NEW MINISERIES — The Retinal Vasculature: A Marker for Ocular, Neurologic and Systemic Disease, **p. 81**

REVIEW® OF OPTOMETRY

January 15, 2017 www.reviewofoptometry.com

CORNEAL DISEASE REPORT

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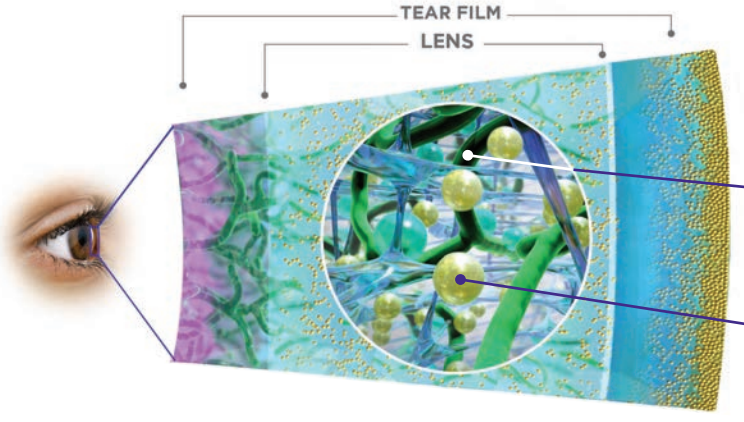

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VOL. 154 NO. 1 ■ JANUARY 15, 2017

IN THE NEWS

The FDA recently granted an **orphan drug designation to Impavido** (miltefosine, Profounda) for the **treatment of *Acanthamoeba* keratitis.** "By creating miltefosine-induced alterations to the membrane architecture of the amoeba, miltefosine allows patients a therapeutic option that has potential advantages over conventional therapy approaches," said CEO Todd MacLaughlan in a press release.

A federal appeals court recently rejected a request by major contact lens makers for a preliminary injunction, which would have blocked **Utah's anti-price fixing law**. Utah passed a law stopping contact lens makers from setting minimum prices for their products, and this **upholds a lower court's ruling that allowed the law to go into effect**.

A new study found 6.9% of 130 study participants developed **cystoid macular edema (CME) following scleral buckling**. The study also found the risk factors associated with CME after scleral buckle included **older age, more extended retinal detachment, macular detachment and external drainage**. Research suggests that clinicians should use caution when employing external drainage in older patients with extensive retinal detachment.

Lai TT, Huang JS, Yeh PT. Incidence and risk factors for cystoid macular edema following scleral buckling. Eye. December 9, 2016. [Epub].

The FDA recently issued a **ban against** the sale, distribution and manufacturing of **powdered medical gloves**, which will go into effect January 19, 2017. The ban was proposed due to mounting evidence that powdered gloves present serious risks to patients such as airway and wound inflammation, post-surgical adhesions and allergic reactions.

Long-term Retinal Effects of Pre-eclampsia

New research suggests clinicians should be wary of traction retinal detachment in patients with this common gestational diagnosis. **By Rebecca Hepp, Managing Editor**

Add retinal disorders to the long list of possible long-term effects of pregnancy, according to a new study. Researchers looked at more than a million women who delivered a baby in Quebec from 1989 to 2013 and tracked later hospitalizations until March 2014. Of the women studied, the 5.8% diagnosed with pre-eclampsia were more prone to retinal disorders and metabolic disease compared with the study participants without pre-eclampsia.

"We have always known women with pre-eclampsia are at risk for retinal vascular disorders during and immediately after their pregnancies," says Jill Autry, OD, RPh, a partner at the Eye Center of Texas ophthalmology center. "Interestingly, this article suggests long-term concerns not only for an increased risk of vascular retinopathies but for other retinal conditions such as traction retinal detachment."

Without adjustments, the study found women with pre-eclampsia had 5.3 times the risk of traction detachments and 3.7 times the risk of retinal breaks. While adjusting for age, parity, period and socioeconomic status had little influence, adjusting for metabolic disorders significantly weakened the associations—for traction detachments and diabetic retinopathy (DR) in particular. Nonetheless, the risks associated with pre-eclampsia continued to be elevated for traction detachments, retinal breaks and DR, the study authors said.

"The study hypothesizes the retinal vascular system may be permanently weakened by pre-eclampsia, as well as the RPE," Dr. Autry says. "This could put the patient at risk for increased vascular disease, retinal ischemia, serous detachments and traction detachments due to subsequent neovascularization. Important to note is that there was not a significant difference found in rhegmatogenous RD, which further supports a vascular association, not a vitreous link."

The researchers also broke down the data by gestational onset of pre-eclampsia and found, compared with patients without pre-eclampsia, women with early-onset pre-eclampsia had 8.4 times the risk of DR and 4.6 times the risk of nondiabetic retinopathy. Women with late-onset pre-eclampsia had only 3.6 times the risk of diabetic retinopathy and 1.9 times the risk of nondiabetic retinopathy compared with no pre-eclampsia.

The study had several limitations, including a lack of information on smoking, ethnicity and drug use, as well as the visual acuity associated

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Pre-eclampsia

continued from page 4

with the retinal disorders. Finally, the study only addressed patients hospitalized, as the administrative hospital data did not include information on outpatient clinics.

"Many patients with pre-eclampsia have risk factors for the development of vascular disease in their lifetime," Dr. Autry says. "Patients older than 40, those with underlying DM and HTN, who are overweight or have kidney disease, a history of blood clots, or autoimmune diseases are all at increased risk for pre-eclampsia and, therefore, at higher risk for the long-term associated chronic illnesses also seen in retinal disorders," she notes. "Certainly, all patients with these risk factors should have regular dilated eye exams over their lifetimes, and maybe we should use a history of pre-eclampsia as a confounding risk factor as well."

Despite these limitations, the researchers admit metabolic diseases explained only part of the issue, suggesting pre-eclampsia could be an independent risk factor for retinal disorders. Further research will help determine whether a history of pre-eclampsia would also be an indication for screening.

Auger N, Fraser WD, Paradis G, et al. Pre-eclampsia and long-term risk of maternal retinal disorders. Obstetrics and Gynecology. December 02, 2016. [Epub ahead of print].

The Root of Space-Flight Induced Visual Impairment

Until now, researchers were unsure of the underlying mechanism that causes visual impairment intracranial pressure (VIIP) in astronauts serving lengthy missions in space. But new research suggests it is related to volume changes in the cerebrospinal fluid (CSF). Concerns arose as the severe structural changes proved irreversible upon return to Earth.

The last decade has seen a pattern of visual impairment in astronauts who flew long-duration space missions, according to researchers. Blurry vision led to further testing that revealed globe flattening and increased optic nerve protrusion. The primary source of the problem was previously thought to be a shift of vascular fluid toward the upper body within the microgravity of space. This new study, however, suggests the microgravity confuses the CSF by the lack of posture-related pressure changes in space.

Researchers used quantitative imaging algorithms to assess any correlation between changes in CSF volume and structures of the visual system. Results showed that, in addition to increased post-flight globe flattening and inflammation at the head of the optic nerve, long-duration astronauts also had significantly greater post-flight increases in orbital CSF volume.

This research is the first to provide quantitative evidence from short- and long-duration astronauts and identify the role of CSF in globe deformations in astronauts with VIIP.

Radiological Society of North America. Cause of visual impairment in astronauts identified. ScienceDaily. November 28, 2016. Available at www.sciencedaily.com/releases/2016/11/161128132831.htm.

Research Links Zika Virus to Glaucoma

When medical history lists the important issues of 2016, the Zika outbreak will certainly be near the top. The first case of Zika-induced microcephaly reached the United States in January 2016.[1] Only a few weeks later, the World Health Organization declared it an international public health emergency, and President Obama sought to infuse $1.8 billion into the fight against Zika.[2,3] By November, researchers had identified several systemic issues caused by the virus—including an association with glaucoma in infants, according to a new case study.

Investigators from Yale University, in partnership with a team in Brazil, published a case report linking exposure to the virus during gestation to the development of glaucoma after birth. The report, published in the November issue of *Ophthalmology*, looked at 13 infants in Brazil who were exposed to Zika *in utero*. The infants were born with normal head sizes, but later experienced slow head growth. Eleven of them were later diagnosed with microcephaly, and one—a three-month-old male—developed glaucoma.[4] This is the first reported link between glaucoma and the Zika virus, the researchers say.

However, this is not the first instance of Zika's potential impact on ocular disease. In May, a *JAMA Ophthalmology* report linked congenital Zika infection with several vision-threatening conditions, such as optic nerve abnormalities, bilateral macular lesions and perimacular lesions.[5]

1. McNeil D. Hawaii reports baby born with brain damage linked to Zika virus. 16 Jan 2016. The New York Times.
2. Sikka V, Chattu V, Popli R, et al. The emergence of Zika virus as a global health security threat: A review and a consensus statement of the INDUSEM joint working group. JGID. 2016 Feb;8(1):3-15.
3. The White House. Office of the Press Secretary. Fact sheet: Preparing for and responding to the Zika virus at home and abroad. 8 Feb 2016. Available at www.whitehouse.gov/the-press-office/2016/02/08/fact-sheet-preparing-and-responding-zika-virus-home-and-abroad. Accessed December 13, 2016.
4. de Paula Freitas B, Ko A, Khouri R, et al. Glaucoma and congenital Zika syndrome. Ophthalmology. 2016 Nov;123(11):S0161-6420.
5. de Paula Freitas B, de Oliveira Dias J, Prazeres J, et al. Ocular findings in infants with microcephaly associated with presumed Zika virus congenital infection in Salvador, Brazil. JAMA Ophthalmology. 2016 May;134(5):529-35.

Video Games & Low Vision

In a study recently published in *Scientific Reports*, researchers from Vanderbilt University and the University of Rochester found action video games (AVGs)—a form of perception training—yield significant peripheral perception improvements in a pediatric low vision study group.[1] These improvements manifested after only eight hours of training and, in a subset, improvements were measurable 12 months later.[1]

"Children who have profound visual deficits often expend a disproportionate amount of effort trying to see straight ahead, and as a consequence they neglect their peripheral vision," said Duje Tadin, PhD, associate professor of Brain and Cognitive Sciences at the University of Rochester, in a press release.[2]

The scientists looked at 24 children and adolescents ages nine to 18 with low vision, and seven pediatric patients with normal vision as controls. The low vision cohort had best-corrected visual acuities between 20/60 and 20/300 and visual fields of at least 35 degrees in both hemifields. No history of cognitive impairment existed in any patient.[1]

The researchers divided the cohort into groups to study three training regimens: (1) a child-friendly, commercially available AVG; (2) a modified attentional tracking (MAT) task designed to mimic task-specific demands within AVGs; and (3) a control game similar to Tetris. The MAT was designed to have participants track multiple moving objects simultaneously while looking for another object that briefly appears and requires a response from the player; it also eliminated undesirable aspects of AVGs such as the need for a high level of hand-eye coordination and age-inappropriate material.[1]

By testing direction discrimination, perceptual crowding and a visual search task, researchers found the AVG group's central and peripheral vision improved by as much as 50% after 10 training sessions.[1]

Paul Harris, OD, who focuses on vision therapy and rehabilitation at The Eye Center at Southern College of Optometry, says AVGs can be beneficial, but clinicians should be careful. "We know not all games will bring the same level of benefits, but AVGs played in moderation and mixed with movement activities in the real world can be incredibly beneficial in helping to increase the ability to search larger areas of the visual environment more quickly and with less effort."

"Studies are continuing to show that, in the right amount and with the right kind of game, patients' visual abilities actually improve in a lasting and positive way," Dr. Harris adds. Vision therapists are incorporating more game play into therapy, he says, and "when supplemental at-home versions of the software can complement what is done in-office, these systems should help to achieve higher levels of cure in shorter periods of time with far more active involvement of our patients." ■

1. Nyquist JB, Lappin JS, Zhang R, Tadin D. Perceptual training yields rapid improvements in visually impaired youth. Scientific Reports. 2016 Nov;6:37431.
2. University of Rochester. Brain training video games help low-vision kids see better. News release. November 28, 2016. Available at www.rochester.edu/newscenter/brain-training-video-games-help-low-vision-kids-see-better-201322. Accessed December 22, 2016.

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Reference: 1. Srinivasan S, Ngo W, Jones L. The relief of dry eye signs and symptoms using a combination of lubricants, lid hygiene, and ocular nutraceuticals. Poster presented at: ARVO annual meeting; April 2015; Denver, CO.

AKORN Consumer Health

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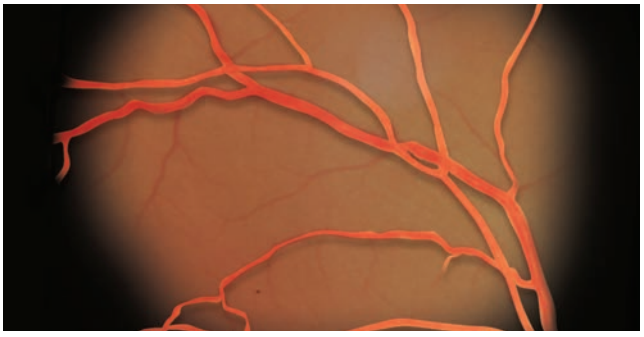
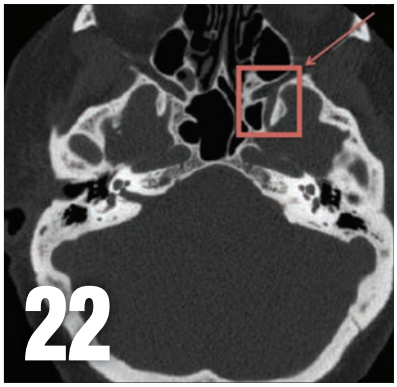
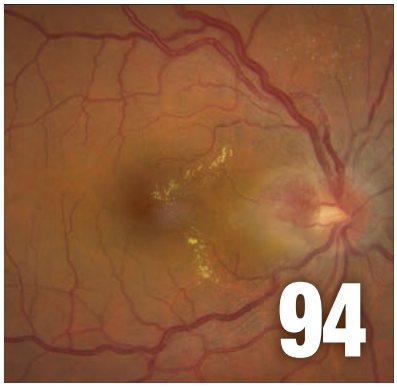


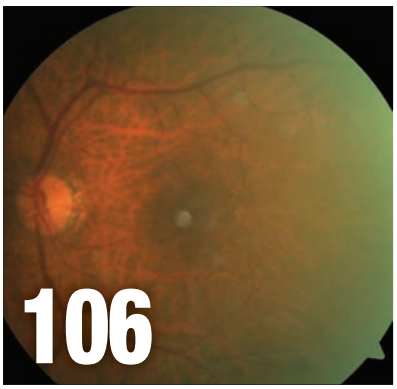
RETINAL VASCULAR MINISERIES:

Departments

Review of Optometry January 2017







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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.

Please see the adjacent page for Brief Summary of Safety Information and visit Xiidra-ECP.com for Full Prescribing Information.

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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.

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Outlook

By Jack Persico, Editor-in-Chief

Give Yourselves a Hand

ODs are taking on more front-line work manipulating ocular tissue rather than merely examining it.

Something interesting has been happening over the last few years: ODs are increasingly using their hands, not just their heads, when caring for their patients. And I don't mean twirling dials on a phoropter or moving a slit lamp joystick around. I'm talking about things like performing SLT for glaucoma, YAG capsulotomy for post-cataract patients, intralesional steroid injections for chalazia and more—procedures that most people, ODs included, had long considered exclusive to ophthalmology.

These are in-office procedures done without the need for an operating room's full complement of technical and human resources. Still, in describing these interventions, you might be inclined to use "the S-word"—surgery. That's a loaded term that riles up those who feel optometrists should stick to making glasses, so we at *Review* try to limit its use to avoid the baggage that comes with it. Strictly speaking, these procedures do meet the definition, as *surgery* derives from the Greek for "hand work." Consulting a dictionary may be an overused way of making a point, but I do find that historical precedent interesting. (Another fun-with-etymology fact for those of us who attend a lot of conferences: *symposium* means "drinking party" in Greek.)

No one expects optometrists to do ILM peels or scleral buckles, but relatively low-risk, high-reward procedures like capsulotomies satisfy an unmet need for patients who can't easily access ophthalmological care. It's the same argument that served optometry well through the TPA wars. And it comes with the same responsibilities: a willingness to study, train and master the tasks expected of you before use. These procedures can't be learned from an article or two; by definition, a hands-on procedure needs to be practiced under the tutelage of a mentor.

Diagnosis and referral will always remain staples of an OD's clinical responsibilities. But since hands-on procedures are one of the biggest growth areas in optometric education, we've devoted this issue's Corneal Disease Report to things an optometrist can do in-office to intervene for patients beyond basic identification and comanagement. In these pages, you'll learn about epithelial debridement and stromal puncture for corneal erosion, EDTA chelation for band keratopathy, amniotic membrane application for wound healing, and how to perform foreign body removal.

You may notice that, this time, we did let the S-word slip in a few times. If you'd like, go ahead and take a minute to celebrate. Possibly at the next symposium.

Two new columns debut this month. Paul Karpecki, OD, our workaholic Chief Clinical Editor, offers personal reflections on trends in practice in an op-ed column called "Through My Eyes." Paul has seen it all, and we look forward to his perspective. Also, Bisant Labib, OD, of PCO highlights the real-world relevance of fundamental principles of care in "The Essentials." Both are sure to be insightful. Enjoy! ■

A New Year in Sight

Setting goals that challenge you personally and professionally yields invaluable experience, growth and excitement. **By Paul M. Karpecki, OD, Chief Clinical Editor**

Take out a pen and paper right now. Write down at least five, but preferably 10, goals for 2017. This may seem like a lot, but once you run through the following categories—family, career, practice/business, fitness, faith, social and charity—you'll already be well on your way.

Next, make certain that your goals include specific, yet realistic, timelines. You may want to write the goals in the present tense, as if you've already achieved them: "Our practice's gross income is up more than 20%, and income from medical eye care services exceeds 30% as of December 31st, 2017."

Finally, place your list of goals where you'll see it frequently. During my residency, I stuck my list on my bathroom mirror. I was amazed that, within a year, I had achieved all 10 goals. Seeing them every morning helped me focus my efforts for the day. And this continues to serve me well even today.

Does goal-setting work? Yes! In 1979, Harvard Business School researchers asked the graduating class, "Have you set written goals and created a plan for their attainment?" The results: 84% had no set goals, 13% had goals but hadn't written them down and 3% had written goals as well as a concrete plan to attain them. You can probably infer the final outcome. By 1989, the 13% with goals were earning twice as much as the 84% who had none. However, the 3% with written goals were actually making more than 10 times as much as the rest of the class.

Six Steps to Success

Here are some other helpful tips to help you achieve your goals:

1. Think big, but keep it manageable. Small goals tempt us because they're easier to achieve. But "think big goals and win big success," as David Joseph Schwartz said, challenges us to aim higher. However, if an idea seems too big, and is not broken into manageable steps, most people will never begin. Strike a balance: push, but don't paralyze, yourself.

2. Believe in a higher purpose. In my life, this has had many meanings and includes my faith. But the concept of a higher purpose could mean that we see our role in society as saving vision, preventing blindness and enhancing lives, not simply having a 9-to-5 job. I assure you the former will make for a far more enjoyable life and rewarding professional career.

3. Prioritize. We are all so much busier in recent years, and smartphones and social media make it difficult to separate our professional and personal lives. Just remember that there truly is a limit to the number of productive hours in a day. Know your strengths and limitations, and prioritize your time to avoid burnout. Otherwise, both your family and career will suffer.

4. Give back. In lecturing, writing and research, I've had people ask, "Why do you freely share so much of the knowledge you've worked an entire career to obtain?" Those who think like that miss out on the greatest experiences in life. Many people have shared their insights with me throughout my career. Donald Korb is a great example. He knows more about ocular surface disease than I can ever hope to learn. By generously sharing his knowledge and experience, he saved me years if not decades of mistakes. Without him and so many others, there is no chance that I could provide the level of clinical care I do today.

5. Be humble. It's easy think we already have all the answers and experience we need; I can assure you that's never the case. People who go far ride on the shoulders of the giants who came before them. Family, friends, colleagues, staff, professors, mentors and religious leaders all likely contributed to where you are today—to who you are today.

6. Create your future. It's said that the best way to predict the future is to create it. Each of us has the ability to tailor our future through the choices we make, the passion in our heart and the vision we have of what can be. Sometimes we can get so lost in our work that we lose sight of the experience gleaned from moment to moment. Eckhart Tolle noted that "the power for creating a better future is contained in the present moment: You create a good future by creating a good present."

In fact, real achievement may not be reaching a certain goal but appreciating and enjoying all the experiences along the way. ■

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Cover Your Assets

Patient education is tricky, but I've got a system that really works—as long as "huh?" counts as an answer. **By Montgomery Vickers, OD**

I obsess about making sure I cover all the bases when communicating with patients. Due to my controlling and paranoid personality, I am always trying to get patients to understand their eyes and my treatment plans.

Big deal, right? I don't think you understand; I try *way* too hard to cover my, uh, assets.

Example 1:

Contact lenses can be, sometimes, pretty often in fact, a way to be less dependent, mostly, on glasses, at least for most people. But not everyone who tries them will like them because we are all different, and even your right and left eye may have differing opinions about contact lenses, but what is success anyway? Any questions?

The number one question after I say this has always been, "Huh?"

Example 2:

What is astigmatism? Well, I have been explaining it for 37 years now and I really don't think I have ever done a good job because it's hard to explain. I can show it to you and you might say, "Oh, I get it!" or maybe not. So, do you really want me to try to explain it?

The response after this? "Huh?"

Example 3:

We don't really know whether myopia control actually will work for your child. It might or it might not, and he might get more myopic or he might not; he might change a little or he might change a lot. Research has taught us we don't really know, and if I could predict the future I would live in Vegas, and I don't. Wanna try it?"

I know what they're thinking. "Huh?"

Example 4:

Glaucoma glaucoma glaucoma. Ancient Greeks thought it meant you had a cataract and your eye shined. Hope that helps. Here's your prescription.

I think this one really helps, don't you? "Huh?"

Example 5:

Do we accept your insurance? I think it would be better if my staff explained the insurance and I saved my brain for important matters such as that horrible bump on your eye that may lead to enucleation and possible death if it's not removed in time, although it's probably just a freckle on your eye and shouldn't be a concern, but hard to tell, OK?

"Huh? What bump? OMG!"

Example 6:

What about LASIK? According to our testing, you are, on paper, probably, a decent candidate for any number of refractive surgical techniques, contact lenses or glasses. So you are a good, or at least fairly good, person to get a second opinion regarding your options; each could be beneficial or lead to blindness, or something in between, and LASIK is irreversible. Totally your call.

"Huh?"

Oh, did I mention that I am thinking about recording every conversation with every patient so I can, with authority, say "See! I never explained astigmatism after all, so how could I be wrong?" Unfortunately, no storage system is large enough to handle my explanation of every possible scenario to every single patient. Now, could you sign and date this column and send it back to me so I'll know you understand? ■

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Cruisin' to Heal a Bruisin'

When presented with ecchymosis, how thoroughly should you evaluate before you hand patients the frozen green beans and say, "rest up?" **Edited by Paul C. Ajamian, OD**

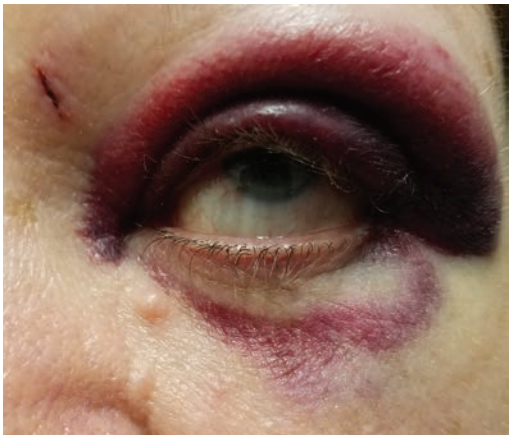
Q A 69-year-old recently presented with a bruised eyelid after taking a spill on the sidewalk. I normally just use a cold compress to treat discomfort and send them on their way. Is there anything else I should be doing?

A "While this looks like a straightforward case of ecchymosis, you can't be dismissive," says Joseph Sowka, OD, a professor of optometry at Nova Southeastern University College of Optometry. He says it's crucial to thoroughly check the patient for rare instances when the situation is more complicated than it seems at first glance. "You need to do a full evaluation from the front to the back when recent trauma is involved. Though problems here are unlikely, check to ensure that the globe is intact, the anterior chamber is formed, and that there is neither cell nor flare present."

Heed the following four-point plan in all cases of bruising, Dr. Sowka advises.

1. Listen for Crepitus

Dr. Sowka says that palpating the eyelid and periorbital region can help you identify whether the patient has experienced trauma significant enough to break bones. "As you palpate the eyelids, you are looking and listening for the telltale crackling of crepitus, which is air that has invaded the lid tissue. This indicates that an orbital wall has fractured." Another tip: "Test the skin sensation of the lower eyelid. Loss of sensation also indicates an orbital fracture and neuronal compromise," says Dr. Sowka. And, if you suspect a break, X-ray or computed tomography (CT) is helpful to confirm the diagnosis.



As swollen and dramatic as this looked at onset, the problem resolved within a week after we ruled out damage to the eye itself.

2. Check the Retina

Dr. Sowka says that, in any case of blunt trauma to the eye and periorbital region, dilate and perform binocular indirect ophthalmoscopy to check for retinal tears and detachments. "It's important to be sure that neither a tear nor a detachment has occurred, because the force from the injury may have disturbed the vitreous enough to make these complications possible." Ultra-widefield imaging has its place, but this isn't one of them. Commotio, peripheral breaks and retinal elevation have to be evaluated in stereo with the trained eye of the optometric clinician.

3. Watch for Symptoms of Emergent Cases

If altered mentation exists, or if the patient presents with a severe headache or somnolence, Dr. Sowka says it's necessary to refer for an urgent CT. Further, he says to be aware of severe bruising. "If a patient received trauma to the eye substantial enough to cause severe ecchymosis, then they received enough trauma to induce a subarachnoid or other type of intracranial hemorrhage," notes Dr. Sowka. "While we hate to send people to the ER unless absolutely necessary, it is difficult to get patients in to see an orbital specialist or neurologist at a moment's notice. The ER can be the best entry point into the system, but be sure to send a detailed note along with the patient so that the physician knows why they are being sent in."

4. If All's Clear, Let it Heal

"Once all of these precautions have been taken and serious sequelae have been eliminated, you can now treat the patient with reassurance," says Dr. Sowka. In some cases, he says, cool compresses may ease any discomfort and give the patient something to do. Otherwise, no further treatment is needed. ■

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Nerves in a Tight Spot

When a patient presents with suspected cranial pathology, knowing the nooks and crannies the nerves call home can guide you toward a diagnosis. **By Bisant A. Labib, OD**

In this new column, "The Essentials," I hope to reinforce the basic science principles and clinical techniques essential to optometry. The hope is that by revisiting these concepts in both a succinct and clinically relevant manner, we may advance our understanding as both scientists and clinicians, and ultimately provide better and more comprehensive patient care. Sometimes, recognizing a new angle on the staple anatomy, physiology and techniques can provide us with fresh, new insight into diagnosis and management.

A Case of the Nerves

A 52-year-old Caucasian male presents to your office with unilateral orbital swelling, pain and vision loss of one week's duration. Examination also reveals restricted abduction and a hyper deviation in his left eye. His ocular history is otherwise non-contributory. His systemic history is positive for a previous diagnosis of squamous cell carcinoma (SCC) of his hard palate one year ago, for which he had undergone surgery and radiotherapy at that time. No lymphadenopathy—visible or palpable mass—is present.

What is your primary differential? Is the patient's history pertinent to his current clinical presentation?

The evaluation of the cranial nerves is an essential part of any eye examination. If an abnormality is found, we focus on identifying the underlying etiology and, if necessary, localizing the suspected lesion through careful history, extraocular muscle evaluation and a basic neurological exam. Often, when see multiple cranial neuropathies, our first instinct is to evaluate for pathologies located within the cavernous sinus. While this is an appropriate differential consideration, as it contains multiple cranial nerves, we frequently fail to recognize that this isn't the only site where several nerves are closely confined in a small space.[1-3]

Table 1. Review of Pterygopalatine Fossa

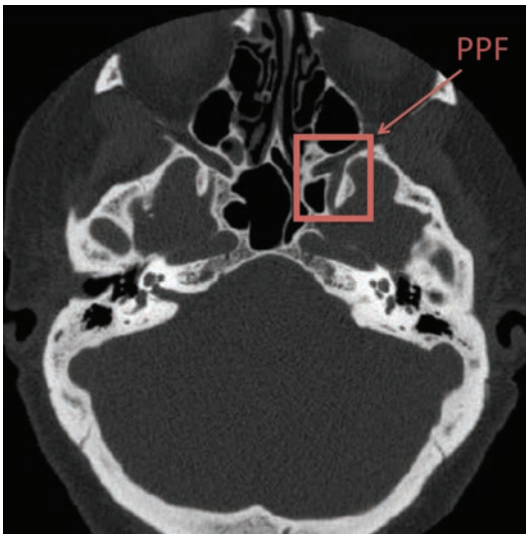
Opening	Contents	Innervation
Pterygomaxillary fissure	• Posterior superior alveolar nerve • Maxillary artery	Sensory stimulation to infratemporal maxillary
Foramen rotundum	• Maxillary nerve (CN V2)	Sensory stimulation to mid portion of the face
Vidian canal	• Vidian nerve, artery, and vein	Parasympathetic stimulation to the nose, palate and lacrimal gland
Pharyngeal canal	• Pharyngeal branch of the maxillary nerve and artery	Mucosa of the nasopharynx
Inferior orbital fissure	• Zygomatic branch of maxillary nerve • Infraorbital artery and vein	Lacrimal gland
Greater palatine canal	• Greater palatine nerve	Sensory and parasympathetic stimulation to mucous membrane of hard palate
Lesser palatine canal	• Lesser palatine nerve	Sensory and parasympathetic stimulation to soft palate, tonsils and uvula
Sphenopalatine foramen	• Sphenopalatine artery and vein • Nasopalatine nerve	Mucosa of anterior hard palate and nasal septum

Same Face, New Space

The pterygopalatine fossa (PPF) is a bony space located anteriorly on each side of the skull base. This structure houses the pterygopalatine ganglion, the largest of the four parasympathetic ganglia of the head and neck. The potential for multiple cranial neuropathies exists not only because this ganglion resides within the PPF but also because this fossa acts as a passageway between several cranial compartments. Thus, it serves as a conduit for disease to spread to numerous, otherwise isolated, anatomical locations.[3]

The PPF is located amidst the maxillary, sphenoid and palatine

bones and contains several openings and foramina (*Table 1*). The PPF is in communication with the orbit, oral cavity, nose, infratemporal fossa, cavernous sinus and the skull base, to name a few.[1-2] Let's review two of these openings and structures, focusing on those that act as a passageway for disease to spread to affect orbital structures.



This computed tomography scan shows the location of the pterygopalatine fossa.

The foramen rotundum. This space is in direct communication within the PPF, where the maxillary nerve passes. The maxillary nerve is the second branch of the trigeminal nerve (CN V_2), and innervates sensation to the mid portion of the face, including the lower portion of the eye.[1,2] Since this branch also runs through the cavernous sinus, any pathology within the PPF can spread directly into the cavernous sinus, and ultimately the brain, via this opening. It can be examined clinically with the cotton wisp test to check for the sensitivity in the location of each branch of the trigeminal nerve on either side.

The inferior orbital fissure. This opens into the superior portion of the PPF, allowing direct contact with the orbital cavity. Passing through the inferior orbital fissure is the zygomatic branch of CN V_2, and the infraorbital artery and vein. Since there is no barrier separating the inferior and superior orbital fissures, disease can easily spread from the PPF to the inferior orbital fissure, and ultimately to the superior orbital fissure, which contains cranial nerves III, IV, VI and V1.[1,2]

Clinical Impact

Why do all these openings and connections matter? Pathologies such as infections and neoplasms, which may otherwise be confined to a certain anatomic location, can easily travel via these connections to remote compartments.

In our case presentation, cavernous sinus pathologies such as a fistula are appropriate differentials. However, a tumor may spread from the PPF to the orbit through the inferior and superior orbital fissures and present in similar fashion. In this case, our patient was diagnosed with recurrent SCC involving orbital metastasis. So, be sure to bear in mind the other tight spaces that can harbor the pathologies causing your patients to experience multiple cranial neuropathies.[4,5] ■

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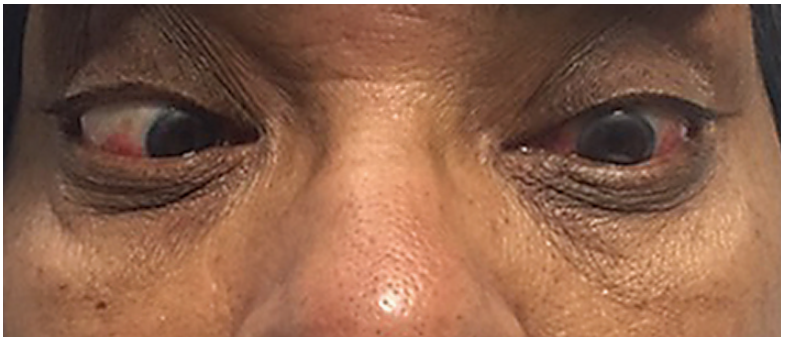
Seeing Halos, No Faith Needed

While temporal artery biopsies are the standard to confirm giant cell arteritis, sonography is a noninvasive alternative. **By Michael Trottini, OD, and Michael DelGiodice, OD**

A 66-year-old Indian female was examined as an inpatient after she experienced an episode of diplopia following a headache. She reported that the headache, which was present for one month, started around both temples and the occipital region and eventually localized to only the left temple. She was also experiencing double vision for the past two days, which prompted her to go to the emergency room. The patient was found to have a left sixth nerve palsy (CN VI). A CT scan was performed, which was normal. The patient was admitted, and neurology recommended MRI and MRA, which were also normal. At this point, our expertise was consulted.



This patient presented with a complete left sixth nerve palsy.

Exam and Diagnosis

The patient was examined at her bedside. She appeared to be in significant discomfort due to her head pain. She denied jaw claudication or scalp tenderness, though she did report increased fatigue and generalized weakness over the past few weeks. Her visual acuities were 20/30 OD and 20/30 OS. No afferent pupillary defect was noted. Confrontation testing was normal. There was a complete left CN VI nerve palsy. External and anterior segment exams were grossly normal with the exception of bilateral inflamed pingueculae which, according to the patient, had been noted for years. Dilated fundus exam was unremarkable. Her medical history was positive for hypertension, for which she was prescribed carvedilol; however, she reported the hypertension has been under very good control.

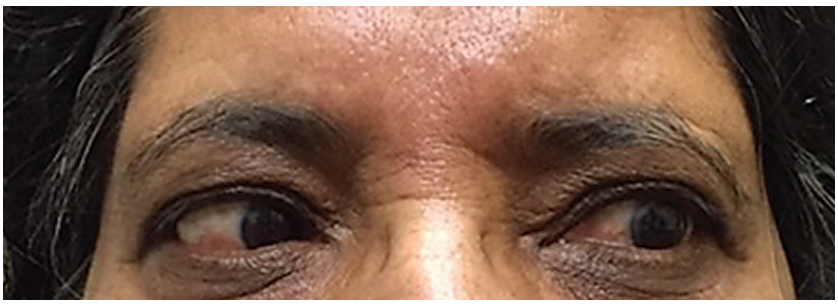
We confirmed the diagnosis of a left CN VI nerve palsy. Given her normal neuroimaging along with her headache, fatigue and weakness we ordered an ESR and CRP, which were elevated at 80mm/hr and 8.2mg/L, respectively. We started her on 60mg of oral prednisone daily and ordered a temporal artery ultrasound. Twenty-four hours later, the patient was re-examined. Her nerve palsy was unchanged, but she reported almost complete resolution of her headache. Her temporal artery ultrasound revealed a "halo sign" within the left temporal artery, which is indicative of giant cell arteritis (GCA).

