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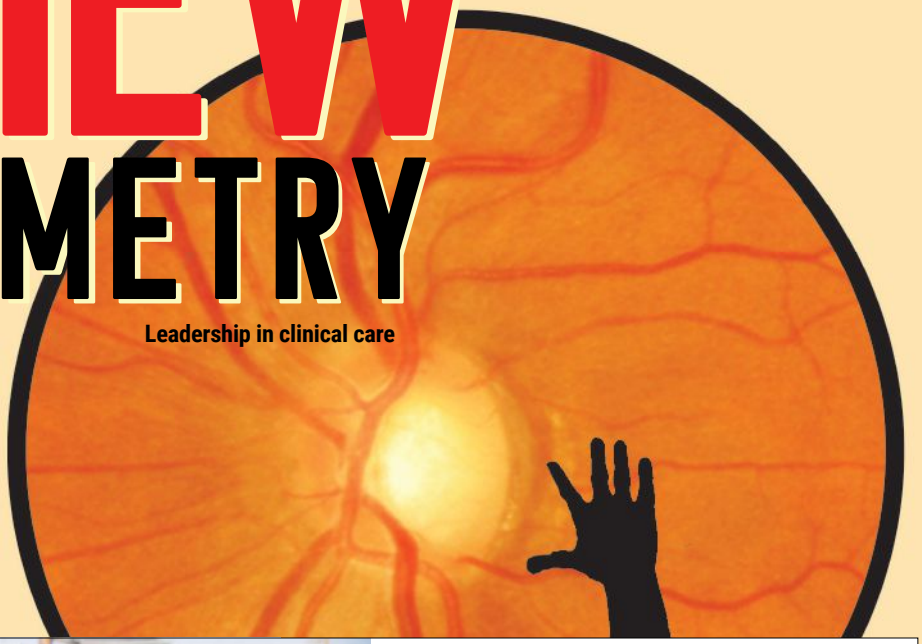

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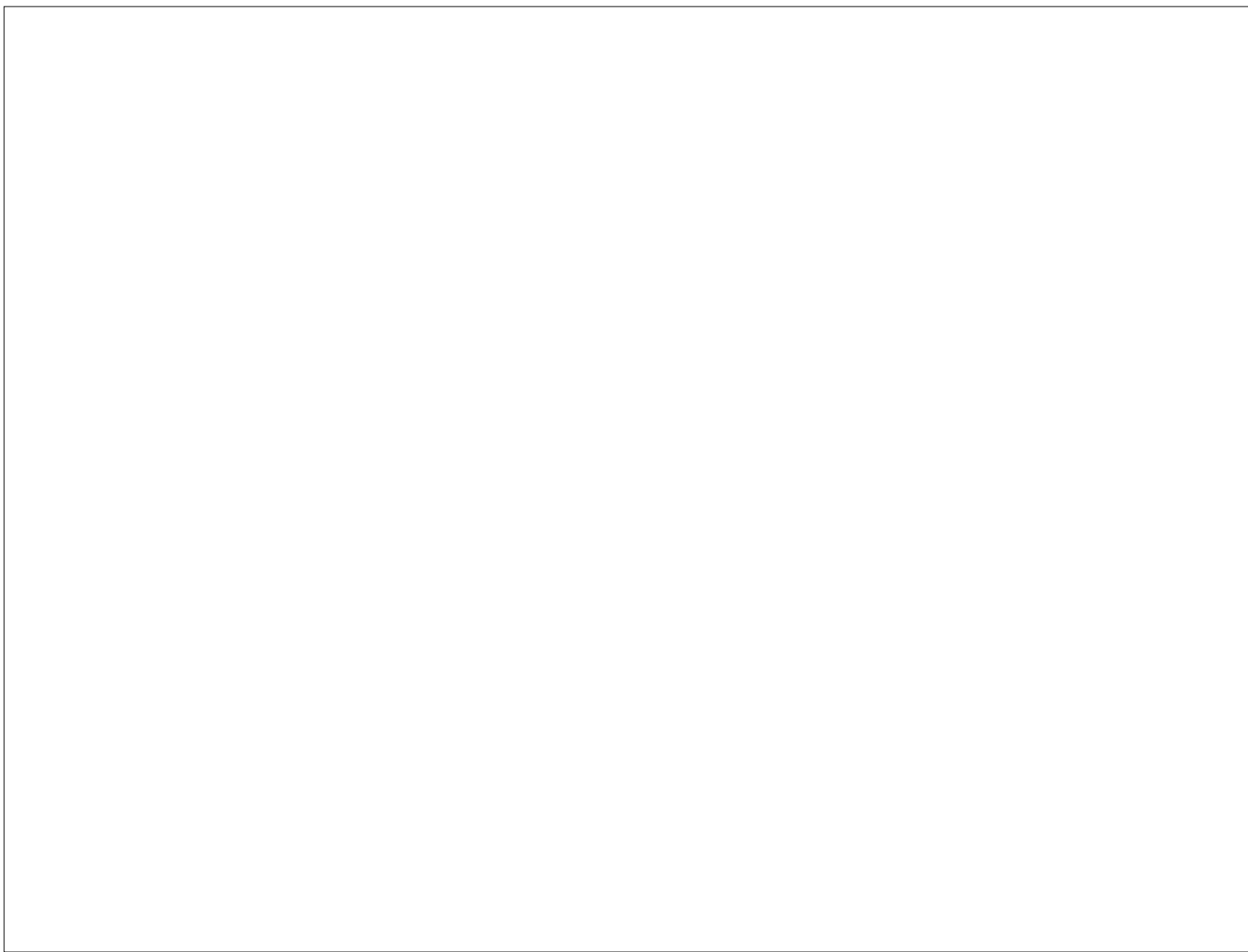

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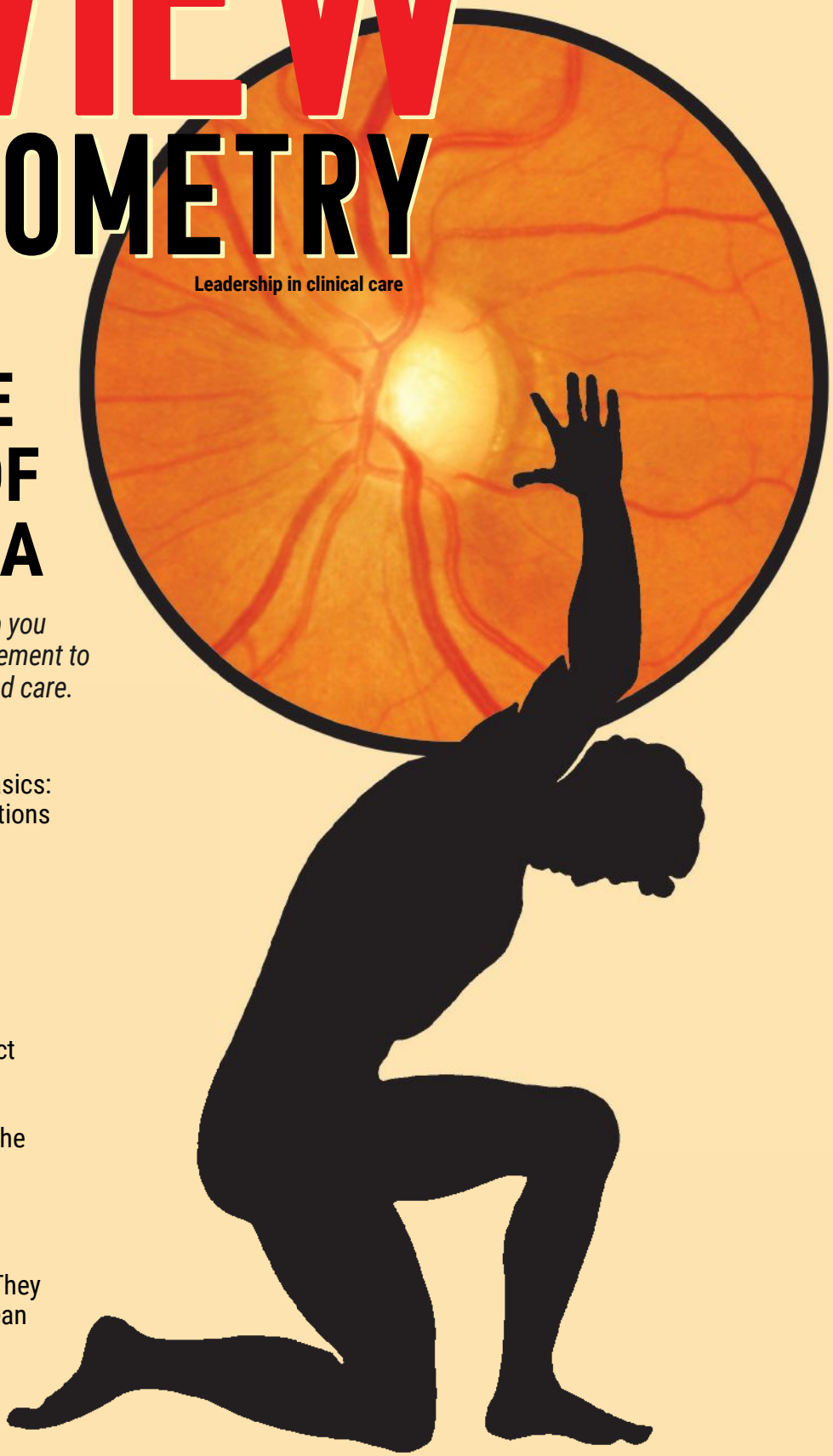

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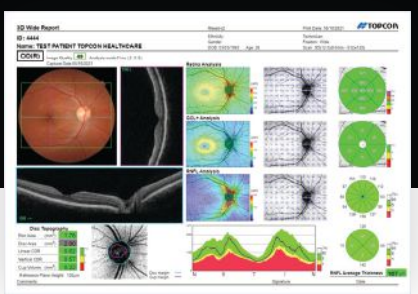

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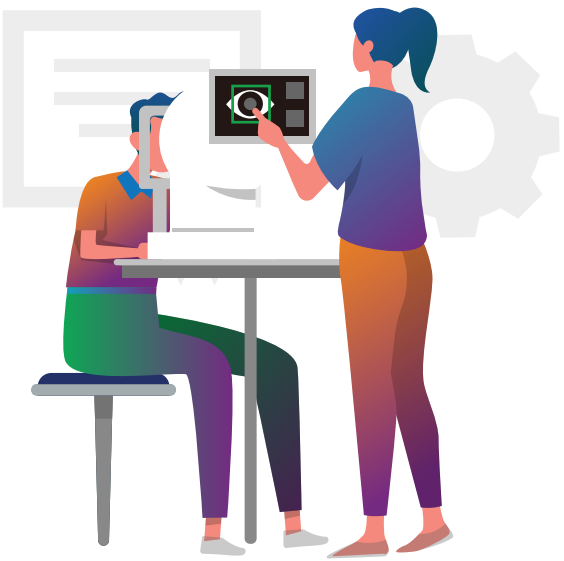

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TOPCON Healthcare

Iowa Gets Anesthesia Injections as Other States Pursue More Scope Gains

The law took effect July 1. In New Hampshire, a bill allowing ODs to administer certain vaccines heads to the governor, while NJ and Nebraska continue advocating for optometric laser rights.

In June 2020, Iowa was in hot pursuit of injection rights for several clinical indications, including subconjunctival injections to treat ocular conditions, intralesional injections to treat chalazia, botulinum toxin (including for cosmetic purposes) and injections to counteract an anaphylactic reaction. Due to last-minute negotiations to get the bill passed, a line was added omitting the use of injectable anesthetics.

In this year's legislative session, Iowa optometrists fought to reintroduce this line to the scope of practice, and they were successful. On April 28, Governor Kim Reynolds signed HR 347, allowing the nearly 1,400 ODs in Iowa to use injectable anesthetics when appropriate to practice optometry as licensed in the state. The exact line added to the practice scope reads that licensed ODs in Iowa have the right to use "local anesthetics prior to a minor surgical procedure authorized by this chapter."

"We went back to the legislators this time and explained that we really couldn't properly utilize injections without having access to the anesthesia portion," says Don Furman, OD, president of the Iowa Optometric Association. "The clarification allowed the original injections law to function as everyone originally intended it to."

The legislation received strong bipartisan support from both the Iowa Senate (48-2) and House (90-8). While the opposition expressed concern about the absence of additional training guidelines in HR 347, Dr. Furman explains that this is because "all relevant coursework was included in the original training requirements [in the 2020 bill]."

As all states pushing scope legislation would echo, OD-legislator relationships are key to ensuring that the individuals voting on the bill understand its importance. "Due to our efforts in building grassroots relationships with many of our state legislators, we were able to have factual discussions regarding how the original wording was a limiting factor in providing needed care to patients across the state," notes Dr. Furman. "We appreciate all of our legislators that provided bipartisan support for this language clarification, and we thank them for listening."

The updated law went into effect on July 1.

Proposed Laser Legislation Moves Forward in New Jersey

The prospect of optometric laser authority is growing closer for the nearly 1,300 ODs licensed in New Jersey, who haven't seen a change to their practice scope in almost 15 years aside from COVID emergency regulations. In May, the state introduced two identical bills to the Assembly (AB 5445) and Senate (SB 3841) proposing to allow New Jersey optometrists to perform three laser procedures—trabeculoplasty, capsulotomy and iridotomy—as well as remove chalazia, skin tags and other lesions. Additionally, the bills propose an expansion of optometrists' vaccination and prescription authority.

Photo: NJSOP

Optometrists Chris Quinn and Jessica Garden testified in favor of New Jersey's laser bill, AB 5445, on behalf of the NJSOP during a Committee hearing last week.

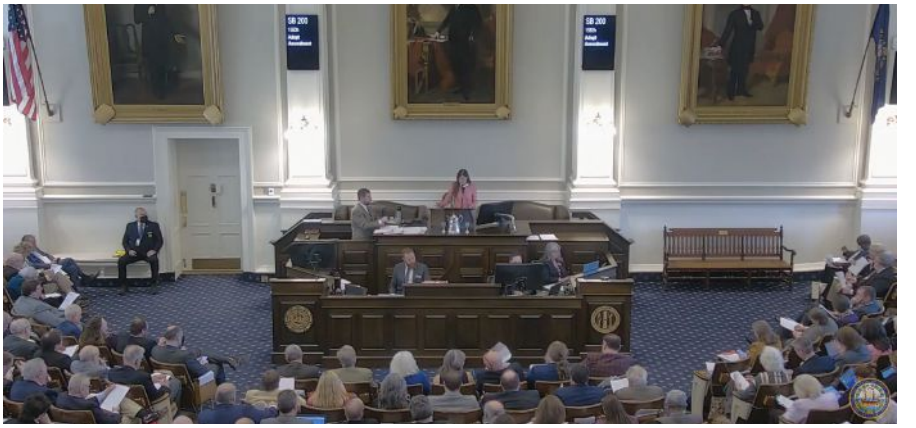
The Assembly bill was transferred to the Assembly Oversight, Reform and Federal Relations Committee on June 22. That same day, after hearing the testimonies of Chris Quinn, OD, and Jessica Garden, OD, of the New Jersey Society of Optometric Physicians (NJSOP), the Committee voted unanimously in favor of AB 5445 and sent it forward into the hands of the Assembly Regulated Professions Committee, which is next in line to debate the legislation in the coming weeks. If the bill passes that Committee, it will then be heard by the full Assembly. Meanwhile, SB 3841 is still awaiting a hearing within the Senate Commerce Committee.

During the Committee last month, Dr. Quinn—an optometrist practicing in Middlesex County and a past president of the NJSOP—remarked on the stand that "There will be three million New Jerseyans over the age of 60 by 2030, an increase of nearly a million individuals. These individuals will require increased healthcare services from a system and workforce that are already strained, but optometrists can be part of the solution."

Dr. Garden, who is also an NJSOP member and practicing optometrist in Hudson County, also pointed out during her testimony that there are nearly two times as many optometrists in New Jersey as there are ophthalmologists, and ODs serve as the primary eyecare provider for more than two-thirds of the state population. "This legislation allows optometrists to provide care when and where it's needed and will lower costs by eliminating duplication of services and additional co-pays, healthcare costs, caretaker arrangements, travel time and time spent with blurry vision," Dr. Garden told Committee members. "According to a 2019 report, issued by New Jersey-based Avalon Health Economics, nationally expanded optometric scope of practice results in an annual system-wide savings of $4.6 billion." She also cited a 2018 report from the US Department of Health and Human Services, which advised that "states should consider changes to their scope of practice statutes to allow all healthcare providers to practice the type of their license utilizing the full skillset."

NJSOP executive director, Keira Boertzel-Smith, JD, says, "The NJSOP thanks Drs. Chris Quinn and Jessica Garden for testifying on behalf of NJSOP." She adds that several new sponsors have signed onto the legislation in the last few weeks to help strengthen the support for the bill, which, if passed, would make New Jersey the 11th state in the country to permit the use of optometric lasers.

To learn how you can support New Jersey's legislative battle to add lasers and other procedures to its optometric practice scope, please contact the NJSOP.



An amendment to SB 200 was proposed in the New Hampshire House to delay mRNA vaccines by two years, which was denied with a vote of 105-275.

New Hampshire Vaccine Bill Awaits Governor's Signature

After passing both the Senate and House in early June, a bill in New Hampshire that would allow optometrists to administer FDA-approved vaccinations to adults for influenza, COVID-19 and shingles is on its way to the desk of Governor Chris Sununu for his signature, which is expected in the coming days or weeks. If SB 200 becomes law, it will increase the number of healthcare providers in the state able to administer these vaccines by several hundred.

In the House, a potentially disruptive amendment was introduced that would have delayed the bill's inclusion of mRNA vaccines by two years due to concerns regarding insufficient research on the vaccine's potential side effects. However, the House denied the amendment with a vote of 105-275, allowing the final bill to retain language that will permit ODs to administer mRNA COVID-19 vaccines to their patients.

Other minor amendments included in the final version of SB 200 relate to the qualifications of optometrists who wish to administer these vaccines to their patients. For example, unlike the introduced bill, the final document states that ODs must have at least $1,000,000 of professional liability insurance coverage and have active certification in basic cardiopulmonary resuscitation, along with other requirements.

The new law will take effect 60 days after Gov. Sununu's signature.

Nebraska SLT Bill Stalled Until 2024

On January 10, Nebraska introduced LB 216, a bill proposing to authorize the state's optometrists to perform selective laser trabeculoplasty (SLT), a noninvasive procedure that's increasingly being recognized as a first-line treatment for glaucoma. The legislation was last heard by the Health and Human Services Committee on January 26, where it currently remains awaiting a vote that's expected sometime next year.

The Nebraska Optometric Association (NOA) commented recently that it will be continuing its advocacy efforts with Committee members to vote the bill out of Committee during the 2024 legislative session. Nebraska ODs who want to participate in advocacy efforts can contact the NOA to learn how they can help strengthen optometry's voice in the state's ongoing battle for scope expansion.

Keep an eye on *Review of Optometry*'s online News Feed to stay informed and read periodic updates on new developments in various states' legal battles for scope expansion.

Keratoconus Prevalence 10x Higher Than Previous Reports

The greater sensitivity of Scheimpflug imaging is revealing cases that may otherwise have gone undiagnosed.

The exact prevalence of keratoconus has often been a matter of debate, as people of certain ethnicities (*i.e.*, those of Middle Eastern descent) are known to have much higher likelihood, but the condition is still considered a rare corneal disease globally. A seminal paper on the topic from 1986 pegged it at one case per 2,000 individuals.

A recent German study investigating the current prevalence of keratoconus and possible associated factors offered updated numbers. The team found that the prevalence of keratoconus in a mainly Caucasian population was approximately tenfold higher than previously reported in the literature when using the latest diagnostic technologies (Scheimpflug imaging). Contrary to previous assumptions, the researchers did not find associations with sex, existing atopy, thyroid dysfunction, diabetes, smoking or depression.

In the population-based, prospective Gutenberg Health Study, 12,423 subjects aged 40 to 80 were examined at a five-year follow-up. Subjects underwent a detailed medical history and a general and ophthalmologic examination including Scheimpflug imaging.

Of 10,419 subjects, 0.49% had keratoconus. This puts the prevalence closer to 200 to one for a Caucasian population. This prevalence was approximately equally distributed across different age groups. No gender predisposition could be demonstrated. Logistic regression showed no association between keratoconus and age, sex, BMI, thyroid hormone, smoking, diabetes, arterial hypertension, atopy, allergy, steroid use, sleep apnea, asthma or depression.

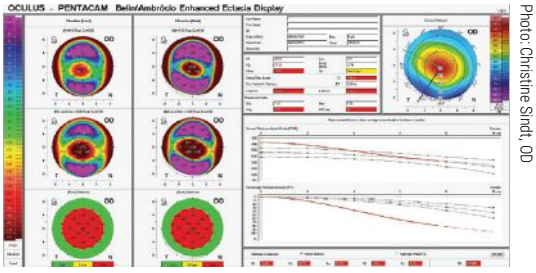


Photo: Christine Sindt, OD

In a study of over 10,000 predominantly Caucasian people, 0.49% were found to have keratoconus.

The researchers concluded that the study design and Scheimpflug analysis "enables a reliable statement on the prevalence and association with possible risk factors."

Marx-Gross S, Fieß A, Münzel T, et al. Much higher prevalence of keratoconus than announced results of the Gutenberg Health Study. Graefes Arch Clin Exp Ophthalmol. June 14, 2023. [Epub ahead of print].

Thicker Choroid Observed in Alopecia Areata

The pathogenesis of alopecia areata (AA) may involve an autoimmune mechanism mediated by T-cells. In some cases, ocular abnormalities such as cataract, tear film disruption and chorioretinal changes have been reported, leading researchers to investigate how the condition may affect retinal layers and choroidal structures. Their study found that the following may be observed in AA patients: T lymphocyte-mediated hair follicle damage, choroidal melanocyte damage and inflammation. They also concluded that choroidal thickness may increase secondary to melanocyte inflammation.

The researchers examined the right eyes of 42 AA patients and 42 controls with SD-OCT. They observed that in alopecia patients, choroidal thickness was significantly greater in the subfoveal, temporal and nasal regions.

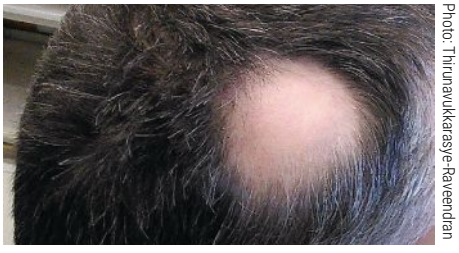


Photo: ThirunavukkarasyeRaveendran

Melanocytes in the choroid may be the link to the observed inflammation, as alopecia is mediated by T lymphocyte activity against pigmented cells.

The average thickness of the following layers was not different between alopecia patients and controls: ganglion cell layer, inner plexiform layer, inner nuclear layer, outer plexiform layer, outer nuclear layer, retinal pigment epithelium (RPE), inner retinal layers and photoreceptor layers.

"Considering that the main pathophysiology in AA is T lymphoid-mediated inflammation against melanocytes, the fact that we were unable to identify any significant difference in thickness between the macula and RNFL can be attributed to the absence of melanocytes in the macula and RNFL," the researchers explained in their paper. While the RPE does contain melanocytes, the authors hypothesized that the lack of a difference between RPE thickness in patients and controls may be attributed to the amount of melanin pigment and its position and distribution in RPE, as prior research has shown that RPE-related melanosomes may become displaced under various light frequencies (*i.e.*, on OCT images).

The team concluded that due to their thicker choroids, patients with alopecia should be closely monitored for possible posterior segment disorders.

