and threat of vision loss. For the majority of cases, gradual thrombosis, fibrosis and spontaneous involution occurs. For this reason, most patients can safely be observed. In all patients with this diagnosis, a systematic work-up for hypertension and systemic vascular disease should be pursued.

Indications for focal laser treatment include vision loss due to chronic macular exudates or edema. Laser photocoagulation directly to, or around, the macroaneurysm can improve vision in some patients.[3] Laser photocoagulation may be performed directly to the macroaneurysm with intent to speed involution and decrease leakage. Indirect laser may be applied to the adjacent retina with aim to stop or decrease leakage progression toward the macula. Some complications to focal laser therapy include retinal hemorrhage, laser-induced retinal damage or epiretinal membrane formation.

Recently, investigators have studied intravitreal injections of anti-vascular endothelial growth factor (VEGF) as a treatment option for RAM with macular edema. These injections are used to reduce VEGF-associated increased vascular permeability and

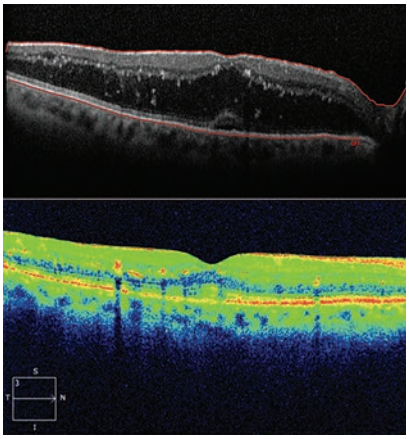

Fig. 5. Above, OCT at presentation showing macular edema. Below, OCT one month after focal laser photocoagulation with improvement in edema.

dilatation of the retinal artery.[4] In patients where a non-clearing vitreous hemorrhage is present, consider a pars plana vitrectomy. This decision is made typically after three months of observation.[1]

Visual prognosis is favorable in most patients with RAM, and observation alone is typically adequate treatment. However, in cases of macular threat, treatment options are available and referral to a retinal specialist is indicated. Accurate diagnosis and comanagement are crucial to save vision and help prevent complications from uncontrolled hypertension.[1]

Our patient was seen by the retina service a few days after the initial presentation. The decision was made to perform focal laser, due to the extent of macular involvement. One month after laser photocoagulation, the patient's visual acuity improved to 20/40 OD. Fundus photos and OCT were also obtained at that visit (*Figures 4 and 5*).

The patient returned for a three-month follow-up visit. At this visit, visual acuity was stable at 20/40 OD. Another OCT was performed showing more improvement in the macular edema, although many exudates still present (*Figure 6*).

Another three months later, the patient presented with a stable visual acuity of 20/40 OD. OCT was performed showing recurrence of fluid superior to the macular threatening the fovea (*Figure 7*). Another round of focal laser was performed. The patient will continue to be followed approximately every three months until resolution. ■

Dr. Diamantakos is a resident at Bascom Palmer in Miami.

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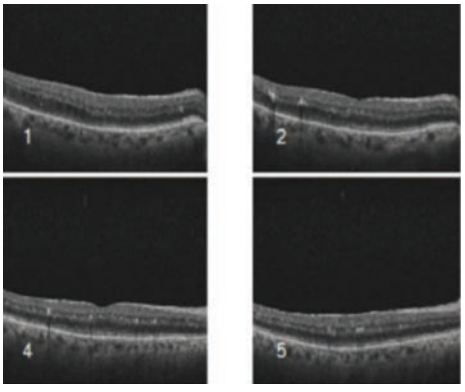