The patient was discharged from the hospital and maintained on 60mg prednisone daily. She was referred to rheumatology to manage her GCA and prednisone tapering. One week later, the patient was examined in our office, and we noted a dramatic improvement in the nerve palsy. Repeat ESR and CRP were ordered and reduced at 45mm/hr and 0.9mg/L, respectively. As of our last visit, her nerve palsy had completely resolved and she remains symptom-free on a low dose of prednisone.

Discussion

GCA is a granulomatous vasculitis affecting medium- and large-sized arteries in older individuals.[1] While the temporal artery is often involved, GCA can affect the aorta, cranial arteries and arteries elsewhere throughout the body.[1] From an ocular standpoint, GCA can cause sudden and usually severe vision loss from arteritic ischemic optic neuropathy or central retinal artery occlusion.[2] Additionally, GCA can lead to cranial nerve III, IV and VI palsies, where the third and sixth nerves are most commonly affected.[3]

Most CN VI palsies in older individuals are vasculopathic in nature; however, a number of



One week after commencing oral anti-inflammatory therapy, this patient showed dramatic improvement of the sixth nerve palsy. It is now completely resolved as of this patient's last examination.

different etiologies exist, including compressive lesions, acute intracranial ischemia, papilledema, herpes zoster virus and GCA.[4] When diagnosing a CN VI palsy, evaluate for other accompanying symptoms that may suggest a specific etiology. Although our patient had a history of hypertension, her headache, fatigue and weakness were suspicious for GCA, which prompted us to order the ESR and CRP laboratory tests.

Confirmation: Rite of (Diagnostic) Passage

Although the patient's symptoms, findings and laboratory studies were very suggestive of GCA, it is still recommended to obtain a temporal artery biopsy if you suspect GCA. These patients will require long-term steroid management, which has the potential to cause of number of side effects, so absolute confirmation is essential. While temporal artery biopsy is the gold standard in diagnosis of GCA, it is an invasive surgical procedure. Temporal artery ultrasound can be an efficient and noninvasive alternative with comparable sensitivity and specificity of 85% and 90% respectively.[1] In GCA-positive patients, the sonogram shows a halo within the temporal artery due to edema of the arterial wall—referred to as a positive "halo sign."[5] A positive Doppler along with elevated serologic studies as well as clinical symptoms of GCA, as seen in this case, makes the diagnosis highly probable; however, a negative result does not rule out the condition.[1]

Treatment Outcome: What to Expect

Once steroid treatment is initiated, the nerve palsy and other constitutional symptoms will generally show rapid improvement, as was the case with our patient.[6] Although GCA is chronically managed by rheumatologists or vascular specialists, patients will often present initially to us, the optometrists. It is always important to be aware of the various ocular manifestations of GCA in order to lead to a prompt diagnosis. ■

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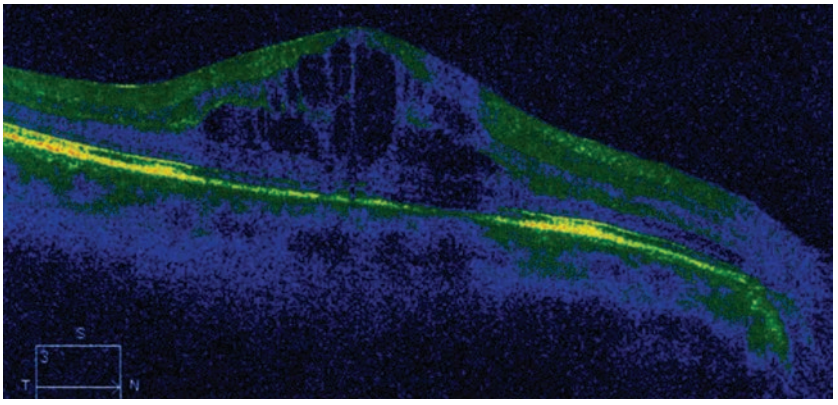
When You See CME

Approaches to managing this common finding. **By Joseph W. Sowka, OD, and Alan G. Kabat, OD**

Three weeks after uncomplicated cataract extraction, a 67-year-old male mentioned that his right eye—the one that had been operated on—wasn't as clear as he had hoped. He was also undergoing treatment with a topical prostaglandin analog for primary open-angle glaucoma, which he stopped prior to surgery and recently restarted. His best-corrected acuity was 20/50 OD and 20/25 OS. Fundus examination showed a mild macular disturbance, and SD-OCT revealed pronounced cystoid macular edema (CME) as the cause of his visual reduction.



This OCT image shows an eye with CME following travoprost treatment.

Inflammation

Various factors and mechanisms are involved in CME pathogenesis, including the release of inflammatory mediators such as prostaglandins.[1-4] These mediators disrupt the blood–aqueous barrier (and blood–retinal barrier), leading to increased vascular permeability.[2-4] Any disease process that can break down these barriers can induce CME.[2-21] Light toxicity from an operating microscope may contribute to free radical release with subsequent prostaglandin synthesis.[2-5] Prostaglandins contribute to tissue inflammation, increasing vasodilation and vasopermeability.[2] Exogenous prostaglandin analog use in the management of glaucoma has been anecdotally noted to cause CME.[2,9,10] This is more prevalent in patients who have undergone incisional ocular surgery with an opened posterior capsule, which, theoretically, allows easier access deep into the eye.[2,9,10]

Pathogenesis

CME is not a diagnosis but a finding occurring from numerous causes; it is named for its intraretinal polycystic petaloid (like the petals of a flower) fluorescein angiographic appearance.[1-6] Initiating factors include preservatives in ophthalmic medications, topical prostaglandin analogs, topical beta-blockers, retinal vein occlusion, diabetes mellitus, central serous chorioretinopathy, anterior or posterior uveitis, pars planitis, retinitis pigmentosa, radiation retinopathy, posterior vitreous detachment, epiretinal membrane formation, macular retinal telangiectasia, post YAG laser procedure and blunt trauma.[2-18] After cataract surgery, the second most common cause of CME is diabetes.[2]

Detection

The predominant symptoms caused by CME of any etiology is visual distortion (metamorphopsia) and acuity reduction.[2-18] Visual acuity may be minimally affected or significantly reduced.[3-18] While the incidence of pseudophakic cystoid macular edema (PCME)-related symptoms (defined as symptomatic vision loss 20/40 or worse) is low (approximately 0.1% to 2.35% of all cases), an estimated 20% to 30% of patients undergoing phacoemulsification demonstrate some form of mild PCME on angiography.[4] The rate has been estimated as high as 41% using SD-OCT.[3] Fortunately, most patients who have PCME detected only with these tests have no visual disturbances and require no intervention.[4]

Therapies

When CME is caused by conditions such as diabetes, retinal vein occlusion, retinitis pigmentosa or uveitis, the treatment is dictated by standard-of-care for the causative condition.[19-34] Cases of CME arising from diabetic retinopathy or retinal vein occlusion would warrant consideration of focal/laser photocoagulation of the leaking perifoveal capillaries, alone or in combination with injections of anti-VEGF drugs

such as bevacizumab, ranibizumab or aflibercept or intravitreal steroid injection implants.

Medications for CME include oral nonsteroidal medicines, such as ibuprofen and indomethacin, and the corticosteroid prednisone. Topical nonsteroidal medications such as ketorolac, nepafenac and bromfenac have also been successful. Topical corticosteroid drops such as prednisolone acetate, loteprednol etabonate and difluprednate can be added for unresponsive or more severe cases.[2-5,34,35] Common dosing ranges from QID to Q2H, dictated by severity and symptoms. Duration of therapy may be several days to months.[2-18,34,35]

Oral carbonic anhydrase inhibitors (CAIs) such as acetazolamide and methazolamide have been documented as helpful in recalcitrant cases of CME.[36] These agents increase active transport by the retinal pigment epithelium to facilitate fluid movement from the retina through the choroid.[36] They work best in cases caused by diffuse retinal pigment epithelial failure (retinal dystrophies).[36] Likewise, topical CAIs such as dorzolamide or brinzolamide can also be used.

The majority of cases of symptomatic CME following cataract surgery resolve spontaneously without intervention within eight months, and many cases resolve faster.[2-6,34] In rare instances, CME can remain detectable in excess of five years, though patients may not be visually disturbed.[2]

Upon discovery of the patient's CME, the topical prostaglandin was replaced by a fixed combination of brimonidine 2%/timolol 0.5%, and bromfenac was initiated. Fortunately, the CME resolved over several weeks and his vision returned to normal. ■

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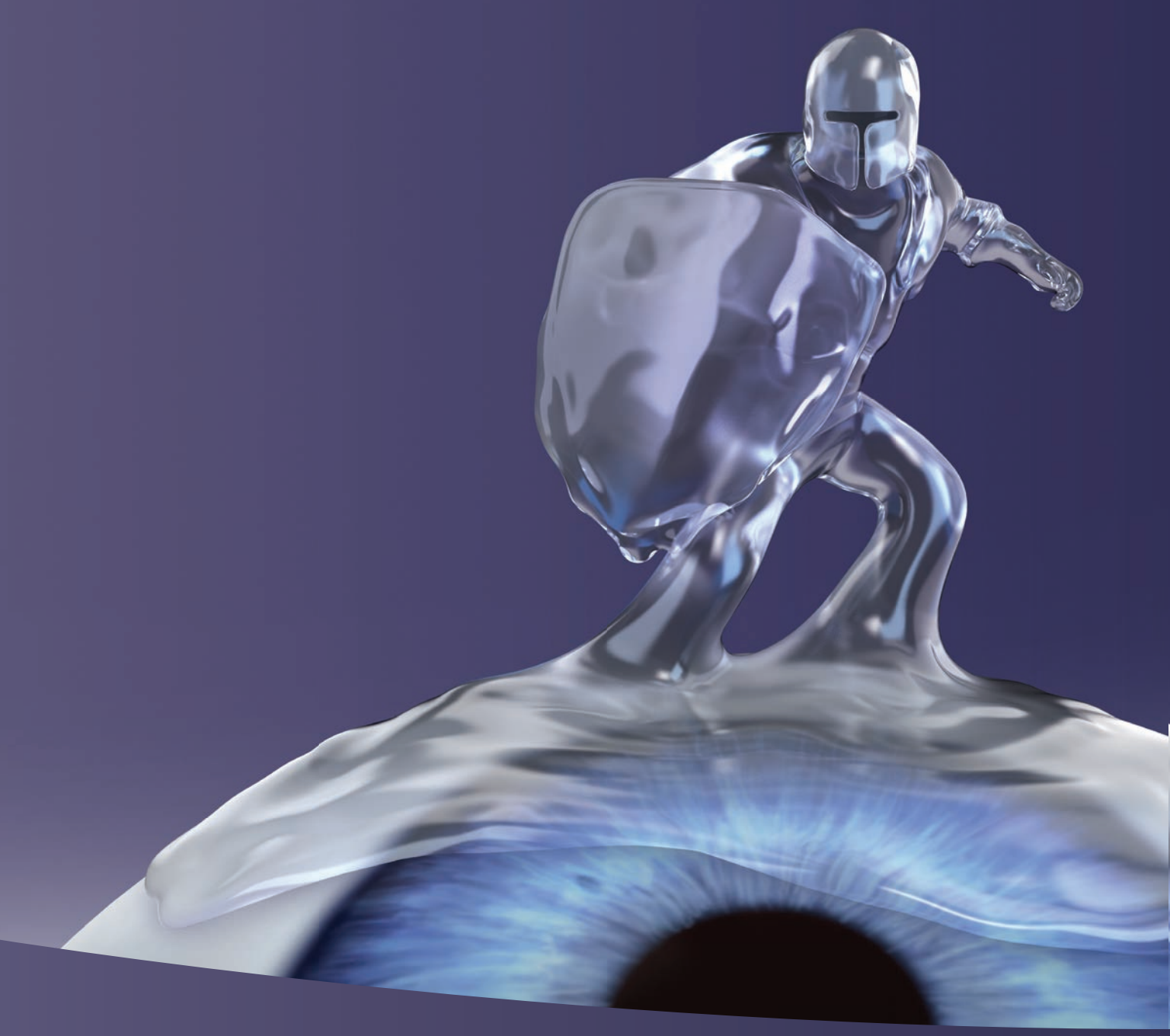

Indications and Usage
BromSite™ (bromfenac ophthalmic solution) 0.075% is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.

Important Safety Information

- **Slow or Delayed Healing:** All topical nonsteroidal anti-inflammatory drugs (NSAIDs), including BromSite (bromfenac ophthalmic solution) 0.075%, may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.
- **Potential for Cross-Sensitivity:** There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including BromSite (bromfenac ophthalmic solution) 0.075%. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.
- **Increased Bleeding Time of Ocular Tissue:** With some NSAIDs, including BromSite (bromfenac ophthalmic solution) 0.075%, there exists the potential for increased bleeding time due to interference with platelet aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

  It is recommended that BromSite be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.
- Use of topical NSAIDs may result in keratitis. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs, including BromSite (bromfenac ophthalmic solution) 0.075%, and should be closely monitored for corneal health. Patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular

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surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients. Post-marketing experience with topical NSAIDs also suggests that use more than 24 hours prior to surgery or use beyond 14 days postsurgery may increase patient risk for the occurrence and severity of corneal adverse events.

- BromSite should not be administered while wearing contact lenses. The preservative in BromSite, benzalkonium chloride, may be absorbed by soft contact lenses.
- The most commonly reported adverse reactions in 1% to 8% of patients were anterior chamber inflammation, headache, vitreous floaters, iritis, eye pain, and ocular hypertension.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit www.fda.gov/medwatch or call 1-800-FDA-1088.

Please see brief summary of full Prescribing Information on the adjacent page.

NSAID=nonsteroidal anti-inflammatory drug.

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SUN OPHTHALMICS

BromSite™ (bromfenac ophthalmic solution) 0.075% Brief Summary

INDICATIONS AND USAGE

BromSite™ (bromfenac ophthalmic solution) 0.075% is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and prevention of ocular pain in patients undergoing cataract surgery.

DOSAGE AND ADMINISTRATION

Recommended Dosing

One drop of BromSite should be applied to the affected eye twice daily (morning and evening) 1 day prior to surgery, the day of surgery, and 14 days postsurgery.

Use with Other Topical Ophthalmic Medications

BromSite should be administered at least 5 minutes after instillation of other topical medications.

Dosage Forms and Strengths

Topical ophthalmic solution: bromfenac 0.075%.

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Slow or Delayed Healing

All topical nonsteroidal anti-inflammatory drugs (NSAIDs), including BromSite (bromfenac ophthalmic solution) 0.075%, may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

Potential for Cross-Sensitivity

There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including BromSite (bromfenac ophthalmic solution) 0.075%. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

Increased Bleeding Time of Ocular Tissue

With some NSAIDs, including BromSite (bromfenac ophthalmic solution) 0.075%, there exists the potential for increased bleeding time due to interference with platelet aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

It is recommended that BromSite be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

Keratitis and Corneal Reactions

Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs, including BromSite (bromfenac ophthalmic solution) 0.075%, and should be closely monitored for corneal health.

Post-marketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients.

Post-marketing experience with topical NSAIDs also suggests that use more than 24 hours prior to surgery or use beyond 14 days postsurgery may increase patient risk for the occurrence and severity of corneal adverse events.

Contact Lens Wear

BromSite should not be administered while wearing contact lenses. The preservative in BromSite, benzalkonium chloride, may be absorbed by soft contact lenses.

ADVERSE REACTIONS

Clinical Trial Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in clinical practice.

The most commonly reported adverse reactions in 1–8% of patients were: anterior chamber inflammation, headache, vitreous floaters, iritis, eye pain and ocular hypertension.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no adequate and well-controlled studies in pregnant women to inform any drug associated risks. Treatment of pregnant rats and rabbits with oral bromfenac did not produce teratogenic effects at clinically relevant doses.

Clinical Considerations

Because of the known effects of prostaglandin biosynthesis-inhibiting drugs on the fetal cardiovascular system (closure of ductus arteriosus), the use of BromSite during late pregnancy should be avoided.

Data

Animal Data

Treatment of rats with bromfenac at oral doses up to 0.9 mg/kg/day (195 times a unilateral daily human ophthalmic dose on a mg/m^2 basis, assuming 100% absorbed) and rabbits at oral doses up to 7.5 mg/kg/day (3243 times a unilateral daily dose on a mg/m^2 basis) produced no structural teratogenicity in reproduction studies. However, embryo-fetal lethality, neonatal mortality and reduced postnatal growth were produced in rats at 0.9 mg/kg/day, and embryo-fetal lethality was produced in rabbits at 7.5 mg/kg/day. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Lactation

There are no data on the presence of bromfenac in human milk, the effects on the breastfed infant, or the effects on milk production; however, systemic exposure to bromfenac from ocular administration is low. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for bromfenac and any potential adverse effects on the breast-fed child from bromfenac or from the underlying maternal condition.

Pediatric Use

Safety and efficacy in pediatric patients below the age of 18 years have not been established.

Geriatric Use

There is no evidence that the efficacy or safety profiles for BromSite differ in patients 65 years of age and older compared to younger adult patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis and Impairment of Fertility

Long-term carcinogenicity studies in rats and mice given oral doses of bromfenac up to 0.6 mg/kg/day (129 times a unilateral daily dose assuming 100% absorbed, on a mg/m^2 basis) and 5 mg/kg/day (540 times a unilateral daily dose on a mg/m^2 basis), respectively revealed no significant increases in tumor incidence.

Bromfenac did not show mutagenic potential in various mutagenicity studies, including the bacterial reverse mutation, chromosomal aberration, and micronucleus tests.

Bromfenac did not impair fertility when administered orally to male and female rats at doses up to 0.9 mg/kg/day and 0.3 mg/kg/day, respectively (195 and 65 times a unilateral daily dose, respectively, on a mg/m^2 basis).

PATIENT COUNSELING INFORMATION

Slow or Delayed Healing

Advise patients of the possibility that slow or delayed healing may occur while using NSAIDs.

Concomitant Topical Ocular Therapy

If more than one topical ophthalmic medication is being used, advise patients to administer BromSite at least 5 minutes after instillation of other topical medications.

Concomitant Use of Contact Lenses

Advise patients not to wear contact lenses during administration of BromSite. The preservative in this product, benzalkonium chloride, may be absorbed by soft contact lenses.

Sterility of Dropper Tip/Product Use

Advise patients to replace the bottle cap after use and do not touch the dropper tip to any surface as this may contaminate the contents.

Advise patients to thoroughly wash hands prior to using BromSite.

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SUN OPHTHALMICS

Hone Your Compliance Skills

Know how to establish medical necessity and follow compliance protocols for all your corneal disease patients. **By John Rumpakis, OD, MBA, Clinical Coding Editor**

Managing the anterior segment in today's ophthalmic practice can be complicated; there are so many different aspects to consider when it comes to disease states and proper evaluation. You really have to be on top of the clinical research to be able to identify potential areas of diagnosis and treatment. Patients can present with any number of ocular complications, including ocular allergy, dry eye, meibomian gland dysfunction, ocular infection (with and without systemic involvement), keratoconus, irregular astigmatism and corneal complications secondary to contact lens wear or topical medications, just to name a few.

Recording the Medical Visit

While gathering the pertinent information from the patient's history and ocular exam is paramount to reaching the correct diagnosis, it's also critical to properly create the medical record. Your listening skills and the technology you employ will help determine how accurately you capture all of that information in the medical record. Keep in mind that the bar for clinical detail in the record has been raised significantly with the incorporation of the ICD-10 in October 2015.

All clinicians must adhere to the same fundamental principles throughout the patient encounter, starting with the initial meeting, whether it be on the phone, online or in your office. The first step is to capture the true nature of the patient's reason for the visit. If the patient initiates the call, find out why they are contacting you. Was it because they are returning for follow up or additional testing? If so, that means you have to pull up their medical record to find out what you are actually having them back for. Of course, it is imperative to capture or verify every patient's insurance information and deductible status on each and every visit.

The severity of the problem a patient presents with or for which you are having them return for follow up determines the level of history you need to perform, which then governs the level of examination you need to perform. Combined, these two points provide you with the clinical information necessary to perform the appropriate level of medical decision-making that leads to a proper diagnosis. With that under your belt, you can establish the diagnosis, implement a treatment plan and follow the patient accordingly.

Medical Necessity

With all of the technology we have today, it is very important to not lose sight of the fact that medical necessity has to be established for every special ophthalmic test you order and perform. Technology cannot replace your clinical examination, but should be used to complement or augment your testing protocol. For example, you cannot take a picture of the anterior segment just because you want to—you must have a specific reason for taking the picture and demonstrate the necessity in the record. Also remember, just because a test is deemed a bilateral test doesn't mean that you perform it bilaterally when you have a unilateral condition. In cases such as this, the ICD-10 laterality and the CPT laterality must match, most likely through the use of appropriate modifiers.

Coding protocols also are important to follow when initiating a treatment plan. For example, if you were treating moderate to advanced dry eye, you cannot automatically jump to using an amniotic membrane for treatment. You must first establish that less invasive methods of treatment—such as a pharmaceutical regimen or punctal occlusion—have been tried and failed. This is what establishes the medical necessity of the amniotic membrane. And, most importantly, you must understand carrier policy when treating a patient. In this dry eye case, for example, you must make sure the amniotic membrane you chose is approved for use on the ocular surface and delivers the best outcome, as not all amniotic membrane technology is equal in delivering clinical outcomes.

It is critical that you hone your corneal disease compliance skills in accordance with your clinical acumen; your patients deserve the best outcomes provided by an appropriate diagnosis and treatment—in the end, your practice will be compliant, safe and profitable. ■

Send questions and comments to ROcodingconnection@gmail.com.

Corneal Disease Report

The OD's Guide to Managing Recurrent Corneal Erosion

Whether it's medical or procedural, optometry can combat this painful condition.

By Aaron McNulty, OD

Recurrent corneal erosion (RCE) is a clinical syndrome characterized by inadequate epithelial basement membrane adhesions, resulting in repeat episodes of corneal epithelial defects.[1] These episodes are typically acute and may involve symptoms ranging from mild irritation to significant pain.[1-3] The average age of onset is the fourth or fifth decade, with a slight female predominance.[1,3]

It's a condition that can leave patients with a fair amount of discomfort. Luckily, the optometrist can help. This article offers keys to understanding RCE, its diagnosis and treatment options.

Diagnosis

RCE is diagnosed based on clinical signs and patient history, so a thorough history is necessary; don't forget to ask about prior episodes of corneal trauma.[1] Patients will typically describe symptoms that occur during sleep or upon awakening and may include redness, photophobia and tearing.[1,2]

While the lids are closed during sleep, superficial epithelial edema may lead to decreased epithelial adhesion. Opening of the lid or rapid eye movement produces a shearing force on the epithelium, leading to erosion.[3] Corneal signs may range from focal superficial punctate keratitis to a full-thickness epithelial defect.[1]

Optometrists can debride the epithelium at the slit lamp under topical anesthesia using a foreign body spud.

A detailed slit lamp examination should be performed with fluorescein staining and retroillumination, and the fellow eye should be examined for signs of basement membrane dystrophy.[1]

Microform erosions consist of minor episodes lasting as little as 30 minutes and typically have an intact corneal epithelium upon examination.[2,4] Macroform erosions are more severe episodes with epithelial defects or areas of edematous, poorly adherent epithelium. These may last for days and are associated with severe pain, eyelid edema, decreased visual acuity and extreme photophobia.[2,4]

If an exam does not reveal obvious epithelial defects, an adhesion test can assess for inadequate epithelial-stromal adhesion. A dry cellulose surgical sponge is gently passed over the area of suspected epithelium. If the intact epithelium is movable, the adhesion test is positive.[1]

Etiology and Pathophysiology

RCE is commonly associated with prior corneal trauma or underlying corneal disease. The most common underlying etiologies are trauma (45% to 69%) and epithelial basement membrane dystrophy (EBMD) (20% to 30%).[1] Causative trauma is typically a shallow corneal injury such as an abrasion from a fingernail, piece of paper, or tree branch.[3] Prior trauma classically leads to macroform erosions.[3] In contrast, EBMD classically leads to microform erosions.[3] The estimated incidence of RCE following traumatic corneal abrasion ranges from 5% to 25%.[1]

Normally, the corneal epithelium is anchored to the basement membrane and Bowman's layer by specialized adhesion complexes. These complexes consist of hemidesmosomes and anchoring fibrils.[1] Trauma and corneal dystrophies have the potential to disrupt the

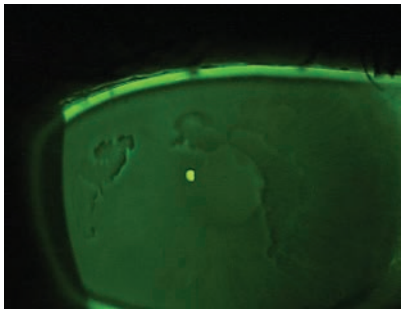
adhesion complexes, which predisposes the epithelium to repetitive erosions.[1] The exact mechanism of the failure of adhesion complexes is not fully understood, but researchers propose there are pathologies or absence of the basement membrane or hemidesmosomes.[3] This leads to repetitive elevation of the epithelium, which causes formation of further abnormalities in the basement membrane.[3]

Patients with RCE have increased activity of matrix metalloproteinases (MMP)-2 and -9. These enzymes can adversely affect the basement membrane and anchoring fibrils, thereby causing dysfunctional adhesion complexes.[1,3] Further, there are high rates of meibomian gland dysfunction (MGD) and ocular rosacea in eyes with non-traumatic corneal erosion.[3] Diseases with high colonization of *Staphylococcus epidermidis* tend to have higher levels of bacterial lipases, which act upon meibum to produce toxic free fatty acids. Investigators believe these fatty acids interfere with the epithelial healing process and predispose patients to erosions.[3] Therefore, many medical treatments are aimed at decreasing MMP activity, or managing MGD, or both.

Treatments

The two primary therapeutic goals for RCE are to facilitate rapid re-epithelialization and relieve pain. A secondary goal is to prevent future occurrences of erosion.[3] Medical therapy typically results in resolution of the epithelial defect.[1] Frequent nonpreserved artificial tears help re-epithelialization, but do not seem to help in the prevention of recurrence.[1,3,5]

A topical nonsteroidal anti-inflammatory drug (NSAID) may be prescribed to reduce pain,



This patient exhibits negative staining at the slit lamp, which is indicative of epithelial basement membrane dystrophy.

although long-term use should be avoided as they may delay epithelial healing.[6] Topical prophylactic antibiotics should be used to decrease the risk of microbial keratitis.[1] For large epithelial defects or patients in significant pain, oral opioids (such as hydrocodone with or without acetaminophen) may be necessary to provide adequate pain control.[7]

Medical therapy is typically the initial therapeutic choice to prevent recurrences, although 60% will have persistent symptoms following medical treatment.[8] Treating underlying lid disease, such as MGD and blepharitis, significantly decreases the frequency of recurrent erosions.[9] MMP-9 inhibitors, such as topical steroids and doxycycline, also speed resolution and help to prevent further recurrences.[10] Topical ointments may be used at bedtime for lubrication. These are often continued for several weeks until the epithelium is tightly adhered to the stroma.[1] Hypertonic ointments are often prescribed at bedtime for weeks to months to complete deturgescence of the corneal epithelium and improve adhesion.[11] However, these ointments may be irritating for some patients due to the salt content.[1] Hypertonic drops may also be helpful (and less irritating), although the contact time of a drop is less than an ointment. Erythromycin ointment provides some antibiotic prophylaxis and may reduce MMP-9.[1,11] The use of autologous serum may be effective at preventing recurrence in select patients.[3]

Bandage contact lenses are often used to protect the epithelium from the shearing force of the lids.[1,12] When using a bandage lens, the clinician should take care to avoid tight lens syndrome.[1] This condition involves acute tightening of the contact lens, which leads to decreased lens movement, inflammatory debris beneath the lens, increased inflammation and pain.[1] The use of a relatively flat base curve and topical NSAIDs can help avoid tight lens syndrome.[1] Nonpreserved artificial tears help to flush inflammatory debris and improve comfort. Topical prophylactic antibiotics should be used to decrease the risk of microbial keratitis, which may be caused by extended use of bandage soft lenses.[1,11] Patients may wear bandage contact lenses continuously for six to 12 weeks to allow for restoration of tight epithelial basement membrane adhesions.[13] The lens must be replaced as appropriate.[1,2]

Despite treatment of acute episodes, some patients will continue to have minor and major RCE occurrences. For recalcitrant cases, surgical therapy may be necessary. Surgical intervention helps to prevent further recurrences by stimulating new and stronger epithelial adhesion complexes.[1,2,8]

Epithelial Debridement

Mechanical debridement of loosely adhered or nonadherent epithelium provides a smooth basement membrane to which healthy epithelium may re-adhere.[1] This is a safe and relatively noninvasive procedure that is typically performed at the slit lamp under topical anesthesia.[1,8] The patient is prepared by

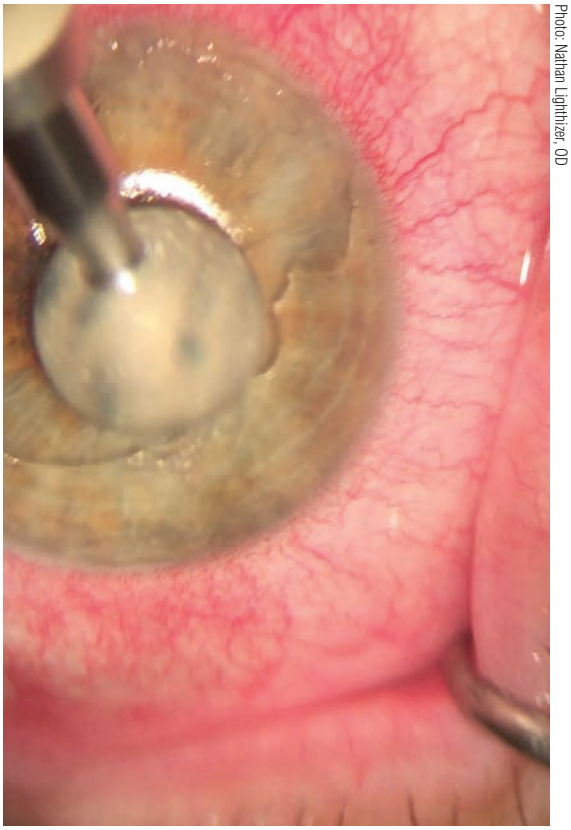


Photo: Nathan Lighthizer, OD

A diamond burr can be used to lightly buff Bowman's layer until a smooth surface is achieved.

instilling topical anesthetic in both eyes.[2] Topical prophylactic antibiotics may be used, and an eyelid speculum is often helpful.[2] Depending upon practitioner preference, various instruments may be used to remove loose epithelium.[8] A methylcellulose spear-shaped surgical sponge (i.e., Weck-cel) is a safe and effective option.[1,8,14] A Kimura spatula may also be used since its blunt edges make it unlikely to damage Bowman's membrane.[2,8] Occasionally, sharper instruments such as a scalpel blade are sometimes advocated; other authors contend that sharp instruments are inappropriate for this.[1,2] Remove any loose epithelial debris with jeweler's forceps or a cellulose surgical sponge.[8]

Loose epithelium is removed to the point of tight adherence.[11] Aggressive removal of the epithelium near the limbus can damage stem cells; therefore, a protective band of epithelium should be maintained 1mm to 2mm from the limbus.[3,8] Bowman's layer is lightly debrided to remove the epithelial basement membrane.[2] Cyclopentolate is instilled.[11]

A bandage contact lens should be placed for two days to two weeks, and topical antibiotics and nonsteroidal drops prescribed.[2] Bedtime ointment may be considered for three to six months.[2]

Diamond Burr Polishing

Following debridement of loose epithelium, diamond burr polishing may be performed. Compared with simple debridement, polishing may remove more abnormal basement membrane. This can provide a smoother surface and stronger epithelial-stromal adhesion, which should enhance the outcome.[14]

Diamond burr polishing may be safely performed at the slit lamp with a handheld, battery operated 5mm diamond burr.[11,14] After debriding loose epithelium as described previously, a diamond burr is used to lightly buff Bowman's layer until a smooth surface is achieved.[2,14] This takes approximately five to 10 seconds, although some sources advocate up to 30 seconds.[8,14] Vertical or circular motions may be employed.[8,14] Vigorous polishing should be avoided, as it may breach Bowman's layer and cause postoperative corneal haze.[14]

A bandage contact lens is placed, and antibiotic and nonsteroidal drops are prescribed.[2]

Anterior Stromal Puncture

This technique, which has been compared to spot welding in metalworking, is performed at the slit lamp under topical anesthetic. Multiple shallow penetrations are made through the epithelium into the anterior stroma. This forms scarring attachments and improves epithelial adhesion.[15] Specialized instruments may be used to prevent corneal perforation. Stromal puncture may be performed through loose epithelium without performing debridement. Fluorescein helps to visualize puncture marks. Topical NSAIDs should be used to control postoperative pain. Prophylactic antibiotics should also be applied to prevent microbial keratitis.[15]

Punctures should be placed 0.5mm to 1mm apart within the entire erosive area. The treatment zone should extend 1mm to 2mm into normal margins to prevent recurrence. Treatment of the visual axis is controversial; investigators have yet to reach a consensus as to whether stromal puncture causes decreased acuity or glare.[15]

Transplantation

Amniotic membranes exert anti-inflammatory and anti-scarring effects on tissue.[16] They contain tissue inhibitors of MMP-9.[16] Transplantation of an amniotic membrane as a biologic bandage may be beneficial following epithelial debridement.[16] Techniques for placement of amniotic membrane vary based on the type of membrane used. Antibiotic drops may be used with the membrane in place.[16]

Expected Outcomes

Debrided epithelium is typically re-epithelialized by three or four days, although this depends on the area debrided.[14] There may be mild corneal haze for three to four weeks; this rarely may persist as a long-term complication.[8,14]

The literature still lacks strong evidence regarding the efficacy of various RCE therapies. A Cochrane systematic review included seven randomized controlled trials, all of which were considered "poor quality."[12] The level of evidence was found to be insufficient for the development of management guidelines.