Oren B, Aksoy Aydemir G, Duzayak S, Kiziltoprak H. Evaluation of retinal layers and choroidal structures using optical coherence tomography in alopecia areata. Medeni Med J. 2023;38:140-7.

Diabetic Retinopathy Management Protocols for Optometry

Paul Chous, MA, OD, FAAO
Chous Eyecare Associates

Dorothy Hitchmoth, OD, FAAO
Dr. Dorothy Hitchmoth, PLLC

Bobby "Chip" Wood, OD
Wood Vision Source, Coyote Optical

In your opinion, are there clear protocols in optometry for managing patients with diabetes?

Dr. Chous: Unfortunately, there are not. This unmet need in our profession creates a lot of variation in patient care and, ultimately, in patient outcomes.
Dr. Wood: I couldn't agree more. We absolutely need some basic guidelines and concrete strategies that standardize how we meet this growing patient need.
Dr. Hitchmoth: Some would argue that a dilated fundus exam and visual acuity check tick the box, but in my experience, it's not enough. In many cases, these basics don't give us the confidence to say that we're doing all we can for patients.

What more can optometrists do without putting too much strain on their practices and staff?

Dr. Chous: I've been giving this a lot of thought this past year and I think it's helpful to look at the fundamentals of diabetic retinopathy management across broad categories. We need to 1) detect, 2) grade, 3) assess risk, 4) manage, and 5) support.
Dr. Wood: As basic as this sounds, it can be a tall order. Grading and assessing risk require a lot of skill and time, and are arguably subjective.
Dr. Hitchmoth: Subjectivity is a big part of the problem. What's needed is a blueprint that provides some guidance on putting the puzzle pieces together.

If you looked at these five categories one by one, starting with detection, what would you put forward as essential practice guidelines?

Dr. Hitchmoth: I would start by saying that we need to approach diabetic retinopathy as a chronic progressive disease.
Dr. Wood: Exactly. And being a chronic progressive disease implies that you can detect it before it becomes advanced disease. The question is, how do we do this?
Dr. Chous: To begin, we need to use both structural and functional testing. OCT-A is a real game changer in structural testing. And on the functional side, although the standard of care for the assessment of vision loss due to diabetic retinopathy is high-contrast visual acuity, evidence shows it is insufficient.
Dr. Hitchmoth: I advocate for electro-diagnostic testing (ERG), preferably utilizing the additional measure of pupillometry, as in the DR score offered by the RET*eval*® device, since this provides a direct reading of retinal health.

In the grading category, what do you recommend?

Dr. Chous: At the most basic level, diabetic retinopathy should be graded at the time of diagnosis and at each subsequent visit. Charting is also important and should include a record of structural retinal damage.
Dr. Wood: Quantifying retinal cell function is likewise essential. For this, I use ERG. ERG is a measure of the function of the retina, the health of the cells, and the risk of disease progression that is fast and easy to perform using the handheld RET*eval* device.

How do you assess risk?

Dr. Chous: Here again, both structural and objective functional measures are crucial, and the two may not align, which makes things tricky.
Dr. Hitchmoth: We may be used to seeing structure first when we rely on visual acuity, but when using objective tests such as ERG, functional loss can precede identifiable structural damage. That's important information that plays a role in how I monitor and manage the patient moving forward.

Do you have any guiding principles in terms of management?

Dr. Chous: The time between retinal examinations depends on risk assessment, but no matter how severe or early the disease is, I strongly believe that multi-disciplinary resources are required to manage all diabetic retinopathy patients.
Dr. Hitchmoth: Good nutrition is also essential and is something we should emphasize with our patients.

Finally, in terms of support, what can optometrists do to help patients who have diabetes?

Dr. Wood: First and foremost, we need to provide comprehensive patient education and strategies to help prevent disease progression.
Dr. Chous: To that end, it's important to emphasize the asymptomatic nature of DR at its earliest, most treatable levels of severity and encourage patients to achieve individually optimized metabolic control in concert with their diabetes physicians.

Choriocapillaris Exhibits Changes with Alzheimer's

Using OCT-A, researchers found microvasculature alterations to this structure and the retina.

A new study outlined how the eye may be connected with neurodegenerative disease. Specifically, retina and choriocapillaris vascular structure characteristics were analyzed to look for biomarkers of Alzheimer's disease. Since the brain and retina share embryologic origins and are affected through similar vascular changes, the researchers thought OCT angiography (OCT-A) of these eye structures might reveal telling changes.

OCT-A was performed on 18 patients with early Alzheimer's disease and 18 age-matched controls. All participants also underwent neurologic and ophthalmic examinations. What they found was that the choriocapillaris exhibited a significant flow area reduction in the Alzheimer's disease group. Subsequently, early Alzheimer's may impair circulation of the structure.

The authors do mention that the choriocapillaris doesn't share the same embryologic origins as the retina. However, its close relation to responsibility for nourishment and metabolism of retinal photoreceptors may make it susceptible to retinal damage from Alzheimer's. Postmortem studies reveal beta amyloid plaques aggregated in retinal vessels, thus the vascular structure and fluid dynamics of the choriocapillaris may be vulnerable to damage from this accumulation, even in the choroid, leading to possible modification of its anatomy and physiology.

The authors add that they found a trend of vessel density reduction of the superficial capillary plexus and another trend, although statistically insignificant, of reduced vessel density of the deep capillary plexus in mild cognitive impairment, which agrees with previous reports. One report describes this finding as the potential result from direct beta amyloid accumulation inside vessel walls, causing loss of microvasculature and consequent reduction of vessel density through a local inflammatory process.

The early patients with Alzheimer's in this study and preferential involvement of the superficial capillary plexus is consistent with a prior report finding early involvement of the inner retina and superficial capillary plexus. Outer retina involvement was only seen with late impairment.

Based on their results and corroborated by similar studies' findings, the authors stated "it has been hypothesized that OCT-A data from patients with Alzheimer's could be used as an alternative biomarker to those currently available that may allow more easily accessible diagnosis and follow-up parameters for the disease, applicable even on a large scale."

They did recognize that "improved software for OCT-A devices is necessary, especially regarding choriocapillaris flow area assessment, and further studies are warranted to better understand the retinal and choroidal vascular changes in Alzheimer's patients."

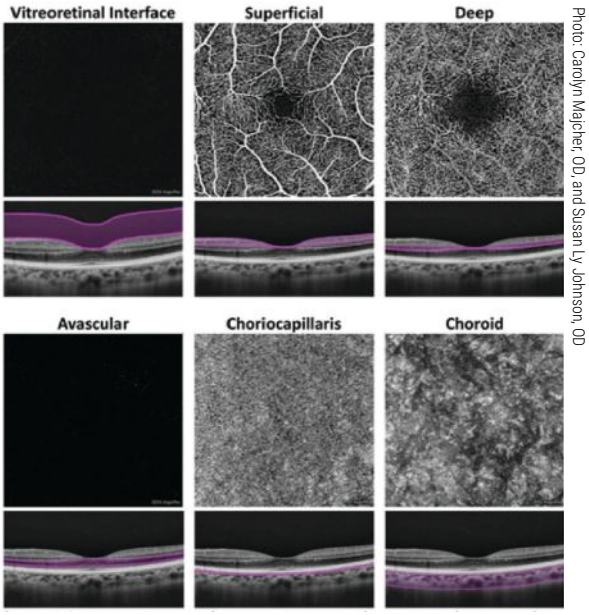


Photo: Carolyn Majcher, OD, and Susan Ly Johnson, OD

Accumulation of beta amyloid macroscopically induces a wide range of vascular abnormalities, including vascular attenuation, vessel tortuosity, narrowed veins, reduced branching complexity and increased width of vessels.

Di Pippo M, Cipollini V, Giubilei F, Scuderi G, Abdolrahimzadeh S. Retinal and choriocapillaris vascular changes in early Alzheimer disease patients using optical coherence tomography angiography. J Neuroophthalmol. June 23, 2023. [Epub ahead of print].

IN BRIEF

Peripapillary Microvascular Perfusion Linked to Renal Function. Researchers in China evaluated the association between peripapillary microvascular perfusion and renal function in individuals with type 2 diabetes but no diabetic retinopathy. Their findings confirmed a relationship. In particular, **peripapillary vessel density and choriocapillaris flow void density percentage were independently correlated with renal function.**

A total of 1,629 patients underwent 6x6mm optical OCT-A centered on the optic nerve head. Swept-source OCT-A assessed various microcirculation parameters.

Compared with individuals without chronic kidney disease, **peripapillary vessel density was significantly lower in those in the chronic kidney disease group and worsened as estimated glomerular filtration rate (GFR) declined.** GFR is a measure of how much blood passes through the kidneys per minute. After adjustment for covariates, higher GFR was significantly associated with higher peripapillary vessel density in the radial peripapillary capillaries, in the superficial capillary plexus, in the deep capillary plexus and lower choriocapillaris flow void density percentage in the entire images. The parameters in the inner ring of the radial peripapillary capillaries, deep capillary and choriocapillaris flow void density percentage were significantly associated with microalbuminuria.

"Our study results further support the theory that microvascular screening of ocular [structures] has potential value for detecting microvascular damage in the kidney due to diabetic nephropathy," the researchers wrote in their paper for the journal *Ophthalmology Science*. "Further longitudinal studies are needed to clarify the peripapillary vessel changes during chronic kidney disease progression," they concluded.

Guo X, Zhu Z, Cheng W, et al. In vivo visualization and quantification of optic disc microvasculature for assessing renal dysfunction. Ophthalmol Sci. July 3, 2023. [Epub ahead of print].

Compromised Kidney Function Associated with RNFL, GCIPL Thinning

This pattern should be closely observed to differentiate between neuroretinal damage caused by glaucoma and that associated with chronic kidney disease.

Previous studies have investigated the relationship between chronic kidney disease (CKD) and retinal nerve fiber layer (RNFL) and ganglion cell-inner plexiform layer (GCIPL) thickness, but findings have been inconsistent. In a new multi-ethnic Asian population study, researchers investigated the association of kidney function status with RNFL and GCIPL thickness and found that compromised kidney function is linked to damage in both structures.

A total of 9,594 Asians eyes from the Singapore Epidemiology of Eye Diseases Study and 87,649 Caucasian eyes from the UK Biobank were included, making this one of the largest studies to date investigating this association, according to the authors.

In individuals with CKD and suboptimal kidney function, significant RNFL and GCIPL thinning was observed and was largely consistent across Asian and Caucasian eyes. These findings further support the notion that individuals with CKD may be more susceptible to RNFL and GCIPL thinning, according to the authors, which is an important marker for glaucoma development.

CKD and reduced estimated glomerular filtration rate (eGFR) were associated with thinner peripapillary RNFL in Asian eyes. Similarly, in Caucasian eyes, reduced eGFR was associated with thinner macular RNFL. Consistently, in Asian eyes, the team observed that CKD and reduced eGFR were associated with thinner GCIPL. CKD was also associated with GCIPL thinning in Caucasian eyes.

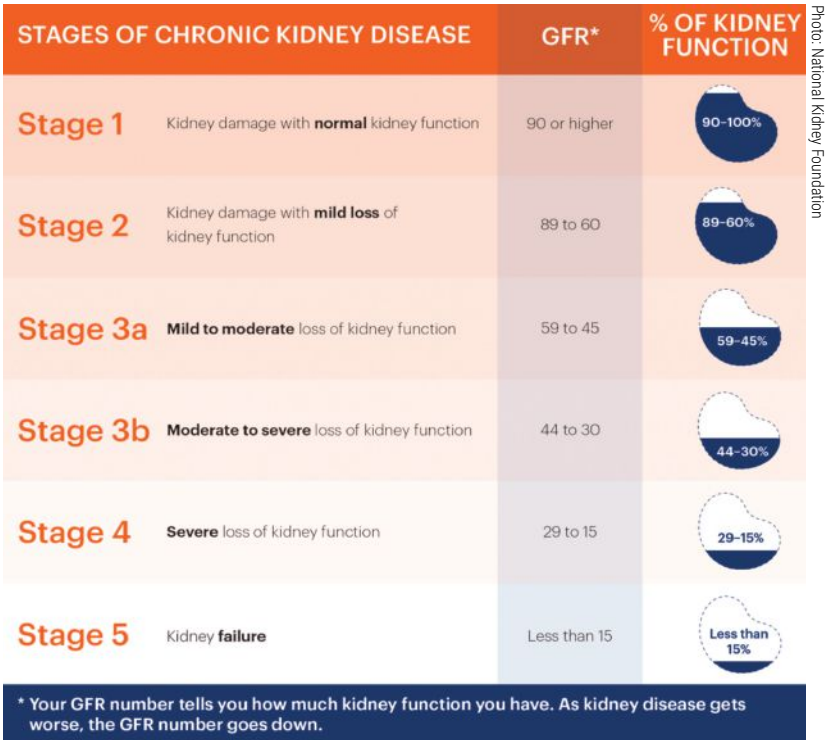


Photo: National Kidney Foundation

Chronic kidney disease and compromised kidney function are associated with thinner RNFL and GCIPL in both Asian and Caucasian eyes, according to this study.

"Across Asian and Caucasian eyes, when evaluating the different stages of kidney disease, we observed a significant trend between declining kidney function with thinner RNFL and GCIPL," the authors wrote in their paper for *Ophthalmology Science*. "Taken together, these findings across Asian and Caucasian eyes further corroborate the overall relationship of kidney function with RNFL and GCIPL thickness."

The authors found it interesting that RNFL and GCIPL thinning were more prominently observed in Malay and Indian eyes, which may be partially explained by the inherent thinner RNFL and GCIPL profiles in these patients, "thus potentially predisposing them to be more susceptible to retinal microvasculature damage from CKD," they explained in the study.

The association between kidney disease and neuroretinal thinning may be explained by shared structural and pathophysiological mechanisms that affect both the kidney and retina, as both are more vulnerable to microvascular damage from systemic disease. "Additionally, pathogenic mechanisms such as chronic inflammation and oxidative stress have been known to cause injury to retinal and renal layers," the authors noted.

"Furthermore, given that RNFL and GCIPL thickness are established markers of glaucoma, it is advisable for clinicians to closely observe the pattern of RNFL and GCIPL loss as a means of distinguishing between glaucomatous and CKD-related neuroretinal loss," they continued. "On this note, individuals with CKD may warrant regular eye examinations."

Majithia S, Chun Yuen Chong C, Chee Li M, et al. Associations between chronic kidney disease and thinning of neuroretinal layers in multi-ethnic Asian and Caucasian populations. Ophthalmol Sci. June 14, 2023. [Epub ahead of print].

How Today's Digital Demands Impact Contact Lens Patients

How digital devices affect the eye

Since 2019, digital device use has increased 35%,[1] with adults now using desktop computers and mobile devices for more than 13 hours per day.[1] Looking at digital screens can result in 60% less blinking, which can compromise a patient's tear film and may cause discomfort.[2,3] As a result, optometrists may need to ask additional questions of their regular device users and consider alternative contact lens options.

During the pandemic, eyecare professionals began noticing an increase in digital eye strain. This has been validated in a study where multivariate analysis revealed associations between digital eye strain and the following

device, age, optical correction, employment status, gender, the use of drops, and duration of use.[4]

With 71% of contact lens wearers admitting to increased screen time for work and life since 2020,[5] digital devices have the potential to impact many patients, given that more than 40 million people in the United States wear contact lenses.

patients, 75% agreed they want more from their contact lenses, including increased comfort and clarity.[5]

Life demands **more of our eyes**

Adults spend 13+ hours daily on digital devices: **35% increase** since 2019[1]

60% less blinking from looking at digital screens compromises the tear film and can cause discomfort[2,3]

Blue-violet light is **all around us**. These shorter wavelengths scatter light more and can impact visual clarity.[4]

These symptoms get **worse as we age**

1. Eyesafe estimate based upon Nielsen Q3 2019 Total Audience Report. 2. Tsubota K, Nakamori K. Dry eyes and video display terminals. N Engl J Med. 1993;328(8): 584. doi: 10.1056/NEJM199302253280817. 3. Patel S, Henderson R, Bradley L, et al. Effect of visual display unit use on blink rate and tear stability. Optom Vis Sci 1991;68(11):888-892. doi: 10.1097/00006324-199111000-00010. 4. JJV Data on File 2022. Blue-Violet Filter Utilized in ACUVUE® OASYS MAX 1-Day Contact Lenses.

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1. Eyesafe estimate based upon Nielsen Q3 2019 Total Audience Report.
2. Patel S, Henderson R, Bradley L, et al. Effect of visual display unit use on blink rate and tear stability. Optom Vis Sci. 1991;68(11):888-892.
3. Tsubota K, Nakamori K. Dry eyes and video display terminals. N Engl J Med. 1993;328(8):584. doi: 10.1056/NEJM199302253280817.
4. Alabdulkader B. Effect of digital device use during COVID-19 on digital eye strain. Clin Exp Optom. 2021;104(6):698-704.
5. JJV Data on File, survey fielded to 468 contact lens wearing patients in the US in April 2022.
6. Cope JR, Collier SA, Nethercut H, Jones JM, Yates K, Yoder JS. Risk Behaviors for contact lens–related eye infe-ctions among adults and adolescents — United States, 2016. MMWR Morb Mortal Wkly Rep. 2017;66(32):841-5.
7. JJV Data on File 2022. Blue-Violet Filter Utilized in ACUVUE® OASYS MAX 1-Day Contact Lenses.
8. JJV Data on File 2022. TearStable™ Technology Definition.
9. JJV Data on File 2022. Effect on Tear Film and Evaluation of Visual Artifacts of ACUVUE® OASYS MAX 1-Day Family with TearStableTM Technology.
10. JJV Data on File 2022. Material Properties: 1-DAY ACUVUE® MOIST, 1-DAY ACUVUE® TruEye®, ACUVUE® OASYS 1-Day with HydraLuxe™ Technology and ACUVUE® OASYS MAX 1-Day with TearStable™ Technology Brand Contact Lenses and other daily disposable contact lens brands.

Also Available in Multifocal

Why does blue light matter?

Data is limited about whether or not blue light exposure affects ocular health, but it is well established that shorter wavelength blue-violet light scatters more, and this can impact visual clarity.[7]

Many eyecare professionals are reporting that their patients are asking if they should be concerned about blue light exposure from digital devices and when outdoors.

Baley Petersen, OD.
Daniel Island Eye Care
South Carolina

"Whether they work outside, spend their time out on the water, or, like so many, spend long hours on digital devices, many of my patients know about blue-violet blocking glasses and are proactively asking if this is an option in contact lenses.

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ACUVUE® OASYS MAX 1-Day lenses harness an unprecedented combination of technologies designed to help meet the demands of today's digital generation.[8]

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The visual needs and demands of patients have ultimately changed over time and will continue to evolve. It is important for eye care professionals to continue to consider alternative contact lenses and how they may provide a better visual experience for patients and potentially better outcomes.

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Study Identifies Optimal Ocular Hypertension Testing Intervals

Visual field monitoring frequency can be customized for each patient depending on risk, but researchers recommend at least once or twice per year.

Catching visual field progression as early as possible can help patients retain more functional vision, but considering the burden that additional testing places on patients and clinics, it's important to find the right testing frequency. Published last month in the *Journal of Glaucoma*, the first study to identify optimal testing frequency for detecting visual field progression in ocular hypertensive patients reported that once- and twice-yearly visual field testing is most ideal for most hypertensive patients.

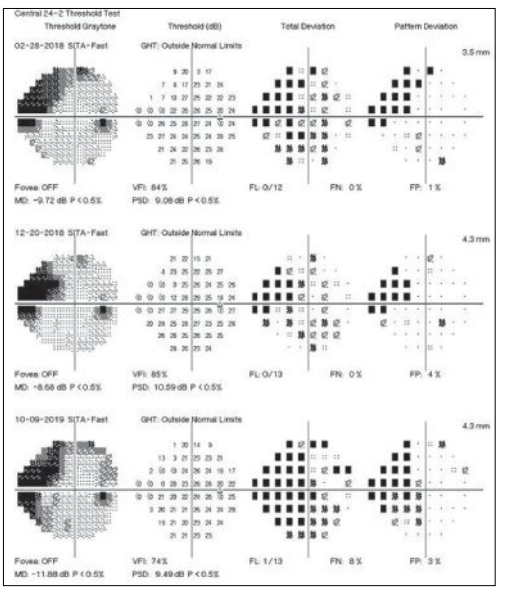

Photo: Brian D. Fisher, OD

Identifying optimal visual field testing frequencies can help reduce clinic burden.

The researchers analyzed 16,351 reliable 30-2 visual field tests from 1,575 eyes in the Ocular Hypertension Treatment Study (OHTS) observation arm. Using computer simulations (n=10,000 eyes) based on mean deviation values and residuals of risk groups, they estimated time to detect progression at testing intervals of four, six, 12 and 24 months (progression: -0.42dB/year). Time to detect a -3dB loss was considered an estimate for clinically meaningful perimetric loss.

At 80% power and -0.42dB/year progression, they found that the best tradeoffs to detect clinically meaningful significant changes in visual field loss were six-month intervals for high-risk patients, six-month intervals for medium-risk patients and 12-month intervals for low-risk patients.

The researchers emphasized in their paper that rapidly progressing ocular hypertensive patients should be monitored and tested more frequently to catch potential glaucoma conversion. The testing interval used in the OHTS was six months, considered optimal by the present study whose investigators note that clinical trial conditions and resources rarely align with real-world situations, where frequent visual field testing is often challenging.

"In light of the OHTS findings regarding risk calculation," they wrote in their paper, "clinicians can now customize the frequency of testing for each patient once the baseline risk variables are collected. This may ultimately reduce costs to patients and the healthcare systems as well as minimize risks associated with unnecessary office visits."

"Since previous findings have presumed no clear benefit from intense monitoring of ocular hypertensive patients, a combination of visual field tests and structural analyses may enable further spacing of those intervals," the authors concluded. "Furthermore, our results may help reduce the burden of frequent office visits, particularly in low-risk patients."

Melchior B, De Moraes CG, Paula JS, et al. What is the optimal frequency of visual field testing to detect rapid progression among hypertensive eyes? J Glaucoma. June 21, 2023. [Epub ahead of print].

IN BRIEF

Posterior Staphyloma High Risk Factor of Myopic Maculopathy. In a new Spanish study, researchers analyzed posterior staphyloma cases for the incidence and severity of myopic maculopathy and its repercussions on visual prognosis. Included were 473 eyes from 259 high myopic patients (70.7% female). After looking at multimodal imaging, the researchers observed posterior staphyloma in 69.4% of eyes. These eyes were older, had longer axial length, worse BCVA and greater stage in each of the ATN grading system components, which classifies myopathy according as atrophic, tractional or neovascular. **Macular involvement with staphylomas had worse BCVA, greater axial length and ATN. Eyes with pathologic myopia and severe pathologic myopia saw posterior staphyloma presence risk of 89.8% and 96.7%, respectively. Posterior staphyloma was the best predictor of BCVA for myopes.**

Of all the posterior staphylomas, 73.4% were primary. Subtypes by frequency were peripapillary (type III), then inferior (type V), narrow-macular (type II) and wide-macular staphyloma (type I) at 20.1%, 16.8%, 16.5% and 11.6%, accordingly. These percentages differ from previous reports that show wide-macular type was the most common, followed by narrow-macular, which is likely because this study cohort was Caucasian-Mediterranean.