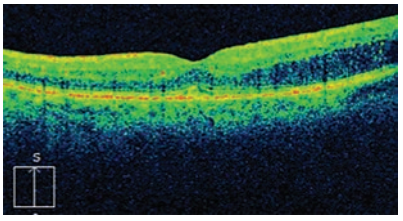
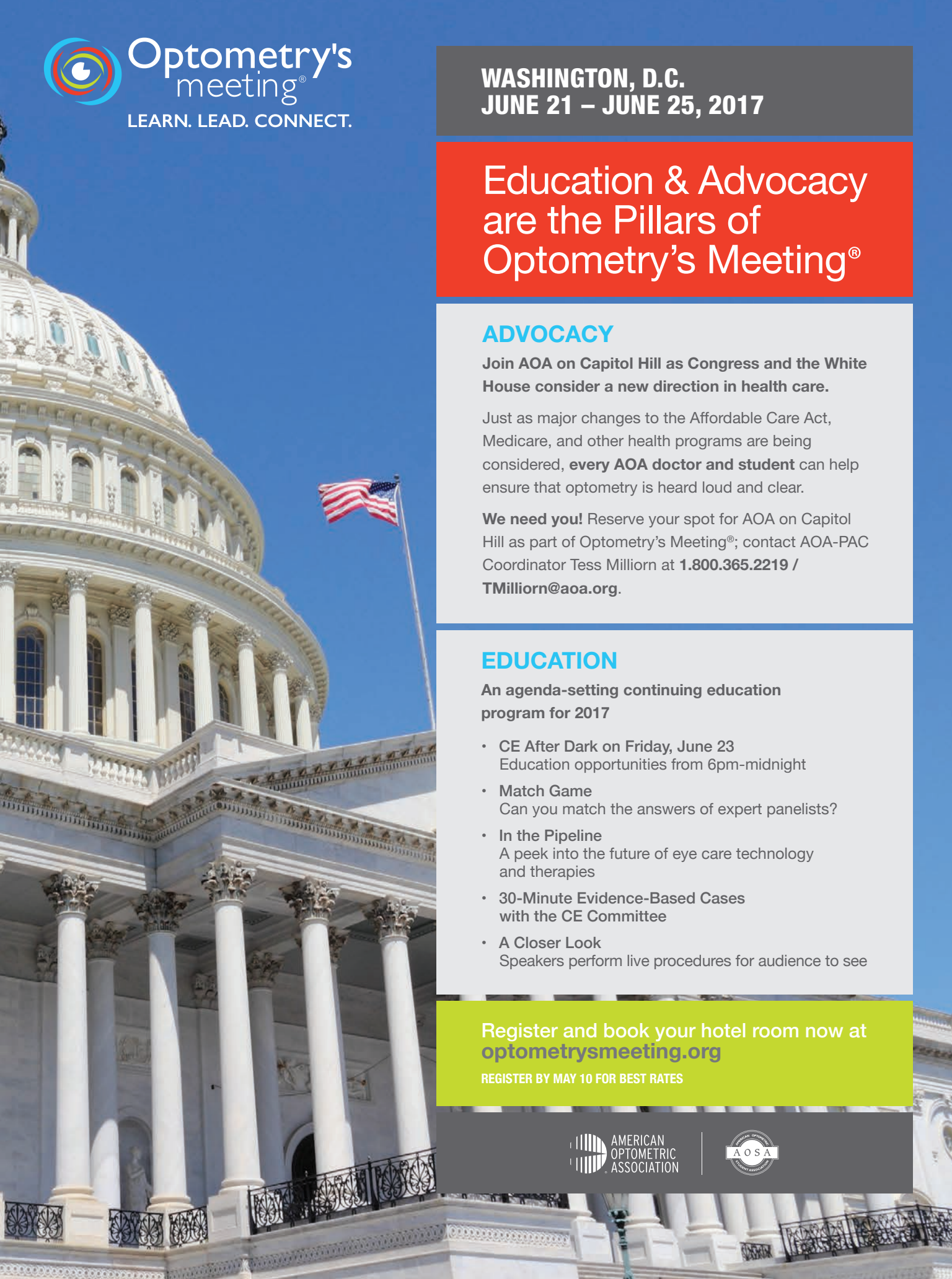


Fig. 6. At left, OCT of the right eye showing exudates with resolution of fluid.