A double-masked randomized controlled trial in Hong Kong (n=48) compared simple epithelial debridement with debridement with diamond burr polishing.[14] The authors found fewer recurrences and less need for repeat intervention in the diamond burr group over six months of follow-up. The incidence of major recurrences was 4% in the diamond burr group vs. 56% in the simple debridement group. Minor symptoms recurred in 20% (diamond burr) vs. 65% (debridement). Additional interventions were needed in none of the diamond burr subjects and 52% of the debridement group.[14]

Although debridement aids the resolution of the acute erosive episode, evidence that debridement alone can prevent additional episodes is lacking.[1,8] However, simple debridement can successfully convert most patients with macroform erosions to microform erosions.[2]

A small study of 11 eyes with history of RCE examined the effect of amniotic membrane transplantation over 10 to 16 months of follow-up. Eight eyes had previous failure with conservative medical treatments. The authors performed debridement using a surgical sponge followed by placement of amniotic membrane. Only one eye recurred. Interestingly, 10 eyes had improvement in best-corrected visual acuity.[16]

Recurrent corneal erosion is relatively common, and may not be adequately managed with medications. Surgical intervention may enhance outcomes and reduce recurrences. Epithelial debridement with diamond burr polishing is a safe, effective procedure for the treatment of this condition. ■

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Corneal Disease Report

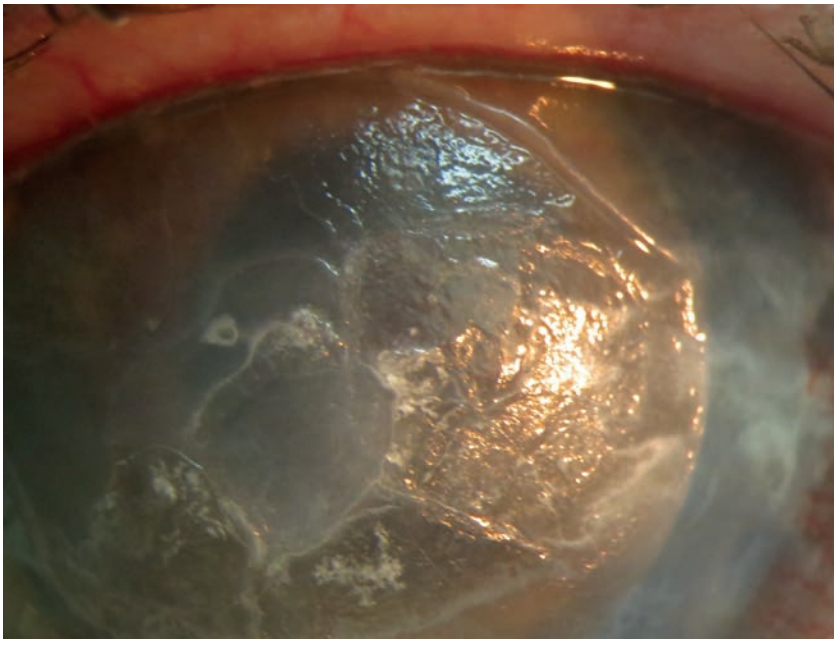
A Hands-on Approach to Band Keratopathy

Following this protocol can give ODs control over a vision-threatening condition.

By Thomas J. Stokkermans, OD, PhD, Pankaj C. Gupta, MD, MSc, and Rony R. Sayegh, MD

Uncovering the underlying causes of band keratopathy (BK) is, by no means, a simple task, but it is something every optometrist is equipt to handle. The process requires a comprehensive approach to gathering the patient's history and employing testing techniques. On top of that, the skilled clinician is responsible for deciding whether—and when—to treat. If the case calls for it, the OD can often treat noninvasively in an outpatient setting at the slit lamp.

This article provides a detailed look at each step of treating a BK patient, from presentation to surgical management.



This patient displays band keratopathy in a pre-phthisis non-seeing right eye. EDTA-assisted removal was initiated to resolve the non-healing central defect.

Presentation

Patients with band keratopathy may present for care with a variety of complaints. Cases of decreased vision, foreign body sensation, eye irritation, photophobia or concern about why their eye's appearance has changed all have the potential to be BK.[1] Early BK may go unnoticed by the patient and only become apparent upon routine slit lamp examination. In many cases, however, BK is associated with long-standing ocular disease, and the patient is fully aware of the condition.[1]

One study shows the most common causes of BK are chronic (28%) and idiopathic (26%) corneal edema.[2]

A thorough consideration of the differential diagnosis, possible causes and treatment options is essential. Clinicans must emphasize the risk of vision loss and treatment options, as patients who are asymptomatic may not consider cosmesis reason enough to undergo surgery.

BK is characterized by the appearance of an interpalpebral, horizontal, opaque grayish-white band across the central cornea. It is formed by the precipitation of

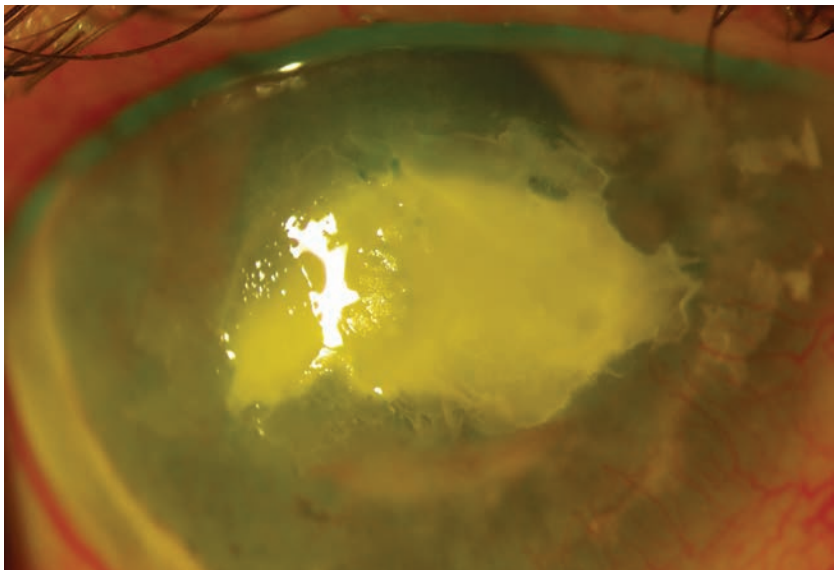
calcium salts on Bowman's layer, directly under the epithelium.[1] The extreme periphery of the cornea may be spared because of the presence of limbal blood vessels exerting a buffering effect. Holes in the plaque are often present and are caused by corneal nerves crossing Bowman's membrane to the epithelial surface. The band usually initiates in the periphery and progresses towards the center, but may, on occasion, begin centrally. Calcium deposits may be very fine or thick and plaque-like. Thick plaques have a tendency to partially flake off, especially in the periphery. This will cause epithelial defects and pain. In those patients with otherwise healthy eyes, visual acuities will decrease in proportion to the density of calcium salt deposition on the central cornea.

Local Causes

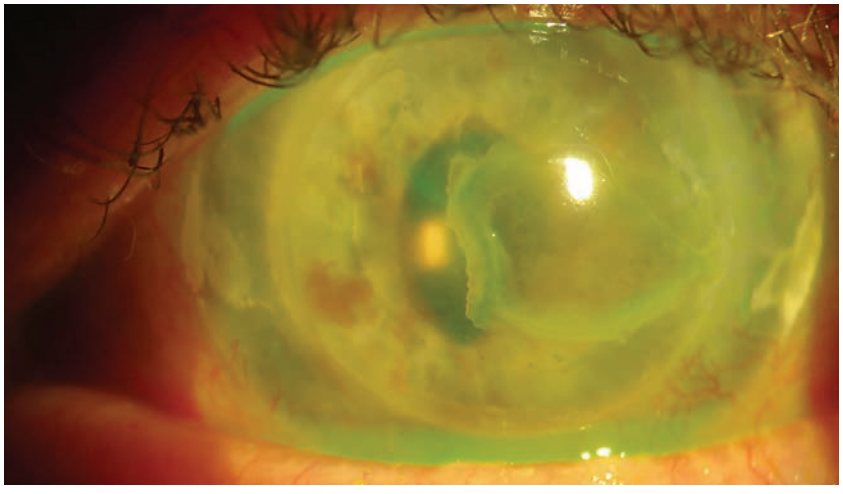
The underlying cause of BK is abnormal levels of calcium and phosphate, which are both present at near their solubility limit in tears, aqueous humor and corneal tissue. Increased evaporation of tears promotes precipitation of these salts, especially in the interpalpebral area. Therefore, keratitis sicca is a significant risk factor for BK and should be ruled out as a cause. Even when calcium and phosphate levels are normal, elevation of the surface pH (alkalosis) favors precipitation. Alkalosis can be seen in chronically inflamed eyes and may explain the increased risk of BK in patients with chronic uveitis.[3-5] Conditions such as juvenile idiopathic arthritis with uveitis, chronic herpes simplex and zoster keratitis, sarcoidosis, discoid lupus erythematosus and tuberous sclerosis are all associated with BK.[3-5]

Endothelial compromise and associated corneal edema may also result in calcium deposition and BK. This process is sometimes seen in aphakic patients who have silicone oil inside the eye, and seems to be due to the oil's contact with the posterior cornea.[6-8] One study concluded that BK was one of the main complications in 8% of patients treated with silicone oil in whom the oil remained in the eye for an average of 30 months, which is significantly longer than usual.[6] The exact reasons for this association remain unclear.[7,8]

Ocular conditions that are associated with BK, but for which the mechanism is not clear, include end-stage glaucoma, corneal dystrophies and neurotrophic keratitis.[9,10] It is possible that endothelial compromise plays a role in some of these conditions.



This image shows the same eye as seen on page 36, post procedure. Unfortunately, the eye became phthisical and had to be enucleated.



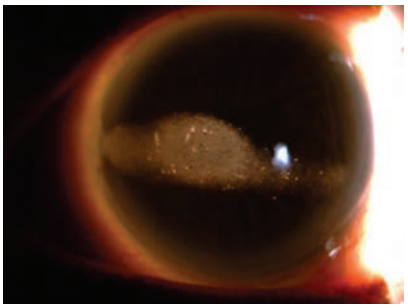
Recurrence of BK in seeing left eye of same patient. This eye with ACIOL and penetrating keratoplasty for band keratopathy had recurrence despite efforts to address systemic causes (patient discontinued vitamin D).

A number of topical medications can cause calcium precipitation and BK, including ophthalmic drops containing phosphates, such as steroid phosphates and other eye drops containing phosphate buffers.[11] One study shows the risk for BK doubled when corneal alkali burns were treated with ophthalmic drops containing phosphate.[12] Pilocarpine containing mercury-based preservatives was shown to increase the risk for BK as well.[12] Mercury initiates changes in the corneal collagen that, in turn, causes deposition of calcium. Some surgical procedures that change the corneal surface or the endothelium increase the risk for BK, as does the use of some early viscoelastic preparations and, as mentioned, the intraocular presence of silicone oil and the intraocular use of tissue plasminogen activator.[12]

Finally, patients exposed to mercury vapor or calcium bichromate vapors, which can occur in certain industrial occupations, can develop BK.[12]

Systemic Causes

Besides local causes of calcium and phosphate imbalance, elevated serum levels associated with systemic disease can tip the balance towards precipitation as well. Especially in patients who present with new-onset BK without any ocular risk factors, a systemic cause should be investigated. Systemic diseases correlated with BK usually are associated with hypercalcemia and include hyperparathyroidism, excessive vitamin D intake, endstage renal disease, hypophosphatasia, milk-alkali syndrome, Paget disease, sarcoidosis, discoid lupus erythematosus, gout (in the form of urate crystals), malignancy (such as iris melanoma) and tuberous sclerosis.[13,14] Milk-alkali syndrome (also called calcium-alkali syndrome), caused by excessive intake of calcium carbonate usually for dyspepsia, is on the rise and is currently the third most common cause of patients admitted to the hospital for hypercalcemia.[15] Hypophosphatasia is a rare inherited mutation in the enzyme alkaline phosphatase that leads to breakdown of bone and teeth. ODs must communicate effectively with the patient's primary care provider to ensure that the appropriate systemic management is completed before initiating corneal treatment. The systemic control of hypercalcemia is complex and may require surgical intervention (such as with an overactive parathyroid gland) or medications that include calcimimetics, biphosphonates and prednisone (depending on the cause of the hypercalcemia). It may result in a medical emergency in the case of extremely high calcium levels, and may require rapid administration of IV fluids and diuretics to avoid heart arrhythmia and damage to the nervous system.[16]



This otherwise healthy eye clearly displays band keratopahty.

Differential Diagnosis

A number of corneal conditions may present similarly to BK.[17,18]

Gout can be associated with corneal uric acid deposits similar in appearance to BK and is actually considered a form of BK by some. Gout is associated with joint pain, swelling and redness.

Interstitial keratitis can present in a similar fashion; however, deeper stromal scarring is expected.

Primary and secondary calcarous degeneration of the cornea, while grossly similar, can easily be distinguished at the slit lamp; as the calcium deposit is present within the stroma as well.[19]

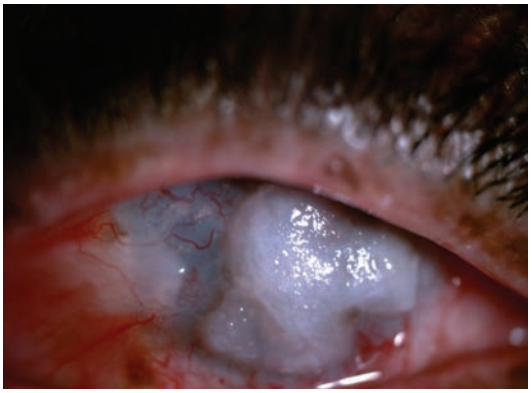
Calciphylaxis, a condition of vascular calcification and skin necrosis, was once thought to be a hypersensitivity reaction to specific antigens, but is now thought to be multifactorial.[20] It is more common in patients with endstage renal disease and generally associated with intensly painful, dark purple skin lesions. This is a potentially fatal disease.[21]

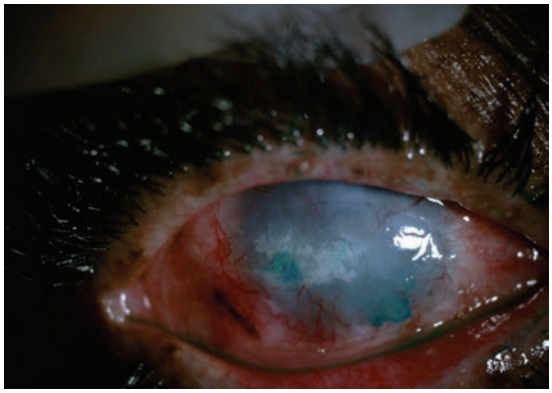
Spheroidal degeneration, also known as Labrador keratopathy, is usually associated with environments with intense chronic UV exposure. The corneal lesions may be more elevated and more yellow in appearance, and often interpalpebral conjunctival findings are found as well.

Ciprofloxacin (and also ofloxacin and norfloxacin) crystalline deposits may also be confused with BK. A detailed history should allow the practitioner to determine its cause. Discontinuation generally leads to resolution, while more extensive deposits may interfere with re-epithelialization.

Advanced basement membrane dystrophy or Salzmann nodular degeneration can cause subepithelial opacification that can grossly appear similar to BK. Unlike BK, it usually has a vascular component, and does not spare the limbus and does not present with clear islands within the lesion.

Familial BK is a rare disorder displaying an autosomal





A patient pre- (left) and post- (right) EDTA assisted scraping of large calcific plaques. The goal with this patient was comfort, not visual rehabilitation.

inheritance (both dominant and recessive inheritance has been reported) that the astute practitioner can uncover in the absence of local or systemic causes after doing a thorough pedigree analysis.[22]

Systemic Considerations

For patients who present with BK in the absence of a known underlying cause, serum calcium and phosphate levels should be obtained along with renal function tests, such as blood urea nitrogen and creatinine. If sarcoid is suspected, either from ocular or systemic findings, angiotensin-converting enzyme testing, chest radiography, or chest spiral CT scanning should be obtained. In otherwise idiopathic cases, parathyroid hormone levels should be checked as well. If surgical treatment is decided by the OD and the patient, treat any underlying systemic or ocular condition first, as otherwise recurrence of BK is highly likely. Dietary modifications are indicated in patients with excessive vitamin D or milk-alkali syndrome.

Non-surgical Management

Many patients will present with BK caused by a history of ocular surgery, chronic inflammation or phthisis. These patients may not be symptomatic and may not benefit visually from surgical treatment. Exercise caution with patients who request surgical treatment solely for cosmetic reasons, as eyes with BK often have other conditions and may not heal as well.[2]

When such a patient presents with symptoms, a non-surgical alternative treatment may include the fitting of a bandage contact lens. Antimicrobial topical therapy should be initiated to reduce the risk of infection in overnight contact lens wear on a compromised cornea. Prosthetic opaque contact lenses can also be fit for cosmetic concerns. Lubrication in the form of artificial tears, gels and ophthalmic ointments may help significantly in patients who present with foreign body sensation, tearing and photophobia and should be first-line treatment. The application of an amniotic membrane device has also been shown to promote healing of BK.[1]

Surgical Management

Once systemic and ocular causes of BK are eliminated and/or treated, and after risks and benefits are discussed with the patient, promptly offering surgical treatment will benefit your patients. One study showed that the majority of patients experienced partial or complete symptomatic relief (98%) while one third of patients improved two lines at two months and 36 months.[2]

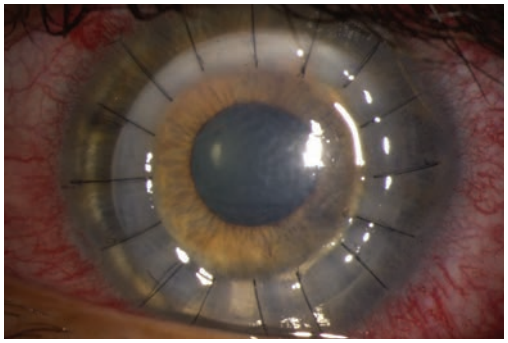
Treatment is relatively straightforward and can even be done at the slit lamp. It always requires removal of the corneal epithelium, followed by superficial debridement (corneal scraping) in the presence of ethylenediaminetetraacetic acid (EDTA).[23,24] In some cases, when the surface is still irregular after the calcium is removed, excimer laser is used to smooth the corneal surface, but this will result in some refractive change.[25]

Patients need to be informed of possible adverse outcomes, including corneal scarring and vision loss, but the incidence of such complications has been reported as close to zero.[24]

Procedure

Removal of calcium is preferably performed under the operating microscope by chelation using a 3% EDTA solution but can be done at the slit lamp if needed. The procedure's steps are:[17]

1. Anesthetize the eye with a topical anesthetic (e.g., proparacaine) and place an eyelid speculum.
2. Debride the corneal epithelium. This can be done with a sterile Beaver blade or an Amoils scrubber.
3. The 3% EDTA solution is then applied to the area of band keratopathy. This is typically done by using a corneal shield/filter paper disc, cut strips of Weck-Cel or sterile cotton tip applicators soaked with EDTA. Alternatively, a reservoir such as a LASIK well can



A patient's left eye following a DALK procedure.

be placed over the cornea and filled with EDTA. The EDTA is applied in three-minute intervals, alternating with thorough irrigation with balanced salt solution. This is done until the calcium clears, which may take 10 to 60 minutes. Care should be taken to avoid toxicity to limbal cells and minimize irritation of the conjunctiva. Thin calcium deposits may come off in five minutes, while thick plaques may take 30 to 45 minutes to dissolve.

Completing the procedure at the slit lamp allows for better visualization. However, when the procedure is performed in upright position, the drainage of EDTA into the inferior fornix increases the risk of a conjunctival chemical burn. Placing sponges containing EDTA on the cornea is much easier in a reclined position as well.

The main advantage of using the EDTA is to minimize damage to Bowman's layer and reduce the risk of an irregular refractive surface that may result from aggressive debridement with a blade. Gentle scraping in between EDTA applications can be performed and may help speed the process.

5. If the corneal surface is extremely irregular after the procedure, polishing the Bowman's layer with a 5mm diamond burr or phototherapeutic keratectomy can smooth the surface. Of note, if any residual calcium is left over, excimer laser treatment will cause worsening of the corneal irregularity, as the laser preferentially ablates the calcium.[25] Alternatively, a gas permeable contact lens can be used afterwards.

6. A soft contact lens is typically placed at the end of the procedure and prophylactic topical antibiotics are used until the epithelial defect has healed. We frequently prescribe topical steroids to modulate healing and reduce scarring. We occasionally use a sutureless amniotic membrane to enhance healing, particularly when delayed epithelialization is anticipated, such as in patients with neurotrophic disease, chronic ocular surface inflammation or advanced age. These cases may be reserved for a specialist since a non-healing epithelial defect may ensue and must be treated aggressivly.

More advanced cases, particularly those that invade Bowman's membrane, may require a more extensive lamellar keratectomy technique such as deep anterior lamellar keratoplasty (DALK).[26]

Extensive keratectomy may cause bleeding from the limbal vessels, particularly in cases associated with superficial corneal neovascularization or interstitial keratitis. This can be controlled with pressure or topical vasoconstrictors, and cautery should be avoided to prevent damage to the limbal stem cells.

Postoperative Care

The patient should be examined five to seven days following surgery. Examination of the epithelium under the contact lens can be performed with fluorescein. Steroids are tapered and the contact lens and antibiotic drops are discontinued once the epithelial defect heals.

Residual anterior stromal scarring may be amenable to excimer laser PTK to improve vision. PTK may also be used to improve the ocular surface and prevent recurrent erosions.

The patient should be checked every three to 12 months, depending on the severity of symptoms. Surgical removal can be repeated if the band keratopathy recurs.

Complications

The main complications related to the removal of calcium deposits on the corneal surface include pain, corneal scarring, corneal edema, infection, decreased vision, non-healing epithelial defect and increased irregular astigmatism. EDTA is toxic to the ocular surface, and inadequate removal during or after the procedure will cause a chemical burn. Recurrence is common, and repeated treatments may be needed. Recurrence is most common in cases of uveitis-induced BK.[1,2]

Occasionally, a mild subepithelial haze can be seen weeks after EDTA chelation, which may resolve on its own. A mild topical steroid (e.g., fluorometholone 0.1%) may help to resolve this haze. If there is significant damage to the Bowman's membrane, the haze may be permanent.

Significant BK is a disease that can and should be treated by EDTA-assisted surgical removal. BK in otherwise healthy patients should be evaluated for systemic causes, including hypercalcemia. Treatment considerations include the likelihood of visual recovery, the presence of pain, photophobia and foreign body sensation and concern for cosmesis.

The overall health of the eye and its ability to heal after the treatment should also be considered. When surgical treatment is not an option, active lubrication or the use of a bandage or prosthetic contact lens are options as well. ■

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Drs. Stokkermans, Gupta and Sayegh are attending faculty at Case Western Reserve University and provide a team approach for the treatment of corneal disease.

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Corneal Disease Report

Beyond the Basics: Tackling Amniotic Membrane Therapy Complications

We all know its virtues. Here are the problems that can arise and what you can do to avoid them. **By Scott G. Hauswirth, OD**

Although amniotic membrane use isn't new to medicine, it's a relatively recent non-surgical modality within our discipline to assist in wound healing. The versatility of the product and the ability to use a non-pharmaceutical option to stimulate tissue repair and regeneration can provide a significant advantage to patient care at any level.

Virtually any corneal or conjunctival surface disease that involves inflammation may benefit from the use of an amniotic membrane.

With eye care practitioners increasingly embracing medical care of the anterior segment and more companies providing a form of amnion to the marketplace, use of amniotic tissue in optometric practice is becoming more common. But with this increased use comes a few inevitable complications and challenges, including patient selection, application and removal techniques, understanding the patient's physiology and setting appropriate patient expectations. These will all affect how your patient fares in both their actual and perceived response to the therapy and its eventual outcome—expedited ocular surface healing—as well the nature and severity of complications.

Below are a few tips for engaging in successful amniotic membrane therapy and managing common complications you may encounter along the way. Let's take some time to delve into the root causes of the complications we may occasionally face and discuss how to avoid or correct them.

Poor Insertion/ Removal

Properly preparing for any allograft placement procedure can help avoid many of the complications associated with the modality. Poor preparation encourages a rushed technique and may lead to these post-procedural complications.

Corneal abrasions. Abrasions to the corneal epithelium may arise from the lid speculum, forceps, a very aggressive application or removal of an older version of the cryopreserved product containing a bare symblepharon (PMMA) ring (in more recent versions, the ring is wrapped in amnion, providing more cushion) on an unstable surface, or from eye rubbing by the patient.

If induced at insertion, patients will likely report increased foreign body sensation and discomfort, which may range from mild to severe. Generally, the abrasions induced during insertion should not cause much concern, as the proper-

ties of the membrane are intended to accelerate epithelial healing. More troubling are those occurring during removal, perhaps due to unintended contact between a bare symblepharon ring or lid speculum and a newly healing epithelium that may still be inadequately bound to the basement membrane complex and unstable.

To avoid this, make sure most supplies are close at hand and you have enough room to maneuver the patient for insertion. Positioning the patient on their back for straightforward insertion of a lid speculum and slowly draping the tissue over the cornea can help with proper graft placement and resultant retention. Directing patients to look away from the contact point of the speculum also decreases the chance of corneal contact. Rehydration of the membrane can be accomplished next (one drop at a time), and placement of the bandage contact lens should be accomplished prior to removal of the lid speculum.

Educate the patient that eye rubbing is strictly forbidden. Although irritation, discomfort and itching are all possible following insertion of the membrane, it is important to remind the patient that eye rubbing may potentially disrupt the very surface we are attempting to heal—their corneal epithelium. In addition, rubbing the eye can lead to destabilization or premature ejection of the graft, which will lessen the beneficial properties of contact with the membrane.

Poor cornea-contact lens relationship. With application of dehydrated membranes, it is imperative that a contact lens covers the membrane to hold it in place. Selecting the right contact lens is critical to the overall function and retention of the membrane. Too tight a contact lens fit will cause impingement of the limbal stem cell region, which can exacerbate issues with a healing corneal epithelium. Fit too loose and the lens can slide around, leading to premature loss of the membrane and potential ejection. I tend to select a bandage contact lens close to the curvature of the cornea, but in many cases will use an oversized soft contact lens such as a Kontur for improved retention.

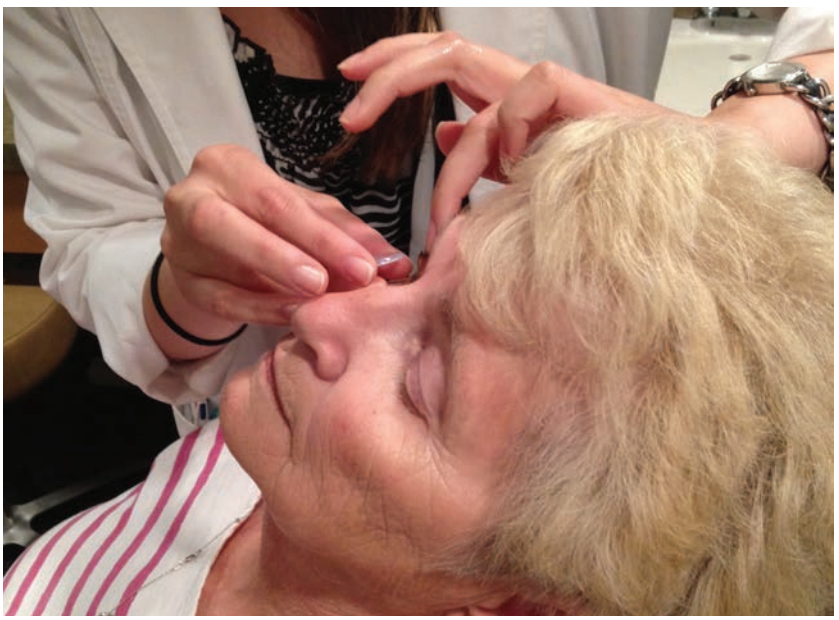
Patient Intolerance

Intolerance of various portions of the amniotic membrane complex is a common yet highly patient-dependent variable. In my experience, the most important issue is setting expectations prior to insertion. Common issues surrounding intolerance are pain or discomfort with either the membrane or the symblepharon ring, improper rinsing and preparation of the membrane or excessive inflammation of the lids or conjunctival surface prior to insertion, which can lead to issues with the fit and movement of the symblepharon ring or bandage contact lens.

Product/Formulation Issues

Some potential complications are related to the specific formulation of amniotic membrane and product you have chosen.

Self-retaining cryopreserved products. With this modality, tolerability of the PMMA ring is generally the largest hurdle to overcome for the majority of practitioners. In my experience, verbalizing to the patient that the first 24 hours *will be uncomfortable* helps them better understand that there is some adaptation to the ring—it is normal and to be expected, and that comfort will generally improve following the first 24 hours. With the exception of patients who also undergo epithelial debridement procedures, it is rare for patients to need additional pain medications. For those who do have increased pain response, occasional use of topical bromfenac or oral ibuprofen may be used to moderate the discomfort. If needed, the amnion tissue can also be excised from the symblepharon ring complex and then draped over the cornea with an



Some of the biggest impediments to success happen during insertion of the membrane. Careful preparation and thorough patient education are critical.

On the Horizon: Amniotic Drops

Soon, patients may have the benefits of amniotic tissue without the potential complicating factors of tissue placement. Drops made from amniotic fluid, reconstituted dehydrated amnion or morselized amniotic tissue will soon be available to practitioners. However, while they may sound similar in terms of therapy, they have their own list of drawbacks and limitations.

In the case of amniotic fluid for ocular surface treatments, very little peer-reviewed evidence exists, with the exception of mouse models of dry eye.[7] But with further research, this therapy may one day provide significant benefits, as one comparative study examining human amniotic fluid vs. human serum in a mouse model shows favorable outcomes.[8] However, in cultured human epithelial cell lines, another study's data favored serum.[9]

Morselized amniotic tissue has demonstrated efficacy in the treatment of non-healing epithelial defects.[10] To make this product, human amniotic tissue is pulverized into a gel-like consistency, which closely approximates the consistency of a cryopreserved product. Thus, researchers hope to find it as effective as the amniotic membrane itself without the added risk and discomfort of the symblepharon ring.

overlying bandage contact lens. This is, however, more technically challenging and time consuming, as the cryopreserved membranes are flaccid and do not position easily.

Stinging on instillation is an issue for patients only when there has not been adequate rinsing done prior to insertion. Cryopreserved amniotic membranes (Prokera specifically) are stored in Dulbecco's modified Eagle medium, which contains amphotericin B and ciprofloxacin, as well as a lower pH, which can cause stinging if not rinsed properly. In our office, we typically will use five 15ml bottles of sterile balanced saline solution for rinsing prior to insertion. This has essentially eliminated this complaint from patients.

Ejection of the ring is a possibility. To minimize this risk, assess the fit of the ring under the slit lamp after insertion. Have the patient look in various gazes to gauge how the edge of the ring is positioned relative to the lid margin. If the upper lid is quite tight, a slightly higher risk exists that the lower portion of the ring will ride up and "teeter-totter," similar to a rigid gas permeable lens. Applying tape to the temporal and/or nasal aspects of the lower lid in this situation to "raise" the lower lid may be useful in reducing ejection. In addition, an upper lid tape tarsorrhaphy, consisting of a single piece of tape positioned laterally to bolster the rigidity of the upper lid, will also improve comfort in many patients, as well as reduce air exposure. However, this needs to be assessed and applied immediately after insertion and before patient discharge to be successful.

If the membrane dissolves quickly, this is likely a sign of either aggressive inflammation or exposure to air, both of which can accelerate breakdown of the membrane. Amniotic membranes sequester inflammatory cells from the ocular surface in their matrix, which may contribute to breakdown of the membrane over time.[1] There is no global period for amniotic membrane insertion, so if the membrane is dissolving rapidly and the patient's condition warrants it, I recommend replacing it with a new one.

Occasionally, patients will complain of increased white discharge after membrane insertion; this seems to be more common in patients with the self-retained product. It is likely associated with irritation to the conjunctiva by the ring and is not harmful to the ocular surface in the vast majority of cases. Most amniotic membranes available on the market are either stripped of epithelium or contain devitalized tissue, which is biologically inert and does not carry complete HLA antigens responsible for an aggressive immunologic attack. In cases where some inflammation of the conjunctiva is present along with a white discharge, a small amount of topical anti-inflammatory is helpful; in my clinic, we typically use loteprednol twice daily, which reduces the amount of discharge and superficial inflammation.

Dehydrated products. The biggest issue here is ejection of the membrane from underneath the bandage contact lens. In my experience, a larger contact lens such as a Kontur 16mm diameter lens can be very helpful at retaining the membrane for the entirety of the treatment. With larger bandage contact lens use, it is imperative that limbal compression be avoided.

Pain can be an issue with dehydrated products, although it is less common in dehydrated products than with cryopreserved products due to the presence of the symblepharon ring in the cryopreserved products. Anecdotally, pain is most frequently found in patients with large epithelial defects.

Improving Odds and Outcomes

While amniotic membranes can be a powerful medium for improving ocular surface health, the key to improving outcomes is choosing your product based on the condition and goals for therapy.

In dry eye patients, amniotic membranes can improve symptoms and ocular surface health for an average of more than four months following application and with an optimal retention time of five days.[2]

This should not be considered a stand-alone therapy—for best outcomes, membranes should always be used in conjunction with other forms of ocular surface therapy. While amniotic membranes provide an immunologic "boost" to the surface, there are many other issues typically in play, especially in dry eye, which should be addressed simultaneously for maximum patient benefit.

Amniotic membranes have been touted to have significant anti-inflammatory, anti-scarring, anti-neovascular, anti-pain and regenerative healing properties; however, patient response is highly variable and not all such advantages can be expected in every patient.

Recently, much of the regenerative properties of amniotic tissue have been attributed to a molecular complex called HC-HA/PTX3, a heavy-chain hyaluronic acid bound to pentraxin-3.[3] Though fresh amniotic tissue has the highest amounts of HC-HA/PTX3, it is almost never used in clinical practice. Cryopreserved amniotic membrane has the next highest amount.[4] Dehydrated products, due to higher levels of processing, have the lowest amounts of HC-HA/PTX3—among the reasons FDA labeling indicates dehydrated products for wound coverage rather than accelerated wound healing. One study examining the healing results following strabismus surgery showed no difference in scar formation in patients using dehydrated tissue vs. none at all.[5] However, other researchers have found dehydrated amniotic membrane tissue to have greater bioavailability and sustained biochemical factor release time than cryopreserved tissue, although the results in this study do not reflect the tissues available commercially in the United States.[6]

Because acute inflammation from certain pathologies may be higher than what the membranes may be able to handle, in certain cases it may be prudent to consider prescribing topical steroids for one week preoperatively to reduce the inflammatory load on the ocular surface.

Lifestyle choices and the overall health of the individual patient will impact the wound healing response. To optimize the environment for ocular surface healing, ask patients about the following in your preoperative discussion of benefits and risks:

- Age and sex hormones
- Dietary habits
- Diabetes and other inflammatory or autoimmune diseases
- Stress, obesity, atopic diseases
- Medications such as NSAIDs, aspirin, steroids, chemotherapy
- Alcohol use and smoking
- Healing from previous surgeries or trauma

All of these factors can negatively impact the ocular surface and the healing response. Patients who have several of these items may actually benefit to a greater degree from amniotic membrane use in healing their ocular surface more quickly than without.

In general, amniotic membrane therapy is a boon for treating ocular surface disease. For patients with moderate to severe ocular surface disease, amniotic membrane therapy can act as a great catalyst to the healing process. It is a synergistic adjunct to pharmacologic treatments and can be beneficial for a broad range of clinical entities and severities of virtually any corneal or conjunctival surface disease. Being able to identify potential issues for patients ahead of time also empowers both the doctor and patient in ensuring compliance and better outcomes. Armed with the right information, you can be confident in providing amniotic membrane therapy to patients in need. ■

Dr. Hauswirth is a practicing optometrist at Minnesota Eye Consultants and an adjunct clinical faculty at Southern California College of Optometry. He is an active industry consultant and speaker. Relevant disclosures: Allergan, Bausch+Lomb, BioTissue, Shire, Sun, TearScience.