Although several factors have an impact on visual acuity in high myopes, **this study found that best predictor for BCVA was the presence of posterior staphyloma, accounting for 12.1% of BCVA variability. What's more, increased axial length was linked to decreased BCVA, explaining 10.9% of variability.**

The researchers elucidate how posterior staphyloma presence **"determines high risk of myopic maculopathy and therefore worse visual prognosis, representing the best predictor for BCVA."**

For clinicians, it is suggested that **"posterior staphyloma should be considered practically as a constant hallmark of pathologic myopia and its severe form determining the follow-up and prognosis of these patients."**

Flores-Moreno I, Puertas M, Ruiz-Medrano J, et al. Influence of posterior staphyloma in myopic maculopathy and visual prognosis. Eye. June 26, 2023. [Epub ahead of print].

Parents Lack Eyecare Knowledge at Kid's Expense

Timing is critical if any vision problems arise in children, especially because many are asymptomatic. This reinforces the obvious: the importance of children undergoing eye exams at a young age, but instead, many are not screened. In a new study, researchers explored the role of parental health beliefs in parents seeking eye exams for their children.

A total of 100 parents whose children underwent an eye exam in Israel completed a questionnaire. Results showed that only 29.6% of parents knew that a vision screening was performed in first grade, and 10% were unsure where to find local eye care for their kids.

When looking into parental misconceptions, 19% of the parents were concerned their child would unnecessarily be prescribed glasses, and 10% believed glasses weaken a child's eyes.

This study shows that knowledge deficits may also be a barrier. Only 60% of respondents knew that vision screenings in schools do not check all vision problems, and only 55% knew that intermittent squinting between ages one and seven is not normal.

"Only 28% of the parents knew that wearing eyeglasses under age seven—when necessary—strengthens vision," the authors explained in their paper. "This study revealed that health beliefs play an essential role in parent seeking of eye care for their children," they concluded "Namely, parents will seek an eye exam for their child if they believe their child is susceptible to vision problems, are free of misconceptions, have adequate knowledge regarding vision and eye exams in children and are aware of available services. Thus, interventions that aim to improve parental education about eye care and examination timing, while raising awareness regarding childhood vision problems, dispelling misconceptions and providing parents with practical information regarding available services, are needed. It also seems that national public health messaging is needed to reach as many parents as possible."

Photo: Getty Images

Interventions are needed to improve parental education on child eye care and exam timing.

Masarwa D, Niazov Y, Natan MB, Mostovoy D. The role of parental health beliefs in seeking an eye examination for their child. BMC Ophthalmol. June 13, 2023. [Epub ahead of print].

Multifocal CLs No Threat to Kids' Accommodation

Though some effect was observed in a recent study, there were no untoward consequences long-term after four and a half years of wear.

Among the concerns on doctors' minds when contemplating myopia management interventions is the potential adverse effects of a given therapy—always a concern in any clinical scenario but all the more so in a developing child. Although use of multifocal contact lenses can alter accommodation somewhat, no long-term study had previously evaluated if the modality could affect a patient's ability to read comfortably and accurately over a prolonged period. To investigate this potential effect, study researchers compared the accommodative response to a 3.00D stimulus between single vision, +1.50D add and +2.50D add multifocal contact lens wearers during three years of wear. Accommodative amplitude, lag and facility between the three groups were then compared after 4.7 years of wear on average.

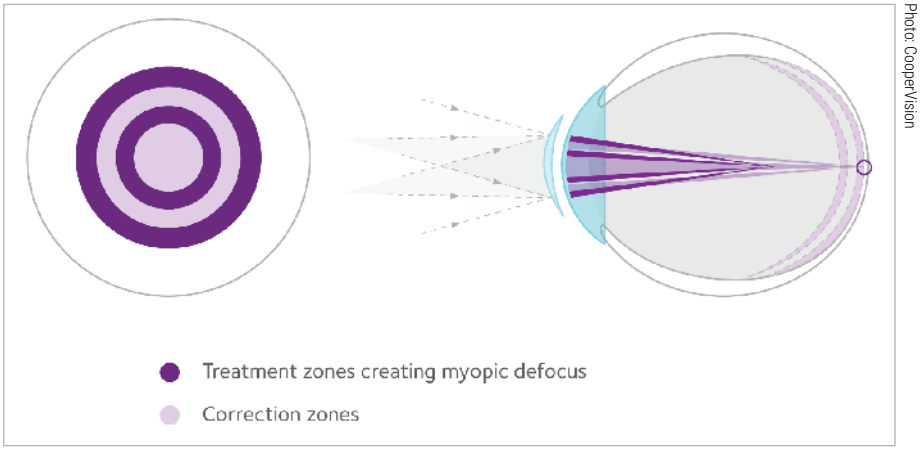

Photo: CooperVision

Accommodative amplitude, lag and facility was not affected long-term for children wearing multifocal contact lenses for myopia control.

Participants in the landmark BLINK study conducted by Coopervision, totaling 294 children aged seven to 11, were randomly assigned to wear one of the three types of soft multifocal soft lenses: single vision, +1.50D add or +2.50D add center-distance. Accommodative response to a 3.00D stimulus was recorded at baseline and annually for three years. Objective accommodative amplitudes, lead/lag and binocular facility with ±2.00D flippers were measured after 4.7 years.

The strength of the lenses did seem to have an intermediate effect on accommodation before the final measurements at 4.7 years. The +2.50D add lens wearers saw lower accommodative response by at least 0.50D to a 3.00D stimulus over single vision wearers for three years; the +1.50 add wearers also experienced lower accommodative response of almost 0.75D over single vision wearers, but this reduced until there was no difference between these two groups at final visit and persisted for only two years.

After adjusting for clinic site, sex and age group, there were no clinically relevant differences of the three groups for accommodative amplitude, accommodative lag or accommodative facility after the average 4.7 years of wear.

Mapping their results onto other studies, the researchers note that accommodative amplitude was not affected by long-term multifocal lens wear, as seen in prior literature, but the accommodative amplitudes measured in this study were lower overall than in two previous studies. They attribute this difference to their use of objectively measuring amplitudes, whereas the other two studies measured subjectively, which can overestimate accommodative amplitude.

Only one previously conducted study looked at long-term multifocal contact lens wear in children. During a contralateral trial, the children wore one single vision lens and one dual focus lens in the other eye for 10 months, with no resultant use of the add power reducing accommodation, even after the dual focus lens was worn in one eye for 10 months.

Accommodative facility has been studied regarding its effect after wearing multifocal contact lenses, but only in short-term studies of less than two weeks. These reports indicated reduced accommodative facility does exist in young adult multifocal wearers, but the results of the current study do not indicate any long-term reduction of accommodative facility. As such, accommodative facility may be reduced while wearing multifocals, but after nearly five years, binocular accommodative facility did not display difference for single vision vs. multifocal wearers, likely due to wearing the treatment and not because of changes in accommodative ability of participants.

The authors of the present study concluded in their paper that "eyecare practitioners prescribing multifocal contact lenses for myopia control should not be concerned about causing long-term effects on accommodation."

Chandler MA, Robich ML, Jordan LA, et al. Accommodation in children after 4.7 years of multifocal contact lens wear in the BLINK Study randomized clinical trial. Optom Vis Sci. June 26, 2023. [Epub ahead of print].

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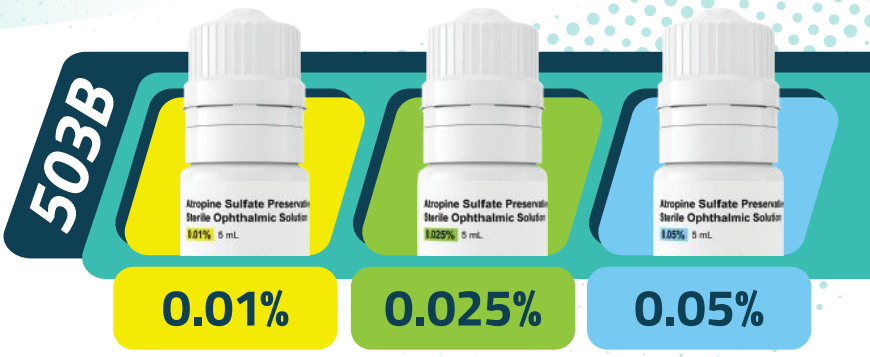

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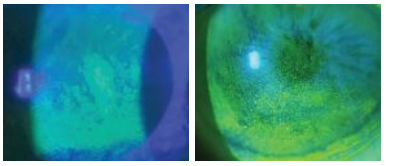

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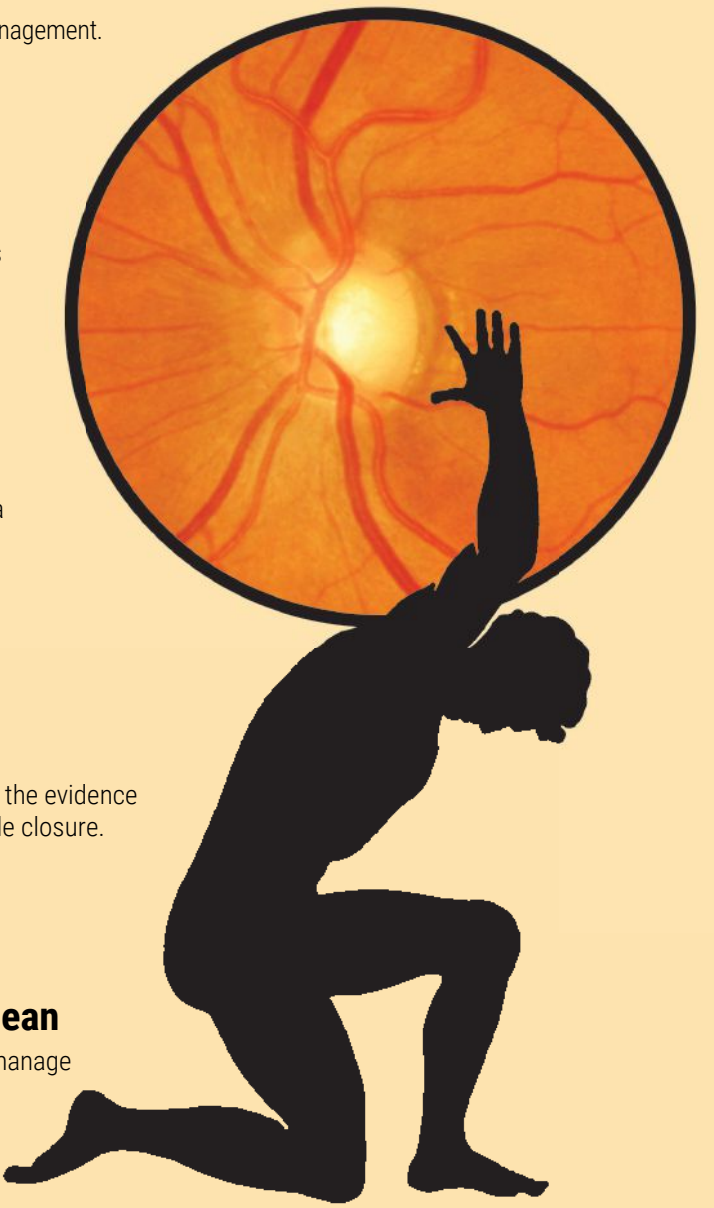

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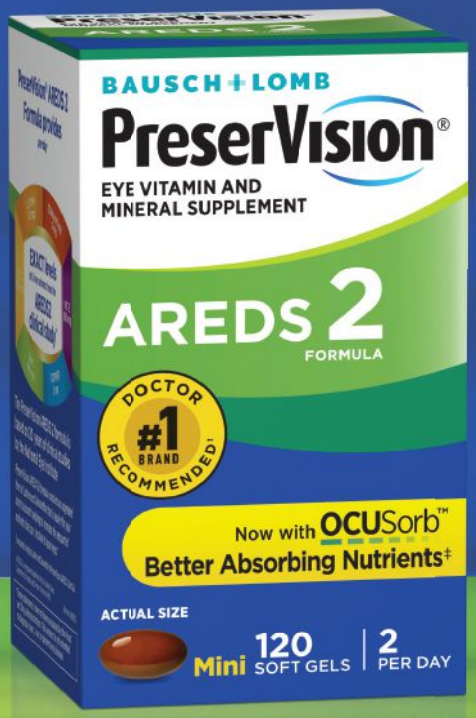

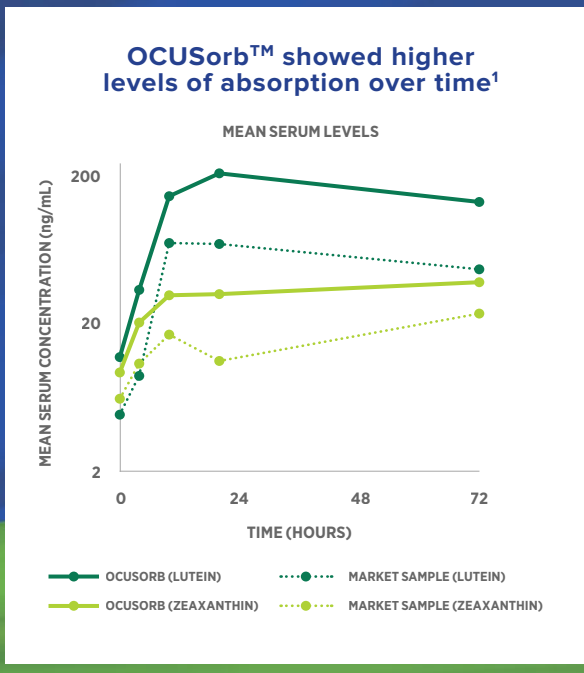

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1. Compared to the market sample. Kotagiri SR, Morde A, Rai D, et al. Ophthalmol Ther. 2022;11(4):1463-1477

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BY JACK PERSICO
EDITOR-IN-CHIEF
OUTLOOK

Clinical Cocoons

Enticing AI solutions are no substitute for insights that come from doing the work yourself. Here's help in breaking through.

Five or 10 years from now, glaucoma diagnosis will probably be a lot easier, thanks to inevitable advances in artificial intelligence. It's easy to paint AI as a panacea for countless difficult or tedious tasks throughout society, and I'm leery of making uncritical assumptions. Glaucoma is in fact more slippery than other diseases on the radar of AI researchers. Especially in its earliest stages, its presence is much less concrete than something like diabetic retinopathy, where fundus images alone are definitive and hence AI systems can be trained on large datasets of confirmed cases. By contrast, in glaucoma the wide variability in optic nerve anatomy makes it hard to draw a sharp line between normal and abnormal, so AI metrics will be more couched in probabilities than certainties.

Still, any data-driven field that creates huge reference sets to scan is going to get an AI boost at some level. At this year's ASCRS meeting, one glaucoma expert even speculated that since AI's predictive algorithms are getting so good, it may one day put visual field testing out of business. Why muck around with all that subjective testing if structural imaging will get you answers that are as good or better?

In some ways, I actually hope AI's benefits in glaucoma are still a few years away. You've surely heard (from me and countless others) that ODs are the only realistic solution to the delivery of glaucoma care in America. With far fewer ophthalmologists in practice and that profession's high degree of subspecialization, there's not nearly enough capacity in the MD ranks to serve millions of glaucoma patients in a way they need and deserve.

Optometry's capacity in glaucoma is gaining steam—medication prescribing rights in all 50 states and SLT in 10 of them—but the profession is still held back by structural problems in insurance billing and patient access, as well as a reluctance among some to really dive into the messy work of full-scope glaucoma care. "The general tendency of ODs who manage glaucoma is to prescribe a prostaglandin analog, and if the patient needs escalation of therapy, they refer the patient to ophthalmology," says Danica Marrelli, OD, this month in "Avoid These Common Glaucoma Mistakes" on page 64.

If optometrists tend to hit a wall in their uptake of glaucoma responsibilities—wherever that may be for each individual—I worry that handing them too many AI tools might blunt their ability to work through tricky clinical problems themselves and, in so doing, gain vital insights into the disease itself. I'm reminded of an allegory used nearly 20 years ago on ABC's TV show *Lost* that has stuck with me ever since: how a moth must dig at its cocoon to break out of it and can only survive because that effort prepared it for the world. "Struggle is nature's way of strengthening," a mentor figure explains.

Our 29th annual glaucoma report targets dozens of areas where some ODs struggle to move beyond the fundamentals. If that's you, we hope this issue helps you break out of that cocoon and emerge stronger than ever. You'll have to put it into practice—no article can give you everything you need—but once you know the disease better than any AI ever could, you'll be able to use diagnostic technology as tool instead of a crutch. ■

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References: 1. Walkden A. Amniotic membrane transplantation in ophthalmology: an updated perspective. *Clin Ophthalmol.* 2020;14:2057-2072. **2.** Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II definition and classification report. *Ocul Surf.* 2017;15(3):276-283. **3.** Jones L, Downie LE, Korb D, et al. TFOS DEWS II management and therapy report. *Ocul Surf.* 2017;15(3):575-628.

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BY PAUL M. KARPECKI, OD
CHIEF CLINICAL DITOR

Put the Patient First

SLT and other glaucoma treatments should be more accessible.

Optometry had nothing to do with an insufficient number of ophthalmologists, especially in rural communities, but this issue must be solved. Access to quality eye care, and in particular laser procedures—as evidenced by the Laser in Glaucoma and Ocular Hypertension (LiGHT) study—is essential. While politicians and lobbyist groups might forget the importance of the patient in medical decision-making, current trends and technologies will soon make it so they can't.

Trends

It is estimated that there are about 19,000 ophthalmologists in the US, similar to what it was 25 years ago.[1] There are over four million cataract surgeries performed per year and aging Baby Boomers could increase that to five or six million within a decade. If you remove subspecialities such as retina, oculoplastics, neuro, academics and those who focus on primary eyecare services, there isn't a sufficient supply of surgeons for the cataract demand alone.

While optometry isn't seeking to perform complex surgeries, laser procedures—something we've been trained extensively in—would allow surgeons to focus on the high number of cataract and intraocular surgeries.

Patient Need for SLT

The LiGHT Trial's six-year results for POAG and ocular hypertension were released last year. Patients in the selective laser trabeculoplasty (SLT) arm showed equal safety but better long-term disease control than those in the drops arm.[2] They also showed a reduced need for incisional or advanced glaucoma procedures compared to those taking drops. Most telling is that a statistically significant number of patients in the drops arm exhibited glaucoma progression compared to those receiving SLT.

> **These innovations and current trends will help refocus future glaucoma treatment decisions back on the patient.**

In rural communities where there is less access to ophthalmologists and/or glaucoma specialists to perform SLT, patients may not receive these timely and essential treatments.[3]

Helpful Innovations

Many glaucoma patients discontinue the use of IOP-lowering drops due to irritation and ocular surface disease (OSD). Patients requiring prostaglandin analogs and BAK-preserved drops tend to experience problems sooner and require an alternative to maintain targeted IOP.

Innovations such as the Durysta implant are very helpful, but this requires a procedure that not every optometrist can perform as determined by the state they practice in. SLT is a mainstay and gaining traction as the primary treatment for open angle glaucoma due to OSD issues with drops and the results of the LiGHT Study.

A future springboard to making laser trabeculoplasty the primary treatment for glaucoma is something called direct selective laser trabeculoplasty (Belkin Vision). With a single touch of a button, it can treat 360° (or 180°) of the trabecular meshwork and provides a fully automated treatment experience with built-in safety features. This automated digital technology administers 120 perfectly placed laser shots that effectively lower IOP.[4] Significantly, a gonio lens is not required to perform the procedure.

The Future is Clear

The patient needs to be the primary focus in decisions regarding access to essential procedures and technology—it's that simple. Ophthalmology shortages are due to the low number of residencies, greater demands in subspecialties like retina and an aging Baby Boomer population. The result: limited access to procedures like laser trabeculoplasty and delayed cataract surgery, which is already occurring and will only worsen over time.

Innovative laser technologies and ocular surface–sparing long-duration therapeutics will provide the solutions glaucoma patients need to stave off progression, but there still has to be a well-trained provider; that is where optometry has proven itself in the states where laser privileges exist. ■

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About Dr. Karpecki

Dr. Karpecki is the director of Cornea and External Disease for Kentucky Eye Institute, associate professor at KYCO and medical director for the Dry Eye Institutes of Kentucky and Indiana. He is the Chief Clinical Editor for Review of Optometry and chair of the New Technologies & Treatments conferences. A fixture in optometric clinical education, he consults for a wide array of ophthalmic clients, including ones discussed in this article. Dr. Karpecki's full disclosure list can be found in the online version of this article at www.reviewofoptometry.com.

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Théa
let's open our eyes

BY MONTGOMERY VICKERS, OD

CHAIRSIDE

Recheck, Remake, Repeat

Here's what I've learned from the annual glasses-check patients. You're welcome.

In my office in West Virginia, we referred to glasses checks as a "Recheck Rx." Here in Texas, everyone calls them a "Spec Check." I doubt that these visits only occur in West Virginia and Texas. What do you call them?

I know the practice management gurus want you to train yourself to be happy these patients made an appointment for this recheck. They use phrases like, "Look at it as an opportunity to problem solve and keep the patient for life." Uh, once you've remade the dude's glasses three years in a row, maybe the luster of "keep the patient for life" kinda wears off, right?

I think that no matter what, you will always find these visits stressful. I have spent the better part of my career studying rechecks looking for patterns to try to prevent rechecks instead of just expecting them to happen. I've learned a few things:

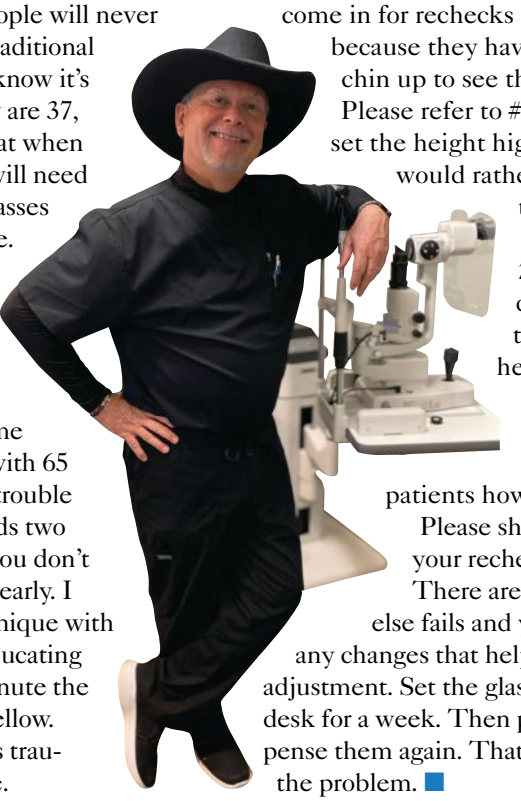
1. If the patient gets their first progressive add at some jackleg glasses store, you can expect a call from them. No matter what you do it's hard to get the message of, "You get what you pay for" across. There are crappy progressives out there, y'all.

2. If a patient has had refractive surgery, they will lie like dogs to avoid getting used to (or as they see it, being dependent on) glasses. My mentor Dr. Bodie used to say, "Don't put them in a bifocal until they beg you for one." Clinically, I have seen a steady progression of astigmatism that ends up screwing up a patient's distance vision if they just fight the eyestrain all day instead of gracefully accepting their presbyopia. Oh, and they don't think buying cheap over-the-counter readers is an admission they need prescription glasses. Really?

3. Thirteen-year-olds would rather have blurry vision than wear their first pair of glasses, so Mom will bring them in for rechecks since she never sees them wearing their glasses.

4. Computer people will never be satisfied with traditional progressives. You know it's true, so when they are 37, start explaining that when they are 43, they will need a second pair of glasses for their workspace.

If you get them used to the idea, they will be less apt to commit seppuku when the time comes. The lady with 65 pairs of shoes has trouble accepting she needs two pairs of glasses if you don't start orienting her early. I use the same technique with cataracts; I start educating the patient the minute the lens looks a hair yellow. Makes referral less traumatic in the future.