Fig. 7. Above, this OCT shows the recurrence of fluid superior to the fovea.



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Concussion, CTE and the Visual System

Current research suggests a role for optometric care on the playing field and in other settings where concussion and traumatic brain injury are prevalent.

By Melinda Wolter, OD, Carlo J. Pelino, OD, and Joseph J. Pizzimenti, OD

In our last column, we described chronic traumatic encephalopathy (CTE) as a progressive neurodegenerative disease that occurs in association with repetitive mild traumatic brain injury (mTBI).[1] Concussion, while likely related to mTBI, is a separate and distinct condition characterized by trauma-induced alterations in a patient's mental status.[2,3]

Although the majority of CTE patients report a history of concussions, it's not a prerequisite for diagnosis, suggesting that even sub-concussive hits are sufficient to lead to CTE. The chronic and repetitive nature of the head trauma sustained, often in certain sports and military activities, is the most important driver of CTE.[3,4] Research suggests tau protein pathology occurs uniquely in those regions of the brain that are most susceptible to stress during trauma.[1,2,5,6]

Research has also found CTE-associated pathology in the retina, primarily in the ganglion cell layer.[7] Patients who have suffered an acute concussion commonly report symptoms of visual blur, field loss, diplopia and photosensitivity. Ophthalmic sequelae associated with concussion, TBI and CTE can be visually debilitating and may be sight threatening.

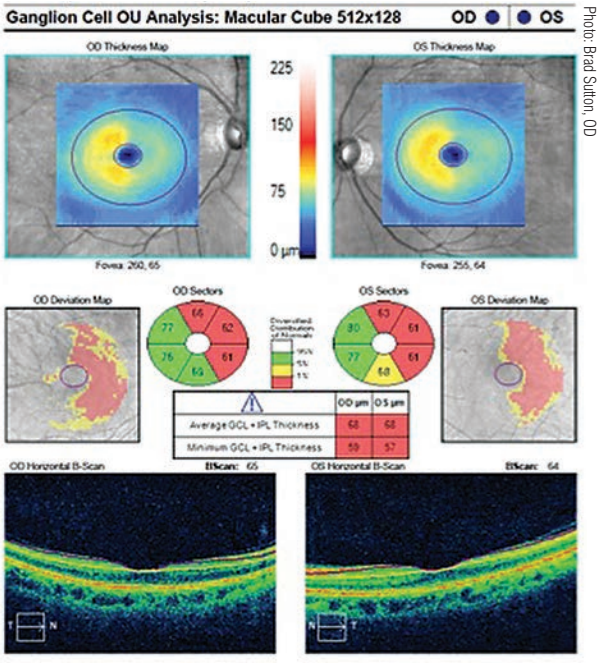


Photo: Brad Sutton, OD

OCT Macular cube with ganglion cell analysis in a post-TBI patient shows a distinct pattern of thinning in each eye.

Table 1. Diagnosing Concussion[3,4]

A suspected diagnosis of concussion may include features of the following clinical domains:

- Symptoms may be somatic (e.g., headache), cognitive (e.g., feeling as if in a fog) or emotional (e.g., mood changes).
- Physical signs (e.g., loss of consciousness, amnesia).
- Behavioral changes (e.g., irritability).
- Cognitive impairment (e.g., slowed reaction times).
- Sleep disturbance (e.g., drowsiness).

If any one (or more) of these components is present, clinicians should suspect a concussion and institute the appropriate management strategy.