My Take on Treating RCE

Amniotic membranes are often used for cases of recurrent corneal erosion (RCE). My treatment for patients with RCE includes epithelial debridement and gentle diamond burr polishing, along with cryopreserved amniotic membrane. Retrospective analysis reveals that the recurrence of erosions in patients receiving the combination of diamond burr polishing and cryopreserved amniotic membrane was roughly half the recurrence in patients receiving the diamond burr polishing with a bandage contact lens.[11]

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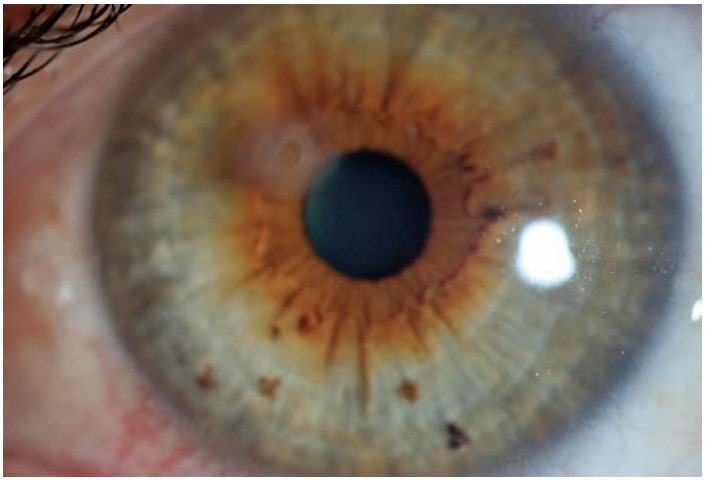
Corneal Disease Report

No Insult to Injury: Managing Foreign Body Removal

Here's what you need to know about this common corneal trauma to yield the best outcomes for your patients. **By Aaron Bronner, OD**

Ocular surface foreign bodies are a frequently encountered form of ocular trauma, which account for roughly 40% of all ocular traumas and are responsible for nearly 2% of all emergency room visits.[1] Patients generally present to the clinic with a very clear history of being struck in the eye with foreign material, but occasionally they have no history other than recent- onset irritation. The material may be metallic, glass, stone or organic and, to some degree, the type should help determine the treatment course. Though patients often have severe discomfort, the level of morbidity seen as a result of foreign body injury is typically mild.



This patient was referred in for evaluation of scar caused by a foreign body and rust ring removal.

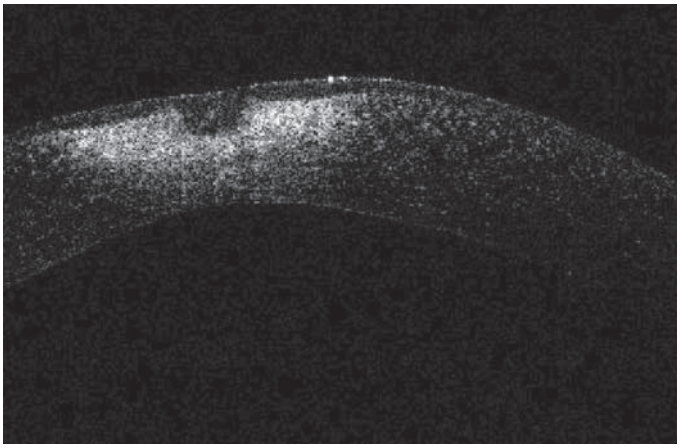
While the actual diagnosis of a corneal foreign body is generally easy to arrive at, the treatment of these injuries warrants more than a kneejerk response. As with any injury to the eye, diagnostic and therapeutic considerations with corneal foreign bodies should include diagnosing the precise nature of the injury, assessing your ability to treat the injury in the acute phase without worsening the course and, given the nature of the foreign body, anticipating and treating any long-term sequelae.

Identifying the Culprit(s)

Prior to simply removing the offending agent, it's important to carefully assess the overall status of the eye, the nature of the foreign body and the depth of the injury. Patient- and material-specific features have the potential to increase the risk of complications and should shape the short- and long-term treatment course.

It's easy to get swept away in the emotion of identifying a problem and offering a treatment; however, before a foreign body is removed and the case is closed, the involved eye needs to be carefully assessed to ensure no secondary ocular surface foreign bodies exist and that there are no signs of a retained intraocular foreign body. Clinicians should carefully assess the anterior segment and scrutinize the cornea, as well as the bulbar and palpebral conjunctiva with and without fluorescein dye—which will highlight areas of epithelial disruption. Corneal assessment should rule out

any subtle full-thickness lacerations (which, in the case of small foreign bodies, may be self-sealing due to the heat of a penetrating injury). Iris and pupillary abnormalities, even a subtly peaked iris, also indicate a possible retained intraocular foreign body and should prompt gonioscopy (after foreign bodies have been removed and the globe is relatively patent with a formed anterior chamber and normal intraocular pressure).



This corneal OCT of the patient from first image shows significant corneal scarring too deep for PTK. This case highlights how aggressive use of an Alger brush for rust removal can lead to significant corneal scarring.

Although the anterior chamber will often have a subtle traumatic iritis, if this iritis remains chronic after the material is removed, this is a strong indicator for retained intraocular material, prompting closer examination. Any disruption to the lens or capsule will result in near immediate and significant cataract development, also indicating intraocular penetration and guiding evaluation. If these indicators of intraocular material exist, the patient should be dilated at the initial visit.

The clinician also needs to be aware of the patient's previous ophthalmic history. Previous corneal surgery, particularly LASIK, can impact prognosis when dealing with a foreign body that has penetrated into the flap interface. Issues with epithelial ingrowth may develop in this scenario. Keratoplasty patients also need to be flagged, as rupture of the interface could occur with aggressive removal, particularly in relatively fresh transplants. These patients are at a greater risk for drug-resistant superinfections.

Nature of the Foreign Body

The foreign body's makeup is most typically related to the specific history at the time of the injury. Welding and grinding histories will produce metallic foreign bodies, striking tools will produce stone/ceramic or metallic objects and landscaping injuries (often caused by string trimmers) will involve organic or stone material (though the stone material in these cases should be treated similar to organic material, as it pertains to infection risk).

Finally, pet tarantulas, while infrequently encountered, are a well-described source of ocular surface foreign bodies, as their leg hairs may periodically end up on the ocular surface when a patient who had recently handled their pet rubbed their eyes. These fibers are barbed and can embed themselves readily into the cornea as well as the conjunctiva.

As with any foreign body, primary material considerations include the formation of corneal rust with metallic ferrous material, risk of infection with organic material or risk of contamination with fungal material or atypical bacteria species when the material is from an unclear environmental source.

Clinicians should carefully assess the depth of the foreign body prior to removal, as deep glass, ceramic or stone need not be removed if it doesn't impact vision, and very deep metallic or organic material should likely be referred to a specialist due to risk of penetration and advanced scarring.

Though it may seem simple to assess depth, in many cases it can be difficult to clearly demarcate the level of penetration; thus, close examination with a thin optic section is warranted. In unclear cases, corneal OCT can clearly demonstrate zones of penetration.

The depth of the injury should also be considered prior to using an Alger brush burr on corneal rust rings. Alger brush burrs are widely reported as having a pressure-sensitive clutch that will prevent the mechanism from penetrating Bowman's membrane; however, if the foreign body itself is penetrating Bowman's membrane, there is no longer an effective resistance to initiate the stop, which can lead to wide scarring if used aggressively.

In cases of penetrating injuries, you should stabilize the globe and then refer for specialist evaluation.

The Acute Injury

Barring a penetrating or inert/deep foreign body, the material should be removed with the patient under topical anesthesia in the clinic. With good patient cooperation, this is possible without a lid speculum, but

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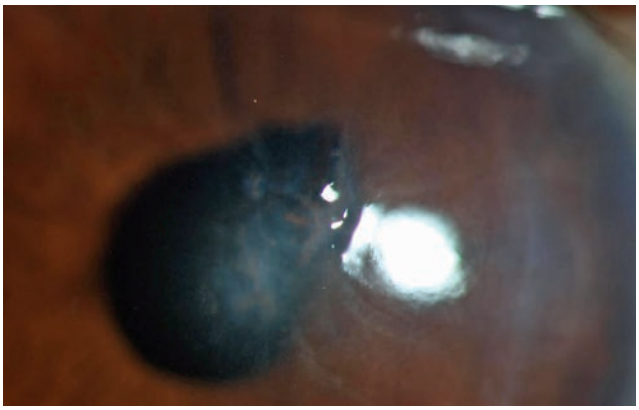
when blepharospasm is intense, clinicians should use a speculum. In very superficial cases, the material may often just be wiped away with a cotton-tipped applicator. In deeper cases, more invasive means are necessary.

Depending on clinician preference, there are a number of acceptable devices for removal of a corneal foreign body: golf spud, jeweler's forceps, magnetic probe or small-gauge needles. All instruments should be sterile. The goal is total removal of the material and any small particles left behind after removal of the primary foreign body. However, stromal disruption will lead to scarring, and broad disruptions here should be limited when not necessary.



Deep stromal retained foreign body from a string weed trimmer. Note the distortion of the pupil, indicating the injury was penetrating and highlighting the potential for a retained intraocular foreign body. Given the nature of the injury, there is a significant risk for microbial keratitis or endophthalmitis.

Any foreign body containing iron will cause rust deposition to the adjacent cornea shortly after contacting the ocular surface. The mechanism probably involves the immune response to a ferrous foreign body as opposed to simple inoculation and diffusion, and is not related to the thermal status of the foreign body.[2]

Regardless of the precise physiologic origin of corneal rust rings, their presence will often induce inflammation and slow down healing and result in localized stromal necrosis, as opposed to the numerous other forms of iron deposits that occur within the cornea such as Hudson-Stahli lines, Stocker lines and Fleicher rings. These should generally be removed as thoroughly as possible when encountered.[3,4] As with removal of the foreign body itself, rust ring removal can be accomplished with several different devices, most popular among these being a small-gauge needle and an ophthalmic burr. Clinical studies show more even and complete removal of the rust with burr compared with manual removal with a needle, and also facilitates more rapid healing; however, one animal model of rust ring removal showed a tendency for deeper scarring when the burr was used.[1,5] Again, though removal of corneal rust will help facilitate a rapid healing response, widespread stromal application of the burr can lead to significant scarring. Removal of all rust material over several visits, as more peripheral rust material may migrate superficially, may be preferable when the ring is large and deep and some material isn't easily removed. During this period, rust that doesn't stymie corneal healing can be left in place.[6]

Once removal of the foreign body and any rust ring has been accomplished, the patient should be treated in a similar fashion as patients with a corneal abrasion. Topical antibiotics should be applied in all cases. While generic ophthalmic antimicrobials are acceptable in cases without concerning history, in those with a concerning history a newer generation fluoroquinolone should be prescribed. In these cases, I generally prefer Vigamox (moxifloxacin 0.5%, Alcon) due to its lack of preservative. Though clinicians should be aware of the risk for fungal infection and extend follow-up intervals and total follow-up course in the setting of high-risk foreign bodies, treatment with a prophylactic antifungal is not warranted in most cases.

For comfort, cycloplegia can be helpful and limited dosing with topical ophthalmic NSAIDs may also reduce pain, though these drops may occasionally lead to corneal healing issues. A bandage contact lens may also be used until closure of the epithelial defect. More advanced therapy with amniotic tissue could be used but is not necessary in most cases. A corticosteroid (alone or as a combination antibiotic topical steroid) should generally not be used in cases of organic corneal foreign body (even with traumatic iritis) until epithelium has healed due to the risk of potentiating severe infection. In cases where scarring that limits vision is a concern, amniotic tissue may be applied, as it may help mitigate superficial scarring risk to some degree. Follow-up should occur shortly after to ensure appropriate healing and allow for removal of a bandage soft contact lens when used.

Post-Trauma Considerations

Follow-up considerations of corneal foreign bodies should also

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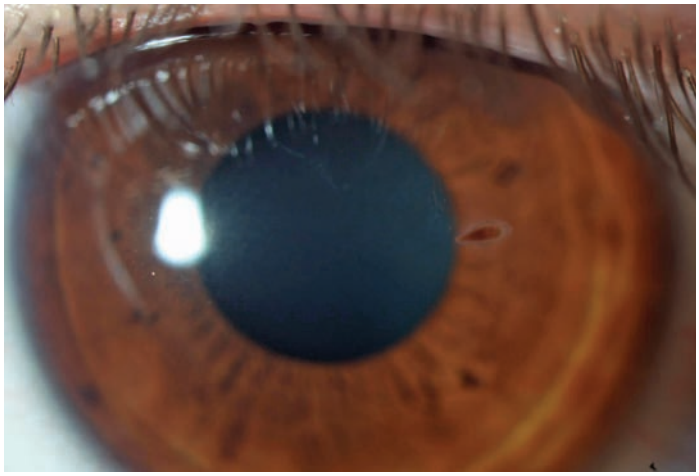
involve treatment of any sequelae that may arise. To allow timely diagnosis of complications, in addition to follow-up one to two days after injury, clinicians should follow up approximately a week later, though these recommendations may vary on a case by case basis. Problems that develop days and months following the original injury could be as mundane as a poorly healing eye or as significant as microbial keratitis. Occasionally, a foreign body and its removal may leave a visually significant scar, which should be assessed for its ability to be removed.



Plant seed corneal foreign body carries increased risk of microbial fungal keratitis.

What Can Go Wrong?

Sometimes, patients with foreign body removal present upon follow up with complications, such as:

Non-healing wound. In almost all cases, epithelial defects from corneal foreign bodies heal quickly and without complication once the foreign body and any rust ring has been removed. Non-healing most typically occurs when a corneal rust deposit is not sufficiently removed, and results in an area of necrosis. At this point, an Alger brush or small-gauge needle will often more easily remove the residual corneal rust compared with the initial visit. Any necrotic tissue, which also retards epithelialization, should also be debrided. If you aren't sure whether you are dealing with necrotic tissue or an infiltrate, which can look similar (though behave quite differently when

mechanically debrided—necrotic tissue is generally softer and more easily debrided than an infiltrate), culturing the material on a prepackaged swab would be appropriate. In cases where there is no necrosis or remaining corneal rust, neurotrophy, exposure or severe ocular surface disease could be the culprit, as each of these can slow healing and should be carefully assessed and treated. Although they aren't necessary in most cases of corneal foreign bodies, in any non-healing corneal defect, a sutureless amniotic membrane is a great option to speed things up. Continuing antibiotic therapy at effective dosages is necessary as long as an epithelial defect persists.

Infection. Non-surgical trauma of the ocular surface is the greatest risk factor for infectious keratitis in developing countries and is also responsible for a significant proportion of cases in the United States. Fungal infection carries a well-known association with corneal trauma from plant matter, but other infectious etiologies, such as non-tuberculous mycobacteria, *Nocardia* and *Acanthameoba* all are distributed widely throughout the environment and are associated with external trauma. Foreign body injuries from suspicious sources should be followed closely for a longer period and should likely be treated with stronger antibiotics than those from cleaner material. Infiltrates that develop from sites of external traumas need to be cultured and treated aggressively, or referred to a specialist, as in many of these cases you are dealing with an atypical organism.

Recurrent corneal erosion (RCE). This is a frequently encountered clinical entity that is often associated with trauma, in most cases a superficial laceration of the corneal epithelium and Bowman's membrane by a fingernail. Given the shared traumatic etiology, a corneal foreign body injury may seem like a likely source for RCE to develop from. The reality, however, is that foreign bodies rarely cause this condition. The rationale for this difference has to do with depth of injury and the pathophysiology of RCE. Any injury that removes epithelium but doesn't impact Bowman's membrane will heal uneventfully. Any injury that removes epithelium and irregularly disrupts Bowman's membrane but doesn't disrupt the stroma has a greater chance for leading to RCE, as the epithelial anchoring complexes are disrupted in these cases. However, any injury that irregularly disrupts

the epithelium, Bowman's membrane and stroma has a low rate of RCE because of the scarring associated with activation of keratocytes (which occurs in cases of stromal trauma). This leads to strengthening of the epithelial-stroma adhesion and a low risk of RCE. In most cases, corneal foreign bodies penetrate through to the stroma, so there is very little association with RCE.

A small piece of retained glass is present in the mid stroma. The material is out of the visual axis and inert and so can be left alone.

Post-traumatic Scars

Scarring occurs in all cases of stromal injury and some degree of it should be expected after foreign body removal. In many cases of small focal injury, this scarring doesn't impact vision to any significant degree, even when the visual axis is involved. Occasionally, however, with a large, widespread (such as occurs from shattered glass) or deep foreign body injury, stromal scarring may be significant and resultant disruption to vision may occur. In these cases, surgical options may be considered. For any surgery, it is best to have the patient wait a minimum of six months following the injury to allow the eye to heal completely. If vision or keratometric measures change significantly over this period, the patient should wait another six months; for any surgical fix it's important to have a relatively stable cornea. Once the cornea stabilizes, surgical options to consider include: corneal transplant; penetrating keratoplasty (PK) or deep anterior lamellar keratoplasty (DALK) for deep central corneal scars; or phototherapeutic keratectomy (PTK) for anterior stromal scarring.

While transplant for a foreign body scar is uncommon, PTK is frequently used in this capacity. PTK uses the excimer laser to remove corneal tissue and can quite effectively treat superficial opacity or even zones of irregular corneal astigmatism, both frequently encountered sources of vision loss from corneal scars. In most cases, as with traditional PRK, the surgery center won't remove tissue beyond a residual stromal bed of 300µm to 350µm and so the scars need to be anterior. Further, as the procedure results in removal of corneal tissue, a flattening effect occurs, which reduces myopia or increases hyperopia, a feature that can be useful in some cases and a drawback in others. Antihyperopia treatments can be used when this shift is not desirable, but hyperopic laser treatments aren't as accurate or effective long-term as myopic treatments.

It should also be noted that any excimer application for irregular astigmatism secondary to a scar has less precise outcomes and appropriate patient counseling about the goal of the procedure (reducing, but perhaps not eliminating, irregularity) is crucial. As part of the workup for these patients, a diagnostic rigid gas permeable (RGP) spherocylinder over-refraction can be useful to determine the amount of reduced vision from corneal irregularity (which the RGP will correct) or opacity (which the RGP will not correct) and can help guide surgical decision-making.

For deep or full-thickness scars, PK and DALK may be options to consider. Given the expense of the surgery, length of recovery, risk of complication and uncertain refractive endpoint, PK and DALK should be reserved for visually significant scars that cannot be correct with an RGP.

Given the frequency with which corneal foreign body injuries occur, most ODs are well-versed in their management, though if you are not used to performing manual manipulations to the eye, or haven't dealt with one of these cases in time, some subtler aspects of their care can be overlooked. As with the management of any acute ocular injury, it's important to be mindful of both acute considerations (material, depth, degree of compromise to ocular tissue) and chronic considerations (potential for scarring, infection and poor healing) prior to initiating treatment to ensure best outcomes and appropriate patient expectations. ■

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Advancing Our Knowledge of Dry Eye Disease

By Paul M. Karpecki, OD, FAAO; Whitney Hauser, OD; and Katherine Mastrota, OD

The dry eye population is estimated to be more than 10 times that of other common conditions such as glaucoma.[1] The ongoing Beaver Dam Offspring Study (BOSS) provided a baseline for estimating the level of dry eye disease (DED) in the general population of US adults.[2] In that study of 3,257 participants, ages 21 to 84 years, Paulsen and coworkers reported an overall prevalence of DED symptoms of 14.5%—or nearly 30 million people.[2]

As high as this may seem, these numbers are likely to increase dramatically in the near future as a result of the aging US population. There are currently more than 100 million adults in the US over the age of 50, with another 10 million expected by the year 2020.[3,4]

Diabetes is also likely to have an impact on dry eye disease prevalence. Diabetes rates have been steadily rising for the last 40 years and there is no indication that this rate is going to decline any time soon.[5,6] Twenty-nine million Americans (9.3%) have diabetes,[6] and an older study found that half of this population had dry eye.[7]

Digital device use may be another huge driver of dry eye disease in coming years, with their use creeping into almost every part of our lives. A recent study by the Vision Council found that, on average, roughly 88% of adults spend more than two hours per day using a digital device, while approximately one in 10 people spend at least three-fourths of their waking hours on a digital device.[8]

Unfortunately, despite rising prevalence, only a small fraction of patients receive treatment for their dry eye,[2,9] and the consequences of this cannot be overstated. Dry eye is much more than a nuisance. Complications include greater risk of eye infection and ocular surface damage, which can lead to inflammation, corneal surface abrasion and ulcers, contact lens intolerance and vision problems if left unaddressed.[10] The relevance of degradation in quality of life, likewise, should not be minimized as it is known to heighten the risk of psychosomatic disorders, such as depression, stress and anxiety.[11,12] And, in severe cases, patient utility

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Goal Statement: On completion of this educational activity, participants should have a better understanding of conventional testing for dry eye disease, and new and advanced diagnostic technology making diagnosis less time consuming and more precise, along with intermediate and long-term therapeutic interventions for treating and managing the dry eye patient.

Faculty/Editorial Board: Paul M. Karpecki, OD, FAAO, Whitney Hauser, OD, and Katherine Mastrota, OD

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assessment scores are comparable to those of acute angina and dialysis patients.[13,14]

The time to act is now. We must actively embrace the advanced knowledge of dry eye that now exists and utilize any tools at our disposal to help diagnose disease sooner and treat it more effectively.

KEY PREDISPOSING FACTORS

- Advanced age
- Female gender
- Hormone replacement therapy
- Systemic antihistamine use
- Lack of healthy essential fatty acid intake (e.g. omega-3 fatty acids)
- Connective tissue disorders
- Refractive surgery
- Androgen deficiency
- Contact lens use
- Rosacea
- Certain medications (e.g., some antidepressants, diuretics, beta-blockers, isotretinoin)
- Diabetes
- Chemotherapy
- Low humidity environments
- Cigarette smoking

THE EVOLVING ROLE OF DIAGNOSTIC TECHNOLOGY IN CLINICAL PRACTICE

The signs of dry eye that doctors see and the symptoms that patients feel always begin at a cellular level. Indeed, the impetus of inflammation is appreciated at a biochemical level before its impact is seen at the slit lamp. Ocular surface stress and damage trigger an acute inflammatory response. The body's innate reaction to the initial insult is a release of acute response cytokines that increase inflammatory cell production, expression of intercellular adhesion molecules and activation of antigen presenting cells.[15] T-cells migrate to ocular surface tissues and potentiate a chronic autoimmune response that results in a decrease in goblet cell density and apoptosis. This inflammatory domino effect results in overexpression of MMP-3 and MMP-9 (matrix metalloproteinase) and breakdown of the epithelium.[15]

Our goal, of course, is to intervene sooner and to recognize that first acute response that will inevitably morph into a state of perpetual inflammation that ultimately leads to chronic, progressive ocular surface disease. Indeed, without timely diagnosis, dry eye disease will only get worse and more difficult to manage. As such, all eye care practitioners should be actively looking for dry eye in our patients—whether or not they are symptomatic.

There's no question that can be a challenge. Research shows that fewer than 60% of dry eye patients are symptomatic.[16] As such, the use of symptoms alone in diagnosis will likely result in missing a significant percentage of dry eye disease patients, particularly those with early or mild disease.[16] Furthermore, this could have considerable impact—particularly in patients undergoing cataract or refractive surgery, as patients with dry eye disease have less than optimal visual results.[16]

Fortunately, a better understanding of conventional testing as well as new diagnostic technology have made dry eye diagnosis far less time consuming and much more precise. Of course, as is the case with many conditions, no single finding or test alone will provide all of the answers we need to initiate effective treatment; but together, our enhanced knowledge, combined with improved tools can help better inform our clinical decision-making for the short- and long-term benefit of patients suffering from or at risk of developing dry eye disease.

CONVENTIONAL TESTING

One way to raise your probability of success in diagnosing dry eye disease is to employ advanced testing, such as osmolarity and meibography.[17] But since many doctors may not yet have access to these technologies, it's important to know how to make the most of conventional testing. This includes the case history, surveys, visual acuity, slit lamp observation, dye testing, tear volume testing and topography.

• ***History.*** Case histories are not the be-all and end-all of diagnosis, but they are essential when diagnosing dry eye disease. When evaluating the history, look at the number of predisposing factors a patient may display (*see "Key Predisposing Factors"*). This approach alone may not be 100% accurate in establishing a diagnosis, but combined with testing, it can help confirm the disease. A patient with a significant number of predisposing factors should heighten your suspicion and prompt testing.

• ***Surveys.*** These have come a long way and have an important place in dry eye diagnosis. They help bridge the gap when there is a disconnect between signs and symptoms, and offer objectivity where none might otherwise exist. Furthermore, many useful surveys are now in circulation. One of the most widely used is the Ocular Surface Disease Index (OSDI). Despite some limitations,[18,19] the OSDI has excellent reliability and validity, as well as good sensitivity and specificity.[19] It also discriminates well between normal, mild to moderate and severe cases. The Standard Patient Evaluation of Eye Dryness (SPEED) and the Dry Eye Questionnaire 5 (DEQ-5)[20] are also commonly used to give objective value to subjective complaints. Other surveys, such as Impact of Dry Eye on Everyday Life (IDEEL), National Eye Institute's Visual Function Questionnaire (NEI VFQ-25) and The Short Form-36 (SF-36) provide information about the patient's quality of life, which is an important measure in any chronic disease.

• ***Visual acuity.*** Visual acuity is tricky because it's not qualitative. For example, 20/20 doesn't mean much if you have to help a patient along by prompting her to blink. That's 20/struggle—not 20/happy. Furthermore, the urge to blink is frequently a response to blur, which is a strong indicator that a patient has dry eye. Unfortunately, clinicians don't often consider dry eye as the primary diagnosis when they encounter a complaint of blurred vision, although in fact this may be the only key symptom reported with almost all levels of dry eye disease. Whether it's transient blurred vision secondary to tear film instability in early disease or

persistent blurred vision secondary to central corneal staining in advanced disease, blurred vision is a diagnostic sign worth careful investigation.

• ***Slit lamp observation.*** The search for dry eye at the slit lamp doesn't begin and end at the cornea. Indeed, you want to look for superficial punctate keratitis, filaments and corneal dystrophies, but the lids and the conjunctiva provide many other clues. When examining the lids, pay careful attention to positioning, laxity, lash alignment and overall lid hygiene. When examining the conjunctiva, be on the lookout for conjunctivochalasis, exposed concretions, pinguecula, pterygium, hyperemia and papillary reaction.

• ***Dye testing.*** Vital dye staining information may be the first indicator that the patient's signs and symptoms don't match up. The three ophthalmic dyes are 2% sodium fluorescein, 1% lissamine green and rose bengal. Fluorescein is the most commonly employed dye in optometric and ophthalmological practices; however, lissamine can help you obtain excellent images that will allow you to recognize early signs of disease. Also, to get a truly detailed picture, both are required. Fluorescein is used to identify desiccated or injured cells and to perform a fluorescein tear break-up time (FTBUT). Corneal staining—particularly central, macropunctate or confluent—is an indicator of late-stage dry eye disease. Lissamine green, on the other hand, stains dead or devitalized cells.[21] Lissamine green is useful in evaluating conjunctival damage, conjunctivalchalsis and the line of Marx along the lid margin. The line of Marx is a distinct zone of histologically parakeratinized cells that anchor the tear film. It's important to pay special attention to this since anything that changes the line of Marx will change the way the tear film operates. (*See Figures 1 and 2*). Rose bengal can provide valuable information too. However, patients frequently complain that it stings.

Photos: Whitney Hauser, OD

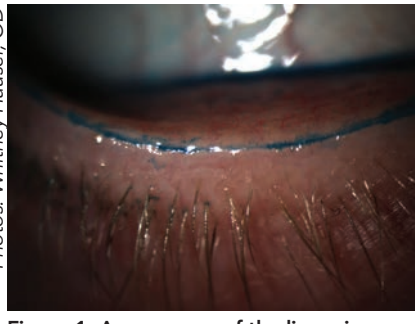

Figure 1. Appearance of the lissamine green-stained line of Marx in a healthy eyelid. The line of Marx represents the muco-cutaneous junction of the eyelid.

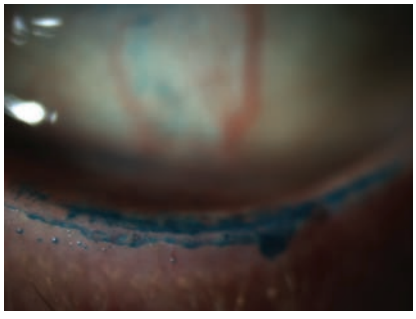

Figure 2. Lissamine green staining of the line of Marx. Notice the abnormal undulations of Marx line in lid margin disease and anterior shift of the line. In the healthy eyelid, the line of Marx smoothly parallels the contour of the lid margin and the line is positioned posterior to the glands.

• ***Tear volume testing.*** For obvious reasons, tear volume testing is a staple in dry eye diagnosis. Options include Schirmer's testing and phenol red thread. Schirmer's is the gold-standard in terms of research, but it does require anesthesia and it takes about five minutes. Phenol red thread, on the other hand, can be performed without anesthesia and takes only takes 15 seconds, making it a valuable alternative.

• ***Topography.*** Though not often thought of as a test for diagnosing dry eye, if properly reviewed, this test is often a first indicator of dry eye disease, especially when used in surgical practices prior to cataract surgery. Topography can detect subtle irregularities to the ocular surface and, as such, is an excellent tool for the detection of dry eye.[22] The appearance of inferior steepening due to epithelial dehydration is a tell-tale sign that sometimes looks a bit like keratoconus.[23] Other topographical findings of dry eye disease include irregularly shaped placido discs and differences in average keratometry readings between eyes.[22,23]

ADVANCED TESTING

With good reason, point-of-care testing is finding its way into more and more practices. These reliable diagnostic tests can quickly provide clinical direction, tracking progress, helping determine the most appropriate therapy and, more importantly, determining who has true dry eye and who doesn't. Newer tests include meibography, lipid layer thickness (LLT) assessment, blink analysis, tear osmolarity, MMP-9 analysis, noninvasive Keratograph break-up time (NIKBUT), microscopy, allergy testing, and the Sjögren's disease (Sjö) test.

• ***Meibography.*** Our ability to image the meibomian glands has significantly changed how we treat dry eye and how we educate patients about the importance of treating their disease. Meibomian glands plug, swell, become serpiginous, truncate and atrophy—in that order.[24] As such, simply seeing a capped gland doesn't tell you much. Without looking inside, you will never really know how many of them are truly viable, which means you might suggest a treatment, like warm compresses, that will never offer meaningful relief to a patient who only has three or four viable meibomian glands.

• ***Lipid layer thickness (LLT) assessment.*** Fluctuating vision is a hallmark of dry eye and an insufficient lipid layer is believed to be the most likely cause.[25] While fluorescein TBUT is still used in most clinics, automated assessments of the lipid layer have taught us a lot about the ocular surface and provide a wealth of useful knowledge. For example, the Lipiview II employs interferometry to evaluate the lipid layer thickness, and the Keratograph 5M evaluates noninvasive TBUT. Being armed with the knowledge that a patient's dry eye is driven by a deficient lipid layer will let you know that treatment should include a lipid-containing artificial tear and therapies that encourage meibomian gland expression.

• ***Blink analysis.*** Don't underestimate the value of a healthy blink. You might be surprised by how many of your patients' dry eye problems are caused by or made worse as a result of blink pattern. New technology can evaluate patients' routine blink characteristics, including blink rate and partial or incomplete closure. You can also use this informa-

tion and video footage to help educate patients about how blinking contributes to their condition. The information can be used to help encourage treatment compliance and/or blinking exercises.

• ***Tear osmolarity.*** Osmolarity testing indicates whether or not the patient has a higher salt content than normal: As the volume of aqueous declines, the salt concentration in tears increases. Hyperosmolar status, whether through decreased tear production or an increased evaporative state, indicates reduced aqueous levels.[26] This test can help make a dry eye diagnosis without relying on symptoms alone. Indeed, this is the primary purpose of tear osmolarity testing. However, it also useful for monitoring patients to determine whether they are responding favorably to treatment.

• ***Matrix metalloproteinase-9 (MMP-9) analysis.*** This point-of-care diagnostic test provides both qualitative and quantitative information that can aid the diagnosis of dry eye. MMP-9, a proteolytic enzyme produced by stressed epithelial cells, has been shown to increase in dry eye patients.[27] A positive reading indicates that the sample contains more than 40ng/ml, which indicates inflammation. Elevated MMP-9 does not automatically imply that a patient has dry eye since this can also be increased in other ocular surface disorders. However, MMP-9 has been correlated with dry eye[28] and is a good indicator that further investigation is warranted.

TRADITIONAL RISK FACTORS NEED NOT EXIST

It is worth noting that although DED has traditionally been associated with aging, in the overall BOSS group, symptoms were also prevalent among younger subjects.[1] In other words, dry eye should not be ruled out simply because a patient is young—particularly if the patient is a contact lens wearer. Indeed, younger age, male gender and the lack of other traditional risk factors should no longer limit further investigation into a patient's dry eye status.

Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry eye in the Beaver Dam offspring study: prevalence, risk factors, and health-related quality of life. Am J Ophthalmol. 2014 Apr;157(4):799-806.

• ***Noninvasive Keratograph break-up time (NIKBUT).*** Aside from sparing the patient from the instillation of dye, this technology is much more precise than a slit lamp observation. Compared to putting in some fluorescein, asking your patient to blink, and then silently counting "one Mississippi, two Mississippi," this scientific technology is light years ahead in terms of objectivity. NIKBUT uses placido disc ring-based corneal topography to measure initial and average breakup. This unit also can help determine tear film quality. Using white or infrared illumination, you can measure the amount of tears at the lower tear meniscus. Finally, interferometry can be performed, allowing you to see particle spread while capturing lots of images and video.

• ***Microscopy.*** These non-contact devices reveal cell loss in the endothelial cell layer. Cell loss can be set in motion by several factors, such as extended contact lens wear, corneal disease, ocular surgery and, of course, dry eye. One benefit of specular microscopes is that they offer objective data that can be monitored over time to measure improvement. The images they provide also can be valuable for patient education.

• ***Allergy testing.*** There's no question that allergy and dry eye overlap. Diagnosing dry eye disease can be challenging in this population, particularly when a patient is taking antihistamines. In such cases, it is helpful to dig deeper. New point-of-care allergy testing is quick and easy to perform. It takes approximately three minutes to perform and 10 to 15 minutes later, you get information on a panel of 60 allergens that are ocular-specific and regionally specific. The Ocular Allergy Diagnostic System (OADS) is very similar to a prick test that you might receive in an allergist's office. However, it uses a plastic applicator instead of needles.

• ***Sjögren's testing.*** Sjögren's is notoriously underdiagnosed but, thanks to new tests, optometrists may be able to detect it sooner. Sjögren's syndrome is associated with a 16-fold increased risk of development of lymphoma,[29] so finding it sooner not only helps guide ocular treatment, it could also save lives. To perform the Sjö test, a doctor or technician obtains blood on a collection card and sends it to a lab for analysis. The results are usually back in seven to 10 business days. Alternately, patients can be referred for a blood draw that is then sent to the proprietary lab for processing.

ELIMINATE GUESSWORK

Like diabetes and hypertension, dry eye disease is a chronic, progressive disease that affects millions of people.[30] While there is no "cure" for dry eye, timely identification and more specific knowledge about a patient's individual presentation can help guide treatment decisions, providing symptomatic relief and preventing escalation.

The best strategy is not to depend on any single test or marker. Dry eye disease (DED) is one of the most pervasive eye conditions in society today. As such, less common diseases can be misdiagnosed as dry eye, forcing the patient to undergo a potentially unnecessary regimen while simultaneously delaying treatment for the real problem. As in glaucoma diagnosis, no single test should be called upon to provide all of the information needed. Instead, a serial approach of multiple tests based on presentation is preferred. Though it may be viewed by some as more expensive or time consuming, going the extra mile in the diagnostic phase can save your patient both clinically and financially in the months and years to come.