5. I am not the boss any more. I am a mere junior associate and love every minute of it. But if I were the boss, I would inform the patient who walks with their Rx, in writing, that (a) they need to be sure to ask the glasses provider what their refund policy is so when, not if, they have trouble with the glasses they can get their money back and come here so we can help them get the best quality lenses and (b) there will be a refraction charge for any rechecks on glasses not purchased here or for any adjustments, repairs, replacement nose pads and drinks of water from our fountain. You get paid to provide your time and expertise. Hey, it was the patient who chose #2 instead of #1, right?

6. Set the stupid seg height 2mm or 3mm higher than your optician measures. There is a real trend in this computer age of patients who come in for rechecks and remakes because they have to tilt their chin up to see the computer. Please refer to #4 above or set the height high enough. I would rather they have to tilt their chin down to drive 20 minutes per day than have to tilt their head back 10 hours per day. Glasses are a tool. Teach patients how to use it.

Please share with me your recheck trends. There are patterns. If all else fails and you cannot find any changes that help, try a desk adjustment. Set the glasses on your desk for a week. Then personally dispense them again. That often solves the problem. ■

About Dr. Vickers **Dr. Vickers** received his optometry degree from the Pennsylvania College of Optometry in 1979 and was clinical director at Vision Associates in St. Albans, WV, for 36 years. He is now in private practice in Dallas, where he continues to practice full-scope optometry. He has no financial interests to disclose.

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*Prescription market data, Dec. 2022 – S01K without cyclosporine.
†In a chronic dry eye patient usage study, participants from a variety of socioeconomic backgrounds answered questions about iVIZIA. There were 203 chronic dry eye patients, ranging from ages 28-80, who used their current eye drops before switching to iVIZIA for 30 days.[1]
‡To limit blurriness when using contact lenses, remove contacts, apply drops, then insert contacts.

Reference: 1. Data on file.

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BY BISANT A. LABIB, OD

Macular Focus

Pinpoint your knowledge toward understanding how the structures here give rise to various conditions.

The macula is a small, highly-specialized area of the retina that is responsible for providing our sharpest acuity. Its unique anatomical and biochemical features distinguish it from the rest of the neighboring as well as peripheral retina and contribute to its susceptibility to certain ocular disease processes. When we explore the details of this region, we are better able to understand the pathogenesis of many macular conditions.

Anatomical and Biochemical Features

The macula is approximately 5mm to 5.5mm in size and is further subdivided into a central 0.35mm fovea. Additional surrounding areas include the parafovea and perifovea. Note that the highest density of cone photoreceptors is located in the fovea, approximating 50 cone cells per 100µm and resulting in the ability to perceive sharp visual detail. The fovea is also uniquely composed of fewer layers than the rest of the neurosensory retina, limited only to the thin inner plexiform layer, outer nuclear layer, photoreceptors and retinal pigment epithelium (RPE). This alteration allows for the tight packing of cones in this space. As we move away from the fovea and to the more peripheral areas of the macula, both cones and rods begin to occupy the space.[1]

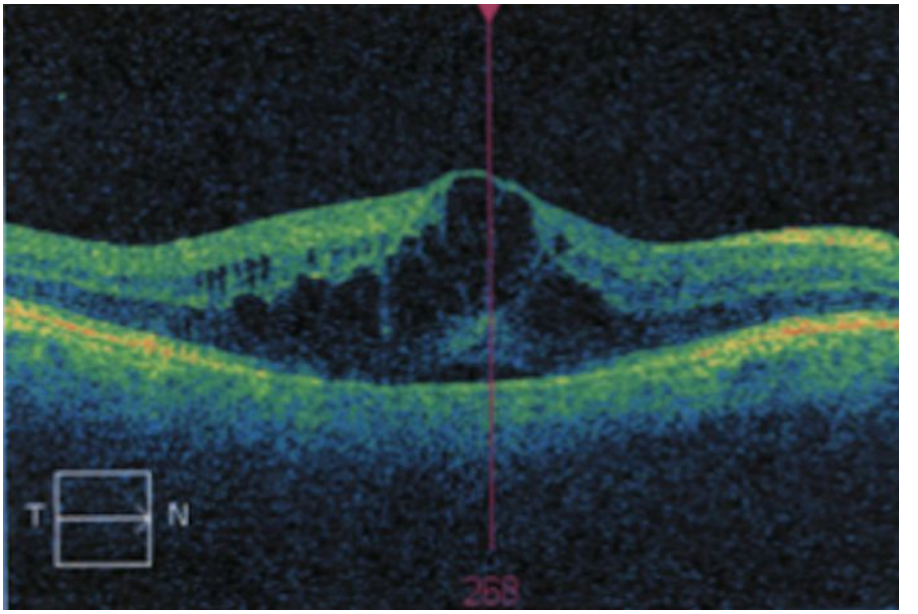
Directly adjacent to the RPE layer is the underlying choriocapillaris, which is the primary vascular supply of the macula. Within the innermost macula, there is a lack of vasculature, termed the foveal avascular zone. This is a unique distinction in that the rest of the retina is supplied by the central retinal artery system and underlying choroid.[1,2] Despite the lack of vasculature, the macula exhibits a high degree of metabolic activity. Light is continuously being synthesized to vision, requiring a substantial amount of oxygen. As such, the retina is one of the highest oxygen-consuming tissues in the body.[2]

Clinical Applications

Given these characteristics alone, the macular region is more susceptible to certain disease processes that do not normally occur otherwise throughout the remaining retinal anatomy. If we apply the principles mentioned above, we are able to better understand the pathophysiology as it correlates to various conditions.

Cystoid macular edema (CME). This condition is generally caused by a breakdown of the blood-retinal barrier and the resultant thickening from fluid accumulation within the neurosensory retina. This manifestation may occur from primarily ocular conditions or secondary to systemic disease conditions. Examples of such cases are uveitis, diabetes, vein occlusion, retinitis pigmentosa, vitreomacular traction or following cataract extraction.[3] Because the blood-retinal barrier is compromised, fluid leaks from across the retinal vessels and RPE into the perifoveal tissues.[2]

Histological studies have suggested the presence of fluid is most common in the outer plexiform layer of the fovea, as well as Henle's layer.



Cystoid macular edema resulting from fluid accumulation.

About Dr. Labib **Dr. Labib** graduated from Pennsylvania College of Optometry, where she now works as an associate professor. She completed her residency in primary care/ocular disease and is a fellow of the American Academy of Optometry and a diplomate in the Comprehensive Eye Care section. She has no financial interests to disclose.

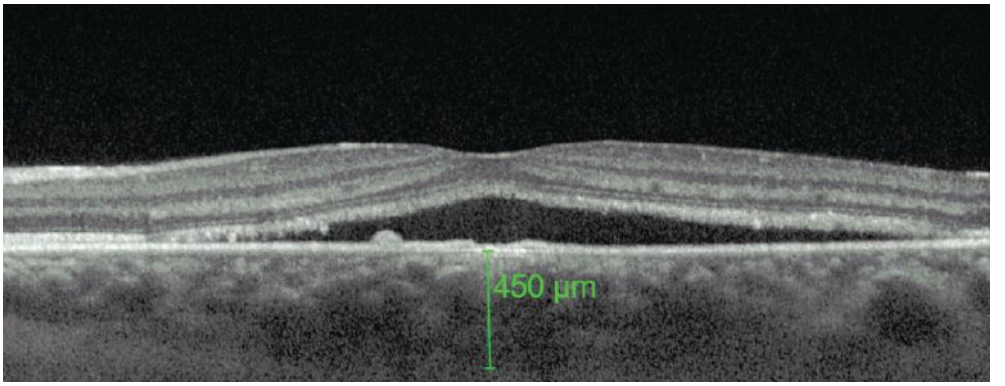


Photo: Mohammad Rafieetary, OD

A thicker-than-average choroid is characteristic of CSCR.

Cystic spaces have been noted to be greatest in the outer plexiform layer. While it is unclear why the leakage is confined to the macula, it has been suggested that it is due to the high metabolic activity and avascularity in the foveal region, which prevents adequate resorption of fluid. It is also speculated that, since the internal limiting membrane is thinnest over the fovea, there is less barrier to prevent the diffusion of inflammatory mediators.[3,4]

Central serous chorioretinopathy. Recent studies using indocyanine green (ICG) angiography have demonstrated multifocal areas of choroidal vascular permeability secondary to ischemia, stasis or inflammation, suggesting that the choroid is the primary site of pathology.[5,6] In patients with this type of chorioretinopathy, increased choroidal thickness has been reported. This variability in size is due to the dilatation of large, hyperpermeable choroidal blood vessels.

Superficial to this thickened layer is an area of medium- and smaller-sized blood vessels known as the inner choroidal layer. In regions where there is marked choroidal thickening, the adjacent inner choroidal layer is thinner than normal tissue due to primary atrophy or direct compression by the underlying dilated vessels. This direct compression and resultant mechanical stress can also lead to reduced RPE adhesion, alteration of RPE hydroionic regulation and RPE atrophy. A combination of these events will ultimately manifest clinically as a pigment epithelial detachment.[6] Since the fovea lacks vasculature and is composed of fewer layers, it is more susceptible to choroidal permeability.

Macular glaucoma. Standard and routine glaucoma testing involves the use of optic nerve OCT to measure retinal nerve fiber layer thickness around the optic nerve head along with a VF 24-2 to test function. However, because the macula contains 30% to 50% of the total retinal ganglion cells (RGCs), scanning this area allows a sampling of the majority of the cells implicated in glaucoma.[7,8]

The ganglion cell and nerve fiber layers constitute 30% to 45% of the total thickness of the macula. Even though the macula, typically defined as the central eight degrees from the foveal center, represents approximately 2% of the retina, it still contains half of all RGCs. In addition, the macula does not contain blood vessels as the optic nerve head does, making it a simpler structure to analyze. Increasing evidence suggests that macular damage is manifest in early or mild glaucoma, where it was once previously thought to be characteristic of advanced stages. To detect such damage using OCT, the RGC and inner plexiform layer (RGC+) should be analyzed.[8]

Full-thickness macular hole. Macular holes are thought to be a result of anteroposterior traction from the vitreous. As mentioned earlier, the internal limiting membrane in the region of the fovea and macula is thinner than in the rest of the retina. As the membrane is in direct contact with the posterior vitreous cortex, tractional forces would impact this area to a greater degree.[9]

Age-related macular degeneration (AMD). While this is a complex and multifactorial condition, it is well-established that the macula is a highly metabolic area. It also contains the highest cone density, requiring phagocytosis of outer segments by the RPE. This profound task leads to oxidative stress on the macula, one of the key pathogenic features of AMD development.[2]

Without the knowledge of the anatomy and biochemistry of the macula as it differs from the other parts of the retina, many macular conditions are not readily understood. In fact, diseases of the macula which were once thought to be idiopathic or of unknown etiology are better recognized today with advancements in technology that allow for more precise examination of this highly specialized area. ■

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NOW APPROVED: the first and only FDA-approved treatment for GA secondary to AMD[1]

GA unravels so much

Save retinal tissue by slowing progression[1-3]

INDICATION

SYFOVRE™ (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

IMPORTANT SAFETY INFORMATION

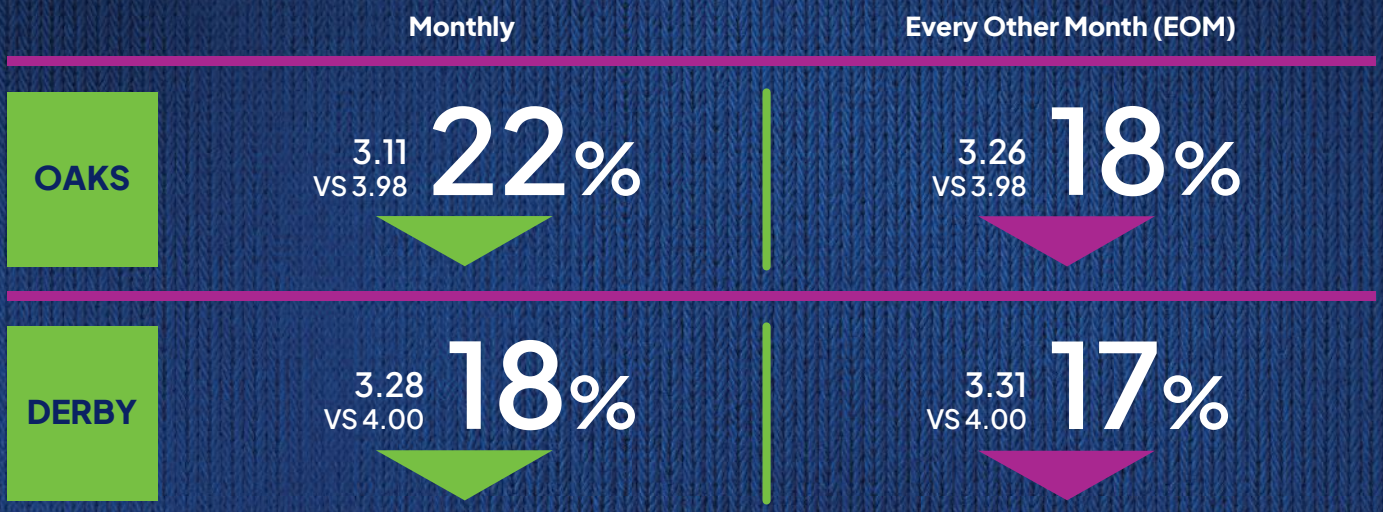
CONTRAINDICATIONS

- SYFOVRE is contraindicated in patients with ocular or periocular infections, and in patients with active intraocular inflammation

WARNINGS AND PRECAUTIONS

- **Endophthalmitis and Retinal Detachments**
  - Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
- **Neovascular AMD**
  - In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.
- **Intraocular Inflammation**
  - In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves, patients may resume treatment with SYFOVRE.

SYFOVRE achieved continuous reductions in mean lesion growth rate* (mm^2) vs sham pooled from baseline to Month 24[1]



SE in trials (monthly, EOM, sham pooled): OAKS: 0.15, 0.13, 0.14; DERBY: 0.13, 0.13, 0.17.

*Slope for baseline to Month 24 is an average of slope of baseline to Month 6, Month 6 to Month 12, Month 12 to Month 18, and Month 18 to Month 24.[1] Based on a mixed effects model for repeated measures assuming a piecewise linear trend in time with knots at Month 6, Month 12, and Month 18.[1]
AMD=age-related macular degeneration; GA=geographic atrophy; SE=standard error.

Explore more at SyfovreECP.com

IMPORTANT SAFETY INFORMATION (CONT'D)

WARNINGS AND PRECAUTIONS (CONT'D)

- **Increased Intraocular Pressure**
  - Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

ADVERSE REACTIONS

- Most common adverse reactions (incidence ≥5%) are ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, conjunctival hemorrhage.

Trial Design: SYFOVRE safety and efficacy were assessed in OAKS (N=637) and DERBY (N=621), multi-center, 24-month, Phase 3, randomized, double-masked trials. Patients with GA (atrophic nonexudative age-related macular degeneration), with or without subfoveal involvement, secondary to AMD were randomly assigned (2:2:1:1) to receive 15 mg/0.1 mL intravitreal SYFOVRE monthly, SYFOVRE EOM, sham monthly, or sham EOM for 24 months. Change from baseline in the total area of GA lesions in the study eye (mm^2) was measured by fundus autofluorescence (FAF).[1,4]

References: 1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2023. **2.** Pfau M, von der Emde L, de Sisternes L, et al. Progression of photoreceptor degeneration in geographic atrophy secondary to age-related macular degeneration. *JAMA Ophthalmol*. 2020;138(10):1026–1034. **3.** Bird AC, Phillips RL, Hageman GS. Geographic atrophy: a histopathological assessment. *JAMA Ophthalmol*. 2014;132(3):338–345. **4.** Data on file. Apellis Pharmaceuticals, Inc.

Please see Brief Summary of Prescribing Information for SYFOVRE on the adjacent page.

Apellis

2/23 US-PEGGA-2200051 v1.0

SYFOVRE™
(pegcetacoplan injection)
15 mg / 0.1 mL

SYFOVRE ™ (pegcetacoplan injection), for intravitreal use
BRIEF SUMMARY OF PRESCRIBING INFORMATION
Please see SYFOVRE full Prescribing Information for details.

INDICATIONS AND USAGE

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Active Intraocular Inflammation
SYFOVRE is contraindicated in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

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Neovascular AMD
In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.
Intraocular Inflammation
In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves patients may resume treatment with SYFOVRE.
Increased Intraocular Pressure
Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

ADVERSE REACTIONS

Clinical Trials 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 practice.
A total of 839 patients with GA in two Phase 3 studies (OAKS and DERBY) were treated with intravitreal SYFOVRE, 15 mg (0.1 mL of 150 mg/mL solution). Four hundred nineteen (419) of these patients were treated in the affected eye monthly and 420 were treated in the affected eye every other month. Four hundred seventeen (417) patients were assigned to sham.
The most common adverse reactions (≥5%) reported in patients receiving SYFOVRE were ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and conjunctival hemorrhage.

Table 1: Adverse Reactions in Study Eye Reported in ≥2% of Patients Treated with SYFOVRE Through Month 24 in Studies OAKS and DERBY

Adverse Reactions	PM (N = 419) %	PEOM (N = 420) %	Sham Pooled (N = 417) %
Ocular discomfort*	13	10	11
Neovascular age-related macular degeneration*	12	7	3
Vitreous floaters	10	7	1
Conjunctival hemorrhage	8	8	4
Vitreous detachment	4	6	3
Retinal hemorrhage	4	5	3
Punctate keratitis*	5	3	<1
Posterior capsule opacification	4	4	3
Intraocular inflammation*	4	2	<1
Intraocular pressure increased	2	3	<1

PM: SYFOVRE monthly; PEOM: SYFOVRE every other month
*The following reported terms were combined:
Ocular discomfort included: eye pain, eye irritation, foreign body sensation in eyes, ocular discomfort, abnormal sensation in eye
Neovascular age-related macular degeneration included: exudative age-related macular degeneration, choroidal neovascularization
Punctate keratitis included: punctate keratitis, keratitis
Intraocular inflammation included: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, anterior chamber flare

Endophthalmitis, retinal detachment, hyphema and retinal tears were reported in less than 1% of patients. Optic ischemic neuropathy was reported in 1.7% of patients treated monthly, 0.2% of patients treated every other month and 0.0% of patients assigned to sham. Deaths were reported in 6.7% of patients treated monthly, 3.6% of patients treated every other month and 3.8% of patients assigned to sham. The rates and causes of death were consistent with the elderly study population.

USE IN SPECIFIC POPULATIONS

Pregnancy
Risk Summary
There are no adequate and well-controlled studies of SYFOVRE administration in pregnant women to inform a drug-associated risk. The use of SYFOVRE may be considered following an assessment of the risks and benefits.
Systemic exposure of SYFOVRE following ocular administration is low. Subcutaneous administration of pegcetacoplan to pregnant monkeys from the mid gestation period through birth resulted in increased incidences of abortions and stillbirths at systemic exposures 1040-fold higher than that observed in humans at the maximum recommended human ophthalmic dose (MRHOD) of SYFOVRE (based on the area under the curve (AUC) systemically measured levels). No adverse maternal or fetal effects were observed in monkeys at systemic exposures approximately 470-fold higher than that observed in humans at the MRHOD.
In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.
Lactation
Risk Summary
It is not known whether intravitreal administered pegcetacoplan is secreted in human milk or whether there is potential for absorption and harm to the infant. Animal data suggest that the risk of clinically relevant exposure to the infant following maternal intravitreal treatment is minimal. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when SYFOVRE is administered to a nursing woman.
Females and Males of Reproductive Potential
Contraception
Females: It is recommended that women of childbearing potential use effective contraception methods to prevent pregnancy during treatment with intravitreal pegcetacoplan. Advise female patients of reproductive potential to use effective contraception during treatment with SYFOVRE and for 40 days after the last dose. For women planning to become pregnant, the use of SYFOVRE may be considered following an assessment of the risks and benefits.
Pediatric Use
The safety and effectiveness of SYFOVRE in pediatric patients have not been established.
Geriatric Use
In clinical studies, approximately 97% (813/839) of patients randomized to treatment with SYFOVRE were ≥ 65 years of age and approximately 72% (607/839) were ≥ 75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies. No dosage regimen adjustment is recommended based on age.

PATIENT COUNSELING INFORMATION

Advise patients that following SYFOVRE administration, patients are at risk of developing neovascular AMD, endophthalmitis, and retinal detachments. If the eye becomes red, sensitive to light, painful, or if a patient develops any change in vision such as flashing lights, blurred vision or metamorphopsia, instruct the patient to seek immediate care from an ophthalmologist.
Patients may experience temporary visual disturbances associated either with the intravitreal injection with SYFOVRE or the eye examination. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

Manufactured for:
Apellis Pharmaceuticals, Inc.
100 Fifth Avenue
Waltham, MA 02451

SYF-PI-17Feb2023-1.0

2/23 US-PEGGA-2200163 v2.0

BY JEROME SHERMAN, OD, AND SHERRY BASS, OD

YOU BE THE JUDGE

Blue Eyes Save Lives

As the ciliary body is not observed during a routine eye exam, a melanoma is nearly never detected there until it may be too late.

Many eye clinicians go through their entire career without ever seeing the ciliary body. Most ophthalmic records do not even list the ciliary body as a structure to be assessed. If a malignant melanoma there spreads anteriorly to the iris, it is easier to detect in a blue-eyed patient. The obvious iris lesion in *Figure 1* would be difficult to detect if the patient had dark brown eyes. Eye color may have been the factor in detection and successful treatment. Early detection and intervention are crucial to increase the odds of patient survival.

Case

A 60-year-old Caucasian woman, who was a long-term patient in our private practice (JS), presented for a routine follow-up. The patient had no symptoms and reported excellent vision in both eyes after routine cataract extraction with posterior chamber IOLs several years earlier. She mentioned that her daughter occasionally observed redness in her right eye but only when her mom looked to the left. The external exam was unremarkable, except biomicroscopy that revealed possible sentinel vessels temporal to the limbus in the right eye at eight o'clock. A small, corresponding iris abnormality was noted in this brown-eyed patient.

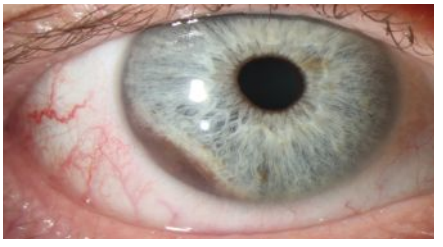

Fig. 1. A different patient than the case presented; note the blue eyes. A ciliary body malignant melanoma is invading the iris from seven to nine o'clock OD. Possible sentinel vessels at nine o'clock secondary to a ciliary body malignant melanoma below. Could this lesion be missed if this patient had dark brown eyes?

This practice had an ultrasound biomicroscopy (UBM) device. Immediate scans demonstrated a mass lesion of the ciliary body at eight o'clock (*Figure 2*). After dilation, ultrawidefield Optos images with and without steering revealed a dark peripheral lesion in the right eye between seven and nine o'clock. A review of previous images about a year earlier without steering revealed a possible smaller lesion in the temporal periphery at nine o'clock in the same eye (*Figures 3 and 4*).

The patient was immediately referred to David Abramson, MD, chief of ophthalmic oncology at Memorial Sloan Kettering in Manhattan, who confirmed the diagnosis of a ciliary body malignant melanoma extending posteriorly to the choroid. The patient was then treated with iodine plaque (I-125). The lesion regressed over the next six months, with a PET scan failing to reveal metastasis.