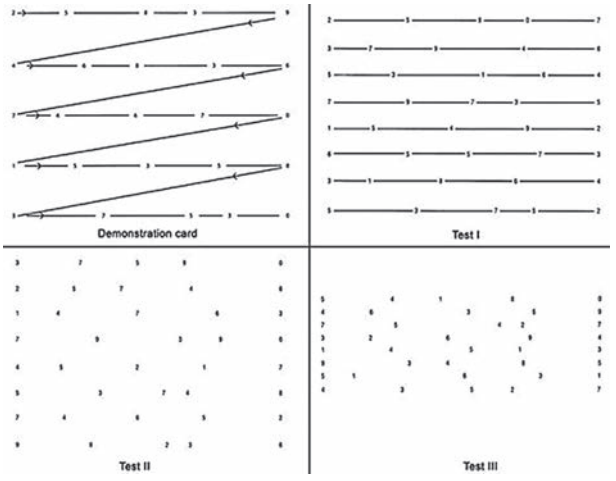
On-site Care

Concussion requires prompt clinical attention. After sustaining a possible concussion, athletes should immediately be removed from play (*Table 1*). Once an mTBI has occurred, the brain is in an extremely vulnerable state and is highly susceptible to additional injury. If a second concussion is experienced before the initial one has resolved, this could result in a potentially fatal brain swelling called second impact syndrome. This is why it is extremely important for athletes still experiencing signs and symptoms of a concussion to avoid risky physical activity. Of all patients who suffer one or more concussions, 10% to 15% have symptoms that continue for three months or longer. These patients are classified as having

post-concussion syndrome.[2,3,4]

Concussion is not a structural change, but rather a metabolic abnormality and therefore not detectable with radiologic studies. Although the detailed neuro-anatomy of concussion is beyond the scope of this column, it is essential clinicians recognize that it involves the cerebral cortex, brainstem and cerebellum. Many pathways are vulnerable, especially those that involve the coordination of movements, and it is logical to assess concussion by evaluating eye movements.

The King-Devick Test (KDT), often used to assess concussion, evaluates saccadic eye movement, which may alert the clinician to a cerebellar disturbance. The test yields an evidence-based, objective, physical measure for determining remove-from-play, thus preventing the cycle of brain re-injury and facilitating prompt entrance into the health care system.[8,9] The procedure is fast, reliable and reproducible, all ideal attributes for sideline screening. According to one study involving boxers and mixed martial arts fighters, the KDT is an accurate and reliable method for identifying athletes with head trauma and concussion.[8]



The King-Devick test evaluates saccadic eye movements and may be used on-site when concussion is suspected.

Table 2. Graduated Return To Play Protocol[4]

Stage 1: No activity—complete physical and cognitive rest.
Stage 2: Light aerobic exercise such as walking, swimming or stationary cycling.
Stage 3: Sport-specific exercise such as skating and running drills.
Stage 4: Non-contact drills such as passing or receiving in football.
Stage 5: Full contact practice following medical clearance.
Stage 6: Return to play—normal game activities.

Cornerstones of Concussion Management

The mainstay of concussion management is physical and cognitive rest until symptoms resolve. This is followed by a graded program of exertion prior to medical clearance and return to playing (*Table 2*). The majority of symptoms related to the head injury will recover spontaneously over several days. During this period of recovery (while symptomatic), it is important to emphasize to the athlete the necessity of both physical and cognitive rest. Activities that require concentration and attention (e.g., scholastic work, video games, text messaging) may exacerbate symptoms and possibly delay recovery.

One study recently described the beneficial effects of post-concussion optometric care. In addition to traumatic structural damage to ocular tissues, patients may present with vergence disorders such as convergence insufficiency, accommodative deficits, fusional instability, oculomotor dysfunction and photosensitivity. Treatment methods may include tinted spectacle correction for full-time wear and conventional oculomotor-based vision therapy. Clinicians should consider a comprehensive optometric approach, as research suggests the injured, young-adult brain has considerable residual visual system plasticity.[10]

Concussion, mTBI and CTE are complex neurological conditions that share the common feature of traumatic injury. As the research continues to evolve, optometrists have the opportunity to "get in the game" and help people who are living with these challenges. ■

Dr. Wolter is in private practice in the Northeast region of Pennsylvania.