NEW UNDERSTANDING IN THE TREATMENT OF DRY EYE DISEASE

Although tens of millions of patients suffer from dry eye disease in the United States alone, less than one million are receiving medical treatment.[2,9] Early, ineffective approaches to treatment may partially explain this unfortunate statistic. However, our evolved understanding of the disease combined with new treatments and well-informed ways to employ them offer more than just hope. We can change the

HOW TO HELP PATIENTS UNDERSTAND THEIR DRY EYE

Perhaps the most important thing you can do when you're talking about dry eye disease is to set appropriate patient expectations. It's essential that patients leave your exam room with the understanding that dry eye is a chronic condition. One way to convey this is by emphasizing the "-itis." For instance, try mentioning conditions such as blepharitis, keratitis and meibomitis. This will help you draw a parallel between dry eye and other diseases that patients are more familiar with, such as arthritis. Patients understand that if you have arthritis, it's a life-long condition that requires ongoing medical treatment for effective control. Dry eye, like arthritis, can cause flare-ups, which are not a reflection of a doctor's inability to manage condition. Rather, these episodes are an expected manifestation of this chronic, progressive disease.

course of this disease and give patients an opportunity to live a less symptomatic life, despite the chronic nature of the condition.

IMMEDIATE INTERVENTION

There are a lot of dry eye treatments on the market and many of them are fantastic. But dry eye is complex. Unless it is very mild and a patient is in the beginning stages of disease, no one treatment alone is likely to provide satisfactory results if used exclusively for months and years to come.

When treating dry eye and ocular surface disease, you have to look at the big picture and the whole patient. There's no one silver bullet, especially when the patient has meibomian gland dysfunction (MGD) or lid disease. MGD is an important cause of evaporative dry eye syndrome and may be the most common cause of dry eye worldwide. MGD results in a deficient lipid layer, which in turn allows excessive evaporation of the aqueous layer of the tear film and consequent dry eye signs and symptoms. Conditions like this require immediate short-term intervention followed by long-term maintenance treatment.

Regardless of what we presume may be triggering a patient's dry eye, the goal is to get the lids, glands and the ocular surface functioning at their best. This involves four essential steps. Many clinicians will advocate for one or the other of these. However, none of these should be neglected. By systematically considering the need for treatment in all four areas, you can get your patient on the right path sooner, and prevent this chronic disease from getting worse.

The four areas that ought to be addressed right away in a patient with dry eye are:

• ***Obstruction.*** Treating gland obstruction is like good dental cleaning. It can include lid margin debridement and scaling, hydrating compresses, manual expression and thermal pulsation. (*See Figure 3*).

• ***Bacterial biofilm.*** If a patient has biofilm, address it head on with scrubs or a mechanical treatment such as Blephex, a surfactant cleaner or hypochlorus acid, or antibiotics as needed, depending on severity. Don't overlook this important step toward faster health and comfort for your patient.

• ***Inflammation.*** Try to knock out the inflammation right away in all forms of dry eye disease. For the immediate short-term, you can initiate steroids, doxycycline or a combination agent. Later or concurrently, you can add a longer-term medication to get inflammation under control. For example, cyclosporine or lifitegrast can be utilized with or without the addition of nutritional supplements.

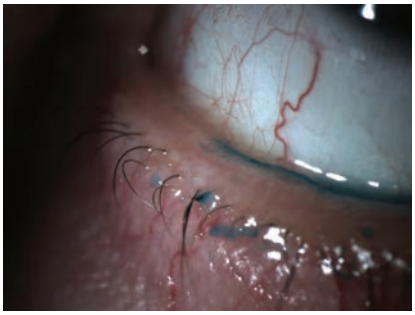

Figure 3. Waxy debris covering the meibomian orifices can be mechanically removed to clear the way for lipid flow from the gland.

• ***Tear film instability.*** Artificial tears get a bad reputation because they will not treat dry eye disease. However, like brushing your teeth every day, artificial tears are important for maintenance and comfort. The key to effective tear supplementation lies in choosing a product that's appropriate for each patient's unique surface condition. A patient with high osmolarity will benefit from a different tear than a patient who is lipid or aqueous deficient with low osmolarity.

BEYOND PALLIATIVE RELIEF

The treatments above, particularly steroids, can offer rapid relief but are by no means a long-term solution. While it is true that you can see outstanding results when you get rid of biofilm, if you put a patient on steroids and follow up with warm compresses, it fails to address the chronicity of dry eye disease. Dry eye is chronic, and once steroids are discontinued, you are left with palliative options alone, as dry eye will once again progress. In fact, research has shown that when artificial tears alone were used for one year, patients experienced a 40% increase in T-cells, which is equivalent to no treatment at all.[31]

Given the progressive nature of dry eye disease, the inflammatory cascade needs to be shut down, rather than merely slowed down. T-cell recruitment and migration must be arrested to prevent cytokine release.

DON'T OVERLOOK CHRONICITY

Dry eye disease occurs when tears no longer provide adequate support to the ocular surface.[15] The lacrimal functional unit (consisting of the lacrimal glands, conjunctival goblet cells, meibomian glands, and their neural and hormonal support structures) is central to the maintenance of a stable tear layer. Without this, tear dysfunction results.

Many environmental and endogenous factors can trigger dysfunction of the lacrimal functional unit, but regardless of what triggers it, dysfunction of the lacrimal functional unit sets into motion a chronic inflammatory reaction that ultimately produces dry eye disease.[15] Furthermore, the dysfunction of the lacrimal functional unit is

perpetuated and sustained by the inflammation itself, and the result is a lacrimal functional unit that cannot produce tears of adequate quantity or quality.

Without an adequately protective tear film, there is continued stress on the ocular surface, leading to a cycle of dry eye disease in which inflammation produces tissue damage, which in turn causes cytokine release. The resulting inflammation then leads to further cytokine release in an ongoing cycle that becomes progressively worse in many patients.[25] It is important to note that even if lacrimal functional unit dysfunction is caused by meibomian gland obstruction and evaporative dry eye, these events will trigger an inflammatory cycle that must be addressed.

THE COMPLEX CHEMISTRY OF CHRONICITY

T-cells contribute to ocular inflammation through the production and release of proinflammatory cytokines.[32] T-cell target recognition occurs through a complex reaction in which a T-cell surface receptor, called lymphocyte function-associated antigen-1 (LFA-1), is able to bind to a ligand on the target cell. This ligand is called intercellular adhesion molecule-1 (ICAM-1). ICAM-1 is normally expressed in low levels on epithelial (and endothelial cells) of ocular tissues, including the cornea, conjunctiva and lacrimal glands, as well as on antigen presenting cells. However, in patients with dry eye, ICAM-1 is overexpressed.[33]

The binding of ICAM-1 to LFA-1 integrin on the surface of T-cells plays an important role in the inflammatory process of dry eye. [36] When ICAM-1 binds to LFA-1, it sets in motion the three key components of an inflammatory response: T-cell activation, recruitment and cytokine release.[33-35] As such, researchers hypothesized that LFA-1/ICAM-1 blocking would be a logical target for treatment.

Indeed, as our understanding of the inflammatory response has evolved, so too has our ability to address it clinically. As we first saw in patients treated with cyclosporine, arresting inflammation is at the heart of successful dry eye treatment. More recently, we are seeing that lifitegrast, a small molecule integrin antagonist, blocks binding of ICAM-1 to LFA-1 on the T-cell surface, inhibiting T-cell recruitment and activation associated with dry eye disease inflammation.[36-38]

CLINICAL DATA

In July 2016, the FDA approved the first in a new class of drugs known as lymphocyte function-associated antigen-1 (LFA-1) antagonists. Commercially known as Xiidra (lifitegrast ophthalmic solution 5%, Shire Pharmaceuticals), the new drug is indicated for the treatment of signs and symptoms of DED. Specifically, this small molecule integrin antagonist blocks the binding of ICAM-1 to LFA-1 on the T-cell surface, inhibiting T-cell recruitment and activation associated with DED inflammation.[36-38] This preservative-free drop comes in individual vials and is dosed BID.

Lifitegrast went though four separate multicenter, prospective, placebo-controlled, randomized, double-masked FDA clinical trials involving more than 2,000 subjects ranging in age from 19 to 97 with a predominance of female patients, at about 75%.[39] Both the active drug and placebo were administered BID for 84 days, and safety and efficacy were determined between the groups.

The study results revealed that the groups using lifitegrast had a statistically significant clinical improvement in signs (inferior corneal staining) and symptoms (eye dryness) compared with placebo. In the OPUS-3 study on symptoms of eye dryness, which involved 355 patients on lifitegrast and 356 on placebo, lifitegrast had a highly statistical improvement compared with placebo at day 84 ($p=0.0007$), day 42 ($p<0.0001$) and at 14 days after initiating therapy ($p<0.0001$).

The most common (>5%) ocular finding associated with lifitegrast was burning, and the most common (>5%) nonocular finding was dysgeusia, or a change in taste sensation. Most adverse events were reported as being mild to moderate in severity, and transient. ■

DON'T OVERLOOK DEMODEX

Ocular *Demodex* infestation is highly age-dependent. In a study of 435 people, infestation was only 13% in individuals ages 3 to 15 vs. 69% in those ages 31 to 50 and 95% in those 71 to 96 years of age. Always be on the lookout for cylindrical dandruff and abnormal lash growth. Overpopulation of *Demodex* mites induces change of tear cytokine levels, IL-17 especially, which cause inflammation of the lid margin and ocular surface.[1]

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This enduring activity may contain discussion of published and/or investigational uses of agents and/or devices that are not indicated by the FDA. Off-label use of a medication or a biological is defined as use for an indication, or in a manner for which FDA approval has not yet been obtained and which is therefore not included on the FDA-approved label or product packaging. Please refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings. Practitioners should critically assess the information herein and are encouraged to consult appropriate resources for any product or device mentioned in this program.

The educational content of this activity has been peer reviewed and validated to ensure that it is a fair and balanced representation of the topic based on the best available evidence.

CE TEST

To obtain two hours of continuing education credit, complete the exam by recording the best answer to each self-assessment question online at: https://www.reviewofoptometry.com/ce/advancing-our-knowledge-of-dry. Or, mail the Examination Answer Sheet on the next page to: Jobson Medical Information, Dept.: Optometric CE, 440 9th Avenue, 14th Floor, New York, NY 10001. A minimum score of 70% is required to obtain a certification of completion. There is no fee for this course.

1. The Beaver Dam Offspring Study (BOSS) reported an overall prevalence of DED symptoms of:
a. 4.5%
b. 14.5%
c. 24.5%
d. 34.5%

2. There are currently more than _____ adults in the US over the age of 50.
a. 10 million
b. 50 million
c. 100 million
d. 200 million

3. How many Americans have diabetes?
a. 9 million
b. 19 million
c. 29 million
d. 39 million

4. Among diabetic Americans, what percent have dry eye?
a. 10%
b. 15%
c. 25%
d. 50%

5. The Vision Council found that, on average, 88% of adults spend more than _____ per day using a digital device.
a. 1 hour
b. 2 hours
c. 3 hours
d. 4 hours

6. The Vision Council found that, on average, one in 10 people spend at least _____ of their day on a digital device.
a. one-eighth
b. one-quarter
c. one-half
d. three-fourths

7. In severe cases of dry eye, patient utility assessment scores are comparable to those of:
a. Acute angina patients
b. Dialysis patients
c. Asthma sufferers
d. Both a and b

8. Research shows that fewer than _____ of dry eye patients are symptomatic.
a. 40%
b. 50%
c. 60%
d. 75%

9. One of the most widely used surveys in circulation that discriminates well between normal, mild to moderate and severe cases of dry eye is the:
a. OSDI
b. IDEEL
c. NEI VFQ-25
d. SF-36

10. This may be the only key symptom reported with almost all levels of dry eye disease.
a. Itching
b. Redness
c. Photophobia
d. Blurred vision

11. When evaluating dry eye at the slit lamp, it is important to look for:
a. Lid laxity
b. Lash alignment
c. Conjunctivochalasis
d. All of the above

12. Ophthalmic dyes that may useful in dry eye management include:
a. 2% sodium fluorescein
b. 1% lissamine green
c. Rose bengal
d. All of the above

CE TEST

13. Corneal staining—particularly central, macropunctate or confluent—is an indicator of:
a. Mild dry eye disease
b. Moderate dry eye disease
c. Late-stage dry eye disease
d. None of the above

14. These topographical signs often point to dry eye disease:
a. Inferior steepening that looks a bit like keratoconus
b. Irregularly shaped placido discs
c. Differences in average keratometry readings between eyes
d. All of the above

15. When a patient's dry eye is driven by a deficient lipid layer, treatment should include:
a. A lipid-containing artificial tear
b. Therapies that encourage meibomian gland expression
c. Allergy medications
d. A and B

16. A positive MMP-9 reading indicates that:
a. The sample contains more than 30ng/ml, which indicates inflammation.
b. The sample contains more than 40ng/ml, which indicates inflammation.
c. The patient definitely has dry eye.
d. The patient does not have dry eye.

17. Sjögren's syndrome is associated with a _____ increased risk of development of lymphoma.
a. 2-fold
b. 6-fold
c. 10-fold
d. 16-fold

18. Research has shown that when artificial tears alone were used for one year, patients experienced a _____ increase in T-cells, which is equivalent to no treatment at all.
a. 40%
b. 50%
c. 60%
d. 70%

19. The lacrimal functional unit consists of:
a. Lacrimal glands
b. Conjunctival goblet cells
c. Meibomian glands
d. All of the above

20. In patients with dry eye, _____ is overexpressed.
a. ICAM-1
b. ICAM-2
c. ICAM-3
d. CAM-4

Examination Answer Sheet

Valid for credit through December 31, 2017

This exam can be taken online at: https://www.reviewofoptometry.com/ce/advancing-our-knowledge-of-dry Upon passing the exam, you can view your results immediately and download a real-time CE certificate. You can also view your test history at any time from the website.

Advancing Our Knowledge of Dry Eye Disease

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

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1 = Excellent 2 = Very Good 3 = Good 4 = Fair 5 = Poor

Rate the effectiveness of how well the activity:

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22. Related to your practice needs: ① ② ③ ④ ⑤
23. Will help you improve patient care: ① ② ③ ④ ⑤
24. Avoided commercial bias/influence: ① ② ③ ④ ⑤
25. How would you rate the overall quality of the material presented? ① ② ③ ④ ⑤
26. Your knowledge of the subject was increased:
◯ Greatly ◯ Somewhat ◯ Little
27. The difficulty of the course was:
◯ Complex ◯ Appropriate ◯ Basic

How long did it take to complete this course? _____

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Last 4 digits of your SS # and date of birth

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State Code and License #: (Example: NY12345678)

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First Name

Last Name

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The following is your: ☐ Home Address ☐ Business Address

Business Name

Address

City State

ZIP

Telephone # ___ - ___ - ____

Fax # ___ - ___ - ____

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

Signature _____ Date _____

Lesson #113881 RO-UAB-0117

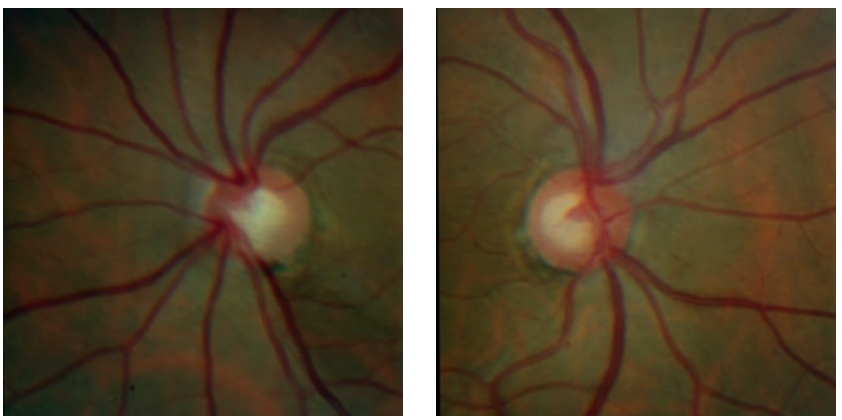
Could This Be Glaucoma?

This patient population is bigger than you think, and knowing when to screen will help you catch even the lesser-known etiologies. **By Rim Makhlouf, OD**

Glaucoma is the second leading cause of blindness worldwide, affecting more than 70 million people.[1] In the United States, open-angle glaucoma (OAG) affects roughly 2.2 million people, with an estimated increase of 22% per decade.[2]

OAG is characterized as primary (POAG) when no cause is identified and secondary otherwise. Most clinicians are on the lookout for the clinical presentations common for POAG, such as optic nerve head (ONH) and retinal nerve fiber layer (RNFL) changes, usually associated with visual field (VF) defects and an open angle on gonioscopy.[3] Numerous risk factors associated with POAG also clue clinicians in on a suspected diagnosis, including higher intraocular pressure (IOP), older age, family history, thinner central cornea, lower ocular perfusion pressure, Type 2 diabetes mellitus, myopia, lower systolic and diastolic blood pressure, disc hemorrhage, larger cup-to-disc ratio and higher pattern standard deviation on threshold VF testing.[3]

Race and ethnicity are important risk factors, as African Americans have a three-fold higher prevalence of OAG relative to Caucasians, and are six times more likely to be blinded by the disease.[4-6] The prevalence may be even higher in Afro-Caribbeans.[5,6] Moreover, recent studies suggest Asian Americans may have higher rates of OAG comparable with Hispanics, and the latter may have rates comparable with African Americans.[7,8]



These ONH images show an inferior temporal NFL defect with a corresponding rim notch in the left eye in a patient with a glaucomatous optic nerve.

Although prompt detection is crucial to preserving vision, diagnosis isn't always cut-and-dry, as both POAG and secondary OAG can present with less common forms. Knowing the clinical presentation of these various glaucomas is key to catching unusual suspects early. This article discusses many of the uncommon presentations of glaucoma, as well as the steps necessary to screen patients properly.

Uncommon POAG

Normal tension glaucoma (NTG) is a form of POAG in which IOP is consistently less than 21mm Hg. Although the pathogenesis is poorly understood, research suggests a number of causative factors independent of IOP, including systemic

and local vascular dysregulation, hematological abnormalities and structural alterations due to neurovascular dysfunction.[9] Researchers believe these factors result in increased sensitivity to a physiologically normal IOP, leading to ONH damage. Systemic conditions that result in ischemic vascular disease, such as diabetes, increase the risk of developing NTG.[10] Other contributing factors may include vasospastic events, hypoperfusion, nocturnal hypotension, hypercoagulability and increased blood viscosity and genetics.[11] Investigators also found NTG is associated with migraines, especially those with visual auras, and sleep apnea.[12]

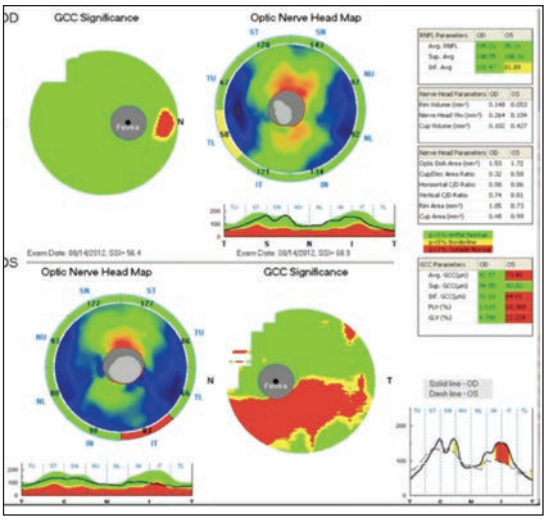
NTG is essentially a diagnosis of exclusion after other forms of optic neuropathy have been ruled out. A thorough history helps uncover previous episodes of increased IOP that might explain the optic nerve damage, including inflammation, ocular trauma or past use of systemic, topical, inhaled or nasal steroids.

Signs of NTG differ only slightly from POAG. For one, VF defects appear to be more focal and closer to fixation early in the disease. Ophthalmoscopically, there is a tendency for more localized RNFL defects, and for the presence of disc hemorrhages and peripapillary atrophy (PPA) often associated with the location of the worst cupping. Lastly, central corneal thickness (CCT) tends to be lower in NTG compared with POAG.[13]

Juvenile open-angle glaucoma (JOAG), a subset of POAG that affects patients between the ages of five and 35, is a rare and usually bilateral condition that affects about one in 50,000 individuals.[14] JOAG is an inherited—autosomal dominant—disease in which gene mutations of the trabecular meshwork (TM) proteins lead to increased aqueous outflow resistance. JOAG patients have a male preponderance, a myopic refractive state and frequently present with headaches, in which case neuroimaging is warranted to exclude other potential etiologies.[15,16] Secondary glaucomas should also be excluded.

Secondary Glaucomas

Secondary OAG is a heterogeneous group that includes a wide range of causes and manifestations. Many may initially present as syndromes requiring regular screening to monitor their conversion into glaucoma. When confronted with a suspected case of OAG, the differential diagnosis is important, as management may differ.

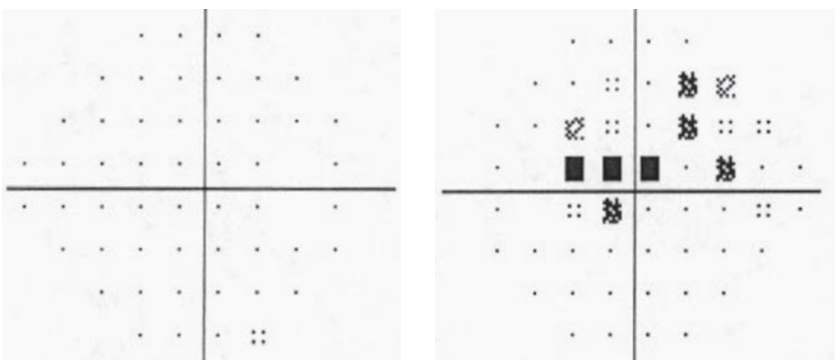


The same patient's OCT is normal in the right eye, but shows an abnormal inferior temporal RNFL thickness as well as an abnormal inferior GCC thickness in the left eye.

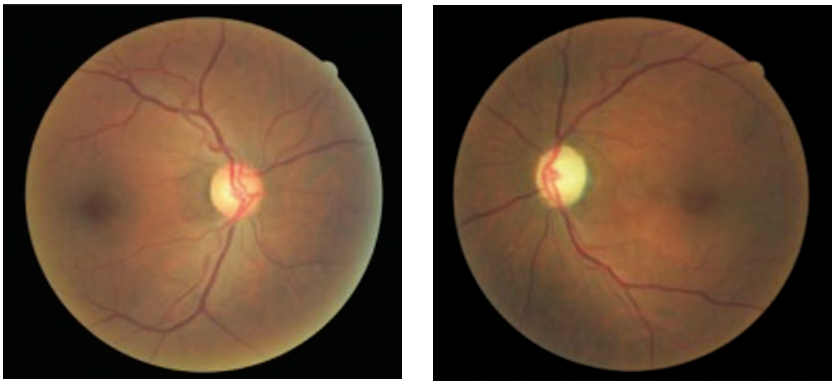
Pseudoexfoliative glaucoma's hallmark is the presence of a fine, flaky material on the anterior lens capsule that coalesces into a characteristic bulls-eye or three-ring sign pattern. Peripupillary transillumination defects occur due to the material rubbing on the iris, with deposition of pigment granules on the corneal endothelium, iris surface and TM similar to pigment dispersion syndrome. Gonioscopy may reveal increased patchy TM pigmentation, usually most marked inferiorly, as well as the presence of clear, flaky material.

Because it is the result of a systemic disease, it is a bilateral condition but often presents unilaterally due to significant asymmetry. ON damage and VF loss may occur more rapidly compared with POAG.

Pigmentary glaucoma is typically a bilateral condition occurring when increased IOP is due to iris pigment dispersion and accumulation at the



The patient's visual field is normal in the right eye but shows a superior paracentral defect with the beginning of a superior nasal step in the left eye.



This patient presented with asymmetrical cup-to-disc ratios, as well as ON pallor in the left eye. VFs revealed a bitemporal hemaniopsia, and MRI confirmed the presence of a large pituitary tumor.

TM. Pigment dispersion syndrome primarily affects young, Caucasian males and patients with myopia. These patients tend to have a more concave approach of the iris, resulting in the pigment epithelium rubbing against the zonular fibers of the lens, which releases iris pigment.

Patients are typically asymptomatic, but episodic rises in IOP secondary to exercise may cause symptoms of colored haloes around lights, blurred vision or subtle ocular pain. Slit lamp examination may reveal a granular brown vertical band along the corneal endothelium known as a Krukenberg's spindle, pigment deposition on the lens, and spoke-like transillumination defects of the mid-peripheral iris. A dense homogeneous pigmentation of the TM and possibly Schwalbe's line, leading to a Sampaolesi's line, is typically seen on gonioscopy.

Traumatic glaucoma results from severe TM dysfunction due to blunt trauma. Clinicians should always suspect traumatic glaucoma and obtain a thorough history whenever they diagnose unilateral glaucoma. Gonioscopy commonly reveals a widening of the ciliary band due to angle recession. Other signs may include irregular and darker pigmentation in the angle, peripheral anterior synechiae or whitening of the scleral spur due to fractured iris processes.

Neovascular glaucoma can be an open-angle process in its early stages due to the presence of fine vessels on the TM, leading to its obstruction and decreased aqueous outflow. Angle neovascularization usually occurs due to retinal ischemia, with diabetes and central retinal vein occlusion accounting for most cases.[17] Ocular ischemic syndrome should be ruled out when neither of these conditions exist. Due to the pathogenesis of the disease, gonioscopy is crucial in its diagnosis.

Uveitic glaucoma, in its open-angle form, usually occurs when chronic—and sometimes acute—intraocular inflammation causes increased IOP from obstruction of the outflow pathways despite an open anterior chamber angle. Mechanical obstruction by inflammatory cells or dysfunction of the TM is common. In chronic cases, permanent scarring and obliteration of TM beams or Schlemm's canal may occur. Development of a fibrovascular membrane may also occur due to the release of cytokines.

Biomicroscopic exam reveals cell and flare in the anterior chamber, and gonioscopy may reveal neovascularization of the angle and peripheral anterior synechiae leading to secondary angle-closure glaucoma.

The Work-Up

With all glaucoma suspects, an extensive history and additional testing are a must. Relevant ocular history includes refractive error, trauma and prior ocular surgery. A history of refractive surgery is associated with a falsely low IOP measurement due to corneal thinning, and cataract surgery may also lower IOP compared with the pre-surgical measurement.[18-22] Systemically, clinicians should ask about migraine, vasospasm, diabetes and cardiovascular disease due to their association with POAG in some studies.[3] Current medications should be thoroughly reviewed, paying special attention to corticosteroid intake. Race and ethnicity is particularly important, as is the severity and outcome of glaucoma in family members.

In addition to common testing during a comprehensive eye exam, clinicians should obtain gonioscopy, CCT measurement and VF assessment, as well as ONH and RNFL evaluation. Since glaucoma is initially an optic neuropathy that affects the peripheral vision in most cases, VA is usually unaffected until the late stages, although it may be affected in early stages, especially in NTG. A relative afferent pupillary defect in the worse affected eye is expected whenever the disease is unilateral or asymmetric.

Anterior segment evaluation, along with gonioscopy, is essential in the differential diagnosis. Both tests are essential to rule out an angle-closure mechanism, which would require a completely different management. Signs include narrow angles, shallow anterior chamber and peripheral anterior synechiae. Anterior segment evaluation and

gonioscopy can also reveal evidence of secondary open-angle mechanisms such as pseudoexfoliation, pigment dispersion, iris and angle neovascularization, angle recession and inflammation.

Fundus examination through a dilated pupil is essential to rule out other abnormalities that may account for optic nerve changes, VF defects or both.[3] Additionally, stereoscopic ONH evaluation is paramount in glaucoma diagnosis. Glaucomatous optic nerve changes include vertical elongation of the optic cup, thinning of the inferior or superior neuroretinal rim, excavation of the cup, thinning of the RNFL, notching of the neuroretinal rim and absence of pallor of the neuroretinal rim.[3] The ISNT rule indicates that normal nerves show a larger rim width **I**nferior, **S**uperior, **N**asal and **T**emporal. Glaucomatous optic neuropathy should be suspected when the ISNT rule is not followed, as is the case in 80% of patients with glaucoma.[23,24] Other features indicating glaucomatous changes include disc hemorrhages, PPA, nasalization of central vessels and baring of circumlinear vessels.[3]

The presence of disc hemorrhages does not necessarily confirm a diagnosis of glaucoma, but may be indicative of ongoing focal disc damage and possible progression.[25,26] They are observed more frequently in NTG than POAG, and their presence warrants a thorough investigation for glaucoma and clinicians should consider initiating an IOP-lowering therapy.[27]

PPA—a clinical finding associated with chorioretinal thinning and disruption of the RPE in the area surrounding the disc—is strongly associated with glaucoma and tends to be larger in NTG.[28] The presence and extent of PPA, especially the beta zone, has been found to have a strong association with both VF and optic nerve progression.[29,30]

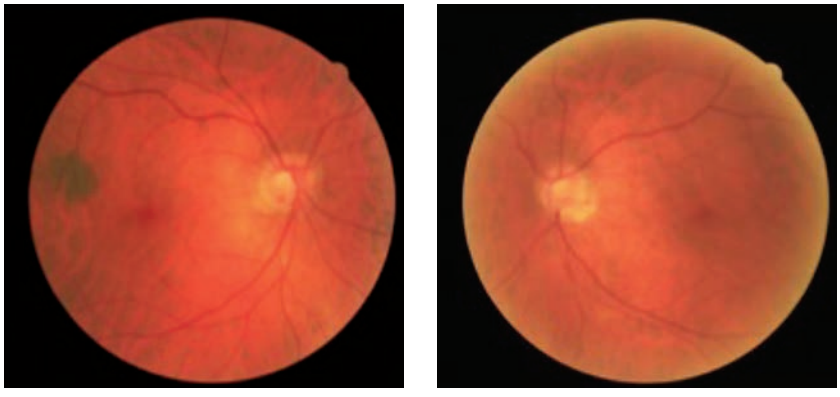
Research shows structural changes may occur before any evidence of functional change is detected with automated perimetry.[31,32] Assessment of structural parameters is therefore important in glaucoma detection, especially when potentially dealing with pre-perimetric glaucoma. In fact, a significant amount of RNFL loss is thought to be required before any visual field defect is detected; thus, quantitative imaging of the RNFL is routinely used as a complement to ophthalmoscopic ONH and RNFL evaluation.[3,33]

Optical coherence tomography (OCT) can help assess the RNFL thickness at the level of the optic nerve and, more recently, the ganglion cell complex (GCC) thickness at the level of the macula. Both structural assessments provide a statistical analysis that compares the measured thickness to a normative database, as well as a trend analysis over time. However, results from these tests should be interpreted cautiously and within the context of clinical examination, as anatomical RNFL variability may lead to a false positive result compared with the normative database.[3,33]

Even though GCC distribution tends to be uniform among individuals, concurrent macular conditions may affect the analysis, leading to falsely normal or abnormal results, depending on the condition and software. Additionally, some patients may show VF loss without the presence of corresponding ONH damage, and the sensitivity of functional and structural tests in detecting glaucoma progression may vary depending on the stage of the disease.[34-36]

Central corneal thickness. Average CCT varies among different races and ethnicities ranging from 534µm to 556µm.[3] The World Glaucoma Association cautions against adjusting the IOP, as CCT has been reported to be a risk factor independent of IOP whereby patients with thinner corneas tend to have a higher risk of OAG.[37,38] Research suggests that differences in corneal biomechanics may be linked to structural differences of the ocular tissues such as the lamina cribrosa, therefore increasing the susceptibility to glaucomatous optic nerve damage under the same IOP in patients with thinner corneas.[39]

Visual fields. The gold standard for glaucoma detection and management is automated static threshold perimetry with white-on-white stimulus. Characteristic glaucomatous VF defects are consistent with RNFL damage and include nasal step,



This patient has tilted discs and POAG OU. Note the inferior temporal disc hemorrhage in the right eye.

arcuate field defect and paracentral depression. General depression may occur, especially in the advanced stages. However, these defects also may be caused by retinal and other optic neuropathies, so the differential diagnosis is important when considering a glaucoma suspect case.

Differential Diagnosis

Optic disc damage and VF defects can be caused by a number of non-glaucomatous disorders—from which glaucomatous damage should be differentiated—such as:

Tilted disc syndrome (TDS) is a congenital anomaly characterized by inferonasal tilting of the optic disc due to incomplete closure of the embryonic fissure. Bitemporal superior VF defects are present in about 20% of patients with TDS and may easily be confused with a chiasmal lesion.[40] More rarely, TDS may cause altitudinal or arcuate defects that may be confused with glaucomatous changes.[41] The differential diagnosis resides in the fact that TDS is generally non-progressive, and VF defects generally do not respect the horizontal midline.[42,43]

Compressive optic neuropathy refers to optic nerve damage due to compression by an extrinsic lesion leading to progressive vision loss. Signs that should prompt neuroimaging, especially when facing a potential diagnosis of NTG, include marked asymmetry or unilateral involvement, unexplained vision loss or vision worse than 20/40, VF defects not corresponding to optic nerve head damage, vertically aligned VF defects, presence of other neurological signs, optic nerve pallor in excess of cupping and age younger than 50.[44]

When faced with a diagnostic dilemma, keep in mind the characteristic features of glaucoma, the differential diagnosis and the clinical presentation of these less common types of glaucoma. ■

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Arm Yourself for Dry AMD

It's imperative we prepare ourselves with up-to-date information for better care of our patients. **By Andrew J. Rixon, OD, Richard C. Trevino, OD, and Roya Attar, OD**

Age-related macular degeneration (AMD) is the leading cause of vision loss in individuals 65 and older.[1] By the year 2020, it will affect an estimated 196 million people worldwide.[1] Vision loss from AMD can be functionally and emotionally debilitating, as it can make it difficult, or even impossible, to read, drive, enjoy certain hobbies and maintain an independent lifestyle.[2]

Approximately 90% of those with AMD have the dry form, for which there is currently no treatment—only lifestyle modifications to reduce risk of progression. Roughly 10% of those with AMD develop choroidal neovascular membranes (CNV), yet it accounts for 75% of severe vision loss in those with AMD.[3]

The capacity for proper detection, education and management of AMD is essential for optometrists, and staying current on the ever-changing body of information surrounding the disease allows for best patient outcomes. This article reviews the pathophysiology of dry AMD, risk factors, diagnostics and patient follow up to ensure clinicians are ready when patients present with suspicious findings. While there is no treatment as of yet, review of current clinical trials suggests one might await us in the future.

Pathophysiology

Retinal health is contingent on the relationship between photoreceptors and the retinal pigment epithelium (RPE).[4] The RPE functions as a protector against photo-oxidative damage to the retina and transports nutrients between the choriocapillaris and retina.[4] To avoid photo-oxidative damage, photoreceptors undergo a daily renewal process where roughly 10% of their volume is shed, then phagocytosed by the RPE.[4]

Foundationally, the accumulation of photo-oxidized debris within and under the RPE is considered the initiating cause of AMD.[5] The debris found within the RPE cells includes a yellow-brownish pigment granule called lipofuscin—a lipid-containing residue from lysosomal digestion with autofluorescent properties.[6]

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Goal Statement: Proper AMD detection, education and management is essential, and staying current on information surrounding the disease allows for best patient outcomes. This article reviews the pathophysiology, risk factors, diagnostics and patient follow up to ensure clinicians are ready for these patients.