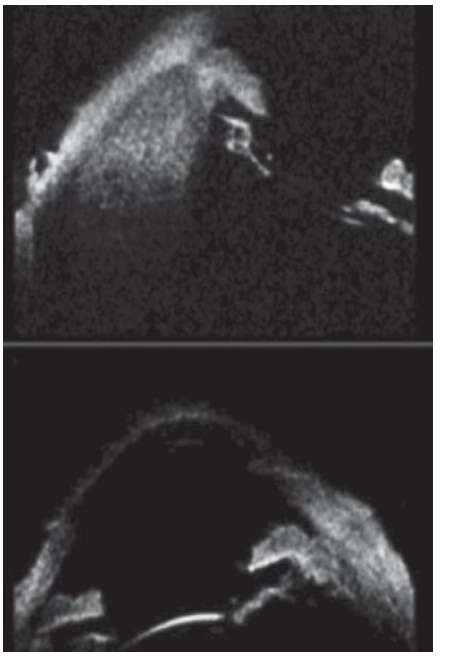

Fig. 2. Two UBM sections of the anterior segment. At eight o'clock (top image) is the ciliary body malignant melanoma. The section through 10 and four o'clock (bottom image) does not reveal any gross abnormality.

You Be the Judge

- If the patient had blue eyes instead, could the detection of the melanoma have been made a year earlier?
- Assuming the patient had blue eyes and not dark brown ones, could a "FAT scan" (see below) performed after the actual diagnosis support successful malpractice litigation?
- Since the patient was under post-op care for bilateral cataract removal and presbyopia-correcting IOLs in the same practice, should the malignant melanoma have been discovered earlier, and hence the prognosis would have been improved?
- Is steering with ultrawidefield imaging the standard of care?

About Drs. Sherman and Bass

Dr. Sherman is a Distinguished Teaching Professor at the SUNY State College of Optometry and editor-in-chief of *Retina Revealed* at www.retinarevealed.com. During his 53 years at SUNY, Dr. Sherman has published about 750 various manuscripts. He has also served as an expert witness in 400 malpractice cases, approximately equally split between plaintiff and defendant. Dr. Sherman has received support for *Retina Revealed* from Carl Zeiss Meditec, MacuHealth and Konan. **Dr. Bass** is a Distinguished Teaching Professor at the SUNY College of Optometry and is an attending in the Retina Clinic of the University Eye Center. She has served as an expert witness in a significant number of malpractice cases, the majority in support of the defendant. She serves as a consultant for ProQR Therapeutics.

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Dr. Nikki Iravani

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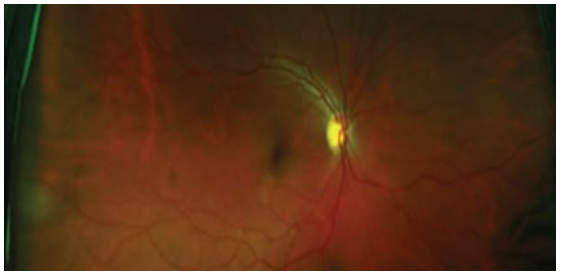

Fig. 3. Optos ultrawidefield image OD about a year prior to the diagnosis. Is the subtle peripheral dark zone between between eight and 10 o'clock normal or an early choroidal melanoma?

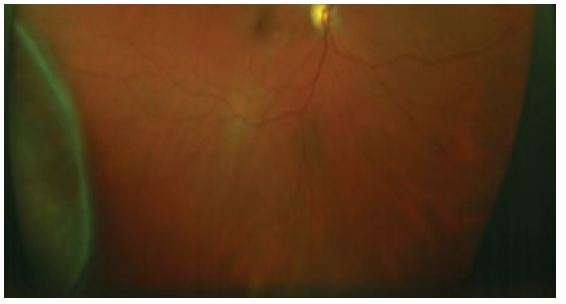

Fig 4. The lesion between seven and nine o'clock is a choroidal melanoma, which is the posterior extension of the ciliary body malignant melanoma.

- If steering was performed a year earlier, could the treatment have commenced a year earlier?

Our Opinion

A "family album tomography" (FAT) scan—careful review of pictures of a patient's face—may sometimes reveal a finding missed by the clinicians providing care to the patient. If our patient had blue eyes and if an iPhone picture of the patient's face was taken earlier, zoomed in and revealed a brown spot on the iris, the plaintiff's attorney and experts could argue that the melanoma had already spread to the iris earlier and was missed during a routine exam.

Steering is considered useful to obtain images of the far peripheral fundus. One could argue whether doing that a year earlier would have detected the melanoma. We recommend steering in the vast majority of cases, but it is unclear whether it is the standard of care right now with ultrawidefield imaging. Binocular indirect ophthalmoscopy is the standard of care and should include steering whenever possible.

Follow-Up

The patient was lost to follow-up, and malpractice litigation was initiated but never completed. An attempt is presently underway to investigate the outcome of this case further from Memorial Sloan-Kettering Cancer Center.

UBM

Only a minority of ophthalmic clinicians have access to this imaging system, and it is often never performed routinely. However, UBM is considered to be ideal in viewing the ciliary body. Structures that are opaque to light can often be visualized with sound. With UBM, the differential diagnosis of a cystic vs. a solid lesion is straightforward in a majority of cases.[1]

B-scan ultrasound is generally not helpful in detecting tumors of the ciliary body, the exception being that if the tumor has spread posteriorly to the choroid and has enlarged considerably. B-scan ultrasound is most useful to detect abnormalities in the posterior segment such as retinal detachments and mass lesions in the orbit. UBM has far better resolution of the anterior segment than B-scan but does not penetrate well. Hence, that is the trade-off, and one technology does not replace the other.

When to Consider UBM

1. When a brown spot is visualized at the far peripheral iris, especially one that was not documented previously.
2. When the angle appears to be narrower in one or several clock hours than in the remaining hours, and gonioscopy fails to reveal its cause.
3. When there is localized perilimbal redness in one zone and in one eye only. Is this evidence of a so-called "sentinel" vessel suggestive of a lesion below?

Finding Uveal Melanomas

These are considered as the most common malignancy of the eye in Caucasian adults and rare, but occasionally encountered, in Black and African American adults. In the Caucasian population, there are approximately four to eight new cases per year per million population. A malignant melanoma can begin in any of the three components of the uveal tract, but only about one in 10 begin within the ciliary body.[2]

An isolated malignant melanoma of the iris is considered to have the most favorable prognosis, and one of the ciliary body and anterior choroid has the worst. The 10-year mortality rate of ciliary body malignant melanoma reaches 30% to 50%. Knowing that the shortest average doubling time of primary uveal melanoma is 154 days, ophthalmic oncologists can calculate the size of the tumor at any previous eye exam.[3]

This information is sometimes used in malpractice cases to prove or disprove that the tumor was detectable. In such cases, the reference is "a like practitioner under like circumstances" and not the specialists at facilities such as Memorial Sloan Kettering.

Of note, Julia Canestraro, OD, is a graduate of SUNY Optometry who is presently at Memorial Sloan Kettering in the Ophthalmic Oncology Service and is helpful in coordinating referrals and follow-ups.

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NOTE: This article is one of a series based on actual lawsuits in which the author served as an expert witness or rendered an expert opinion. These cases are factual, but some details have been altered to preserve confidentiality. The article represents the authors' opinion of acceptable standards of care and do not give legal or medical advice. Laws, standards and the outcome of cases can vary from place to place. Others' opinions may differ; we welcome yours.

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Gut Check

Dry eye problems could be alleviated with diet and lifestyle changes. Here's what to consider.

Q I have several patients who don't respond to medical and mechanical dry eye therapies such as prescription drops, LipiFlow (Johnson + Johnson) or BlephEx. What are my next steps?

A Dry eye disease (DED) has been identified as a multifactorial condition, and there are myriad treatment options to address its causes. But when those fail, we must ask, "Are we missing a bigger picture?" Recent studies have shown that modern lifestyles can contribute to DED, whether it is digital screen use, increased stress or poor sleep and nutrition.[1]

"I believe including lifestyle modifications in our dry eye management should be the standard of care in treating DED," says Mila Ioussifova, OD, of South Waterfront Eyecare in Portland, OR.

Underlying Trouble

With more advanced dry eye treatments like intense pulsed light (IPL), we have learned about the correlation between rosacea and DED, according to Dr. Ioussifova. Rosacea is a common dermatological condition that often manifests with ocular complications like meibomian gland dysfunction (*Figure 1*) and *Demodex* blepharitis.[2,6]

Rosacea is also a complex and multifactorial disease, one in which imbalances in the skin organisms have been identified as its pathogenesis.[3] Recent studies have described that these alterations are due to gut dysbiosis, the alterations in the gastrointestinal (GI) microbiome and its associated pathologies, such as small intestinal bacterial overgrowth, irritable bowel syndrome and inflammatory bowel disease.[5] Consider these issues when treating rosacea and dry eye with IPL yet still noting recurrent flare-ups.

Many pharmaceutical treatments aid to reduce inflammation involved with DED. However, oxidative stress and the dysregulation of redox homeostasis could potentially play a causative role in the inflammatory process and pathogenesis of dry eye.

Studies have shown that patients with DED exhibit higher levels of oxidative stress markers in tears and conjunctival cells and lower levels of antioxidant enzymes, leading to peroxidation of lipids on the ocular surface and DNA oxidative damage in both nuclei and mitochondria, resulting in loss of goblet cell density in the conjunctiva.[4]

Healthy Body, Healthy Eyes

"When managing dry eye patients, we are given an opportunity to look at and treat the whole person by assessing the imbalances in their body to maximize nutrient absorption, antioxidant support and improve detoxification pathways—especially important in those with autoimmune conditions," Dr. Ioussifova emphasizes. "Incorporating nutrition and lifestyle modifications has been crucial in managing some of my most challenging dry eye patients."

She recommends ordering functional testing to assess micronutrient or hormonal imbalances, as well as assessing GI microbiome dysbiosis with stool testing. Ask patients how many hours they sleep, how many times a week they exercise, what they usually eat and how they feel after meals to sense if they have GI disturbances. "You would be surprised how many people report they have GI issues but think those symptoms are normal," she observes. "We may be their first provider to make the connection between their gut symptoms and their rosacea and dry eye flare-ups."

Dr. Ioussifova's favorite comment from her patients is, "I came to you for my eyes, but now my skin is better, my stomach is happier and I have better sleep and more energy."

"When we treat the imbalances in the gut, the root cause of most noncommunicable diseases and address other lifestyle factors, we can help heal the patient's whole body, not just the eyes," she says. ■

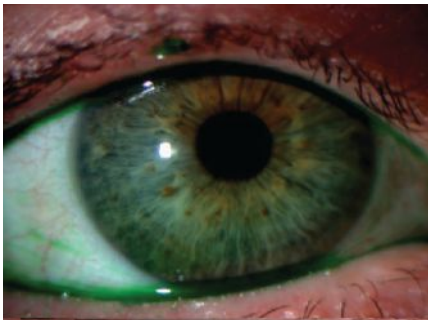

Fig. 1. Ocular rosacea and meibomian gland dysfunction.

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About Dr. Ajamian **Dr. Ajamian** is board certified by the American Board of Optometry and serves as Center Director of Omni Eye Services of Atlanta. He is vice president of the Georgia State Board of Optometry and general CE chairman of SECO International. He has no financial interests to disclose.

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DRY EYE CATALYSTS FOUND IN ALL WALKS OF LIFE

A mammoth report from TFOS documents how patients' ordinary daily activities manifest and perpetuate the disease, and how clinicians can guide them toward better choices.

BY RACHEL RITA, ASSOCIATE EDITOR

A condition as pervasive as dry eye is sustained by the rhythms of modern life. Our reliance on digital screens, our poor sleep habits and dietary choices, the harsh climates we expose our eyes to, the medications we take as well as the conditions they treat, the cosmetics and contact lenses we wear—all these are on-ramps for the family of conditions we call ocular surface disease, chief among them dry eye.

Against this backdrop, in late 2020 the Tear Film and Ocular Surface Society (TFOS) created a new workshop comprised of 158 clinical and academic researchers from 38 countries to systematically evaluate the scientific literature on how a patient's day-to-day experiences—some volitional, some not—give rise to dry eye, digital eye strain, microbial keratitis, pterygia and a host of other conditions.

The TFOS Lifestyle Workshop, as it's called, is a collection of 10 reports just published in *The Ocular Surface* that will surely be the most definitive statement attempted thus far on these often-unavoidable triggers for ocular surface disease. TFOS also released a series of videos in early May that sketch out the key insights of the workshop's eight subcommittees.

Below, we'll walk you through this treasure drove of data using quotes from the video presentations, journal articles and original interviews conducted with several participants for added context.

"People are exposing themselves to so many ocular risk factors nowadays," says Dr. Jennifer Craig, a professor at New Zealand's University of Auckland and Chair of the TFOS Lifestyle Workshop. With the ubiquity of digital screens and the growing popularity of myopia management interventions, this is starting at such a young age; furthermore, people are living longer. "If we're causing damage at a younger and younger age, we've got a lot of years to live with the consequences of that damage." Here's what Dr. Craig and her colleagues advocate in response.

Contact Lens Wear

Patients who wear contact lenses consistently point to convenience and cosmesis as motivators. In literature reviewed by this subcommittee, such individuals reported better quality of life than those wearing glasses among kids, adults and elderly alike, all citing better vision quality and comfort leading to increased satisfaction.

Despite the obvious advantages, especially when playing sports, contact lenses may contribute to or exacerbate dry eye. However, the rate at which that occurs may differ for experienced vs. new lens users. While the contact lens discontinuation rate remains about 25%, the reasons why differ. For new wearers, their most cited reasons were discomfort (35%), lens handling (33%) and loss of interest. However, experienced wearers most often cited ocular discomfort, followed by inconvenience, which may be partially due to said discomfort. Although not a precise complaint, ocular discomfort is often caused by feelings of dryness. This is corroborated by evidence that dropouts have shown shorter tear breakup time, meibomian gland plugging, worse meibum quality and greater likelihood of being diagnosed with dry eye.[1]

Going into greater detail, this subcommittee identified nine areas of lifestyle choices regarding contact lens use and wear that could affect dry eye and other ocular surface effects.

The first category as it relates to contact lenses is how lenses are obtained. "Purchasing lenses from unregulated outlets in particular is a concern for patients wearing cosmetic lenses or sort of party type lenses that certainly impact the risk of microbial keratitis. There's very good evidence around that fact, and some of it relates to lenses being shared with friends," states Dr. Lyndon Jones, of the School of Optometry and Vision Science at University of Waterloo, Canada and the primary author of this report.

Age is a significant risk factor in ocular surface health and continued contact lens success. Children have fewer complications than adults, likely due to parents managing their wear. As the ocular surface worsens with age, so does the contact lens complication rate, to some extent. Complications are highest in young adults, attributed to comparatively poorer adherence to proper hygiene measures. As such, the subcommittee recommends that safety education and continual connection with an eyecare provider are integral parts of ensuring hygiene compliance.

The COVID-19 pandemic brought with it unforeseen complications in all aspects of life and will be discussed in other subsections of this article. However, as it related to contacts, the subcommittee highlighted that there is a great lack of existing evidence for what patients should do when unwell in general, but especially with viral upper respiratory tract infections such as COVID. Long COVID has been linked to corneal epithelial nerve loss and an increase in immune cell density of the cornea, potentially creating long-term impediments to contact lens wear. Furthermore, contact lens wearers who have a lower quality precorneal tear film may experience worsened dry eye symptoms from mask-associated dry eye. Some evidence points to illness mapping onto corneal inflammatory events associated with contact lens wear, prompting Dr. Jones to suggest affected patients "refrain from contact lens wear until they are fully better."

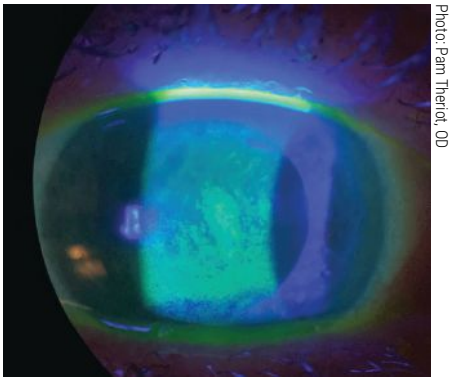


Photo: Pam Theriot, OD

An example of dry eye compromising the ocular surface, seen with sodium fluorescein staining.

Despite this potential link, COVID itself did not end up directly impacting typical contact lens–associated risk factors; instead, performance may have been lessened from mask-associated dry eye, increased screen time and hand sanitizer use.

Other health concerns such as thyroid eye disease and diabetes, both in their ocular manifestations and the medications used, can complicate lens wear. Problems can also arise after cosmetic or refractive surgeries due to potential corneal shape changes, eyelid configuration or contour modifications.

Vision and comfort decline as the tear film thins, leading environmental factors like decreased temperature and humidity to increase dryness of the eyes through a less stable tear film and subsequent tear film evaporation. Also having the ability to impact lens wear negatively are low humidity, high altitude, pollution, wind, dust and fumes.

Reliance on digital devices results in a compromised environment of the ocular surface and exacerbates existing difficulties in contact lens wear, as reduced blink frequency and blink amplitude lead to complaints of eye strain, dry eyes, brining, irritation and blurry vision. The contact lens subcommittee report stresses that it is important to remember that full correction is needed for contact lens wearers to achieve maximal performance, especially when heavily using digital devices. Multifocal performance is better than with monovision lenses and low-level astigmatism should be fully corrected for as well.

Lens wearers with industrial occupations should be cautious of foreign bodies, chemical fumes, vapors and aerosol droplets, as these can pose problems. Flying is also well-known to decrease lens performance from the low humidity and resultant dry environment.

Interestingly, a high risk-taking personality was found to be a better predictor of compliance than factors of age, sex or practitioner perception, with those that possess this trait being much less compliant than their counterparts.

The report notes that 99% of wearers admit they have engaged in at least one hygienic risk behavior, so it's no wonder microbial keratitis and other contact complications account for one million US doctor visits each year. Risk increases with sleeping in lenses, which is the single largest risk factor for serious complications. Others include topping off lens solutions in cases, using tap water to store lenses and infrequent cleaning or replacing of lenses and cases.

Other complications have been reported in contact lens wearers after smoking tobacco, marijuana or e-cigarettes and those under the influence of drugs or excessive alcohol consumption. These included increased inflammatory and infective rates and decreased performance.

Daily disposables are more convenient for patients since there is no upkeep; not surprisingly, they have the highest compliance with lens replacement and the lowest complication rates. Wearers also have fewer inflammatory complications and less severe cases of microbial keratitis. However, patients who inappropriately reuse daily disposables are actually most at risk of developing complications, since the practitioner doesn't go over proper hygiene guidance, as the lenses are meant to be single-use products.

Perhaps related to patients reusing dailies is that they "don't think about contact lenses as being medical devices," Dr. Jones points out. "They think of them as being a commodity

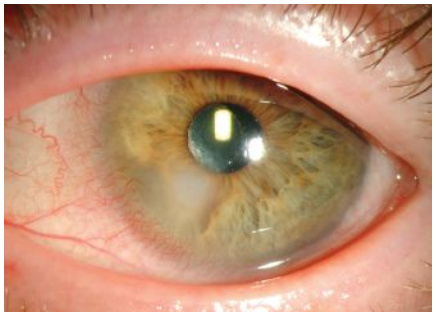


Photo: Christine Sindt, OD

An example of a *Pseudomonas* infection, which can be far more commonly found in nonadherent contact lens patients.

product, so I think the big thing for me is to give practitioners the opportunity to be able to get that message across to patients that lenses are safe—unless you don't do what you're supposed to. In which case, the outcome can be not so nice." This could also have been exacerbated by what he explains as the pandemic causing patients to avoid frequent follow-up to save time and costs, but ultimately contributing to reduced satisfaction with lenses and increased risk.

The systematic review covered by this subcommittee looked at the association of lifestyle factors and soft contact lens dropout. They found, not surprisingly, that the most common reason for dropout was lens discomfort. The most common reason for dropout among presbyopes using multifocals was for vision quality. However, the most common general reason suggests contacts are contributing to concerns of dry eye symptoms in a substantial number of patients.

Use of Cosmetic Products

Few consumer products are as problematic as cosmetics—used worldwide and all throughout history but defined, manufactured and regulated in very inconsistent ways. As the eye makeup industry alone is valued at $15.5 billion, the prominence with which these cosmetics are used should prompt more stringent safety protocols. Unfortunately, this is not the reality of the industry right now, with TFOS outlining that a "number of these ingredients can act as allergens, carcinogens, endocrine disruptors, immunosuppressants, irritants, mutagens, toxins and/or tumor promoters and may damage the ocular surface and adnexa."[2]

In the US, the FDA estimates 12,500 chemicals are used in cosmetics, but less than 20% of those have been reviewed for safety.[2] The US is much more lax than European countries in regulating cosmetic manufacturing; the US has only banned 11 chemicals for toxicity, while the EU has banned or restricted over 1,300.

Covered in the report are the most deleterious offenders known so far that have made their way into cosmetic products, including benzalkonium chloride, chlorphenesin, formaldehyde-releasing compounds, parabens, phenoxyethanol, phthalates, prostaglandin analogues, retinoids (vitamin A metabolites), salicylic acid and tea tree oil (terpinen-4-ol).

Benzalkonium chloride may induce tear film instability, goblet cell loss, conjunctival squamous metaplasia, cell apoptosis and disrupted corneal epithelial barrier. The preservative can result in irritating, burning, itching, foreign body sensation, conjunctival hyperemia, blepharitis, meibomian gland loss, DED, glaucoma surgery failure and anaphylaxis. It's not surprising, based on these manifestations, that the compound has been found toxic to corneal, conjunctival and meibomian gland epithelial cells *in vitro* at levels much lower than those approved for eye makeup use.

Formaldehyde-releasing compounds and parabens are likewise toxic to corneal, conjunctival and meibomian gland epithelial cells. They can cause damage due to mutagenic, carcinogenic and pro-allergenic properties. Parabens, used in over 22,000 US cosmetics, act as allergens and endocrine disruptors while also possessing estrogen potency and anti-androgen activity, with the most common to look out for being methylparaben and ethylparaben. Through these properties, these compounds may increase malignancy risk.

Phthalates are a compound used in cosmetics as solvents in removers or fragrances and are sometimes found as plasticizers in packing materials that can leach into cosmetics unintentionally. They, like parabens, are linked to endocrine disruption and anti-androgen activity as well as reproductive disorders, hepatotoxicity, neurotoxicity and more. They negatively impact corneal endothelial cells' growth and viability. Consequently, dibutyl phthalates have been banned in Europe for cosmetic use, but still exist in many US products.