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Responsibilities: Candidates are expected to be highly knowledgeable in the field of Cornea and Contact Lenses who can develop and teach courses and/or laboratories in the subject area. The candidate must also be able to provide direct patient care and clinical instruction to professional students as well as residents, and be involved in interdisciplinary practice with other educational professionals. Candidates must be willing to actively participate in curricular assessment, professional development, student counseling and service activities within the college, university and the scientific community. Successful candidates are also expected to be involved in research and scholarly activities, and have a sincere commitment to optometric education, community service and patient care. Primary duties include, but are not limited to:

a) **Teaching**
- Developing and delivering lectures and/or laboratories for cornea and contact lenses and related areas, as assigned;
- Embracing and enhancing the didactic philosophies in the O.D. program;
- Maintaining and expanding the high quality clinical practice environment for optometry students on rotation;
- Precepting students on clinical rotation at the Midwestern University Eye Institute-Downers Grove.

b) **Service**
- Helping to maintain and grow the state of the art optometry program with a strong interdisciplinary focus that meets the needs of patients in the surrounding community; is efficient, patient friendly, and cost-effective;
- Working closely together with all optometry and ophthalmology faculty to provide a complete range of eye and vision care services;
- Participating in leadership roles in state, regional, and national optometry organizations;
- Participating on College and University committees, as assigned;
- Participating in College and University service activities.

c) **Scholarly activity**

Engaging in research and scholarly activity, including presentations at scientific meetings, research, and publication in peer-reviewed journals sufficient to qualify for academic advancement in a non-tenure track position.

Qualifications: Candidates must possess a Doctor of Optometry degree from an ACOE-accredited institution, must have completed an advanced degree and/or ACOE-accredited residency in Cornea and Contact Lens, and must be eligible for an Illinois optometric license. Primary eye care clinical expertise is also required.

Contact information: Interested applicants should forward a letter of interest and curriculum vitae to Dr. Joshua Baker, Acting Dean, or Dr. Mary Lee, Vice President & Chief Academic Officer, Pharmacy and Optometry Education; Midwestern University, Chicago College of Optometry, 555 31st Street, Downers Grove, IL 60515; e-mail: jbaker@midwestern.edu or mleexx@midwestern.edu.

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Continuing Education

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1. Complete an accredited residency in medical optometry
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3. Practice in a medical setting for a minimum of two years.#

www.abcmo.org

Visit **www.abcmo.org** to understand how JC accredited medical facilities credential specialists and why specialty certification can enhance the careers of optometrists who complete residencies in medical optometry.

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^ At this time, 127 JC accredited hospitals, clinics and teaching institutions recognize ABCMO specialist certification.
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Product Review

Dry Eye Care

Tear Stimulation

Allergan's TrueTear Intranasal Tear Neurostimulator temporarily increases tear production in adult patients, according to the company. TrueTear is a handheld stimulator with disposable tips that is inserted into the nasal cavity to induce the production of tears.

Visit www.allergan.com.

New Punctal Plug, Lid Cleanser

Oasis Medical now offers a new medium-term punctal occluder, as well as eyelid and lash pre-soaked pads.

The Soft Plug Extended Duration 180 is canalicular and made of an absorbable polydioxanone material. Oasis says it can last up to 180 days and is available in three sizes.

The Lid & Lash cleansing pads (available with or without tea tree oil) are pre-soaked with the original pump formulation for daily eyelid and lash cleansing and hydration. It comes in a count of 60 pads for a true full-month supply.

Visit www.oasismedical.com.

Spectacles

Blue Light-Blocking Reading Glasses

Eschenbach's Polinelli reading glasses block 30% of blue light, and also block UVA and UVB, according to the company. Three AR coatings offer better contrast and sharpness when viewing digital devices, according to Eschenbach.

The thin polycarbonate lenses feature spring-hinge temples. Choose from +1.00D up to +2.50D in 0.50 increments, plus some options up to +4.00D for patients with higher magnification needs.