Faculty/Editorial Board: Andrew Rixon, OD, Richard Trevino, OD, Roya Attar, OD
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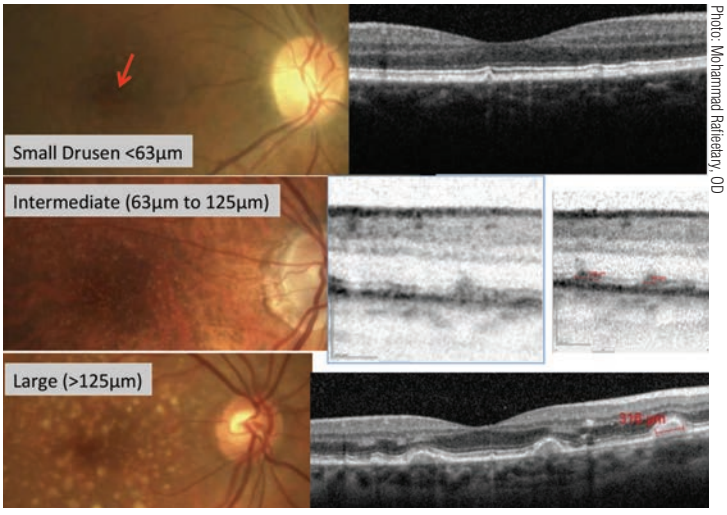

Photo: Mohammad Rafieetary, OD

Fig. 1. Fundus photography with corresponding OCT images of small, intermediate and large drusen.

Drusen, composed of acellular, polymorphous material, is considered the hallmark of early AMD.[7] Hard drusen involve focal thickening of the RPE basement membrane and may become calcified, lipidized, cholesterolized or, rarely, vacscularized.[8] Soft drusen are substantially larger than hard drusen and represent a limited separation of the RPE basement membrane from its attachment to Bruch's membrane.[8]

Drusen size and RPE abnormalities are important risk factors for progression of AMD (*Figure 1*).[9] RPE cells, in response to many negative stimuli, go through morphological changes such as hypertrophy, atrophy and intraretinal migration.[7]

Small drusen (<63µm) are consistent with the normal aging process and have no relevant increased risk of late AMD developing.[10] In fact, small drusen (<31.5µm) are common in persons younger than 50, with reported incidence as high as 95.5%.[3,11,12]

Medium drusen (63µm to 125µm) have not been studied extensively, but a recent study found that patients with large total macular areas involving medium drusen, and closer proximity of these to the fovea, were more likely to progress to early AMD.[13] Medium drusen confers an increased risk of progression to late AMD, although this risk is not great.[10,13] However, the presence of both medium drusen and RPE abnormalities (within two disc diameters of the fovea) increases the risk of progression to late AMD by between four and ten-fold compared with the presence of medium drusen alone.[10,13]

Large drusen (>125µm) are associated with a much higher risk for developing advanced AMD, with an estimated five-year rate of developing late AMD of 13% when found bilaterally without other abnormalities.[10,9] That five-year risk of progression increases to 47.3% when there is the bilateral presence of both large soft drusen and pigmentary abnormalities (*Figure 2*).[10]

The width of a major branch retinal vein as it crosses the optic disc margin is approximately 125µm and is a good reference to estimate the size of retinal drusen.[10]

The natural history of drusen is dynamic, and multiple studies confirm that both resorption of drusen and the formation of new drusen can occur simultaneously in the same macula.[9,14] Recent preliminary SD-OCT studies show a tendency for drusen to increase in volume and area over time, although regression can also occur (*Figures 3a and 3b*).[9,15] In the observation group of one study, the proportion of eyes showing a reduction of ≥50% in the area of drusen within 3,000µm of the foveal center increased over time from 1.2% at six months to 31.2% at five years.[16]

Although regression of drusen volume may seem to be a positive outcome, this usually progresses to outer retinal atrophy and loss of underlying choroidal thickness.[17] Investigators found that larger drusen volume is more likely to spontaneously regress, followed by possible progression to geographic atrophy (GA) or CNV.[9] Additional studies show that increased drusen volume with spontaneous regression is a negative prognostic indicator for advancement of the disease.[18,19]

Reticular pseudodrusen (RPD) has recently been recognized as another expression of AMD. RPD are associated with changes internal to the RPE and are predominantly located outside the fovea. RPD is highly correlated with GA, a known risk factor for advanced AMD.[20] Approximately 30% to 50% of patients with RPD progress to late AMD.[21] In the Beaver Dam eye study, patients with RPD had a six-fold higher rate of progression to late AMD than patients with indistinct soft drusen alone.[22]

Geographic atrophy occurs when the RPE, overlying photoreceptors and underlying choriocapillaris break down in a sharply demarcated area, revealing underlying choroidal vessels.[22-25] Research estimates it accounts for 35% to 40% of late-stage AMD cases.[26] GA develops frequently in macular areas previously occupied by drusen.[24] Once GA develops, the atrophic area typically enlarges slowly and in a non-central location, ultimately involving the

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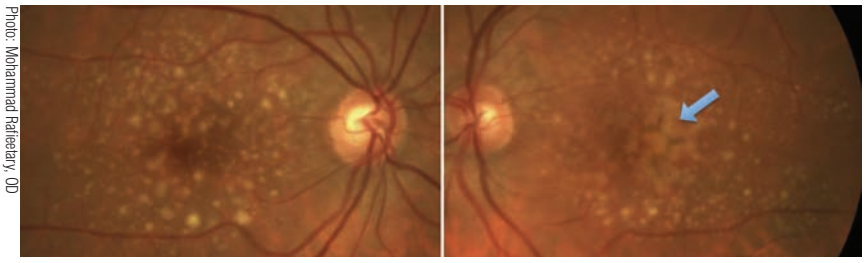

Fig. 2. Both large drusen and pigmentary abnormalities in a patient with a high risk for conversion to advanced AMD.

central macula and resulting in vision loss.[23,27,28]

AMD Risk Factors

Some risk factors for AMD are modifiable, while others are not:

Non-modifiable Risk Factors

Age. The most important risk factor for AMD is age itself. The prevalence of AMD among 60-year-olds is 0.9%.[26,29] At age 70 it rises to 2.8%, and among those older than 80 the prevalence jumps to over 10%.[26,29] Although the reason for this strong association is not clearly understood, both local retinal and broader systemic age-related changes are believed to play a role.

Ethnicity. Research suggests the prevalence of AMD varies widely among racial and ethnic groups. In North America, studies estimate AMD is twice as prevalent among Caucasians compared with African Americans, while late-stage AMD is roughly 10 times more prevalent among Caucasians than African Americans.[29,30]

Genetic factors. Close relatives of people with AMD are at an increased risk for the condition.[31] Studies of twins reveal that the heritability of AMD ranges between 46% and 71%, with severe AMD being more heritable than the mild form of the disease.[32]

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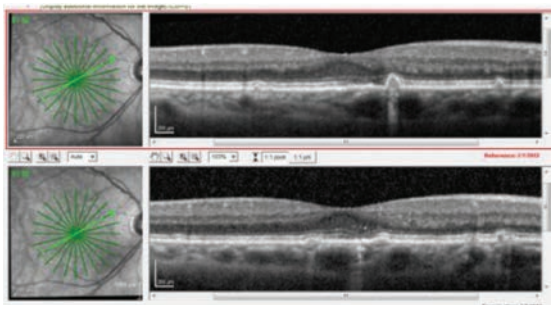

Fig. 3a. Radial OCT slice showing spontaneous regression of large drusen.

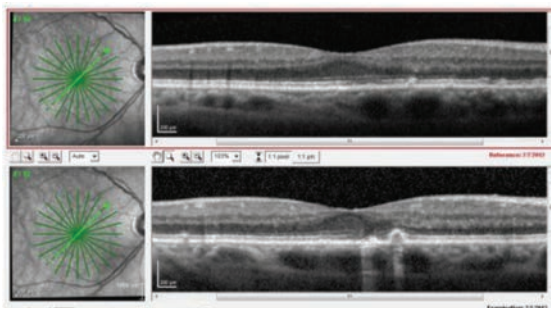

Fig. 3b. Radial slice in same patient, in same time frame, showing increased size and formation of large drusen.

Currently, 52 genes have been identified involved with AMD risk. Two genes in particular seem to convey the greatest risk.[33] One is for a protein in the complement inflammatory pathway known as complement factor H (CFH). The second gene remains elusive, but studies have narrowed it down to either age-related maculopathy susceptibility gene number 2 (ARMS2) or a gene that codes for the protein high temperature requirement factor A1 (HTRA1), which plays a role in angiogenesis.[34]

Both CFH and ARMS2 were associated with higher rates of disease progression in the mostly white participants of the AREDS study, but the effect of these genes may vary with race.[35] For example, it appears ARMS2 has little or no effect on AMD risk in African Americans.[36] The risk associated with these two genes is additive, so a person with both high-risk genes is at greatest risk.[37] Individuals possessing high-risk genes are not only more susceptible to developing AMD, but are also at elevated risk of having the disease progress to legal blindness.

Low macular pigment. This is another important AMD risk factor.[38] Macular pigment is composed of the carotenoids lutein, zeaxanthin and meso-zeaxanthin, which have both blue light filtering and antioxidant properties. Low macular pigment is associated with low dietary intake of foods rich in these compounds such as spinach, kale and eggs. Other factors contributing to low macular pigment include genetics, obesity and smoking.[39]

High macular pigment optical density (MPOD), found using heterochromatic flicker photometry, is believed to protect the retina against photo-oxidative damage caused by blue light.[38] Individuals with low MPOD are at elevated risk of AMD, and may also suffer from decreased visual function owing to the blue light filtering effect of macular pigment.[38]

Modifiable Risk Factors

Tobacco. By far the most important modifiable risk factor for AMD is smoking tobacco products, and it remains the only established causative factor for AMD.[40]

Compared with someone who has never smoked, current smokers have two to three times greater risk of developing the disease.[41] In addition, smokers develop AMD at a younger age than nonsmokers and have a higher risk of disease progression.[42]

Smoking cessation results in a risk reduction that increases with duration of abstinence from tobacco. Several long-term, population-based studies found that former smokers are at only slightly higher risk than individuals who have never smoked.[40]

Lifestyle. In addition to smoking cessation, a number of other lifestyle changes can decrease AMD risk, including maintaining an average body weight, getting regular exercise and eating a heart-healthy diet.[43] In fact, a combination of healthy lifestyle practices might be more important in reducing AMD risk than a focus on any given one. A healthy lifestyle can reduce oxidative stress and inflammation throughout the body, both of which are thought to promote AMD.

Increased exposure to sunlight. This has been identified as a potential AMD risk factor, and it appears to be greatest in those with light hair and eye color.[44,45] Known as the *blue light hazard*, short wavelength, high energy, visible blue light triggers the release of harmful free radicals in the retina that cause oxidative stress, possibly contributing to the development of AMD.[46] Measures that protect the eyes from sunlight, including broad-brimmed hats and blue light filtering sunglasses, can mitigate this risk.[47] The yellowing of the crystalline lens with age will naturally decrease the amount of blue light that reaches the retina as a patient ages. However, cataract surgery can eliminate this protective effect, thereby increasing AMD risk.[41] Many intraocular lens implants now contain blue light filtering properties. The AREDS study found no association between cataract surgery and subsequent progression of AMD.[48]

Associated Findings

Dark adaptation. In addition to a variety of visual changes, self-reported complaints of difficulty under dim lighting or at night are common in patients with AMD.[49] Consistent with this complaint, delayed rod-mediated dark adaptation is characteristic of early AMD, which can also be observed in some older adults with normal macular health, whereas cone-mediated dark adaptation in the same retinal area is undisturbed.[50]

In early AMD, photoreceptor degeneration is associated with decreased light sensitivity in the macula and slowed dark adaptation, despite relatively unimpaired visual acuity.[51] Research suggests this is likely due to changes within the RPE/Bruch's membrane complex, where drusen are formed.[49,51] Drusen accumulate in the aging Bruch's membrane and in the sub-RPE space in

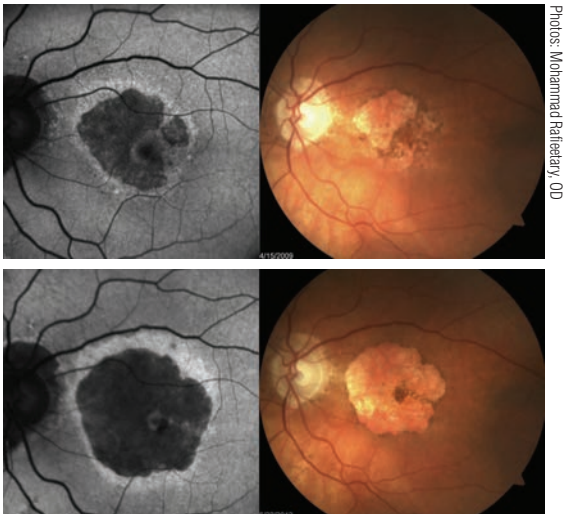

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Fig. 4. Comparison of fundus photography and FAF in GA progression over time. The top FAF and fundus photo are from 2009, the bottom are from 2012.

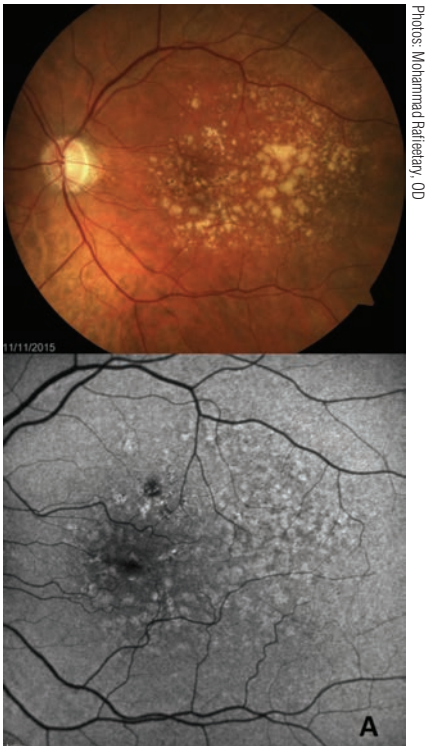

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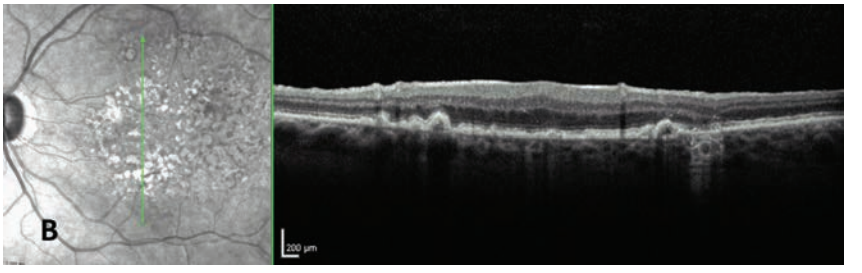
Fig. 5a. FAF more easily highlights early GA formation that is less detectable in fundus examination.
Fig. 5b. GA confirmed with OCT showing increased transmission through to the choroid in region of GA.



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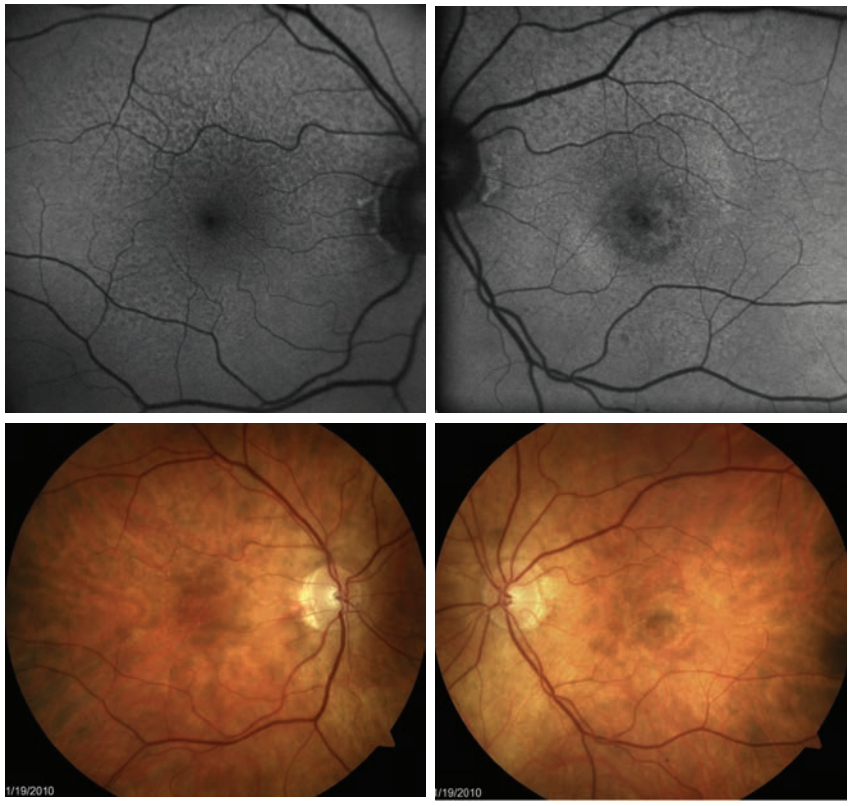


Fig. 6. FAF shows greater extent of RPE abnormality with extrafoveal RPD than is easily seen with fundus photography. This patient also has presence of central CNV OS.

early AMD, disrupting the retinoid cycle and leading to photoreceptor degeneration, with an earlier onset and more severity affecting macular region rods than the cones.[50,52] Other potential factors contributing to the scotopic dysfunction in early AMD include genetic alterations in vitamin A metabolism and age- and disease-related deficits in pathways within the RPE metabolism that remain uncharacterized. Regardless of the exact mechanisms underlying the slowed rod-mediated dark adaptation, a scotopic functional impairment is present in the earliest phases of AMD.[50]

One study concluded that delayed rod-mediated dark adaptation in older adults with normal macular health is associated with incident-early AMD three years later, and thus is a functional biomarker for detection of early disease.[53]

Research has also found increasing age, decreasing visual acuity, the presence of reticular pseudodrusen, severity of AMD and decreased subfoveal choroidal thickness are also associated with dark adaptation impairments.[54]

Imaging in Dry AMD

Standard color fundus photography, although historically useful for classifying the stage of AMD, may not adequately detect some common early and intermediate manifestations.[55,56] RPE damage is a hallmark of AMD, and alterations to the RPE may not be clinically detectable by funduscopy or photography. Drusen and subretinal drusenoid deposits become clinically visible at 30µm while changes in RPE cells are substantially smaller.[57] *In vivo* imaging of the autofluorescent properties of the ocular fundus provides the ability to visualize and evaluate the state of the aging RPE in AMD.[58]

Studies show innate autofluorescent properties originate from the accumulation of fluorescent pigments, known as fluorophores, in the RPE cells, primarily as lipofuscin.[58] Fundus autofluorescence (FAF) noninvasively visualizes these fluorophores with a short wavelength excitation light, followed by capture of the fluorescence signals emitted post excitation.[59] Areas of abnormal autofluorescence are then compared with a normal, homogenous autofluorescent background and are described as having increased or decreased autofluorescence.[60] GA, for instance, exhibits dark areas because of a complete lack of fluorophores.[60] FAF thus provides a topographical rendering of the extent of lipofuscin accumulation in the RPE.[8]

Using these renderings, researchers have described and classified distinct patterns of abnormal fundus autofluorescence in early nonexudative AMD—and, most importantly, suggest they are useful in determining the risk of disease progression.[58,59,61] Furthermore, researchers have used FAF to demonstrate not only progression in patients with GA, but also inhibition of progression when therapeutic intervention is successful (*Figure 4*).[59,62,63] A recent study shows that FAF imaging detects GA earlier than with color photography, in part due to precise delineation of GA borders as a result of superior contrast (*Figures 5a and 5b*).[28] However, FAF's advantage over color photography diminishes over time, with the two modalities ultimately becoming comparable in more advanced cases.[64]

FAF is also highly beneficial in imaging RPD. The appearance of these drusen vary based on imaging techniques, and their extent of involvement can be difficult to detect with fundus evaluation alone.[20]

Follow-up Evaluation

A history and examination are the recommended elements of follow-up visits. The follow-up history should take into account symptoms, including decreased vision and metamorphopsia, as well as changes in medications, nutritional supplements, medical, ocular and social history. The examination on the follow-up visit should include visual acuity and stereoscopic biomicroscopic examination of the fundus.[80,81]

Recommended follow-up intervals, assessment and treatment plans for non-neovascular AMD are listed below.[80,8]

Treatment Recommendations and Follow Up for Non-neovascular AMD

Type of Patient	Frequency of Examination	Follow-up Recommendations	
		Management Plan	Testing
Patients with two or more risk factors for AMD, older than age 55	Annual examination if asymptomatic, or prompt examination if new symptoms	• Patient education • Recommend UVR protection, antioxidant supplementation, home Amsler or comparable monocular near vision self-monitoring weekly	• Baseline fundus photos, repeat every two years or as necessary • Stereo fundus biomicroscopy • Amsler grid • Baseline central 10 degrees • Automated visual field, repeat every two years • OCT and/or fluorescein angiography as appropriate
Patients with hard drusen, pigmentary degeneration or both	Six to 12 months, depending on risk factors	• Patient education • Recommend UVR protection, antioxidant supplementation, home Amsler or comparable monocular near vision self-monitoring twice each week	• Fundus photos, repeat every two years or as necessary • Stereo fundus biomicroscopy • Amsler grid • Central 10 degrees • Automated visual field, repeat every two years • OCT and/or fluorescein angiography as appropriate
Patients with geographic atrophy, VA 20/30 to 20/70	Six to 12 months, depending on extent of atrophy	• Patient education • Recommend UVR protection, antioxidant supplementation, home Amsler or comparable monocular near vision self-monitoring every other day • Monitor for CNV	• Fundus photos every year • Stereo fundus biomicroscopy every interim visit • Amsler grid every interim visit • Central 10 degrees • Automated visual field every one to two years • OCT and/or fluorescein angiography as appropriate
Patients at high risk with soft confluent drusen and granular pigmentary degeneration	Four to six months	• Patient education • Recommend UVR protection, antioxidant supplementation, home Amsler or comparable monocular near vision self-monitoring daily • Low vision consultation and evaluation	• Annual fundus photos • Stereo fundus biomicroscopy every interim visit • Amsler grid every interim visit • Annual central 10 degrees • Automated visual field, • Consider central 30° AVF depending on central fixation • OCT and/or fluorescein angiography as appropriate
Patients with geographic atrophy in both eyes	Six to 12 months	• Patient education • Low vision consultation and evaluation	• Annual fundus photos • Stereo fundus biomicroscopy every interim visit • Annual central 10 degrees • Automated visual field

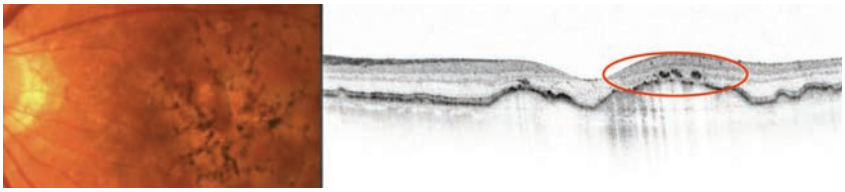
These lesions tend to show well on FAF and infrared reflectance imaging (*Figure 6*).[20]

OCT has become increasingly valuable in AMD assessment, as it provides noninvasive, high-resolution, cross-sectional imaging of both the neurosensory and deeper subretinal layers.[66] SD-OCT has proven useful for evaluating drusen of all sizes, drusenoid PEDs, changes to neurosensory retina overlying drusen, reticular pseudodrusen, retinal pigment abnormalities, GA and age-related choroidal atrophy.[7]

Specifically, small to medium drusen will exhibit variable reflectivity depending on the composition of the underlying material. Large drusen or drusenoid PEDs will often show a dome-shaped elevation of the RPE with a hypo- or medium-reflective material separating the RPE from the underlying Bruch's membrane.[7] Pigment clumping and migration will appear focally hyper-reflective with underlying shadowing (*Figure 7*). Focal loss of RPE will show hyporeflectivity in the RPE and hyper-reflectivity of the underlying choroidal vessels.[7] Lastly, GA appears as areas of sharply demarcated choroidal hyper-reflectivity. There may be associated retinal atrophy manifesting with thinning or loss of the outer nuclear layer and the absence of the external limiting membrane and inner segment-outer segment junctions (*Figure 8*).[7]

Current Clinical Trials

Currently, medical treatment options for AMD are limited to only patients whose disease leads to the development of CNV. With anti-vascular endothelial growth factor (VEGF) treatment for these particular patients, the visual prognosis for exudative AMD has improved drastically, but investigators are still evaluating multiple targets and different



Photos: Mohammad Rafieetary, OD

Fig. 7. Pigmentary migration imaged with OCT shows increased hyper-reflectivity (darker with reverse contrast scan) and causes shadowing of underlying RPE layer.

delivery systems to further improve treatment for those with CNV from AMD. Additionally, researchers are making significant progress in helping dry AMD patients who suffer vision loss from GA.

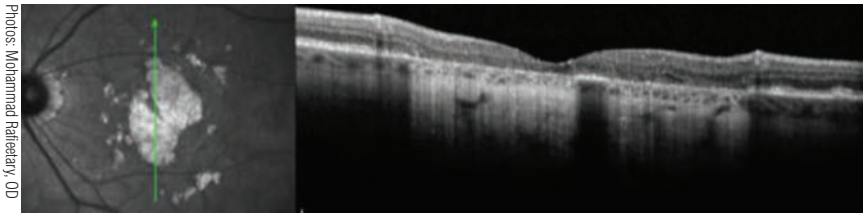
One goal for future AMD treatment is improving treatment efficacy by targeting multiple steps simultaneously in the pathogenesis of CNV development. Two drug targets researchers are currently considering are angiopoietin 2 and platelet-derived growth factor (PDGF), as both play key roles in the formation of new blood vessels.[66] Investigators are also evaluating the molecule RG7716 in phase II clinical trials of the AVENUE study.[67] It is an anti-VEGF molecule, but also exhibits anti-angiopoietin 2 properties.[68] Fovista (Ophthotech) is an anti-PDGF molecule that has completed phase II trials, and preliminary results show increased efficacy when used in conjunction with ranibizumab compared with ranibizumab alone.[69,70] It is currently in phase III clinical trials.[71,72]

Another emphasis in AMD therapy is relieving patient's burden of treatment. Although current anti-VEGF therapy provides extreme improvement in visual outcomes for those with wet AMD, many patients maintain visual stability only with periodic injections, often monthly, for an indefinite length of time. The ongoing LADDER study is evaluating the feasibility of a port delivery system to give sustained release of medication in those with wet AMD.[73] Additionally, the phase III clinical trial HAWK is evaluating the efficacy of an anti-VEGF agent, RTH258, that could decrease the time between retreatment in patients with CNV.[74]

RTH258 is currently the smallest VEGF inhibitor used in human therapy. Due to its small molecular size, it can be given in higher concentrations, hopefully leading to longer duration of action. In initial phase II studies, researchers show it is non-inferior to ranibizumab one-month post treatment and had longer effect of treatment than ranibizumab.[75]

The most promising treatment options on the horizon for GA are complement inhibitors, which aim to decrease the rate of progression of GA. Phase II clinical trials with intravitreal dosing show lampalizumab, a complement factor D inhibitor, is a safe treatment option for GA and has potential efficacy in reduction of GA progression at 18 months.[76] Currently there are two ongoing identical phase III trials, CHROMA and SPECTRI, to determine lampalizumab's efficacy.[77,78]

While lampalizumab is a promising treatment option, other complement inhibitors have failed to show efficacy. For example, eculizumab, a factor C5 inhibitor, failed to show efficacy in reduction of GA progression in phase III clinical trials.[79]



Photos: Mohammad Rafieetary, OD

Fig. 8. OCT image of GA shows increased light transmission to the choroid due to absence of RPE. The outer retinal layers are also lost in the regions of GA.

With rising incidence of AMD in the aging US population, optometrists will have to assess and manage more patients afflicted with this potentially debilitating condition. We must stay abreast of current and upcoming means to diagnose and manage AMD. For example, technological advances in ocular imaging are allowing for quicker detection of small drusen and RPE abnormalities, earlier detection of GA, and improved visualization of retinal structure that was previously unobservable with funduscopy alone.

Additionally, we are often faced with family members seeking answers to their questions and concerns, and we owe it to them to address their trepidations with accurate information on current and future treatment options. We can only serve the best interest of our patients by arming ourselves with the knowledge and skill necessary to manage dry AMD in this ever-evolving landscape. ■

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OSC QUIZ

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1. Which of the following is considered the hallmark of early AMD?
a. Choriodal neovascular membrane.
b. Reticular pseudodrusen.
c. Drusen.
d. Geographic atrophy.

2. What are the dimensions of a large drusen?
a. <30µm.
b. ≥30µm to 63µm.
c. ≥63µm to 125µm.
d. >125µm.

3. What are two important risk factors for progression to advanced AMD?
a. Drusen size and pigment abnormalities.
b. Drusen size and age.
c. Drusen size and dietary intake of carotenoids.
d. Drusen size and hypercholesterolemia.

4. Which statement is true regarding OCT imaging in AMD?
a. Pigment clumping and migration appears focally hypo-reflective on OCT.
b. Choroidal changes in AMD cannot be imaged with OCT.
c. Formation of GA can lead to atrophy of the outer retina, which can be visualized with OCT.
d. OCT can only image large drusen.

5. The five-year risk of developing late AMD is greatest with the presence of:
a. Bilateral large drusen.
b. Bilateral presence of both large drusen and pigment abnormalities.
c. Bilateral pigment abnormalities.
d. Bilateral medium drusen.

6. Which statement regarding the natural history of drusen is true?
a. Drusen are not dynamic.
b. Both resorption and development of drusen can occur simultaneously in the same eye.
c. Spontaneous regression of drusen decreases the likelihood of progression to GA or CNV.
d. Those with lower total drusen volume are more likely to have drusen regression.

7. Fundus autofluorescence imaging noninvasively visualizes which of the following?
a. Cholesterol plaques.
b. Edema secondary to CNV.
c. Fluorophores.
d. Intact choroidal vasculature.

8. Which is true regarding current treatment of dry AMD?
a. There are already FDA-approved injectable medications to treat dry AMD.
b. GA has been shown to stabilize with injection of anti-VEGF molecules.
c. Current treatment of dry AMD is limited to lifestyle modifications and vitamin supplementation.
d. There is currently minimal research being done to improve management of dry AMD.

9. What drug class has a potential medication that is currently in phase III clinical trials and has shown potential for reduction of GA progression in phase II trials?
a. Anti-VEGF agents.
b. Anti-angiopoietin 2 agents.
c. Anti-PDFG agents.
d. Complement inhibitors.

10. Which is not a goal for improving treatment of exudative or wet AMD?
a. Allowing for more frequent injections of anti-VEGF agents.
b. Targeting multiple steps in the development of CNV.
c. Developing sustained-release delivery systems.
d. Developing novel anti-VEGF agents that have longer duration of action.

11. Which individual would be at greatest risk of developing AMD?
a. 85-year-old Caucasian non-smoker.
b. 95-year-old Caucasian smoker.
c. 85-year-old African American non-smoker.
d. 95-year-old African American smoker.

12.Which of the following lifestyle changes can decrease AMD risk?
a. Spending more time outdoors.
b. Getting regular exercise.
c. Moderate alcohol consumption.
d. Increased consumption of red meat.

13. Which factor has an established causative relationship with AMD?
a. Cataract surgery.
b. Smoking tobacco products.
c. Egg consumption.
d. Second-hand smoke.

14. Which of the below measures would be least effective at decreasing AMD risk?
a. Smoking cessation.
b. Cataract surgery.
c. Wearing sunglasses outdoors.
d. Lutein supplementation.

15 Factors contributing to low macular

OSC QUIZ

pigment include all of the following except:
a. Genetics.
b. Smoking.
c. Low dietary intake of lutein and zeaxanthin.
d. Sun exposure.

16. Which of the following are macular pigments?
a. Zeaxanthin and canthaxanthin.
b. Porphyrin and nasturtium.
c. Lutein and zeaxanthin.
d. Melanin and rhodopsin.

17. The exam frequency for a high-risk AMD patient with soft confluent drusen and granular pigmentary degeneration should be:
a. Every three months.
b. Annually.
c. Four to six months.
d. Every two years.

18. Which of the following is not a potential factor contributing to the scotopic dysfunction in early AMD?
a. Development of intraretinal pigmentary deposits.
b. Genetic alterations in vitamin A metabolism.
c. Age- and disease-related deficits in pathways within the RPE metabolism.
d. A disruption in the retinoid cycle.

19. Which two genes are associated with high risk of AMD development?
a. CYP1B1 and ARMS2.
b. ARMS2 and CFH.
c. PAX6 and CYP1B1.
d. CFH and PAX6.

20. The recommended management plan for a patient with two or more risk factors for AMD and over the age of 55 include all of the following except:
a. Antioxidant supplementation.
b. Home Amsler or comparable monocular near vision self-monitoring weekly.
c. UVR protection.
d. Low vision consultation and evaluation.

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18.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
19.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
20.	Ⓐ	Ⓑ	Ⓒ	Ⓓ

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24. Avoided commercial bias/influence: ① ② ③ ④ ⑤
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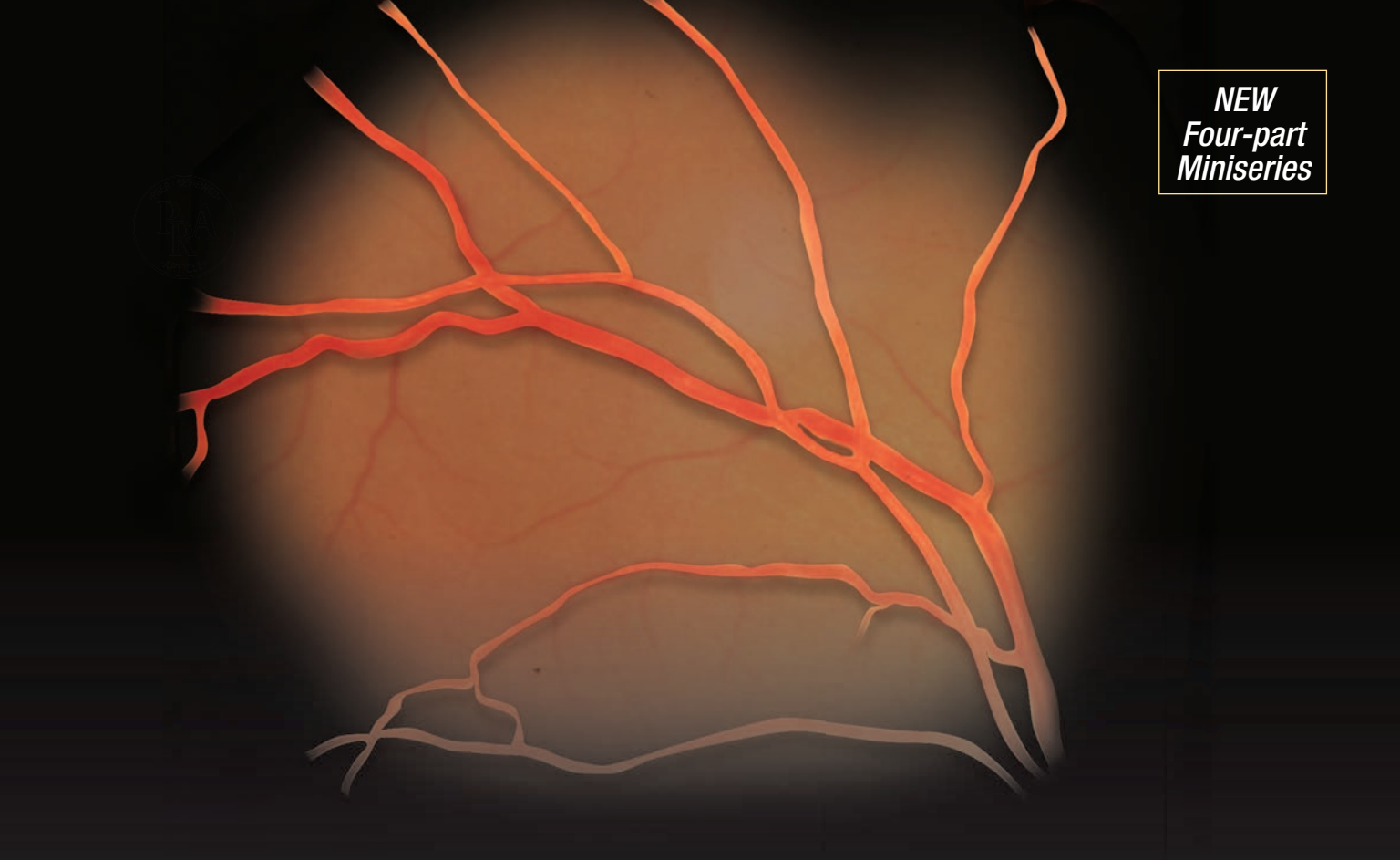


NEW Four-part Miniseries

The Retinal Vasculature: A Marker for Ocular, Neurologic and Systemic Disease

The retina is a unique and fascinating anatomical structure. It's the only part of the central nervous system we can observe noninvasively, along with its associated retinal, systemic and cerebrovascular pathologies. Viewed through direct ophthalmoscopy, indirect ophthalmoscopy, indirect biomicroscopic ophthalmoscopy, ocular photography, fundus autofluorescence, optical coherence tomography (OCT), fluorescein angiography or OCT angiography, qualitative and quantitative retinal observations can reveal unfolding, worsening or impending retinal, systemic, neurologic or cerebrovascular disease.