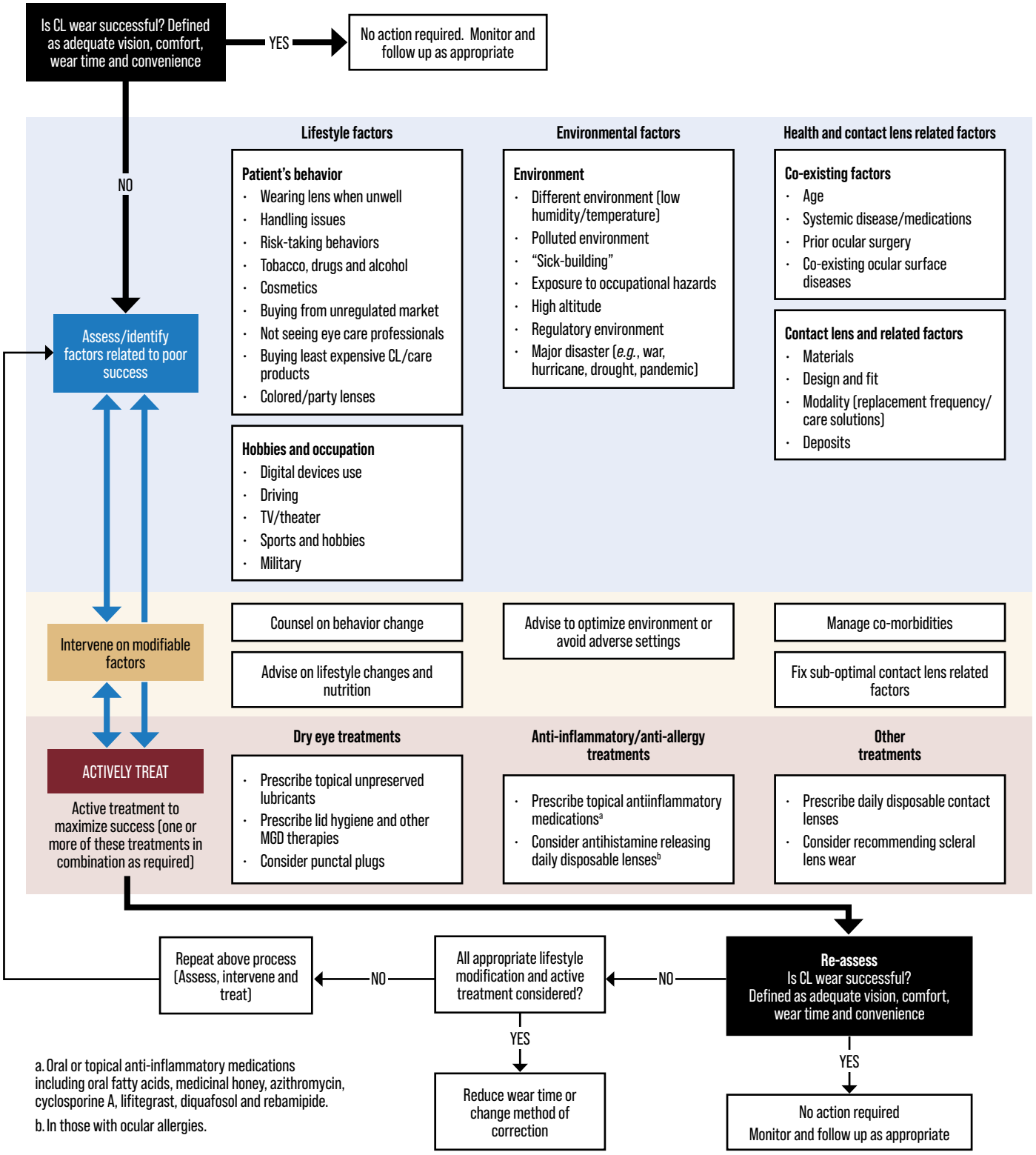
Tea tree oil is another endocrine disruptor with anti-androgen activity, specifically linked to promoting meibomian gland dysfunction. However, unlike the others, it does possess some valid medical uses, like in relieving *Demodex* infestations. However, terpinen-4-ol should be used judiciously since it may contribute to antibiotic resistance in human pathogens, the report says. It may also induce gynecomastia in boys and has been found to kill all meibomian gland and corneal and conjunctival epithelial cells at 1% concentration after only 90 minutes *in vitro*.

Other ingredients often causing ocular discomfort are castor oil, fragrances, gold, heavy metals and talc. These ingredients are often linked to contact dermatitis. Ingredients also causing ocular discomfort but for different reasons are prostaglandin analogs, retinoids and salicylic acid. While retinoids and salicylic acid are not typically used in cosmetics, being placed closely on the skin near the eyes can cause meibomian gland changes and ocular surface toxicity, respectively.[2]

It's not just which kinds of makeup are applied that can cause problems, but how. Sharing eye makeup can introduce bacterial, viral or *Demodex* transmission. Repeatedly using a single cosmetic can introduce microbes into

Potential Management Strategies for Contact Lens Discomfort

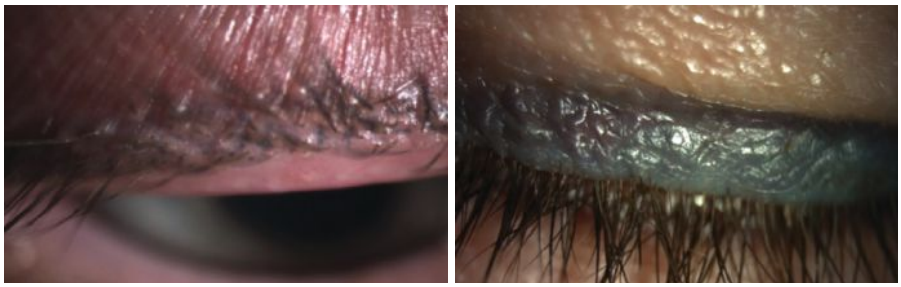
Consensus opinion of the TFOS Lifestyle Workshop Contact Lens Subcommittee.



a. Oral or topical anti-inflammatory medications including oral fatty acids, medicinal honey, azithromycin, cyclosporine A, lifitegrast, diquafosol and rebamipide.

b. In those with ocular allergies.

Photos: Tracy Doll, OD



Inappropriate use of permanent makeup. Both patients have dry eye with MGD.

containers; this has been corroborated by 79% of used mascaras testing positive for *Staphylococcus aureus* and 13% for *Pseudomonas aeruginosa.* Even further, contamination rates are linked to amount of use, product age and the number of users.

Different cosmetics applied on or near the eye vary widely in observed adverse effects. Mascara can migrate to the ocular surface itself through blinking, can block meibomian glands when applied to the mucocutaneous junction of the lid margin and can obstruct the nasolacrimal duct and canaliculi as well as cause contact dermatitis from ingredients. Eyeliner similarly can predispose cosmetics to migrate to the ocular surface when applied to the mucocutaneous junction and contribute to meibomian gland dysfunction. Eye shadow contributes to irritation and eye primers to allergic reactions.[2]

The brushes and sponges used to apply makeup often harbor microbial growth through skin oil, debris and moisture. One recommendation is to use hypochlorous acid wipes as a cleaning solution or makeup remover, since it possesses antimicrobial properties. By contrast, the often-used micellar makeup removers can migrate to under the eyelids and increase tear film evaporation or cause decreased tear stability, while oil-free surfactant removers can cause eyelid irritation.[2]

This subcommittee's systematic review also tackled whether eyelash growth products are linked to ocular surface disease signs or symptoms; based on the current literature, it was unable to come up with clear conclusions.

However, the subcommittee was able to provide some concrete recommendations for the cosmetics industry and/or other stakeholders like the FDA:

1. Provide information about a cosmetic's function, toxicity, indications, contraindications, durability and expiration date, as well as concentration.
2. Perform well-controlled, high-quality studies to examine acute and chronic effects of eye cosmetic ingredients and procedures on the ocular surface and adnexa.
3. Develop guidelines to assess safety and tolerability of eye cosmetic products.
4. Establish more stringent and rigorous oversight of eye makeup industry.
5. Develop standardized and universally accepted definitions of the words 'clean' and 'natural' as they relate to cosmetics.
6. Educate eyecare providers and consumers about risks associated with ingredients in eye cosmetic products.

Digital Device Use

It has been widely recognized that our dependence on modern technology is likely causing all sorts of problems, from cognitive changes in children to sleep problems and much more. While digital eye strain is one such effect, this subcommittee refreshingly does not try to offer admonitions to lower one's digital consumption, recognizing that it's just not feasible in today's world.

Instead, this report covers how digital eye strain is often exacerbated by other underlying conditions and offers solutions as they relate to those. First, though, the group had to define digital eye strain: *the development or exacerbation of recurrent ocular symptoms and/or signs, related specifically to digital device screen viewing.*

This report looked at many different types of displays and their characteristics, such as size, resolution, refresh rate and viewing distance, all of which can have an effect on the ocular surface.

Diagnosing digital eye strain comes with challenges. Two of the most popular questionnaires used in patient screening—the Computer Vision Syndrome Questionnaire (CVS-Q) and the Computer-Vision Symptom Scale (CVSS17)—fail to address whether symptoms are also experienced outside of digital device use. They look at frequency and severity of symptoms, but "there is no criteria to link questionnaires specifically to digital device use and many require only one symptom to be reported, hence we have a very high prevalence," notes subcommittee chair James Wolffsohn, FCOptom, PhD, head of the School of Optometry at Aston University, Birmingham, UK. Reported rates of digital eye strain vary widely, from 32% to 98%, depending on diagnostic criteria and occupation.

Symptoms on the questionnaires include burning, eye pain, headache, redness, photophobia, tearing, repeated/frequent blinking, heavy eyelids, itching, blurred vision, double vision, eye strain and foreign body sensation, many of which could be indications of other underlying problems.

Thus, the subcommittee concluded that "currently there is no robust algorithm to diagnose digital eye strain and many people 'diagnosed' with digital eye strain probably have dry eye disease, uncorrected/not fully corrected refractive error and/or a binocular vision anomaly which have their own diagnostic criteria and established evidence-based management strategies."[3]

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The subcommittee encourages doctors to elicit reports of recurrent ocular symptoms (and possibly signs) specifically when using digital devices. It is important to check with patients that any increase in symptoms or signs while using digital devices is not also occurring during non-digital tasks.

Reasons for digital eye strain occurring are mainly due to mechanisms of blink abnormalities that cause ocular surface and tear film alterations, the report notes. This may be caused by underlying vision or accommodation deficiencies as well as oculomotor function that can induce visual disturbances like asthenopia, blurred vision and focusing and accommodative difficulties.

The report also covered possible management strategies that could improve symptoms of digital eye strain.

"Oral omega-3 supplementation does seem to have a beneficial effect on digital eye strain," Dr. Wolffsohn says. "We know omega-3 is good for ocular health in terms of anti-inflammatory effects, and as we know that ocular discomfort generally has an inflammatory component, this may explain its benefit."

Likely effective management strategies include reminders created through software. These can pop up on a computer or phone screen to notify the user to take rest breaks, provide blink reminders or adhere to the 20/20/20 rule. Other likely strategies are artificial tears, probiotics, eyelid warming, humidifiers and using e-paper devices (like a Kindle) when possible. Notably, however, the blue-light blocking lenses that have become popular in some circles were shown to be ineffective—or, rather, to lack solid scientific evidence of support for recommended use—as was antioxidant supplementation.[3] The report advises practitioners not to recommend patients invest in blue-light blocking lenses, as they are often costly and have thus far failed to show documented clinical benefits.

Photo: Getty Images

While device use can lead to digital eye strain, underlying conditions need to be checked in order to determine if the strain is a symptom originating elsewhere.

Other options center on the task itself, with advice on altering device settings or the type of device being used. It has been found that digital eye strain usually occurs around the four- to five-hour mark, so working for that long or extended past this frame may exacerbate symptoms, explains Dr. Wolffsohn. As well, digital eye strain may be made worse through cognitively demanding material.[3]

A few studies have found more demanding tasks to cause users to reduce their blink rate, since longer fixation is needed to perform said task. Interestingly, this could be a subconscious mechanism to attempt to stay focused by avoiding interruptions. As such, interspersing demanding work with passive activity may prove a good way to tamp down eye strain. Device settings can be changed to help with symptoms, including increasing font size and changing the type to something more easily readable. Bypassing small devices for larger ones and increasing view distance may also provide some benefit, as may using circularly polarized light-emitting displays.[3]

Clarifying what is actually effective will hopefully combat the productivity lost through this condition and improve quality of life.

Medications & Elective Procedures

Just as with cosmetics use, elective (or semi-elective) procedures and medications are meant to enhance quality of life. However, no surgical or medical intervention is without potential side effects, and those impacting the ocular surface are certainly no exception.

Medications can cause ocular surface disease through toxicity of preservatives, ingredients or excipients like surfactants, co-solubilizers and preservative aids, pH or tonicity of the formula or from drug overuse.

Benzalkonium chloride is the main preservative known to cause toxic effects, outlined in the Cosmetics section. Preservatives can also cause allergic and immune-inflammatory effects. Artificial tears, gels and ointments used for dry eye, while offering benefits, can cause their own adverse reactions. If opting for preserved agents, 'soft' or 'disappearing' preservatives like Polyquad, sodium perborate, Purite and SofZia show lower cytotoxic effects to the ocular surface than benzalkonium chloride does, according to the report.[4]

Alternative medicines like aloe vera and manuka honey have both been recommended for dry eye. Note that aloe can result in ocular allergies, redness, irritation or burning, and manuka honey or honey eye drops or gels can produce conjunctival inflammation and should not be used if patients have an allergy to bee products.

Antihistamines, mast cell stabilizers and dual-acting drugs are all anti-allergic therapies known to cause a wide range of negative ocular effects, as can topical alpha-adrenergic receptor agonists and NSAIDs. Antihistamines can have mild side effects. Azelastine and emedastine can cause ocular irritation and dysgeusia, and emedastine can also result in burning, stinging, itching, dry eye, epiphora and visual disturbances. Systemic antihistamines may be more of an issue, as they can decrease aqueous and mucin production from lacrimal glands and goblet cells and induce lacrimal gland vasoconstriction, causing decreased tear production to lead to dry eye disease. Topical versions are

preferred when possible since their adverse effects are lessened.[4]

Sunscreens, topical steroids and various ointments and creams can cause negative ocular effects. Mainly, ones to look out for are topical acne and rosacea meds containing alpha hydroxy acid (glycolic acid), beta hydroxy acid (salicylic acid), retinoids and ivermectin.

Systemic drugs can equally contribute to ocular surface problems, with emphasis in the report placed on conditions of Stevens-Johnson syndrome and toxic epidermal necrolysis. Sao Paulo's José Gomes, MD, lead author of this subcommittee report, brings attention to the fact that these conditions "develop after patients with genetic predispositions take these medications to treat a specific infection and develop an acute reaction that can evolve to chronic cicatricial changes in the ocular surface, compromising the vision of the patient." But even simple cold meds, widely used in the population, can have deleterious effects, he notes.

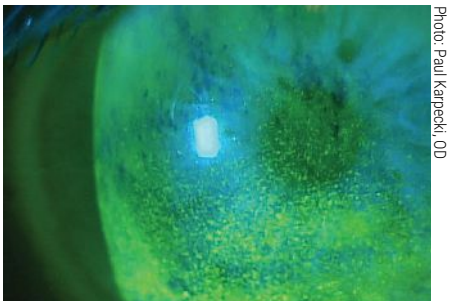

Photo: Paul Karpecki, OD

Benzalkonium chloride can cause a host of problems to the ocular surface; in this case, toxicity is present.

Drug-induced dry eye, whether from topical or systemic compounds, should be treated by identifying the culprit and stopping administration if possible or switching to something else. Topically, this means using preservative-free or low-toxicity preservative drugs.[4]

Surgical procedures focused on or around the eyes—*e.g.*, blepharoplasties, ptosis repair, canthoplasty, brow lifts—can cause various types of ocular surface damage. Botox injection is a first-line therapy for blepharospasm and hemifacial spasm but one study found it induced ptosis in 8.4% to 13.4% of cases, transient tearing in 5% to 10%, dry eye in 3% to 7.5%, photophobia in 2% and ectropion in 1%, the report states.[4]

Conversely, interventions such as punctal plugs and low-level light therapy seem to help with dry eye, the latter specifically improving meibomian gland dysfunction. Pinguecula and pterygium excisions both show some post-op improvement in dry eye symptoms, as does conjunctivochalasis.[4]

Using CO_2 or Er-YAG lasers can result in conjunctival hyperemia, corneal ulceration and bullous keratopathy or ectropion. Refractive surgery's potential to induce post-op dry eye is well known. One study of LASIK patients found dry eye persists in up to 94.8% at one day, 85.4% at seven days and 59.4% at 30 days. More worrying is LASIK-induced neuropathic epitheliopathy, which develops in up to 4% of patients, according to the report. PRK patients had dry eye up to six months post-op

in 43% in one study. However, risk factors are known and screened for: pre-existing dry eye, female sex, Asian race, contact lens use and older age.

Other procedures that have resulted in dry eye are corneal crosslinking (with epi-on displaying better OSDI scores than epi-off), cataract removal and gamma knife radiosurgery for trigeminal neuralgia. With cataract surgery, dry eye improvement typically occurs by three months post-op, though may take up to six in diabetic patients.

Taking the multitude of procedures and medications into consideration, Dr. Gomes points to a few ways to prevent or reduce dry eye and other ocular surface problems. "Adverse events may be reduced by changing to a different class of topical medication, using corticosteroids, lubricating the eyes frequently and reducing exposure to preservatives."

He also puts responsibility on practitioners to "stress that increasing the awareness of the potential risks, benefits and consequences will help patients to make the right decisions when considering when to undergo elective procedures and medications."

Environment & Climate

We cannot easily change the environment we live in, but at least the knowledge of which factors are contributing to ocular surface health can aid in developing solutions.

The climate itself has many contributors to ocular surface status. Extreme high or low temperatures both in- and outdoors have been associated with dry eye, and temperature variations may be related to allergic conjunctivitis. Low humidity has been linked to greater ocular irritation, with one study showing improvement of symptoms with indoor humidity of 30% to 40%. Dry eye symptoms are exacerbated in low humidity environments like in deserts, airplane cabins and during dry seasons.

Wind speed is not well-documented in relation to ocular surface effects, but cases of corneal freezing and frostbite exist in ultra-marathon runners exposed to high wind speed and military freefall parachutists experiencing high wind, respectively. One suggestion for those living or working in cool, low humidity and windy environments is to wear silicone hydrogel contact lenses rather than hydrogels, due to the latter showing greater dry eye and visual disturbance symptoms. Dew point—the temperature at which air must be cooled to reach maximum water saturation—may serve as a protective factor against dry eye with higher levels.

High altitude is known for causing short-term effects of corneal thickening and long-term effects of dry eye and pterygium due to hyperbaric conditions, stronger ultraviolet (UV) radiation compounded by higher number of sunshine hours, low air pressure and dry and cold air. Often coinciding with high altitude, UV radiation is associated with conjunctival and eyelid malignancies and climatic droplet keratopathy; it primarily affects outdoor workers.

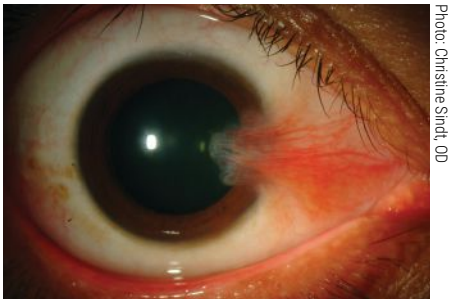

Photo: Christine Sindt, OD

Pterygia are fairly common among those living in higher altitudes or closer to the equator.

Recently, more extreme weather conditions like increased temperatures and precipitation have caused longer pollen seasons and higher indoor and outdoor mold spore concentrations, resulting in more allergic conjunctivitis and ocular allergic symptoms, potentially exacerbating dry eye as well.

Pollution is another source of negative health effects. This subcommittee's systematic review investigated whether specific chemical pollution compounds are related to dry eye incidence. They found it to be greater with exposure to air pollutants of nitrogen dioxide (NO_2) and carbon monoxide (CO), as well as with soil pollution from chromium. NO_2 has been associated with greater ocular irritation, lower tear break-up time and increased meibomian gland dysfunction, while CO is likely associated with increased dry eye symptoms. However, there was no increased dry eye prevalence with particulate matter. Dry eye disease and conjunctivitis have also been correlated with both indoor and outdoor pollution.

Two conditions of note are "sick building" and "sick house" syndromes, which display ocular symptoms. Similar in nature, both describe a scenario where the occupant experiences acute health effects directly linked to spending time in a work building or the home, with symptoms subsiding once away from the premises. Symptoms can range from chemosensory changes to skin symptoms, but as it relates to the eye, the most common side effects are tired or strained eyes, dryness, itchiness, irritation and watering. Since these symptoms may also be signs of ocular conditions of dry eye disease, refractive error or conjunctivitis, it's hard to parse whether symptoms are always due to sick building syndrome or are indicative of a building-related illness.[5]

Either way, patients should be made aware of the possibility of their work and/or living space making their ocular symptoms worse. The syndromes are likely caused by many interrelated factors. This can be seen through the association of sick building syndrome symptoms and female sex, asthma or parental asthma history, pollen or pet allergy, humidity, dampness, office crowding, lack of office cleanliness and more.[5]

The report devotes some attention to the common finding of pterygia, which has a fairly high prevalence of 10% to 12%, with higher incidence closer to

the equator. This is unsurprising as it is linked to prolonged sunlight exposure, higher altitude and outdoor exposure.

Covered last in this section is the range of ocular surface injuries that can occur. Chemical injuries can occur from occupational exposure, especially from construction and agricultural work. Household exposure can result from cleaning agents and hydrogen peroxide. Thermal injuries happen from direct flames, scalding liquid, burning items, curling irons or fireworks. Many of these are risks that people are exposed to daily, so informing patients of the risks of these agents or exposures may help them to be cautious, especially toward their eyes.

Nutrition

Unlike some other categories covered, this subcommittee report found the scientific grounding to be lacking overall in solid evidence across many facets of nutrition, since the literature is sparse. However, there is still enough to look at many aspects and likely associations, or lack thereof, with dry eye.

The most solid evidence exists for dietary components of omega-3 and omega-6 polyunsaturated fatty acids. Omega-6 does not benefit the ocular surface but omega-3 does. Greater omega-6 consumption correlated with a 2.5x higher risk of dry eye, while a 30% reduction in risk was observed with each gram of omega-3 consumed each day. This may be due to omega-6 being more pro-inflammatory while omega-3 exhibits greater anti-inflammatory properties. As such, the ideal ratio of consumption of omega-6 to omega-3 is less than 4:1. Despite this, Maria Markoulli, PhD, MOptom, the primary author of this subcommittee and a member of UNSW Sydney's School of Optometry and Vision Science, still points out that "what we don't yet know is what the optimal dietary intake needs to be to prevent and manage dry eye disease."

Macronutrients most important in maintaining ocular surface health include vitamins $A_{2,3}$, B_{12}, C and D. Vitamin A deficiency can cause reduced or absent goblet cells and corneal punctate keratopathy. Long-term, this deficiency can lead to corneal perforation and other effects. Vitamin B_{12} deficiency was associated with a 1.5x increased risk of having dry eye, the report found. Vitamin C is present in human tears and serves as an antioxidant defense as well as helping heal the cornea following injury, suggesting it could play a role in dry eye if insufficient.

Photo: Getty Images

The Mediterranean diet has been shown to reduce risk of dry eye.

There is much evidence of vitamin D deficiency impacting dry eye, including its ties to the pathogenesis of the disease. Selenium and lactoferrin may play a role in maintaining the ocular surface, as decreased levels of selenium in tears and decreased lactoferrin levels were linked with dry eye.[6]

Although hydration offers plenty of benefits for many organs and organ systems, it does not seem to be indicative of a protective factor against dry eye or other ocular surface outcomes with increased intake, the report found.

Endocrine-disrupting chemicals may be consumed through ingestion, leaching from food containers, and end up changing gut microbiome diversity. Blood concentration of mercury is linked to dry eye symptoms, with main consumption happening through contaminated fish. Alcohol is weakly associated with dry eye, but with no increased risk seen in heavy drinkers. Other dietary factors increasing the risk of dry eye are anorexia nervosa, food intolerance and food allergy. About 14% of those who possess some form of food allergy have allergic conjunctivitis and it puts patients at an almost 1.5x increased risk of dry eye development.[6]

As far as specific habits are concerned, only the Mediterranean diet is directly linked to the ocular surface by decreasing dry eye symptoms and risk of Sjögren's syndrome, likely due to anti-inflammatory properties from olive oil and nuts.