Visit www.eschenbach.com.

Diagnostic Equipment

Slit Lamp Camera Attachment

Haag-Streit's Fundus Module 300 allows non-mydriatic fundus imaging during the slit lamp exam; it attaches directly to the biomicroscope for full, stable exam integration, according to the company. It is compatible with BQ 900, BP 900, BI 900 and BM 900 model slit lamps by Haag-Streit, and can be used in combination with the IM 900 or IM 600. Captured images are transferred to Haag-Streit's EyeSuite software.

Visit hsdriven.com/fundus. ■

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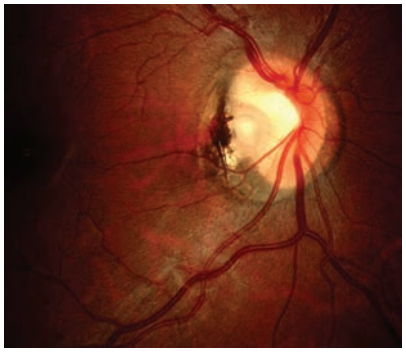
Diagnostic **Quiz**

Ain't It the Pits?

By Andrew S. Gurwood, OD

History

A 74-year-old black male reported to the office with a chief complaint of blurry vision and a black spot in his left eye's field of vision, which he said had existed for many years. He said that he was told "that he had a pit in the back." He was hoping we could prescribe him some spectacles that would improve his vision.



This 74-year-old patient has suffered from blurry, spotty vision in his left eye for years. Can you say why?

The patient's systemic and ocular histories were remarkable for a cerebrovascular accident (stroke) experienced in 2011—with no lasting systemic paralysis and hypertension—for which he was properly medicated with lisinopril and amlodipine. He denied allergies of any kind.

Diagnostic Data

His best-corrected entering visual acuities were 20/20 OD and 20/100 OS at distance and near. His external examination revealed no evidence of afferent pupil defect; however, a left ceco-central superior absolute scotoma was detected using the facial Amsler technique and supported by confrontation fields and Amsler grid follow up. Refraction and pinhole did not improve the acuity.

The biomicroscopic examination of the anterior segment was normal with Goldmann applanation pressures measuring 15mm Hg OU. The pertinent dilated fundus findings are demonstrated in the photograph. The periphery was normal.

Your Diagnosis

Does this case require any additional tests? How would you manage this patient? What is your diagnosis? What is the patient's likely prognosis?

To find out, visit www.reviewofoptometry.com. ■

Retina Quiz Answers *(from page 110):* 1) d; 2) d; 3) b; 4) d; 5) d.

Next Month in the Mag

In June, *Review of Optometry* is proud to present its 8th Annual Retina Report. Topics include:

- *Rethinking Anti-VEGF Protocols for Diabetic Retinopathy*
- *AMD Mimickers: When to Suspect Macular Dystrophy* (earn 2 CE credits)
- *How to Use Advanced Imaging Techniques for Detection and Management of Choroidal Diseases*
- *The 1st Annual ORS Larry Alexander Optometric Residency Case Report Contest (presentation of winning case)*

Also in this issue:

- *Presbyopia Correction by the Drop: Can It Work?*
- *Horner's Syndrome: Your Apraclonide Test Came Back Positive—Now What?*
- *Don't Let Dry Eye or Allergy Prevent Lifelong Contact Lens Success*