Multiple studies demonstrate associations between newly forming and chronic retinal and cerebral vascular disease. Observable changes in retinal vascular architecture, such as increased retinal vein caliber (decreased artery-to-vein ratio), retinal vascular tortuosity, increased prominence of the retinal arterial reflex, venous nicking, "copper" or "silver wire" appearance as well as the discovery of cholesterol, calcium or thrombotic emboli are all associated with concurrent and future cerebrovascular events. These associations support the use of the retinal vasculature as a biomarker for discovering, predicting or monitoring patients for potential retinal, systemic, neurological and cerebral vascular morbidities and risks—essentially broadening the responsibilities of the optometrist.

This four-part series introduces some of the root concepts of the neuro-retinal-systemic connection, along with some normal and abnormal retinal vascular phenomena. I thank each of the author teams. Without their expertise and willingness to participate, this miniseries would not have been possible. I hope this educational experience becomes a useful resource for you in clinical practice.

—Andrew S. Gurwood, OD, Clinical Editor, retinal vascular miniseries

Recognizing Abnormal Vasculature

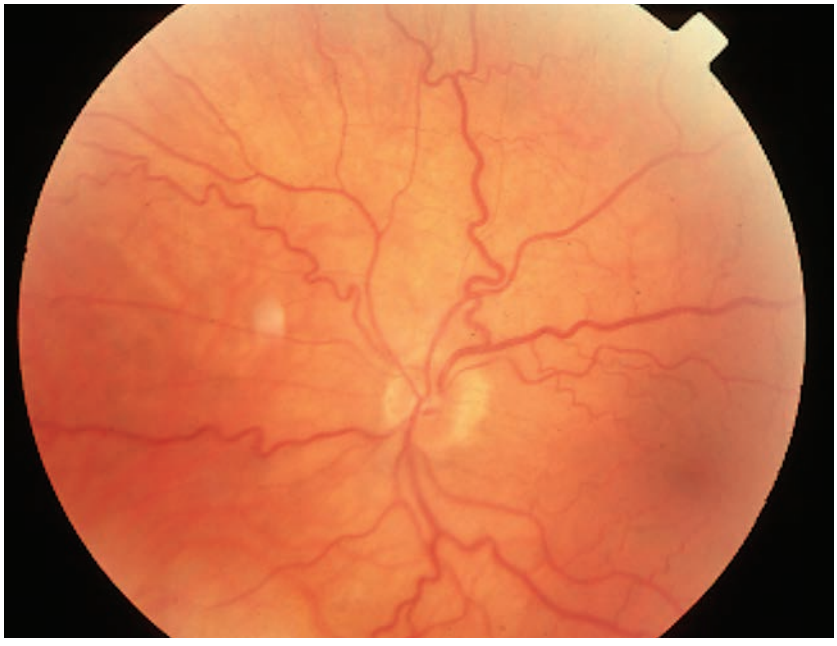
A guide to following and educating patients who face this class of sight-threatening diagnoses. By Leticia Rousso, OD, and Joseph Sowka, OD

When performing fundus evaluations, you may be tempted to focus on the retina and optic nerve while overlooking the status of the retinal vessels. However, the retinal venules and arterioles can provide vital diagnostic information. The eye allows for direct, noninvasive visualization of the body's microvasculature (giving insight into the patient's overall vascular health). The retinal vessels should be studied during clinical examination. Changes in the shape, color and caliber of vessels can represent ocular manifestations of many systemic conditions. Examining the arteriolar-venular caliber ratio can assist in diagnosing vascular abnormalities and associated pathology. A reduced ratio could indicate retinal venular dilation, arteriolar attenuation or both.

Fundus photography can help monitor any changes in retinal vasculature and retinopathy. Using it, you can obtain a side-by-side comparison of the retinal vasculature in each eye—a valuable indicator of worsening or resolving pathology.

Identifying anomalous vasculature, coupled with understanding the fundamental causes of pathological changes, can be crucial for identifying systemic conditions.

Here, we address the pathophysiology and commonly associated conditions that occur when patients present with abnormal vasculature, such as dilated, tortuous retinal veins; dilated nontortuous retinal veins; dilated retinal arteries; tortuous retinal arteries; and narrowed retinal arteries.

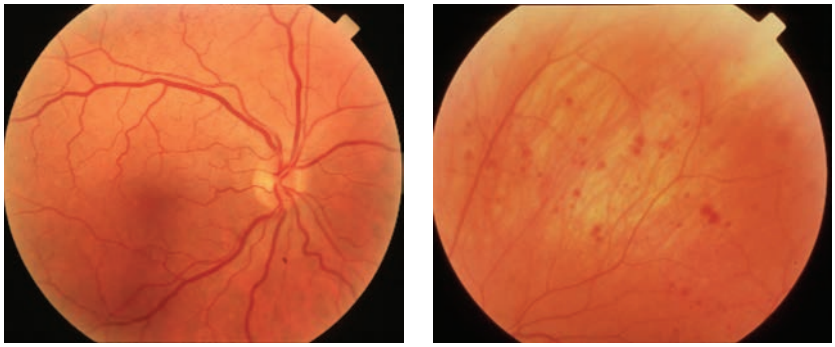


Dilated, tortuous retinal veins in an impending vein occlusion.

Dilated, Tortuous Retinal Veins

Vascular occlusion is the second most common cause of blindness due to retinal disease, following diabetes.[1] The retinal venules typically present as both dilated and tortuous preceding and during a vascular occlusive event. Virchow's triad—a term used to describe various etiologies of thrombosis—consists of hemodynamic changes (blood

stasis), degenerative and mechanical changes to the vessel wall, and blood hypercoagulability.[1,2] If you observe dilated, tortuous retinal venules, consider impending retinal vein occlusion. This condition occurs when a thrombosis exists within the venous circulation causing outflow obstruction within the retina. The thrombosis will cause a buildup of pressure within the venous and capillary system and can potentially cause the leakage of blood or serosanguinous fluid, or both, into the retina. Vision may be lost if leakage occurs in or near the macula, causing secondary edema or ischemia via capillary closure. Possible etiologies include: diabetes, hypertension, cardiovascular disease, hyperviscosity syndromes (anemia and antiphopspholipid antibody state), arteriosclerosis, carotid artery disease, collagen vascular disease and coagulopathies (sickle cell disease).



At left, dilated, nontortuous retinal veins in a patient with blood dyscrasia. At right, midperipheral hemorrhages and dilated retinal veins in ocular ischemic syndrome.

While typical patients who present with a central retinal vein occlusion (CRVO) include middle-aged individuals with a strong systemic history of hypertension, hypercholesterolemia or diabetes, atypical presentations may warrant referrals to rule out hypercoaguable diseases.[1,2] A 25-year-old female presenting with a CRVO without any known vascular diseases would warrant evaluation for autoimmune factors, blood dyscrasia or dysproteinemia. First, rule out specific drugs that have the potential to cause retinal vascular occlusions. Diuretics, oral contraceptives and antipsychotics have all been linked to retinal vascular occlusions and should be considered in these cases.[3]

Identifying the underlying systemic cause of this condition allows for early management and prevention of other harmful sequelae. Many causes of retinal vein occlusion have the potential to threaten systemic circulation and ultimately harm other organs in the body if not identified and treated early.

Venous beading is an ocular sign that connotes the shape and appearance of retinal venules. It is commonly associated with poorly controlled diabetes. This phenomenon is a strong predictor of progression to neovascular, or proliferative, diabetic retinopathy.[2] The beaded appearance of the venule is caused by prolonged cycles of hypoxia with constant dilation and constriction of the lumen due to vascular autoregulation.[4] Recognizing this beaded appearance during clinical examination should prompt a referral to a primary care physician or endocrinologist. Proper referral and management may prevent vision loss by preventing systemic worsening and debilitating retinopathy.

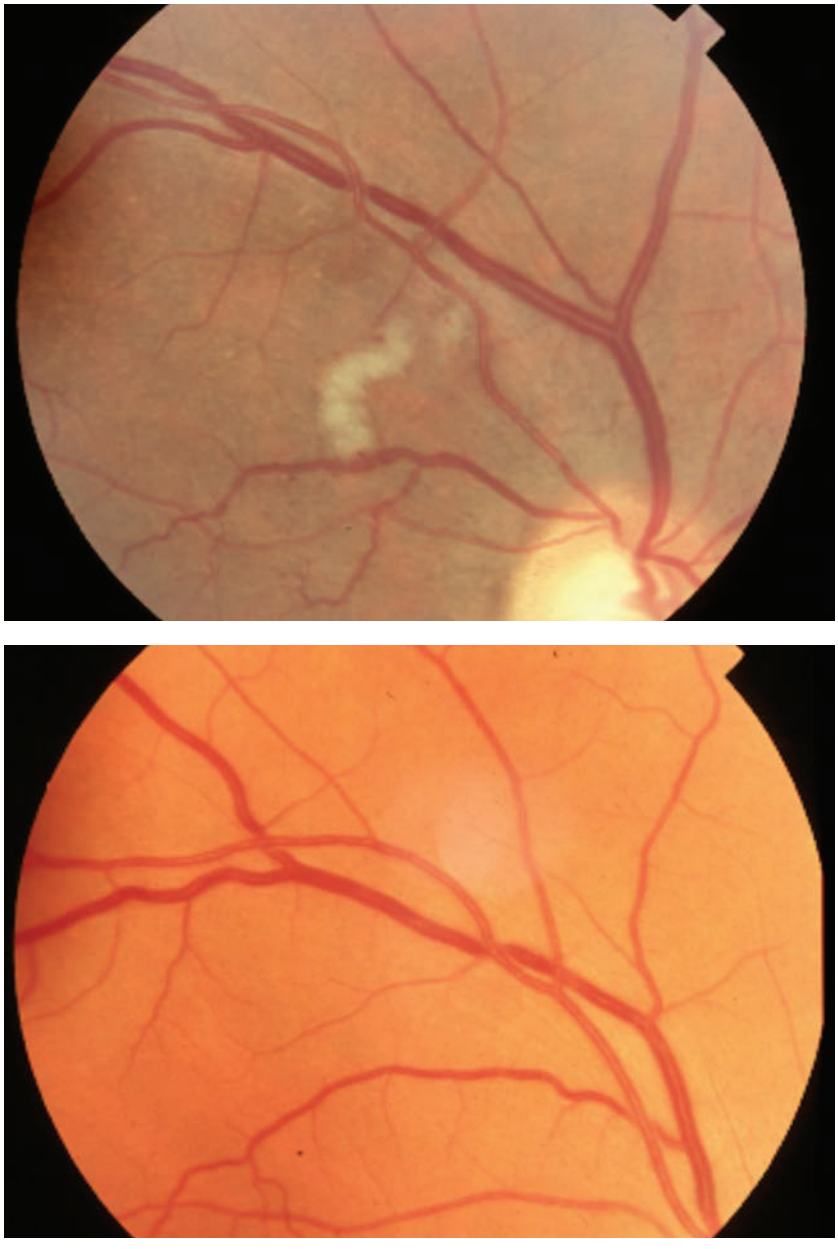
Categories of Vasculature Abnormalities

Dilated, tortuous retinal venules	Retinal vascular occlusion caused by: • Diabetes • Hypertension • Cardiovascular disease • Hyperviscosity states • Arteriosclerosis • Collagen vascular disease • Sickle cell disease
Dilated, non-tortuous retinal venules	Ocular ischemic syndrome caused by: • Atherosclerosis • Dissecting aneurysm of the carotid artery • Giant cell arteritis • Fibrovascular dysplasia • Takayasu arteritis • Aortic arch syndrome • Behçet's disease • Trauma or inflammation causing stenosis of the carotid arteries
Dilated retinal arterioles	Retinal arteriolar macroaneurysm
Tortuous retinal arterioles	Possible association with systemic vascular diseases
Narrowed retinal arterioles	Hypertension, atherosclerosis, retinal artery occlusion

Many studies have reported an association between larger retinal venous caliber and increased risk for cardiovascular disease.[5] Data from the Atherosclerosis Risk in Communities (ARIC) study shows that narrowed arterioles, dilated venules or both are associated with risk of incident stroke events and coronary heart disease events.[5] Retinal venular dilation is hypothesized to reflect the effects of hypoxia, inflammation and endothelial dysfunction.[5]

Consider systemic signs if you suspect cardiovascular disease—shortness of breath, fatigue, irregular heartbeat, pain in chest area or dizziness.[6] If you identify venular dilation in conjunction with other ocular or systemic signs of cardiovascular disease, recommend a cardiovascular workup in comanagement with the patient's primary care provider or cardiologist.

In addition, you may see a few uncommon causes of retinal vein occlusions. One such cause is retinal arteriovenous malformations (Wyburn-Mason syndrome), a rare retinal anomaly in which abnormal blood flow occurs between retinal arterioles and venules, bypassing the capillary bed. This condition is usually congenital and typically presents as a unilateral, dilated and tortuous vascular loop.[7] Retinal malformation can be a presenting sign of simultaneous systemic malformations that occur in the brain.[7]



Above, arteriolosclerosis and venous compression in hypertension. Below, arterial attenuation and arteriovenous nicking in hypertension.

Dilated Nontortuous Retinal Veins

Degenerative changes to the vessel wall can occur secondary to chronic hypertension and atherosclerosis. Blood hypercoagulability can occur due to a blood dyscrasia, dysproteinemia and sickle cell disease, as well as other diseases that cause a hypercoagulable state.[8]

Ocular ischemic syndrome (OIS) is caused by decreased blood flow to the ocular blood vessels, which is due to stenosis or occlusion of the common or internal carotid arteries.[9] The decreased blood flow from the retinal arterioles to the capillaries causes a significant decrease in vascular pressure and secondary venous stasis.[9] In OIS the retinal venules are typically dilated but not tortuous.[9]

Other nonatheromatous causes of OIS include: dissecting aneurysm of the carotid artery, fibrovascular dysplasia, Takayasu arteritis, aortic arch syndrome, Behçet's disease, giant cell arteritis, trauma or inflammation causing carotid artery stenosis.[9]

Ocular hypoperfusion leads to clinical signs of dilated retinal venules as well as unilateral hemorrhages in the mid-periphery of the retina.[9] In addition, OIS patients will usually present with a plethora of anterior segment-related findings—uveitis, hypotony, neovascularization, corneal edema and cataract.[9] Considering the high risk of cardiovascular disease, it is imperative to quickly refer these patients for a full cardiovascular work-up, paying particular attention to the ipsilateral common or internal carotid artery.[9] Clinically, we can evaluate the carotid arteries by auscultation using the bell side of a stethoscope and listening for a bruit—a sound signifying turbulent blood flow due to plaque buildup of the carotid artery. However, a bruit will not be heard if the carotid artery is significantly stenosed.[10]

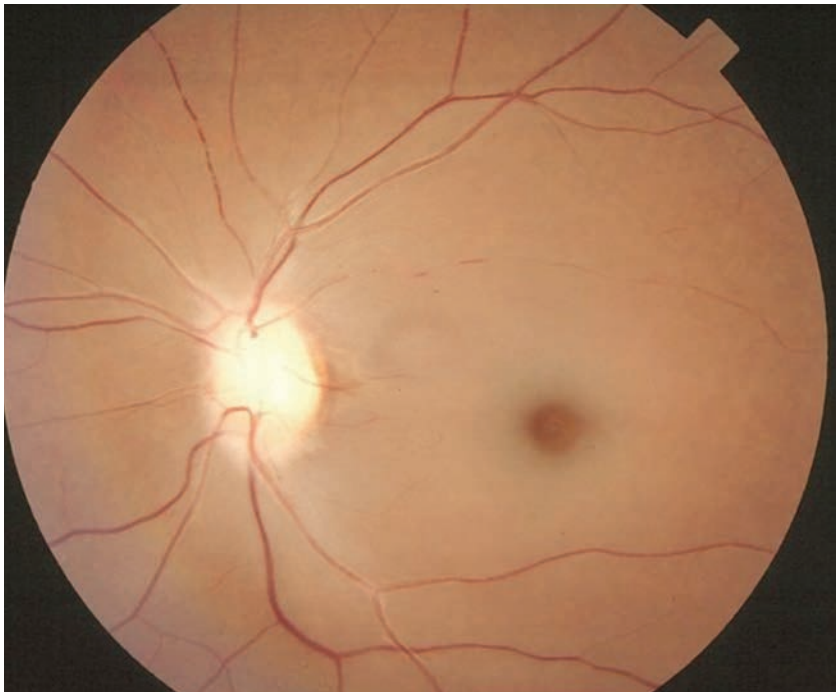
A similar pathophysiology occurs in patients who suffer from a blood dyscrasia or dysproteinemia. Changes in blood composition can lead to a disturbance in blood flow causing potential thrombus formation and vessel occlusion. Blood dyscrasias can present as dilated nontortuous retinal veins with or without retinal hemorrhages.[3]

Dilated Retinal Arteries

The retinal arterioles may also present as dilated, tortuous or narrowed. Retinal arteriole macroaneurysms (RAM), for instance, present as focal dilations in retinal arterioles and are usually caused by systemic hypertension.[11] This condition usually presents within the first three bifurcations in the retina and may be difficult to detect during clinical examination if significant retinopathy exists.[11]

Hemorrhage, exudates and edema all have the potential to affect vision, especially if the lesion is in proximity to the fovea. The lesions tend to occur unilaterally in female patients older than 60 years.[11] Fundus photography, OCT and optical coherence tomography angiography (OCT-A) are ancillary tests that could be useful in imaging the retinal microvasculature documenting RAM location. Prompt evaluation with a retinal specialist is adequate if macular edema or significant retinopathy exists.

Consider a referral to a specialist for a full work-up for hypertension, lipid evaluation and a full systemic vasculitis work-up.[12]



Narrowed, attenuated retinal arterioles in retinal artery occlusion.

Tortuous Retinal Arteries

The significance of tortuous retinal arterioles has been hotly debated in the literature for decades. While some studies suggest that tortuosity may be strongly associated with systemic vascular conditions, others have disproved this theory and have found no apparent correlation.[13] One study concluded that older age, higher blood pressure, alcohol consumption, greater BMI, diabetes and higher HbA1c level are significantly associated with less tortuous arterioles.[13] A smaller study of 218 healthy young Caucasians associates straighter retinal arterioles with higher blood pressure and BMI.[13] Conversely, two small clinic-based studies associate elevated blood pressure with increased retinal arteriolar tortuosity. Therefore, additional larger population-based studies are needed to further evaluate the relationship between arteriolar tortuosity and vascular diseases.

Narrowed Retinal Arteries

Narrowed retinal arteries can occur secondary to atherosclerosis, hypertension or both.[14] Chronic hypertension has the potential to cause many types of ocular findings, including: arteriolar attenuation, arteriole-venule nicking, cotton wool spots, hemorrhage, maculopathy, and optic nerve edema if severe.[14] Retinal

arteriolar attenuation is a defining sign of hypertensive retinopathy.[14] The finding is considered an autoregulatory, physiological response to retinal artery vasospasm.[14]

Chronically elevated blood pressure can cause irreversible arteriolar narrowing and hardening of the arteriolar wall, with an apparent broadening of the arterial light reflex.[14] "Copper" and "silver wiring" are exaggerated forms occurring secondary to increased optical density of the vessel.

The major anatomical difference between retinal arterioles and venules are that arterioles have thicker vessel walls capable of compressing and reducing blood flow through the underlying venule. The sclerotic changes in vessel wall structure from chronic hypertension may have the potential to indent the underlying venule when crossing over it in the retina.[14] This crossing change, known as arteriovenous nicking, can change the hemodynamics within the venule. This condition should be watched closely and managed cautiously, as patients are at increased risk for thrombus formation and secondary branch retinal occlusion. Managing them with periodic evaluation as well as comanaging systemic risk factors with a primary care provider or cardiologist is crucial to prevent future manifestations of the disease.

Retinal artery occlusion is an important consideration when a patient presents with narrowed retinal arteries. These occlusions are commonly caused by emboli, thrombi, trauma or inflammation causing a blockage within the retinal arteriole. Recognizing arteriolar attenuation, in conjunction with other signs of a retinal artery occlusion (pallid edema of the retina, correlating visual field or visual acuity loss, presence of an afferent pupil defect) supports the diagnosis. Fundus photography can aid in side-by-side retinal comparison and identification of reduced retinal perfusion and arteriole attenuation. OCT-A can image the abnormal blood flow through the arteriole system.

Retinal artery occlusion is a significant indicator of systemic disease.[15] All acute cases of retinal artery occlusion warrant immediate referral to a stroke unit for evaluation. It is essential to suspect certain cases of retinal artery occlusions may be caused by giant cell arteritis. Should suspicion be high, immediate evaluation with erythrocyte sedimentation rate and c-reactive protein is required as 5% to 10% of all central retinal artery occlusions are caused by giant cell arteritis.[15]

Atherosclerosis is caused by the hardening of the vessel wall due to the build-up of fatty plaque, causing a reduced arteriole lumen size. The Blue Mountains Eye Study and the Beaver Dam Eye Study revealed smaller arterioles and larger venules were associated with a 20% to 30% increased risk of coronary heart disease (CHD) mortality independent of cardiovascular risk factors.[16] Another study showed that women with larger retinal venules or narrower arterioles each had a 30% higher risk of CHD, even after adjusting for other known cardiovascular risk factors.[16]

Understanding the various conditions that may change the appearance of the retinal vasculature will allow for early management and possible prevention of sight-threatening sequelae. Aside from direct clinical examination, the newly developed OCT-A may prove to be a useful, noninvasive imaging technique of the retinal microvasculature. OCT-A is capable of direct, high resolution imaging of blood flow using the motion from red blood cells within the vessel. Using advanced imaging modalities such as fundus photography and OCT-A will allow for monitoring and detection of vascular changes over time. The status of the retinal vessels can provide much information about our patients' systemic health. The retinal vascular system has a story to tell if you are willing to listen. ■

Dr. Rousso is a faculty member at Nova Southeastern University's College of Optometry.

Dr. Sowka is chief of advanced care and director of the glaucoma service at Nova Southeastern University College of Optometry.

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Tales From TFOS

Ocular surface experts from around the world recently came together to share groundbreaking research. **By Paul M. Karpecki, OD**

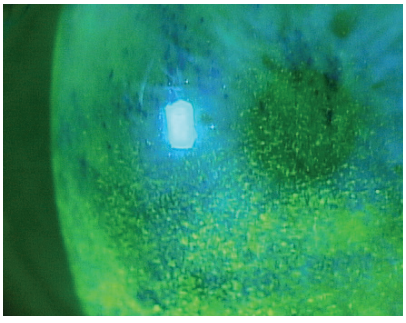
The Tear Film and Ocular Surface Society (TFOS) is an organization that provides incredible insights, research, knowledge-sharing and camaraderie among dry eye disease (DED) experts around the world. Its 8th International Conference, held September 2016 in Montpellier, France, was another exceptional educational event. Here are a few abstract highlights from papers, posters and presentations:

Contact Lenses and MGD

Several presentations and papers, and a session comoderated by me and Donald Korb, OD, showed contact lenses likely contribute to structural changes within the meibomian gland framework, leading to meibomian gland dysfunction (MGD). Video imaging shows contact lens movement along the lower eyelid in the direction of the meibomian glands during a normal blink.[1] Researchers postulate this friction over time may play a role.[1] The research also shows a statistically greater amount of meibomian gland loss in contact lens wearers compared with an age-matched control group of non-wearers.[1]

Eric Papas, OD, conceded that contact lenses may indeed result in structural changes to the meibomian glands, but no study has yet confirmed functional changes directly associated with contact lens wear.[1]

All of this evidence (or lack thereof) suggests we should be monitoring our contact lens patients for structural changes with tests such as meibography throughout their lens wearing life and, once these changes are noted, take steps to educate and treat to minimize functional meibomian gland issues, contact lens drop-out and, potentially, chronic DED.



New research is helping to reshape dry eye screening and diagnosis.

Diabetes and Dry Eye

Research showed a clear correlation between MGD and patients with Type 2 diabetes.[2] One study found patients with Type 2 diabetes had a significantly lower noninvasive tear break-up time, higher levels of inflammation and obstruction of the meibomian glands. In addition, the lipid layer thickness was considerably lower than in normal subjects, resulting in increased subjective symptoms and a decreased quality of life.[2] Another study showed the HbA1c level had a high degree of correlation with the symptoms based on the National Eye Institute Vision Functioning Questionnaire.[3]

Fish Oil, Krill Oil and DED

A recent clinical trial showed that omega fatty acid supplements are a valuable treatment option for DED. Researchers from the University of Melbourne in Australia showed a statistically significant improvement in osmolarity ($p<0.001$) in both phospholipid and triglyceride forms of omega fatty acids when measured three months after the study subjects began taking omega-3 supplements. The results also showed increased tear stability and an improvement in subjective symptoms.[4]

Symptoms But No DED

One poster looked at Tearlab's osmolarity test, particularly when normal readings occur in patients who present with classic symptoms of DED.[5] The patients had normal measurements (in this case, 50 patients with both eyes measuring under 300 mOsmol/L and within 5 mOsmol/L between eyes) with a mean tear osmolarity of 293.33 mOsmol/L (+/- 6.70) and a mean difference of 0.94 mOsmol/L between eyes (+/- 3.18).

An alternate diagnosis was established in 100% of these cases. The most frequent diagnoses were allergic conjunctivitis (24%) and anterior blepharitis (24%), followed by epithelial basement membrane dystrophy (12%), keratoneuralgia (12%), contact lens intolerance (8%), conjunctivochalasis (8%), computer vision syndrome (6%) and trichiasis (6%). Twenty-two percent of patients had more than one diagnosis.[5]

In the past, if a patient presented with fluctuating vision and dry, gritty, red eyes, doctors often initiated dry eye treatment, resulting in patient

and doctor frustration when DED wasn't the appropriate diagnosis. This research suggests normal osmolarity may be beneficial in establishing a differential diagnosis away from DED, even with classic DED symptoms.

Sex and the Eye

Though we have long known women are at a higher risk for DED, new developments led by David Sullivan, PhD, are adding to our body of knowledge. For one, his research reveals that the sex hormone receptors for estrogens and androgens are different between men and women.[6] Because sex hormones can mediate inflammation—among other activities—in the eye, this research may explain why some therapies work and others don't between the sexes, despite similar signs and symptoms.

Furthermore, testosterone deficiency can result in a significant alteration to the glycocalyx make-up on the ocular surface, causing ocular surface desiccation.[6]

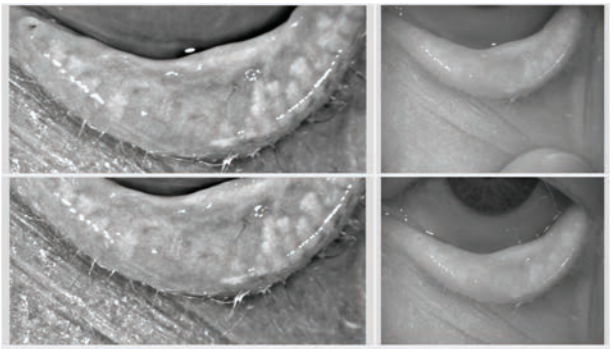
We can't forget the fact that, although DED is multifactorial, meibomian and lacrimal glands play a key role, and the cornea can be the most affected. New research suggests testosterone may also play a key role in corneal protection.[7,8]

Restoring Clarity to the Ocular Surface

Mesenchymal stem cells (MSC) may be the key to restoring transparency in a cornea after ocular injury, a new study suggests. Research shows that MSCs inhibit stromal fibrosis and secrete elevated levels of hepatocyte growth factor, resulting in decreased inflammation.[9]

Wrong Diagnosis for Millions

One of the great things about a symposium such as TFOS is that it leaves you with as many new questions as it does answers. As an example, leave it to Dr. Korb to question the common assumption that DED is underdiagnosed. And I have to agree with him after hearing the presentation; too many times we make a diagnosis based on symptoms that sound like dry eye disease. Or we make the assumption that patients with classic DED need to have treatments that focus on aqueous production and dry eye sequelae, when in fact more than 50% of these patients actually improve significantly from a treatment for MGD.[10] After Dr. Korb's presentation, I had to admit that I, too, believe MGD needs to be addressed in all patients with DED. This shift changes how we think about the disease, and although MGD may be a leading cause of DED, the two are not one and the same.



Meibography can reveal functional meibomian glands, even when none are observable to the naked eye.

No Observable Glands, But Treatment Isn't Futile

Another poster by Dr. Korb and Caroline Blackie, PhD, OD, looked at meibography of the lower nasal eyelid and compared patients with no observable glands with a control group that had roughly five observable glands in the same area.[11] When they tested this area they found that the dry eye patients still had a mean of 1.8 (+/- 1.1) functional glands, even though they were not observable.[11] This dispels the myth that treatment is futile when no glands are seen. In fact, patients with this much structural damage are precisely the patients who require the most aggressive treatment to preserve, and possibly enhance, what little structure remains.

This is only a small sampling of the abstracts, posters and presentations provided at the annual meeting. TFOS is a terrific organization to join if dry eye and ocular surface disease is an important aspect of your practice. It's a valuable resource for researchers and clinicians alike with insights that can be deep into immunology while also extremely practical and clinical. All of the new research it provided clearly shows we have come a long way in the understanding of DED—but we still have a long way to go before we fully understand this complex and multifactorial disease. ■

1. Arita R. Do contact lenses cause clinically relevant meibomian gland dysfunction? Prime Time TFOS Debates 2 presented at the 8th International Conference on the Tear Film & Ocular Surface (TFOS), September 8, 2016; Le Corum, Montpellier, France.
2. Garzon Johanna P, Lopez-Alemany A. Correlation between tear film lipid layer by interferometry and symptoms in diabetic patients with meiboiman gland dysfunction. Poster presented at the 8th International TFOS Conference.
3. Garzon Johanna P, Lopez-Alemany A. Clinical features of meibomian gland dysfunction in patients with diabetes Type 2. Poster presented at the 8th International TFOS Conference.
4. Downie LE, Deinema L, Chinnery HR, Vingrys AJ. A randomized, double-masked, placebo-controlled, clinical trial of two forms of omega-3 supplements for treating dry eye disease. Poster presented at the 8th International TFOS Conference.
5. Brissette AR, Bohm KJ, Starr CE. The utility of a normal tear osmolarity test in symptomatic patients. Poster presented at the 8th International TFOS Conference.
6. Sullivan DA. Liu Y, Ding J, Kam WR. Ménage à trois: sex, sex steroids and dry eye disease. Keynote address presented at the 8th International TFOS Conference.
7. Kadmiel M, Cidlowski JA. Glucocorticoids, sex and inflammation. Keynote address presented at the 8th International TFOS Conference.
8. Clayton J. Studying both sexes: a guiding principle for ophthalmology. Presented at the 8th International Conference on the TFOS.
9. Chauhan S, Restoration of corneal transparency by mesenchymal stem cells. Keynote address presented at the 8th International TFOS Conference.
10. Korb DR. Blackie CA. Is dry eye the wrong diagnosis for millions? Poster presented at the 8th International TFOS Conference.
11. Korb DR. Blackie CA. Can meibography fail to reveal functional gland structure? Poster presented at the 8th International TFOS Conference.

Contain That Ulcer

It's an emergency when a *Pseudomonas* ulcer involves the limbus, and prompt treatment is crucial to keep it from reaching the sclera. **Edited by Joseph P. Shovlin, OD**

Q I recently saw a patient with a significant *Pseudomonas* ulcer in which the edge had reached the limbus. The corneal specialist added an oral antibiotic. Is this necessary, and what's the best option for treatment?

A "A *Pseudomonas* ulcer that spreads to the limbus is a true, globe-threatening ocular emergency," Eric Donnenfeld, MD, national medical director of TLC Laser Eye Centers, says. "Once *Pseudomonas* ulceration reaches the limbus it has the potential to extend into the sclera."

Additionally, a scleral abscess is "much more unresponsive to treatment than a corneal ulceration and often requires enucleation," Dr. Donnenfeld adds, suggesting this is why "most corneal specialists are extremely aggressive in treating infections near the limbus."

"While *Pseudomonas* keratitis can be very aggressive, *Pseudomonas* organisms are generally susceptible to a variety of antibiotics, including aminoglycosides and fluoroquinolones," says Chistopher J. Rapuano, MD, director of cornea services at Wills Eye Hospital in Philadelphia. Early diagnosis and treatment with intensive topical antibiotics early in its course—when it just involves the cornea—often provides rather good results, according to Dr. Rapuano. However, "when the infection reaches the sclera, the clinical results are typically much worse," Dr. Rapuano says, echoing Dr. Donnenfeld's conclusion. "Topical antibiotic therapy just isn't as effective in eyes with infectious scleritis."

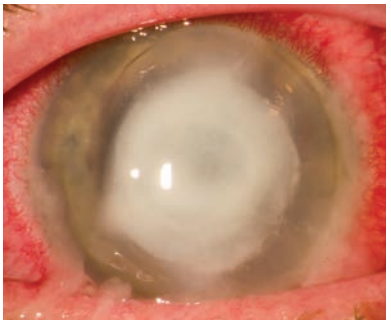


Photo: Christopher Croasdale, MD

Keeping *Pseudomonas* ulcers, such as this one, from extending into the sclera is paramount.

The Ghosts of Treatment Past and Present

"Years ago," notes Dr. Rapuano, "most eyes with *Pseudomonas* scleritis were lost."