Dietary additives or supplementation of certain agents have been studied on their effects on the ocular surface. Caffeine may actually have a slight protective effect against dry eye, as might manuka honey, which decreased allergic symptoms with dietary birch pollen honey. Dr. Markoulli points to "oral ingestion of multiple Chinese herbs that have been reported effective against Graves' ophthalmopathy and dry eye, and curcumin has been found to reduce oxidative stress, angiogenesis and inflammation."

Vitamin A supplements reduce dry eye symptoms compared with no treatment or treatment of cyclosporine, according to the report. Vitamin B_{12} administration similarly improves dryness symptoms. Omega-3 is also effective as a supplement to decrease dry eye symptoms and signs, but optimal dosage, composition and duration of supplementation treatment still needs to be determined.

Nutrition extends beyond the food we eat, also comprising the gut microbiota. As Dr. Markoulli notes, "the gut microbiome plays an important role in the regulation of low-grade chronic inflammation and ecological shifts within the gut microbiome can induce imbalance or dysbiosis, which is associated with chronic disease."

Specifically, dry eye is associated with severe gut dysbiosis and reduced microbiome diversity. Luckily, pre-

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Indication

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

Important Safety Information

- Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients.
- 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.

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*Xiidra reduced symptoms of eye dryness at 2 weeks (based on Eye Dryness Score compared to vehicle) in 2 out of 4 studies, with improvements observed at 6 and 12 weeks in all 4 studies.[1†]

Important Safety Information (cont)

- 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 Brief Summary of Important Product Information on adjacent page.

†Pivotal trial data
The safety and efficacy of Xiidra were assessed in four 12-week, randomized, multicenter, double-masked, vehicle-controlled studies (N=2133). Patients were dosed twice daily. **Use of artificial tears was not allowed during the studies.** The study end points included assessment of signs (based on Inferior fluorescein Corneal Staining Score [ICSS] on a scale of 0-4) and symptoms (based on patient-reported Eye Dryness Score [EDS] on a visual analogue scale of 0-100).[1]

Effects on symptoms of dry eye disease: A larger reduction in EDS favoring Xiidra was observed in all studies at day 42 and day 84. Xiidra reduced symptoms of eye dryness at 2 weeks (based on EDS) compared to vehicle in 2 out of 4 clinical trials.[1]

Effects on signs of dry eye disease: At day 84, a larger reduction in ICSS favoring Xiidra was observed in 3 of the 4 studies.[1]

References: 1. Xiidra [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp. **2.** Data on file. DRF Fingertip Formulary® Novartis Pharmaceuticals Corp; July 2022.

XIIDRA® (lifitegrast ophthalmic solution), for topical ophthalmic use
Initial U.S. Approval: 2016

BRIEF SUMMARY: Please see package insert for full prescribing information.

1 INDICATIONS AND USAGE

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

4 CONTRAINDICATIONS

Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients in the formulation *[see Adverse Reactions (6.2)]*.

6 ADVERSE REACTIONS

The following serious adverse reactions are described elsewhere in the labeling:

- Hypersensitivity *[see Contraindications (4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in 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 practice.

In five clinical trials of DED conducted with lifitegrast ophthalmic solution, 1401 patients received at least one dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had less than or equal to 3 months of treatment exposure. One hundred-seventy 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%-5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus, and sinusitis.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Xiidra. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

Rare serious cases of hypersensitivity, including anaphylactic reaction, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, urticaria, allergic conjunctivitis, dyspnea, angioedema, and allergic dermatitis have been reported. Eye swelling and rash have also been reported *[see Contraindications (4)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

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 premating 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 *[see Clinical Pharmacology (12.3) in the full prescribing information]*.

Data

Animal Data

Lifitegrast administered daily by IV injection to rats, from premating through gestation day 17, caused an increase in mean pre-implantation 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.

8.2 Lactation

Risk Summary

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 *[see Clinical Pharmacology (12.3) in the full prescribing information]*. 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.

8.4 Pediatric Use

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

8.5 Geriatric Use

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

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and probiotics may help to improve dry eye symptoms. This approach to dry eye may be something to look out for in the future, as Dr. Markoulli mentions "the field of modulating the gut microbiome as an intervention to treat dry eye disease is relatively in its infancy."

Diseases related to nutrition can also impact the ocular surface. Obesity, metabolic syndrome, diabetes, cardiovascular disorders, chronic kidney disease, inflammatory bowel disease and irritable bowel syndrome are all linked with abnormal ocular surface changes and increased dry eye prevalence, symptoms and/or signs. Ocular complications can result more often after bariatric surgery due to malabsorption. For some reason, however, hypertension is inversely linked with dry eye prevalence.

Societal Challenges

This section comprises factors that are out of one's personal control and instead are what might be considered issues that need to be addressed by entire countries or cultures.

However, perhaps the most obvious factor beyond our control is our biology and the aging process. Dry eye is increasingly prevalent as age increases and the related condition of meibomian gland dysfunction also increases with age, potentially exacerbating or contributing to dry eye.[7]

Sex is a risk factor for dry eye, with female patients more at risk, as well as observed biological and physiological differences seen in structures of the cornea, conjunctiva, lacrimal glands, meibomian glands and tear film. This yields an almost twofold higher risk for women to develop dry eye compared with men. However, higher rates of asymptomatic meibomian gland dysfunction are seen in Caucasian males.[7]

Southeast Asians have 1.5x to 2.0x higher risk of having dry eye disease and meibomian gland dysfunction, the report points out. Heritability of dry eye seems to sit at about 30% for symptoms and 40% with a previous dry eye disease diagnosis. Signs of dry eye range from 25% to 80% in heritability.[7]

Also outside of many people's capabilities are fixing issues of malnutrition or food insecurity, as without proper nutrition, the eye (as well as the rest of the body) cannot function optimally. Water, sanitation and housing are all factors associated with trachoma development and other waterborne diseases.

Fiona Stapleton, PhD, MCOptom, also a part of UNSW's School of Optometry and Vision Science, specifies as this subcommittee's head that "there's also a very strong link between education and poverty, socioeconomic class and access to health services which will affect both the prevalence and severity of many ocular diseases."

Photo: Jakayla Toney/Unsplash

Global pandemics not only expose vast populations to disease but also to numerous second-order effects, such as COVID's mask-induced dry eye and greater reliance on digital screen time.

Remoteness, geography and seasonality can all impact the types of ocular surface diseases seen and the severity displayed. Along with this, the availability and affordability of services will vary by region. Ocular surface disease presence will be compounded by the cost of diagnostics and treatment, with options of national health services, insurance or out-of-pocket expense weighing on patients with how likely they will be able to afford treatment.

Occupation affects how likely patients are to develop ocular surface diseases. Exposure, both short- and long-term, to corrosives and excess heat can cause acute or chronic ocular surface injury and complications. Cleaners, miners, construction workers, laboratory workers, food industry workers, agricultural workers, fire workers and mechanics should take caution with adequate protective eyewear to minimize their heightened risk of ocular surface burns. Working night shifts is a risk factor for meibomian gland dysfunction, tear film instability and worsening dry eye symptoms. Prison populations experience poorer health outcomes from lack of services, nutrition limitations and lack of awareness of disease. Conjunctivitis, xerophthalmia and pterygia are all conditions overrepresented in this population.

Interestingly, higher education may be associated with dry eye, due to increased screen use in white collar jobs. Related to this, socioeconomic status is well-regarded as a contributor to ocular surface disease more generally, with lower status experiencing greater burden. Accessibility to helpful resources and cost still remain issues to many.[7]

With COVID having disrupted lives since 2019, this subcommittee wanted to clarify how the pandemic has impacted ocular surface diseases. First, they looked at screen time use, implementation of online classes and digital device use during the pandemic. Eye symptoms were found to worsen with exposure to screen time and online learning as a consequence of the pandemic, with no ocular symptoms of dry eye improving with exposure. As well, there was worsening or no change associated with signs and symptoms of dry eye when exposed to the virus.

Strategies to mitigate virus spread, like face masks, were also analyzed. Mask wear was found to both induce and exacerbate dry eye signs and symptoms, as well as cause contact lens intolerance and more cases of chalazia. However, allergic ocular symptoms decreased with mask use, probably from a barrier of the nasal passage to exposed airborne allergens.

Dr. Stapleton explains that since remote, hybrid and flexible work are likely to continue, it is reasonable to assume that frequency and severity of ocular surface diseases will continue along with this. As such, practitioners, she believes, "can be proactive with their patients to mitigate these effects." She also puts into perspective how these larger, societal factors are at play with the ocular surface. "Focusing on social determinants and their interactions, rather than just the cause of the disease, encourages the development of more comprehensive, holistic solutions and a 'whole of society' approach to reducing disease morbidity. It encourages practitioners to have a broader discussion with their patients about lifestyle and social determinants."

Personal & Lifestyle Challenges

In the last of the reports, more patient-specific issues are addressed, covering mental health, physical health and lifestyle choices. Although these factors may not initially seem relevant to the ocular surface, there are some surprising associations.

There has been an increasing awareness of how mental health disorders affect the rest of the body. This report covers mainly the conditions of depression, anxiety and generalized stress.

First discussed was depression. An alarming 29% of individuals with dry eye disease also had depression, as one meta-analysis concluded. A different one was able to determine that dry eye disease patients had a higher frequency of depression. Interestingly, dry eye symptom scores were associated with depression severity scores, but data is much weaker when looking at dry eye signs. Of note, both depression and antidepressant medications may be linked to dry eye with a biologic basis, as evidenced by SSRI antidepressants having been linked with ocular surface changes, too.

Anxiety disorders saw a similar trend as with depression. Several studies reported a link between anxiety and a dry eye diagnosis. A PTSD diagnosis increased odds of a dry eye diagnosis twofold, and anxiolytic use is a strong predictor of dry eye diagnosis as well. Similar to depression, there is an association between dry eye symptoms and anxiety, but not signs. However, much of what's been found was done on veterans, so the general population may exhibit differences.

Relieving dry eye symptoms may help with anxiety, as one study found after treating dry eye patients with various methods for three to six months. While dry eye has not been studied specifically with mental health treatments, therapy has helped with other chronic pain conditions.[8]

Photo: Getty Images

Vaping is just one lifestyle choice patients can make that has direct negative consequences on their ocular health.

The effects of stress on the eye are apparent, as worse self-perceived health status and more psychological stress were both linked with increased susceptibility to aqueous deficient and evaporative dry eye and its symptoms.

When sleep is interrupted, it can cause serious issues to the body. Dry eye patients have poorer sleep quality, spend less time asleep and experience more sleep disturbances. Sleep-related factors like excessive sleepiness, insomnia, high sleep apnea risk and receiving less than five hours of sleep are associated with dry eye symptoms, showing a clear connection between the need for proper sleep and maintenance and repair of the body. Primary Sjögren's similarly exhibits increased sleep disturbances, more night awakenings and obstructive sleep apnea presence. However, being able to get adequate rest may revert some observed ocular surface changes, as this was described in animal models.

Obesity may put patients at risk of worsening dry eye, as it has been connected to evaporative dry eye, tear film instability and meibomian gland abnormalities in function and architecture. Unfortunately, treatment for often comorbid obstructive sleep apnea in obese patients has also been linked to dry eye diagnosis and has shown to cause greater ocular irritation upon initiation, with CPAP device use having been reported to induce ocular manifestations in as high as 50% to 70% of patients.

This subcommittee undertook the task of reviewing chronic pain conditions and whether they are contributive risk factors to dry eye disease for their systematic review. One study cited as much as 17% of patients have at least one chronic pain condition. They reviewed many conditions, but found that some were indeed linked with an increased risk of dry eye. These included migraine with a 1.61x increased risk, fibromyalgia with a 1.91x increased risk, irritable bowel syndrome with a 2.16x increased risk and back pain with a 1.60x increased risk. All these observations suggest a comorbidity between chronic pain conditions and dry eye, but mostly with symptoms.

Drugs can affect the ocular surface differently, depending on the type. Kelly Nichols, OD, of University of Alabama Birmingham's School of Optometry and one of the authors of this report, points to the adverse effects of smoking on ocular surface health.

"Surprisingly, there's not a lot of good data to support that, even though everyone would suggest that probably you shouldn't smoke because it could impact your eyes. It doesn't mean the

association isn't there, just that the literature gives us less guidance than we may want." She advises ODs to look a little more carefully at the tear film, and tear film stability in particular, in a patient who's a smoker. "It could potentially have more impact on the ocular surface, whereas symptoms in that individual may not play as significant a role, or at least they're not telling you that."

Vape users experienced greater dry eye disease symptoms and signs compared to non-smokers, the report found, and cannabis use long-term may decrease corneal endothelial density. Alcohol intake is a contributory factor to dry eye, but this may be part of a wider issue of poor nutrition. Caffeine, however, actually shows evidence of increasing tear meniscus height and Schirmer test values two hours after intake, suggesting it may produce better tear parameters.

Dr. Nichols offers some key takeaways to carry into your practice from the findings of this section. "Many patients are either taking anti-anxiety or antidepressant medications. These therapies, and the underlying conditions, also overlap with sleep disorders, and all of these have potential consequences for the ocular surface. So, asking them about their sleep and the comfort of their eyes might be a really important thing to do. Creating conversations around some of these less obvious connections to dry eye might be a positive outcome of the report."

Takeaways & Concluding Remarks

One of the recurring themes throughout all sections of this massive report is that doctors may need to change some of the recommendations they're giving to patients.

"We have to be very careful that we're not just doing something for the sake of it, that we actually have the evidence behind it to support doing that, and we don't have patients investing money in things that might not work," Dr. Craig cautions.

This might be most evident when reviewing the subcommittees' findings on blue-light blocking lenses, hydration or smoking and their effects on the ocular surface.

"It's a really important area to find out more information, but we need better quality studies. We don't have enough evidence yet. The report isn't saying blue light doesn't elevate certain risks. We need to use that information to help drive future research until we do have enough evidence to decide whether things cause a problem."

Dr. Craig is excited by the prospects for change, and thinks that education on these topics will be reciprocally exchanged by clinicians and their patients

in the wake of the TFOS Lifestyle Report, pointing out that patients now more than ever are engaging themselves in becoming informed about their health.

She hopes that these sort of integral conversations between patients and doctors will "help drive better standards in industry and things like cosmetics. If there's resistance from the professions and from the public, then they may be forced to change some of the components within their cosmetics if they're no longer accepted. If it becomes recognized that they cause problems, I think we should see changes happening there."

Cosmetics is one of the most apparent industries in which regulations and manufacturing processes need to be changed to reflect what is currently known about its effects on health, but this is not the only area that needs change.

Through the combined efforts of all the subcommittee reports, we now know more than ever about a wide range of factors that contribute to ocular surface health. Heed the advice and tips given by the researchers of this report, continue to adapt your recommendations as the literature evolves, and you'll be in the best position to help your patients. ■

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25 Lessons Learned from the TFOS Lifestyle Report

1. A risk-taking personality is a better predictor of contact lens compliance than other demographics.
2. Daily disposable lenses provide the best safety and compliance.
3. Experienced contact lens users may need more emphasis placed on reducing dry eye symptoms.
4. Benzalkonium chloride is a pervasive preservative in cosmetics that causes widespread ocular symptoms.
5. Guidelines need to be developed in safety and tolerability of eye cosmetic products, with more stringent and rigorous oversight of the eye makeup industry.
6. Cosmetics should provide information about function, toxicity, indications, contraindications, durability and expiration date, as well as concentration.
7. Digital eye strain surveys and questionnaires need to more stringently parse out symptoms that overlap in the absence of digital device use.
8. Blue-light blocking lenses display no therapeutic effects on eye strain, but oral omega-3 supplementation does.
9. Digital eye strain often overlaps with underlying problems like dry eye or refractive errors and these conditions should be checked for first.
10. Antihistamines, mast cell stabilizers and dual-acting drugs all can have negative effects on the ocular surface.
11. Benzalkonium chloride in topical mediations and over-the-counter products also causes adverse reactions.
12. Any type of refractive surgery can result in postoperative dry eye; therefore, patients should be checked and treated beforehand in the presence of dry eye.
13. Dry eye is exacerbated by environmental conditions of low humidity, high wind, high altitude and strong ultraviolet ray exposure.
14. Changes in climate across the world have resulted in worse pollen seasons, exacerbating dry eye and allergies.
15. Air pollutants of nitrogen dioxide and carbon monoxide, as well as soil pollution from chromium, are all agents that were shown to contribute to dry eye.
16. Omega-3 consumption and supplementation are both shown to improve dry eye. Supplementation of vitamin A or B_{12} is also helpful.
17. It's important to look out for patients with common food allergies, as their likelihood of having ocular manifestations like dry eye or allergic conjunctivitis is fairly high.
18. Although adequate hydration is necessary, any positive effects this may have on the ocular surface and for dry eye are not yet determined in research.
19. The demographic traits of being female, Southeast Asian, elderly or younger adult patients are at greater likelihood to develop dry eye.
20. Occupations exposing individuals to corrosives or excessive heat can cause ocular surface injury or complications including dry eye.
21. The COVID-19 pandemic has exacerbated dry eye through virus exposure and mask wear.
22. Mental disorders of depression and anxiety are associated with dry eye.
23. Chronic pain conditions of migraine, fibromyalgia, irritable bowel syndrome and back pain all increase the risk of having comorbid dry eye.
24. Smoking has yet to be well-established in any adverse ocular surface effects, although vaping and smoking cannabis have been observed to have negative impacts.
25. Seemingly intuitive advice to give patients—*e.g.*, reduce blue light exposure, stay hydrated, quit smoking—still lacks concrete evidence to confirm the usefulness of recommendations given.

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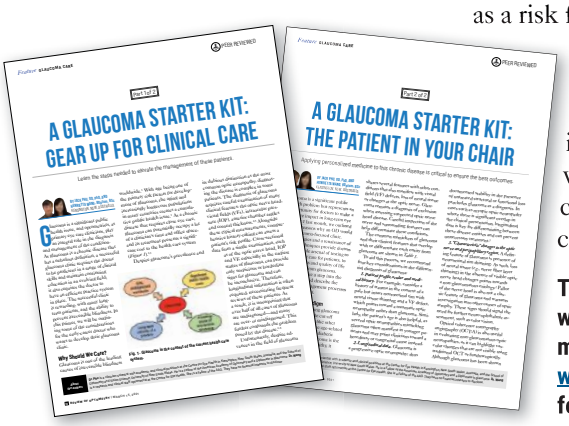
GLAUCOMA CARE BEYOND THE BASICS: ADVANCED TIPS AND CONSIDERATIONS

Discover what skills clinicians should have at this level of management.

BY HENRIETTA WANG, BOPTOM, BSC, AND JACK PHU, OD, PhD
KENSINGTON, NSW, AUSTRALIA

With an increasingly aging population, the prevalence of glaucoma has been projected to reach almost 111 million worldwide by 2040.[1] Optometrists play a critical role in all aspects of a patient's journey with this chronic eye condition, ranging from the initial diagnosis to ongoing management.[2]



In 2021, we published a two-part starter kit article to guide optometrists wanting to set up or further develop their glaucoma clinic. This article is a follow-up that will cover more intermediate or advanced concepts for optometrists such as navigating the challenge of high myopia in glaucoma and strategies for tackling glaucoma progression.

Navigating Care in High Myopia

Myopia has been firmly established as a risk factor for glaucoma development whereby each diopter increase in myopia associated with a non-linear 20% increase in risk of glaucoma which has been shown to accelerate above -6.00D.[3] The concomitant presentation of myopia and glaucoma can pose both a technical and diagnostic challenge to clinicians.

Optical coherence tomography (OCT) is critical in glaucoma assessments. From a technical standpoint, obtaining high-quality artifact-free scans can be difficult in myopic patients. These patients may have anomalous retinal configurations such as prominent posterior staphylomas and peripapillary atrophy, which often result in data loss arising from errors in segmentation or scan truncation.[4]

Although OCT scans in high myopia are associated with a higher prevalence of artifacts, previous work has shown in the majority of cases, these scans still contain sufficient information to cross-sectionally identify glaucomatous features such as retinal nerve fiber

The present article can be read on its own by practitioners already comfortable with the core principles of glaucoma care. For those wishing to review glaucoma management from the fundamentals on up, please find our two prior articles at www.reviewofoptometry.com. They will be linked to the online version of this feature and can also be found in the March 2021 and April 2021 issue archives.

About the authors

Dr. Wang leads the Glaucoma/Neuro-ophthalmology unit at the Centre for Eye Health. She received numerous clinical and academic awards during her undergraduate optometry degree, including a research scholarship for her work in the Retinal Networks Laboratory. **Dr Phu** is clinician-scientist, holding the position of lecturer at the School of Optometry and Vision Science, UNSW. He has published extensively in the field of basic vision science and clinical aspects of glaucoma and maintains a research program in translational clinical research to improve patient care. They have no financial interests to disclose.

layer (RNFL) thinning on circle scans and thickness heat maps.[4]

Therefore, it is still recommended that clinicians review all components of OCT imaging for these patients, including the circumpapillary RNFL thickness values, as well as the RNFL and ganglion cell complex heat maps, to maximize the usable information for glaucoma diagnosis. In particular, clinicians should place more emphasis on interpreting raw data rather than drawing comparisons from normative databases. Patterns of defect that are suggestive of glaucoma include asymmetric loss across the horizontal midline, arcuate like defects and losses that are deepest temporally rather than nasally.

Another clinical consideration optometrists should have in mind when assessing patients with high myopia for glaucoma is the overlap in clinical features between the two entities.[5] High myopia can present with anomalous disc presentations such as tilting or torsion as well as displacement of neural tissue associated with axial elongation.[6] Myopic optic discs can also manifest with glaucoma-like visual field (VF) defects, further confounding accurate diagnosis.[5] As there is no single clinical feature that can be used to definitively distinguish between glaucoma and myopic optic neuropathies, clinicians must instead rely on the difference in natural history to guide differential diagnosis.[5,7]

In contrast with glaucoma, which has a median progression rate of -0.40dB per year,[7] myopic optic neuropathies are typically static or very slowly progressing.[5] Given the variable nature of OCT measurements for progression analysis in these patients, clinicians should rely more upon changes to the disc appearance detected using serial fundus photographs or perimetric progression when assessing these patients.