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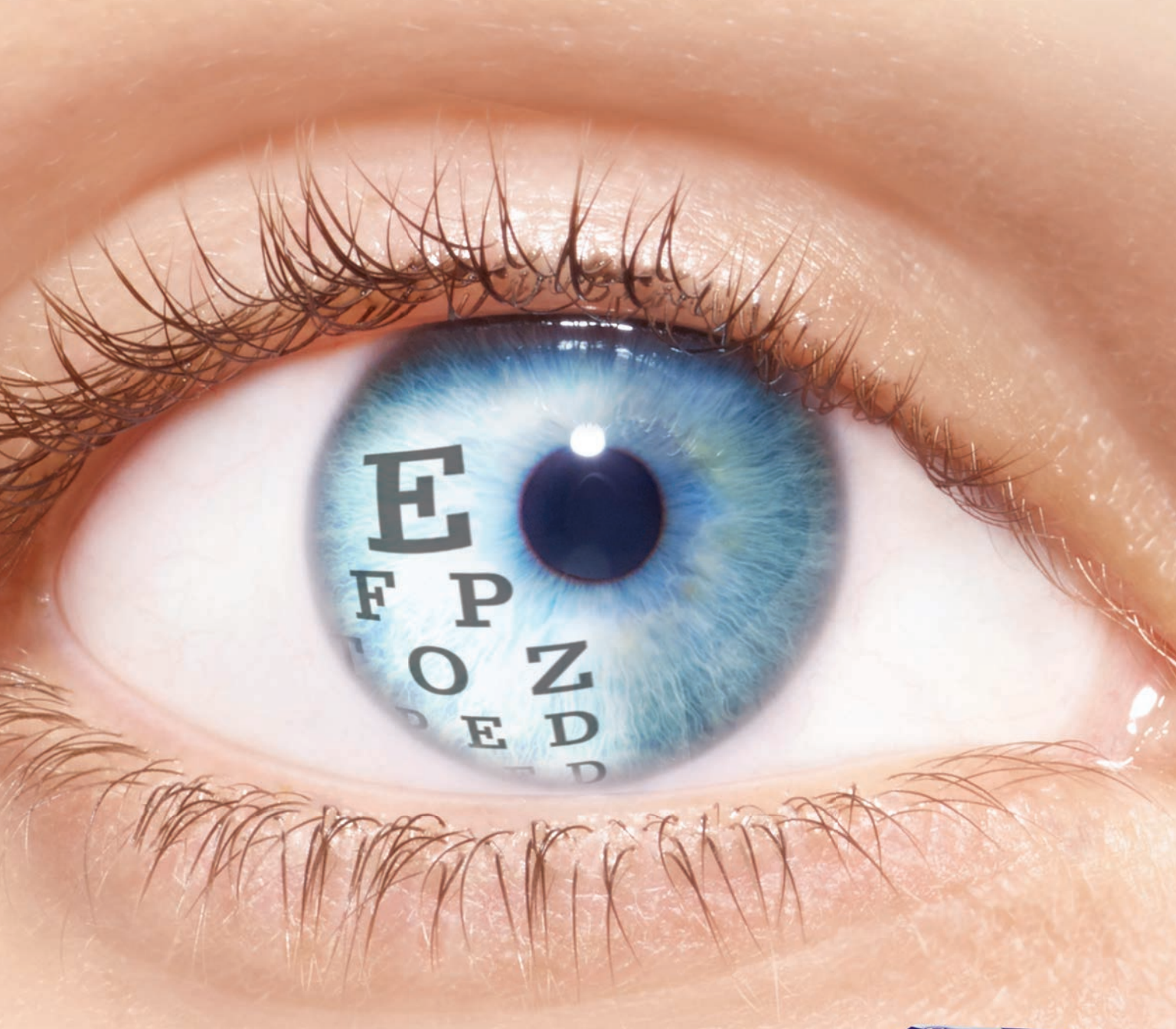
[1]Blackie CA et al. Cornea 2009 (v0.1) p.1.



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*Prospective, randomized, double-masked, single-dose, contralateral eye study, N=40. Lipid layer thickness was measured in nanometers, and baseline measurement was 63.38.

1. Korb D, et al. Evaluation of extended tear stability by two emulsion based artificial tears. Poster presented at: 6th International Conference on the Tear Film and Ocular Surface: Basic Science and Clinical Relevance; September 22-25, 2010; Florence, Italy.

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