Over time, treatment moved from cryotherapy—an improvement on earlier treatments, but still largely ineffective—to systemic fluoroquinolones, which "penetrate the eye rather well," says Dr. Rapuano. "Doctors began using these medications in eyes with *Pseudomonas* scleritis when they became available in the United States in the late 1980s. The success in treating *Pseudomonas* scleritis dramatically improved."[1,2]

Now, "therapy for this type of case might involve the use of topical gram-negative medications such as fluoroquinolone or aminoglycoside every 30 minutes," says Dr. Donnenfeld. "Oral or even IV medications are used, and some specialists will even lavage the subconjunctival space with antibiotics." Both doctors generally agree that moxifloxacin 400mg per day is the most common oral antibiotic used to treat *Pseudomonas* scleritis. "Oral fluorquinolones," says Dr. Donnenfeld, "achieve tissue levels as high as IV medications, which makes them a good choice. However, IV delivery is required when an antibiotic such as the aminoglycoside tobramycin is preferred." Additionally, "hyperbaric oxygen therapy has been attempted in some research facilities, and riboflavin UV crosslinking can be a very effective adjunctive therapy."[3] Crosslinking, Dr. Donnenfeld adds, "is generally reserved for resistant organisms such as fungi or resistant bacteria."

With all this in their wheelhouse, eye care providers still lack a panacea and, "while it is certainly not successful in all cases, the current use of systemic fluoroquinolones has significantly improved our treatment of *Pseudomonas* scleritis," says Dr. Rapuano. Today, eye care providers have a much more effective set of tools at their fingertips, and prevention and early diagnosis are ideal. "The best treatment of a limbal *Pseudomonas* ulceration," posits Dr. Donnenfeld, "is to prevent it from spreading into the sclera." ■

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Smoke (or Vapor) Gets in Your Eyes: Part Two

Traditional pipes, water pipes and electronic cigarettes are highly popular. Are they harming us and our children?

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

Tobacco use kills approximately 440,000 Americans each year, and one in every five US deaths is the result of smoking.[1,2] While the majority of these patients are killed by smoking cigarettes, tobacco use in other forms contributes to worldwide morbidity and mortality.[1-3] Smoked forms of tobacco other than cigarettes, including cigars, traditional pipes and water pipes, erroneously are often perceived as much less hazardous than cigarettes.[3]

New nicotine delivery systems not directly reliant on tobacco, such as electronic cigarettes, are also becoming increasingly popular, especially among teens and adolescents.

Smoking and the Eye

Several ocular conditions are directly or indirectly related to smoking. For one, smoking is an established risk factor for cataract. Cessation of smoking appears to decrease the risk of cataract, but cataract risk among former smokers persists for decades. Formation of free radicals and lower levels of circulating antioxidants may initiate the ocular pathogenesis by oxidative stress. There is evidence of a dose-response effect of smoking on ocular morbidity.[4]

Other associated ocular conditions include age-related macular degeneration, dry eye disease, diabetic retinopathy, ocular ischemic syndrome, retinal vascular occlusions, anterior ischemic optic neuropathy, thyroid eye disease and metastatic carcinoma of the uvea.[5,6]

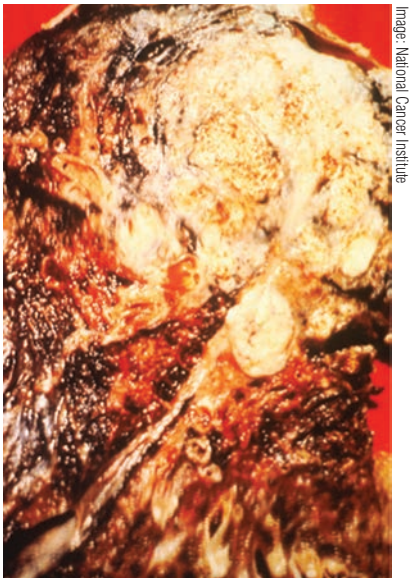

Image: National Cancer Institute

Cross-section of a lung. The black areas indicate the patient was a smoker, and the white area is cancer.

Everything But Cigarettes

Because smoking can have such a profound effect on the eye, optometrists should be aware of the various methods of smoking and be prepared to educate patients on their associated risks. For more information on cigarettes and cigars, see part one, available at www.reviewofoptometry.com/article/smoke-or-vapor-gets-in-your-eyes-part-one.

Traditional pipes are usually composed of a bowl, in which the tobacco is placed for burning, attached to a stem through which the smoke is drawn. The tobacco used in pipes may sometimes be flavored.[5] One study reported that the total particulate matter extracted from pipes was up to 44% more mutagenic per unit of nicotine, relative to cigarette smoke.[7] As with cigars, pipe use is associated with cancers of the mouth, nose and upper airway.[7]

Water pipes—known in various regions by names such as shisha, hookah and narghile—typically employ indirect heating of tobacco (often via charcoal). The smoke generated is passed through a chamber containing water before reaching the user through a hose. The proliferation of water pipe cafes may be due, in part, to the introduction of flavored tobacco preparations.[3,8] Water pipe use appears to be especially popular among university students, many of whom believe it is less hazardous than cigarette smoking.

However, the water in the pipe does not act as a real filter. During a 20- to 80-minute hookah session, users may smoke the equivalent of 100 or more cigarettes.[9] In addition, the use of charcoal as a heating source generates large amounts of

Image: National Cancer Institute

Get the conversation started with these five A's to quitting tobacco.[12]

carbon monoxide and polycyclic aromatic hydrocarbons.[3,6,7] Although the literature on the health effects of water pipe use isn't robust, what little is available indicates water pipe use is associated with cancer, heart disease, lung malfunction, infectious diseases and reproductive side effects.[8]

Nicotine delivery systems not directly reliant on tobacco, such as electronic nicotine delivery systems (ENDS) known as e-cigarettes, are becoming increasingly popular. These devices work by vaporizing a solution containing nicotine dissolved with flavorants in a carrier medium (usually propylene glycol).[3] The nicotine used in e-cigarettes is most frequently derived from tobacco. Companies promote ENDS with claims that they have reduced health risk compared with tobacco use and can be used in situations where smoking is prohibited.[3,10]

Of major concern is their widespread use by teens and adolescents. In addition, studies reveal many e-cigarette smokers are dual users (they also smoke another form of tobacco). The FDA has not found e-cigarettes safe and effective in helping smokers quit.[3,10,11]

With respect to health hazards, data on ENDS are lacking. Nicotine delivered by vapor with few known toxicants should theoretically carry relatively low risks, particularly when compared with cigarettes. The limited data available suggests these products are not likely to approach the health hazards of cigarettes. However, significant concerns exist about the purity of ingredients used, device functionality and quality control, the ease with which devices can be modified by users and the general lack of oversight in manufacturing and marketing.[11]

Smoking Cessation Strategies

Only 20% of smokers will ask for help with tobacco cessation, and for those who attempt quitting tobacco use without assistance, only 10% will be effective long term.[12] Recent research has clarified the addictive nature of nicotine, comparing the dependence to that caused by opiates, cocaine or other illicit drugs.[1,2,12] Pharmacologic and counseling strategies are now the cornerstone of tobacco cessation programs and, taken in combination, can achieve the highest rates of smoking cessation.[12]

Unless there is an obvious contraindication, every adult patient making an attempt at smoking cessation should be offered pharmacologic therapies to improve their chances of success.[12] First-line therapies approved by the FDA include six agents: Wellbutrin SR (sustained-release bupropion, GlaxoSmith-Kline), Chantix (varenicline, Pfizer) and four nicotine replacement therapies (NRTs). These are FDA-approved for adults ages 18 and over who want to quit smoking.[13] Three types of NRTs are approved by the FDA for consumers to buy OTC: nicotine gum, transdermal nicotine patch and nicotine lozenge products. There is one prescription-only nicotine replacement product, under the brand name Nicotrol (Pfizer), which is available both as a nasal spray and an oral inhaler.

NRTs should be used for a short time to help the patient manage nicotine cravings and withdrawal.

Interventions to help smoking and tobacco product cessation should be considered a standard of good practice. Tobacco dependence is a chronic condition, but the evidence suggests safe and effective therapeutic options are available to help aid patients in quitting. Excellent resources are available at http://smokefree.gov. ■

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Fixing a Hole

A patient's blurry vision may have been spotted on an earlier image.

By Philip Kim, OD, and Mark T. Dunbar, OD

A 38-year-old female presented to the eye clinic complaining of progressive blurred vision in the right eye. She had a long-standing medical condition directly related to her retinal diagnosis. She also had a strong family history of cancer—her paternal grandmother had breast cancer, her maternal grandmother had pancreatic cancer, her maternal grandfather had pheochromocytoma and her father had gastric cancer.

Upon examination, her visual acuities were 20/30 OD and 20/20 OS with no improvement after refraction. Her extraocular motilities showed full range of motion, her confrontation fields were full to finger counting in both eyes and her pupils were round and reactive to light with no afferent defect. Her intraocular pressures were 20mm Hg OD and 19mm Hg OS.

Anterior segment exam in both eyes and left eye fundus exam were unremarkable. But the fundus exam in her right eye (*Figure 1*) was notable. A widefield image of the retina was also taken (*Figure 2*), as well as an OCT of the peripapillary region (*Figure 3*). We also had an intravenous fluorescein angiography (FA) from a previous encounter (*Figure 4*).

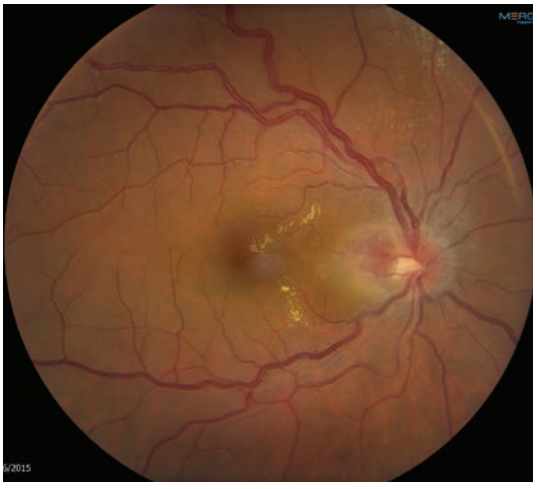

Fig. 1. This fundus photo shows the optic nerve and macula of the 38-year-old patient's right eye.

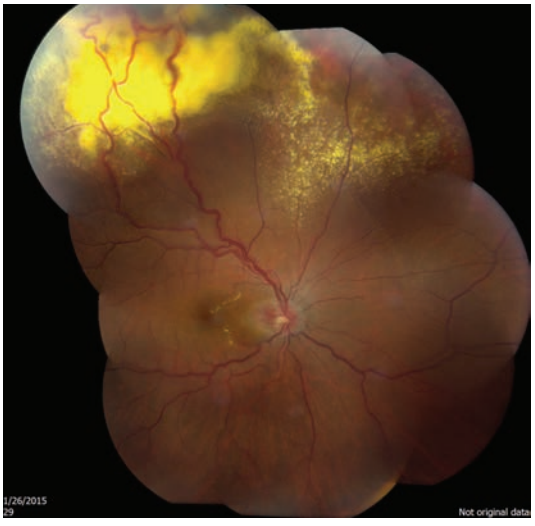

Fig. 2. Note the peripheral changes in this widefield view of the same eye.

Take the Quiz

1. What is the diagnosis of this retinal tumor?
a. Retinal capillary hemangioma.
b. Cavernous hemangioma.
c. Astrocytic hamartoma.
d. Infectious granuloma.

2. Which medical condition is mostly associated with the retinal tumor?
a. Tuberous sclerosis.
b. Neurofibromatosis.
c. Von Hippel-Lindau disease.
d. Sarcoidosis.

3. Which other vital organ can be associated with this condition?
a. Brain.
b. Kidneys.
c. Adrenal glands.
d. All of the above.

4. Which option is to be considered for the treatment of these retinal tumors?
a. Laser photocoagulation.
b. Photodynamic therapy.
c. Observation.
d. All of the above.

For answers see page 106.

Diagnosis

Our patient had a juxtapapillary retinal capillary hemangioma (RCH) that was previously treated with photodynamic therapy (PDT) in 2013 but since developed exudates nasal to the fovea. In addition, the patient also had a superior RCH with marked exudation and another RCH located inferotemporally with mild exudates that was previously treated

with argon laser photocoagulation in 2012 and 2013 (not shown on fundus images).

Upon reviewing the previous images, we noticed the FA displayed early hyperfluoresence in both the juxtapapillary tumor and inferotemporal tumor with prolonged intensity and minimal leakage. The OCT of the peripapillary region of the tumor (*Figure 3*) displays intraretinal fluid and thickening that was not present in the earlier visit.

The compilation of the findings of the fundus images in comparison with previous studies led us to conclude the patient had developed a new RCH in the superior periphery with significant exudation and that the previous juxtapapillary RCH had newly developed leakage.

Discussion

Retinal capillary hemangioma is a benign vascular tumor that extends from the inner retina towards the retinal surface. These RCHs can leak fluid and result in exudative retinal detachments. They are typically described as pink lesions often accompanied by an afferent feeder vessel and an efferent draining vessel to and from the lesion.

RCH can be unilateral or bilateral. One study shows bilateral lesions occurred in 57.9% (unilateral 42.1%) of patients and that 84.7% of the retinal lesions were located in the periphery—the rest were located in proximity to the optic nerve.[1] Although RCH can be an isolated sporadic lesion, it is highly associated with our patient's long-standing systemic disease, von Hippel-Lindau (VHL) disease, a multisystem cancer syndrome that can lead to the development of both benign and malignant tumors. A positive familial history of VHL and the existence of RCH are the diagnostic criteria for VHL syndrome.[2] Without a family history, a person with RCH must also have multiple RCHs in the eye or a hemangioblastoma of the central nervous system in order to meet the criteria.[2]

VHL is inherited through an autosomal dominant fashion and is caused by a mutation in the VHL tumor suppressor. The prevalence is approximately one in every 36,000 births, and penetration is nearly complete by age 65.[2] Approximately half of VHL cases are familial, with the other half being sporadic due to new

mutations. VHL disease is a highly diverse condition that presents itself with more than 40 types of lesions being described in 14 different organs, including retinal capillary hemangiomas, cerebellum or spinal hemangioblastomas, renal pheochromocytomas and carcinomas.[2] The tumors associated with the highest mortality are renal carcinomas and cerebellum/spinal hemangioblastoma—which is why patients require periodic imaging and should be closely monitored by multidisciplinary medical clinicians.[3]

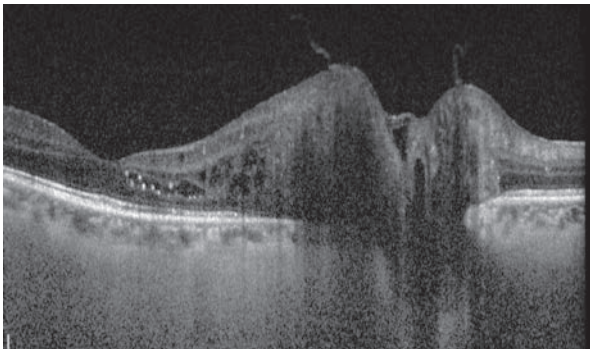

Fig. 3. What can be gleaned from this OCT scan of the optic nerve and macula?

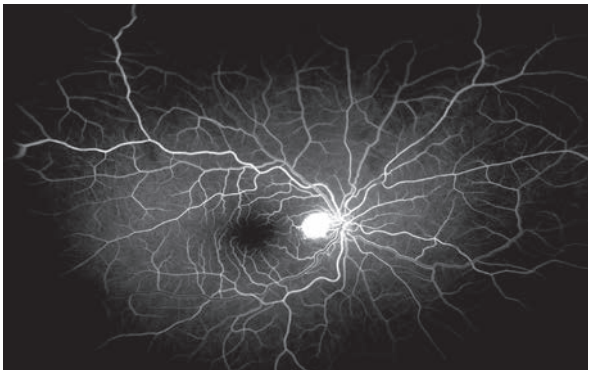

Fig. 4. This is the early venous phase of the fluorescein angiogram of our patient—note the hyperfluorescent lesion involving the optic nerve.

Management

Many proposed treatments exist with RCH, but the efficacy of treatment, as well as the indications for treatment, are based on the tumor's location, size and associated findings. Close observation is often the case for peripheral lesions less than 500µm with no associated exudation, as these peripheral lesions can remain fairly stable.[4] Observation is also indicated for juxtapapillary lesions that do not have active leakage, as they can have a natural history of stability and other alternative treatments may lead to negative sequelae.[5,6] Argon laser photocoagulation has been indicated for peripheral lesions less than 3mm with no subretinal fluid.[7] The photocoagulation itself can either be targeted at the tumor, the feeder vessels or both and has been reported to be 91% to 100% effective in preserving visual acuity at a mean follow-up time of 5.1 years.[7] This treatment is particularly effective for tumors that are 1.5mm or smaller.[7,8] Cryotherapy is an alternative treatment that is proposed when tumors are more anteriorly located, have a moderate degree of subretinal fluid or are larger than 3.0mm.[9]

Furthermore, research shows photodynamic therapy may induce the occlusion of both juxtapapillary and peripheral retinal capillary hemangiomas and can lead to the cessation of leakage.[10]

Anti-VEGF therapy has been tried with both peripheral RCH and juxtapapillary RCH with mixed results. Unfortunately, no large clinical trial has yet examined the efficacy of anti-VEGF agents in the management of VHL patients. In small pilot studies, there has been some success on decreasing exudation, but the anti-VEGF drugs did not seem to have an effect on reduction in the tumor size.[11]

For our patient, both her superior peripheral RCH and juxtapapillary RCH were treated. An argon laser photocoagulation was performed in the superior retinal tumor, which led to the retraction of lipid exudation by the following visit. Furthermore, a half-fluence photodynamic therapy was conducted at the peripapillary region, and the patient regained her vision back to 20/20 OD. ■

Dr. Kim practices at Nova Southeastern University in Ft. Lauderdale, Fla. where he is also a faculty instructor.

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Product Review

Contact Lenses

Rose K2 Soft Lens

A daily wear silicone hydrogel soft lens for irregular corneas, available as a three-month replacement lens, is now available from Menicon.

The Rose K2 Soft lens uses the same five-step fitting method common to all Rose K designs. The design features an aspheric back optic zone, front surface toricity and front surface aberration control, according to Menicon. Additionally, Rose K2 Soft offers precise edge lift control, prism ballast stabilization and reverse geometry for a trouble-free fit, according to the company.

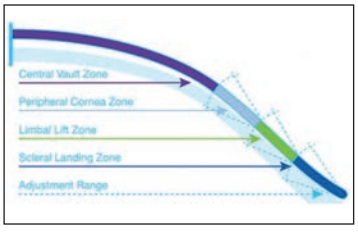
Visit www.roseklens.com.

ZenLens 28-lens Set

Zenlens comes in a new 28-lens set format to help optometrists better assess toricity in their scleral lens patients. Adding to the Zenlens 24-lens Dx format, the new 28-lens set adds four diagnostic lenses with toric peripheral curves. These additions can help specialty lens fitters quickly and accurately assess scleral toricity to better determine proper peripheral lens toricity, according to the company.

Visit www.aldenoptical.com/zenlens.

Center-near Multifocal Scleral Lens



Ampleye now offers optometrists a center-near multifocal with more add options for their patients with presbyopia. The standard center-near multifocal zone of 2.00mm is adjustable from 1.00mm to 4.00mm in 0.50mm steps, and add powers can be specified from +1.00D to +3.50D in 0.25D steps, according to Art Optical.

Visit www.artoptical.com.

Cataract Comanagement

Toric Multifocal IOL

Cataract patients will soon have a new option for correcting their presbyopia and astigmatism simultaneously. Alcon's AcrySof IQ Restor +3.0D multifocal toric IOL is designed to address presbyopia and pre-existing corneal astigmatism at the time of cataract surgery in adult patients who desire good near, intermediate and distance vision with an increased potential for spectacle independence, according to the company.

Already available internationally, Alcon will release the new IOL in the United States on a rolling basis starting in the first quarter of 2017.

Visit www.alcon.com.

Practice Management

Digital Marketing Guide

Acuvue's online marketing guide can help optometrists develop or optimize their digital marketing strategy to encourage new patient visits, stay engaged with current patients and keep patients informed of new contact lens options, according to Johnson & Johnson Vision Care.

The interactive guide includes topics such as targeting prospective patients, practice website development, social media marketing and more. Each chapter concludes with a worksheet to help clinicians map out a digital strategy and next steps.

In addition to the digital guide, optometrists can download and use free digital banner ads, social media posts and email templates.

The digital guide can be downloaded for free from www.acuvueprofessional.com, in the practice resources section, or at www.myacuvueresourcecenter.com (users must register to access additional resources). ■

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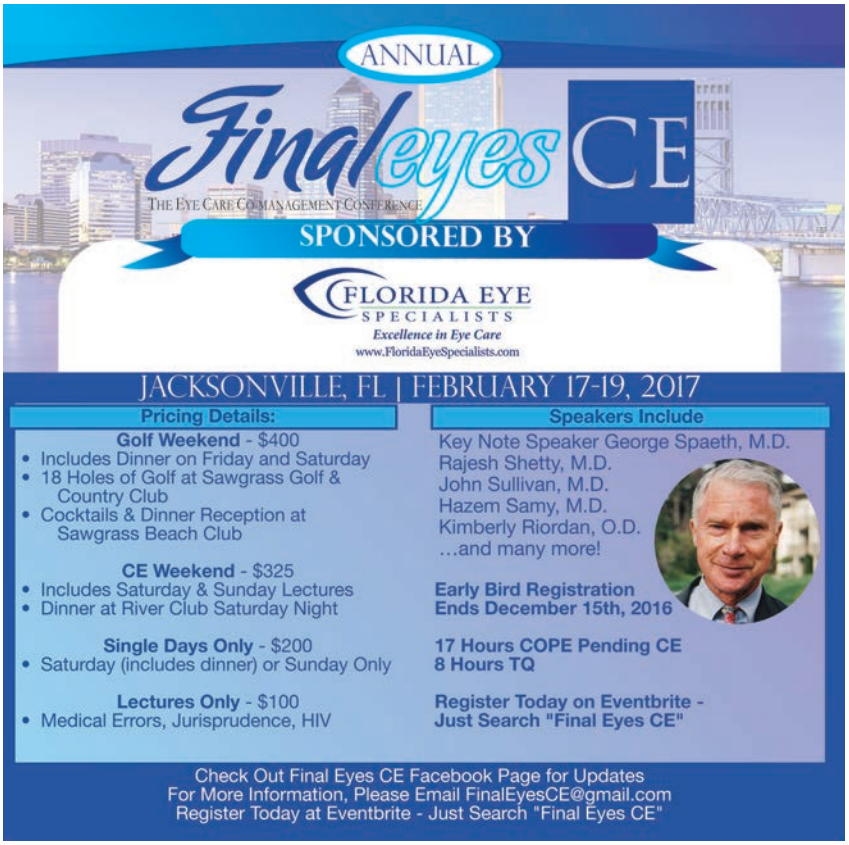

MEDICAL OPTOMETRISTS

The American Board of Certification in Medical Optometry (ABCMO) is recognized at Joint Commission (JC) accredited medical facilities as issuing board certification in the specialty of medical optometry and those ABCMO certifies are eligible for credentialing at these facilities as specialists rather than general optometry practitioners.^

The Joint Commission, the accepted national Gold Standard, reviews and accredits over 21,000 federal, state and local-chartered medical facilities.

To Be Eligible for ABCMO board certification:

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2. Pass the national Advanced Competence in Medical Optometry Examination
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.

For Application procedures see
www.abcmo.org
or contact myers.kenj@gmail.com

^ At this time, 127 JC accredited hospitals, clinics and teaching institutions recognize ABCMO specialist certification.
˙ www.jointcommission.org
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■ **21.** *Envision University Low Vision Grand Rounds.* Envision University, Wichita, KS. Hosted by: Envision University. CE hours: 2. To register, email michael.epp@envisonus.com or go to www.envisionuniversity.org.

■ **22.** *Benedict Professor in Practice Management & Administration.* UHCO Health & Biomedical Sciences Building, Houston. Hosted by: University of Houston College of Optometry. Key faculty: Sam Quintero. CE hours: 8. To register, email optce@central.uh.edu or go to ce.opt.uh.edu.

■ **22-28.** *2017 Island Eyes Conference.* Kauai Marriott Resort, Lihue, Kauai, Hawaii. Hosted by: Pacific University College of Optometry. Key faculty: Pat Caroline, Bradley Coffey, David Kading, Nate Lighthizer, Danica Marrelli, Lorne Yudcovitch. CE hours: 31. To register, email Jeanne Oliver at jeanne@pacificu.edu, call (503) 352-2740 or go to www.pacificu.edu/islandeyes.

■ **23.** *2017 Legislative Conference.* Capitol Plaza Hotel, Jefferson City, MO. Hosted by: Missouri Optometric Association. CE hours: 3. To register, email Lee Ann Barrett at moaed@moeyecare.org or go to www.moeyecare.org.

■ **23.** *IOP Day at the Capital.* Crystal Ball Room, Hoff Building, Boise, ID. Hosted by: Idaho Optometric Physicians. CE hours: 4. To register, email Randy Andregg at execdir@iopinc.org, call (208) 461-0001 or go to idaho.aoa.org.

■ **26-29.** *Global Specialty Lens Symposium.* Rio Hotel, Las Vegas. Hosted by: Pentavision, Contact Lens Spectrum. Key faculty: Joseph T. Barr, Craig W. Norman, David Kading, Scott Read, Stephanie Woo. CE hours: 50 total, 20 per OD. To register, email maureen.trusky@pentavisionmedia.com, call (215) 628-7754 or go to www.gslsynomposium.com.

■ **26-30.** *VT/Visual Dysfunctions.* Southern College of Optometry, Memphis, TN. Hosted by: Optometric Extension Program Foundation. Key faculty: Paul Harris. CE hours: 35. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org.

■ **27-29.** *33rd Annual Palm Beach Winter Seminar.* Hilton West Palm Beach, West Palm Beach, FL. Hosted by: Palm Beach County Optometric Association. Key faculty: Blair Lonsberry, Joseph Pizzimenti. CE hours: 20. To register, email Tamara Maule at pbwinterseminar@gmail.com, call (561) 477-3524 or go to www.pbcoa.org.

■ **28.** *TCOS Winter CE Event.* Marriott Ventura Beach, Ventura, CA. Hosted by: Tri-County Optometric Society. Key faculty: Randall Thomas, Ron Melton. CE hours: 4. To register, email benpalmer.od@gmail.com or go to www.tcosvision.org.

■ **29.** *VOA One-Day CE Conference.* Omni Charlottesville, Charlottesville, VA. Hosted by: Virginia Optometric Association. CE hours: 4. To register, email Bo Keeney at office@thevoa.org, call (804) 643-0309 or go to www.thevoa.org.

■ **29.** *Advances in Anterior & Posterior Segment Management.* Marshall B. Ketchum University, Fullerton, CA. Hosted by: Marshall B. Ketchum University. CE hours: 8. To register, email Antoinette Smith at asmith@ketchum.edu, call (714) 872-5684 or go to www.ketchum.edu/ce.

■ **29.** *Systemic Disease & Oral Pharmaceuticals Day.* SUNY College of Optometry, New York, NY. Hosted by: SUNY Office of Continuing Professional Education. CE hours: 6. To register, email Betsy Torres at ce@sunyopt.edu, call (212) 938-5830 or go to www.sunyopt.edu/cpe.

February 2017

■ **2-4.** *Ski + Learn Optometric/Dental Conference.* Sheraton Steamboat Resort, Steamboat Springs, CO. Hosted by: Optometric Education Adventures. Key faculty: Jack Schaeffer, Robert Wooldridge. CE hours: 12. To register, call Steve Looysen at (701) 952-2020 or go to www.optometricedadventures.com.

■ **2-5.** *VT/Strabismus & Amblyopia.* Office of Robin Lewis, Phoenix. Hosted by: Optometric Extension Program Foundation. Key faculty: Robin Lewis. CE hours: 28. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org.

■ **4.** *Illinois Optometric Association Winter CE Series.* Holiday Inn Matteson Conference Center, Matteson, IL. HOST: Illinois Optometric Association. Key faculty: Mark Dunbar. CE hours: 6. To register, email Charlene Marsh at ioabb@ioaweb.org, call (217) 525-8012 or go to www.ioaweb.org.

■ **4.** *2nd Annual Optometric Glaucoma Symposium.* Palace Hotel, San Francisco. Hosted by: Glaucoma Research and Education Group. Key faculty: Murray Fingeret, John G. Flanagan, Arthur D. Fu, Andrew G. Iwach, L. Jay Katz, Terri Pickering. CE hours: 3. To register, go to www.glaucoma.org/news/events/glaucoma-360.

■ **8.** *Indiana Optometry's Winter Seminar.* Ritz Charles, Carmel, IN. Hosted by: Indiana Optometric Association. CE hours: 7. To register, email Bridget Sims at blsims@ioa.org, call (317) 237-3560 or go to www.ioa.org.

■ **8-9.** *Michigan Optometric Association Winter Seminar.* Kellogg Hotel and Conference Center, East Lansing, MI. Hosted by: Michigan Optometric Association. CE hours: 12. To register, email Amy Root at amy@themoa.org or go to www.themoa.org.

■ **10-12.** *Heart of America Contact Lens and Primary Care Congress.* Sheraton Kansas City Hotel at Crown Center, Kansas City, MO. Hosted by: Heart of America Contact Lens Society. Key faculty: Ed Bennett, Tom Quinn, Christine Sindt, Joe Shovlin, Leo Skorin, Steven Ferrucci. CE hours: 63 total, 17 per OD. To register, email Craig Brawley at president@thehoacls.org, call (314) 799-7934 or (314) 843-5700 or go to www.hoacls.org.

■ **11.** *Winter Thaw.* Embassy Suites, Newark, DE. Hosted

by: Delaware Optometric Association. Key faculty: Andrew Morgenstern, Greg Caldwell, Carol Hoffman. CE hours: 7. To register, email Aaron Yatskevich at ayatskevich@vqeyecare.com or go to deoa.wildapricot.org/event-2327157.

■ **11-18.** *AEA Cruises Caribbean Optometric Seminar*. Aboard Royal Clipper, Caribbean. Hosted by: AEA Cruises. CE hours: 10. To register, email Marge McGrath at aeacruises@aol.com, or go to www.optometriccruiseseiminars.com.

■ **12.** *OptoWest 2017*. San Francisco Marriott Marquis, San Francisco, CA. Hosted by: California Optometric Association. Key faculty: Dawn Pewitt, Adam Shupe, Matthew Earhardt. CE hours: 6. To register, email Sarah Harbin at sharbin@coavision.org, call (916) 266-5022 or go to www.coavision.org.

■ **12.** *Glaucoma Symposium*. SUNY College of Optometry, New York, NY. Hosted by: Office of Continuing Professional Education. Key faculty: Murray Fingeret. CE hours: 6. To register, email Betsy Torres at ce@sunyopt.edu, call (212) 938–5830 or go to www.sunyopt.edu/cpe.

■ **17-19.** *Finaleyes CE 2017*. Baptist Medical Center, DuPont Auditorium, Jacksonville, FL. Hosted by: Florida Eye Specialists, Ted Brink & Associates and Baptist Health. Key faculty: George Spaeth, John Sullivan, Shawn Agee, Rajesh Shetty, Eric Botts, Kimberly Riordan. CE hours: 18. To register, email Susan Frick at finaleyesce@gmail.com, call (904) 200-1857 or go to www.finaleyesce.com.

■ **17-21.** *Annual Winter Ophthalmic Conference (formerly SkiVision)*. Snowmass Village, Aspen, CO. Hosted by: *Review of Optometry*. Key faculty: Murray Fingeret, Leo Semes, Andrew Archila, Eric Schmidt, Fred Edmunds, Jack Cioffi, John Flanagan, Howard Purcell, Jack Schaeffer. CE hours: 20. To register, email Lois DiDomenico at reviewmeetings@jobson.com, call (866) 730-9257 or go to www.skivision.com.

■ **18-25.** *Exploring Specialty Niches Within Optometry*. Royal Caribbean Cruise Line's Harmony of the Seas, Eastern Caribbean Cruise departing Ft. Lauderdale, FL. Hosted by: Dr. Travel Seminars and the New Jersey Society of Optometric Physicians. Key faculty: Edward L. Paul, Jr. CE hours: 16. To register, email info@drtravel.com or go to www.drtravel.com.

■ **19.** *3rd Annual Glaucoma Forum*. Marshall B. Ketchum University, Fullerton, CA. Hosted by: Marshall B. Ketchum University. CE hours: 8. To register, email Antoinette Smith at asmith@ketchum.edu, or go to www.ketchum.edu/ce. ■

To list your meeting, please send the details to:

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Diagnostic **Quiz**

Spotty History

By Andrew S. Gurwood, OD

History

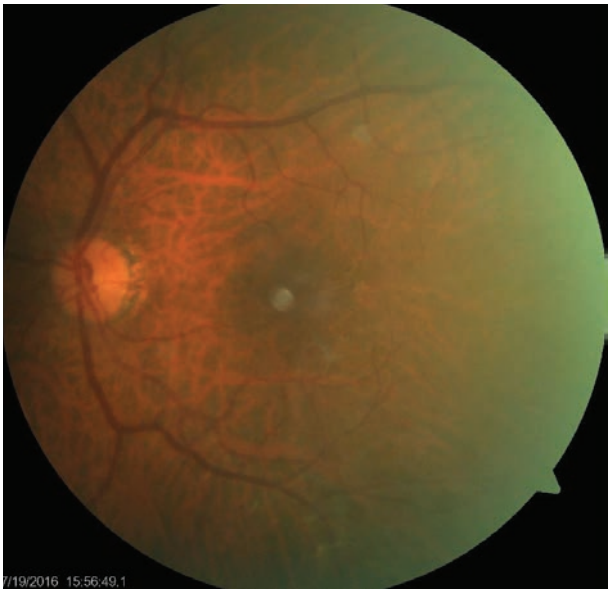
A 65-year-old black male presented with a chief complaint of blurry vision in his left eye. He had been experiencing this issue for two months. He denied any history of trauma or previous ocular illness. His medical history was remarkable for hypertension, for which he was medicated with lisinopril daily. He also denied allergies of any kind.

Diagnostic Data

His best-corrected entering visual acuities were 20/20 OD and 20/50 OS at distance and near. His external examination was normal for extraocular muscle movement, color, brightness and pupils; however, there was a central abnormality discovered using the facial Amsler during confrontational field testing, OS. Biomicroscopy found normal anterior segment structures and open Van Herick angles with Goldmann applanation tonometry that measured 15mm Hg, OU. The pertinent dilated fundus finding is demonstrated in the photograph.

Your Diagnosis

How would you approach this case? Does this case require additional tests? How would you manage this patient? What is the likely prognosis?



This dilated fundus photograph shows the posterior segment of the left eye of our 65-year-old male patient. He presented complaining of blurry vision in his left eye. Can you diagnose the patient's condition based on this information?

To find out, please visit us online at www.reviewofoptometry.com. ■

Retina Quiz Answers *(from page 94):* 1) a; 2) c; 3) d; 4) d.

Next Month in the Mag

In February, *Review of Optometry* will focus on the latest innovations in eye care.

Topics include:

- *Cornea: Stem Cell Therapies in Action*
- *Will Sustained-Release Drug Delivery Reinvent Glaucoma Therapy?*
- *The Life-Changing Capacity of Retinal Prostheses*
- *Will "Smart" Contact Lenses Deliver on Their Potential?*

February's issue will also feature stories on:

- *Identifying and Treating Meibomian Gland Dysfunction and Dry Eye in Younger Patients*
- *Are You Missing These Optic Nerve Disorders?* (earn 2 CE credits)
- *Congenital Anomalies of the Retinal Vasculature*

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1 After 1 week of wear; data on file.

2 The Vision Council. Eyes overexposed: the digital device dilemma: 2016 digital eye strain report.

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