An example showing the static nature of myopic optic neuropathy is shown in *Figure 1*. This 47-year-old patient was closely monitored over a 14-month period given the myopic configuration of the discs and low

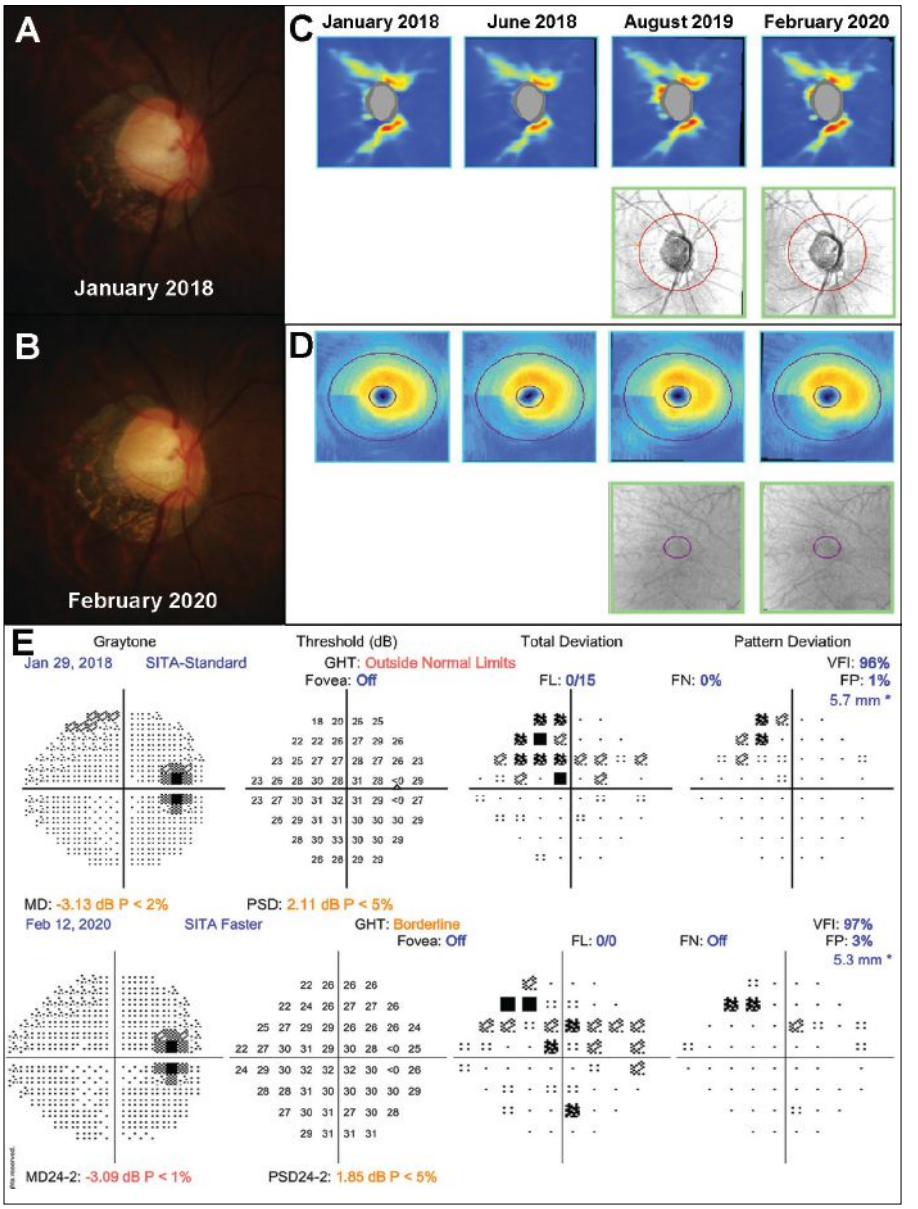


Fig. 1. An example of myopic optic neuropathy in a 47-year-old patient. *A to B:* Fundus photographs showed no change in the disc appearance between January 2019 and February 2020. *C to D:* There was no evidence of structural progression on the RNFL and ganglion cell inner plexiform layer (GC-IPL) guided progression analyses. *E:* 24-2 SITA-Standard VFs also did not show worsening of the existing superonasal defect.

intraocular pressures (IOPs; 14mm Hg OD and 14mm Hg OS). Her structural and functional findings were stable over this period thus supporting the leading diagnosis of myopic optic neuropathy.

Although progression is the one of the most definitive ways for differentiating between glaucoma and myopic optic neuropathy, clinicians may still make the decision to treat in the absence of longitudinal data showing progression. Some factors that may cause clinicians to lean more towards treating rather than monitoring at the initial visit include high IOPs in the context of thin central corneal thicknesses, and central or extensive field defects.[8]

In particular, it is difficult to ascertain the true IOP in patients that have undergone refractive surgery involving the cornea whereby in most instances,

IOP is under-estimated in this subset of patients.[9] In patients with central or extensive field loss, given the existing level of functional loss and potential functional impact, clinicians may err on the side of caution and initiate treatment without confirming progression to preserve as much existing vision as possible.

Clinical tip #1: OCT measurements relevant to glaucoma are often confounded in patients with high myopia. Clinicians should place more emphasis on using raw data as well as longitudinal data to make a more confident glaucoma diagnosis.

No One Approach

In more recent years, there has been a paradigm shift towards greater personalization of glaucoma care.[2,10] In our previous articles, we briefly discussed the importance of understanding glaucoma disease trajectory to determine the need for treatment. Side effects associated with eye drops or laser, cost of treatment, the need for ongoing reviews and even the diagnosis of glaucoma are all factors that can reduce a patient's quality of life.[11,12] Thus, the provision of glaucoma care should balance between preserving a functional level of vision for the patient and ensuring they maintain a reasonable level of quality of life.

There are several factors that clinicians need to consider when making the decision to treat or to escalate treatment. First, it is important for clinicians to establish progression rate and location of vision loss if relevant to prognosticate the patient's risk of vision loss if their glaucoma is left untreated.[2] While there are several risk factors associated with glaucoma, the most definitive risk factor for blindness within a patient's lifetime is the severity of glaucoma at the point of diagnosis.[13-17]

In patients with pre-perimetric or early glaucoma, close monitoring with reviews every four to six months can help identify catastrophic progressors.[18,19] In patients with existing vision loss without historical data to establish

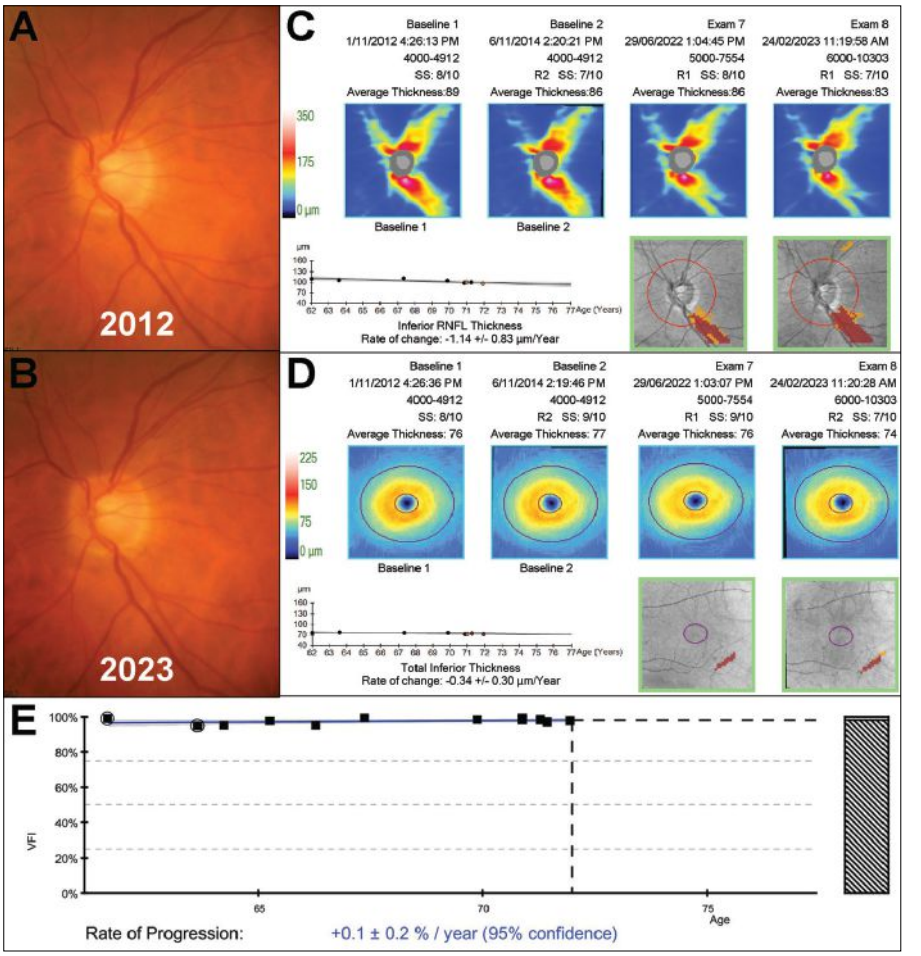


Fig. 2. An example of a 72-year-old patient with slow progressing untreated normal tension glaucoma monitored over an 11-year period. *A to B:* Fundus photographs showed subtle thinning of the inferior neuroretinal rim between 2012 and 2023. *C to D:* Structural progression analyses showed slow inferior thinning on both the RNFL and ganglion cell-inner plexiform layer printouts. *E:* VF index progression analysis showed no evidence of associated functional deterioration.

progression rate, clinicians can stratify risk of progression by extrapolating natural history based on the subtype of glaucoma.

For example, from a statistical standpoint, patients with high-tension phenotypes of glaucoma or pseudoexfoliative glaucoma are more likely to progress faster compared with patients with low-tension phenotypes.[7] Secondly, the trade-off between a patient's likelihood of vision loss based on their disease progression rate over their lifetime, current stage of glaucoma and adverse effects associated with treatment needs to be considered. A 2017 study that evaluated the long-term clinical course of patients with "pre-perimetric" low-tension glaucoma found that over half of these patients did not develop a VF defect.[20] Similarly, a 2015 study that compared outcomes for newly diagnosed open-angle glaucoma patients prescribed latanoprost vs. placebo also showed that over 25% of untreated patients did not demonstrate VF progression over the study period.[21]

These findings support the notion of close observation for newly diagnosed low-tension open angle glaucoma to determine disease progression rate and better understand the patient's risk of vision loss within their lifetime. An example of a 72-year-old patient with slow-progressing untreated normal

tension glaucoma monitored over 11 years is shown in *Figure 2*. Given the slow rate of progression on both structure and function in conjunction with low IOPs (range of 9mm Hg to 15mm Hg OD and 10mm Hg to 15mm Hg OS), the overall risk of vision loss within this patient's lifetime is fairly low.

The discussion to watch vs. to treat should be made in discussion with the patient whereby the risks and benefits are presented to them for them to make an informed decision. Clearly document the details of the conversation as well as the patient's decision in their clinical record.

There are several strategies clinicians can adopt when stratifying risk of blindness in glaucoma patients. To make an individualized projection of disease progression, clustered or more frequent testing may be more appropriate, as this provides clinicians with additional data points to detect change. For example, previous work suggests a minimum of six VFs within a two-year period is most ideal for detecting mean deviation loss.[22] This approach is most useful in pre-perimetric stages of disease where it may be difficult to differentiate between early disease manifestation and normal aging changes.[23]

An alternate method for risk stratification is the use of IOP characteristics such as response to osmotic stress or diurnal pressure fluctuations.[24] In addition to differentiating between low- and high-tension phenotypes, assessing pressure characteristics can also help determine the most appropriate option for treatment (*i.e.*, topical therapy vs. selective laser trabeculoplasty as first-line therapy)[25] or titrating treatment intensity.[26]

Clinical tip #2: Apply a personalized approach to deciding when to watch and when to treat or escalate for newly and previously diagnosed glaucoma patients.

Beyond Traditional Strategies

Recent developments in testing technologies have modernized the workup for diagnosing and monitoring glaucoma. One such example is the introduction of shorter test algorithms for assessing VF such as SITA Faster, which has been shown to significantly reduce testing time while providing near identical results to slower test strategies such as SITA Fast.[27] A major obstacle to assessing visual function in glaucoma has been the variable nature of perimetric test results, which confounds assessment of the structure-function relationship and disease progression.[28]

Despite many authoritative sources recommend performing multiple VFs to overcome this obstacle and improve the amount of useful clinical data for glaucoma diagnosis or monitoring,[22,28] previous work has shown these recommendations are not widely adopted into clinical practice with the majority of newly diagnosed open-angle glaucoma patients receiving fewer than three VFs within the first two years after diagnosis with an average of less than one field per year during follow-ups.[22,28,29] The development of shorter testing algorithms allows for multiple field tests to be routinely performed at each visit to obtain a suitable number of field test results: this technique is known as "front-loading fields".[18,19] This technique increases the likelihood of obtaining a reliable VF result.[19]

By front-loading VFs at six-monthly intervals, catastrophic progression (defined as mean deviation progression rate of greater than -2dB/year) can be detected six to eight visits faster than a non-front-loading approach.[18] By adopting a front-loading approach to VF testing using shorter test strategies, clinicians are able to improve glaucoma diagnosis confidence or progression detection rates, overcome issues with poor reliability associated with shorter tests and reduce the need for additional visits to obtain enough usable VF data.[18,19]

Another recent addition to traditional strategies for glaucoma care is the adoption of "glaucoma supplementary testing" through the addition of ancillary tests that aim to help clinicians with risk stratification and treatment titration. There has been a move away from

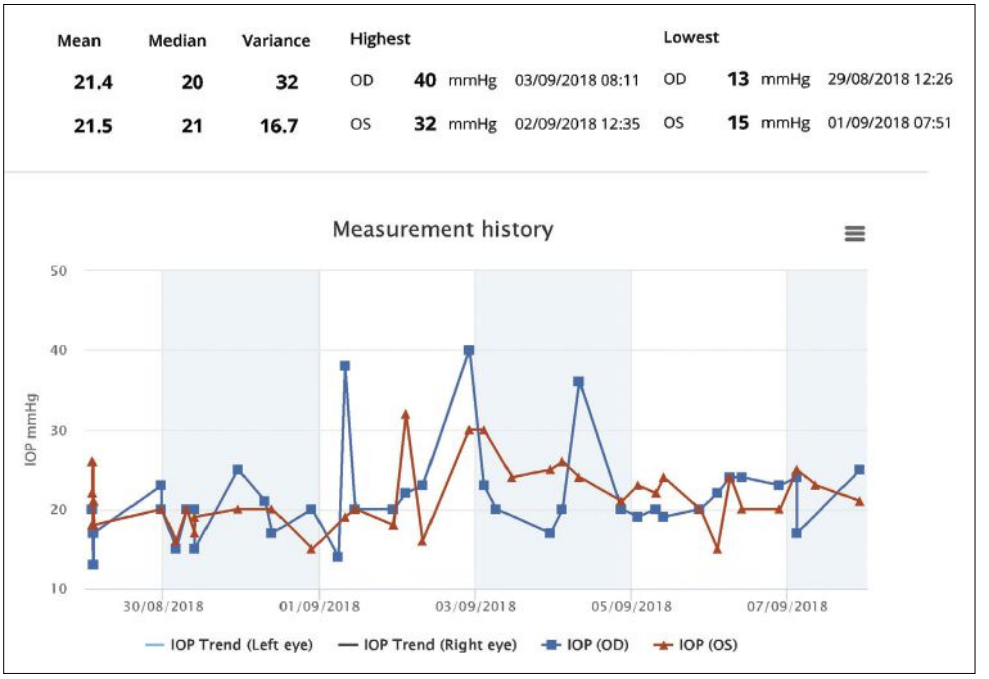


Fig. 3. iCare Home monitoring phasing results for a patient with pseudoexfoliation syndrome and no structural or functional evidence of glaucoma. In-office IOP measurements for this patient ranged between 14mm Hg to 19mm Hg OD and 15mm Hg to 19mm Hg OS.

single applanation pressure measurements to a more holistic approach to assessing IOP characteristics such as diurnal fluctuations or peak IOP.[30] As discussed above, identifying the peak IOP can guide treatment selection and phenotyping of glaucoma to assist with risk stratification.[26] Previous work has shown almost 70% of peak IOPs are measured outside of regular office hours with a predilection for peaking at nighttime.[31]

While historically patients were required to be hospitalized to obtain these measurements, the development of new technologies and techniques such as the water-drinking test or patient-driven home-monitoring devices for measuring IOP has enabled comprehensive evaluation of IOP to be feasibly implemented in practice.[32] Recent work has shown IOP peaks identified with the water-drinking test and the iCare Home device to be highly comparable; thus, these can be used interchangeably if needed.[33] Identifying a patient's peak IOP can help clinicians set treatment targets and stratify progression risk.[34] It can also be used to identify potential intraocular spikes that occur out of office in patients with treated but progressive glaucoma despite IOPs appearing to be on target during in-office measurements.[31]

An example of iCare Home phasing results for a patient with psuedoexfoliative syndrome with no structural evidence of glaucoma is shown in *Figure 3*. In-office IOPs measured across three visits ranged between 14mm Hg to 19mm Hg OD and 15mm Hg to 19mm Hg OS. iCare Home monitoring was deployed to assess the extent of her diurnal pressure fluctuations. This revealed a peak pressure of 40mm Hg OD and 32mm Hg OS. Given these findings, she was started on Travatan eyedrops (travopost ophthalmic solution, Novartis) at night in both eyes.

Clinical tip #3: Adding newer techniques and technologies such as front-loading fields or at-home IOP monitoring devices adds an extra dimension to glaucoma assessments.

> **The development of new technologies and techniques such as patient-driven home-monitoring devices has enabled comprehensive evaluation of IOP to be feasibly implemented in practice.**

Holistic Care

In addition to assessing for out-of-office IOP spikes, 31 clinicians should consider the role of systemic comorbidities in contributing to glaucoma disease progression. The pathophysiology of glaucoma is complex, involving not only intraocular pressure but also vascular flow to the optic nerve head.[31,35] As such, systemic vascular disease may impact the risk and management of patients with glaucoma.[36] Several large-scale studies have highlighted associations between common vascular and metabolic diseases, including hypertension and diabetes, and the development and progression of glaucoma.[37-39]

In patients with on-target IOPs who continue to demonstrate glaucoma progression, it may be necessary to consider the role of systemic vascular diseases. Further, although vascular risk factors have been classically associated with normal tension glaucoma, it is now recognized that it is also relevant to high pressure phenotypes.[40] Clinicians therefore need to consider vascular contributions irrespective of baseline pressures.

A focal point in the pathophysiological pathway between systemic vascular disease and glaucoma progression is the effect each condition has on ocular perfusion pressure around the optic nerve head.[41] Technologies such as OCT angiography (OCT-A) may facilitate the measurement of ocular blood flow (*Figure 4*).[42] However, there remains limited information on how to correlate outputs from OCT-A with risk related to vascular disease. It is possible for clinicians to estimate ocular perfusion pressure by considering mean arterial pressure and IOP.[43] However, similar to OCT-A indices, there is no evidence-based cutoff for a target ocular perfusion pressure.

Much like out-of-office IOP measurements, there may be value in obtaining ambulatory blood pressure measurements to examine its diurnal variation, especially nocturnally.[44,45] Specifically, the concept of diurnal ocular perfusion pressure relates to the prescription of topical beta-blocker therapy for glaucoma. It is now recognised that beta-blocker medications dosed once daily in the morning provides comparable IOP control to twice-daily medications.[46] Given the option to dose morning or night, it may be preferable to dose in the morning to reduce the potential effects on nocturnal blood pressure.[47]

Systemically, the optometrist or ophthalmologist can also liaise with the patient's other doctors to optimize control of the systemic vascular risk factors. A strategy such as 24-hour ambulatory blood pressure measurement in conjunction with IOP phasing can provide valuable insights into the ocular perfusion pressure throughout the day.[48] Clinically, we must recognize that blood pressure that is overly reduced through medications potentially increases the risk of glaucoma progression.[44,45]

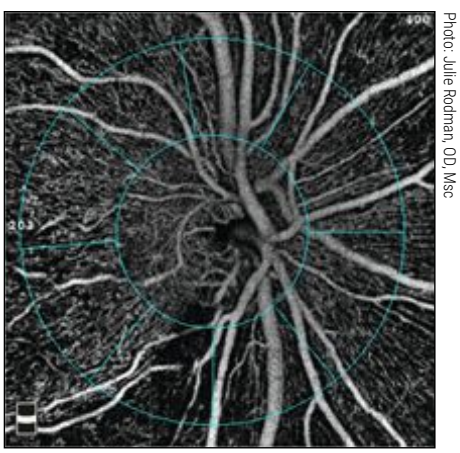


Photo: Julie Rodman, OD, Msc

Fig. 4. By monitoring blood flow within the retina, OCT-A provides a way to assess the health of the ganglion cells that are affected in glaucoma.

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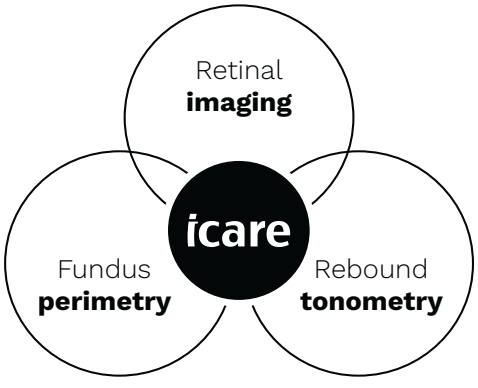

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Aside from the intimate link between ocular perfusion pressure and systemic blood pressure, the control of other systemic diseases may play a role in glaucoma progression.[36] Some studies have suggested that elevated blood sugar levels may be associated with higher IOPs and glaucoma progression risk.[49] Other conditions in which blood flow is dysregulated, such as obstructive sleep apnea, vasospastic disorders (including migraine) and thyroid disease, may also present a similar increase in risk.[50-52] The presence of glaucoma progression with these comorbidities may warrant communication with the patient's other doctors to optimize their management, as control of those factors may also assist in glaucoma management.

Clinical tip #4: Optimizing a patient's glaucoma care extends beyond testing in the consulting room. Encouraging optimal control of a patient's vasculopathic risk factors has implications for disease progression.

Takeaways

Because glaucoma is a chronic disease, the delivery of care encompasses many aspects that range from accurate diagnosis to systemic implications for ongoing management.

While the multifaceted nature of care may present several challenges to clinicians, they also present the opportunity for these clinicians to apply a personalized and holistic approach to improving patient outcomes. ■

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AVOID THESE COMMON GLAUCOMA MISTAKES

Experts share their management missteps and clinical pearls to ensure an optimal outcome for all patients.

BY CATLIN NALLEY
CONTRIBUTING EDITOR

Glaucoma—a lifelong, vision-threatening disease that requires ongoing management—is one of the most common conditions optometrists see in clinical practice. As primary eye care providers, ODs are in a prime position to not only identify patients with glaucoma, but also monitor and successfully treat the condition in the long-term.

"Glaucoma care is an ever-evolving field, and we have to adapt with it. New therapies, both topical and surgical, continue to emerge, scope expansion brings greater accessibility to already existing treatment options, imaging techniques constantly improve and new diagnostic tools emerge as well," says Jessica Haynes, OD, a consultative optometrist at the Charles Retina Institute in Germantown, TN. "We have to be able to determine which treatment options are right for our patients and also which tools and devices are right for our practices."

Below, ODs with extensive glaucoma experience share common management missteps—in no particular order—that can be detrimental to patients and providers, as well as clinical pearls and advice to help fellow optometrists optimize their approach to this disease.

Misinterpretation of the Evidence

OCT has become a critical component of glaucoma diagnosis and management; however, this can lead to poor clinical decisions if the results are not interpreted appropriately. "Relying on OCTs regression analysis alone for diagnosing glaucoma is a major mistake," notes Joseph Shovlin, OD, of Scranton, PA.

"When providers rely entirely on OCT regression analysis—ignoring potential for misinterpretation—it's estimated that about 40% of patients diagnosed with glaucoma are being treated for something they actually don't have," he says. "This is one of the many reasons some estimates show up to 40% of patients being treated for glaucoma actually don't have it. But, we're certainly not suggesting not to treat when there is any concern or some doubt surrounding a diagnosis."

There are number of reasons "red" (false positive) and "green" (false negative) disease can be misinterpreted, according to Dr. Shovlin. For example, common "red" disease causes include wrong birthdate entered (listed as younger); 15% to 20% of normal patients have a "split bundle defect" that may cause a dip into the red zone for regression analysis; and temporal (myopes) or nasal (hyperopes) vessel insertion with displacement.

In the case of "green" disease, Dr. Shovlin notes the potential causes such as wrong birthdate entered (listed as older) and patients whose retinal nerve fiber layer (RNFL) starts high and declines over time but still read as normal for their age (green depiction). "They might lose 10% and still read as green, but that is abnormal," he says. "Look at the top printout for symmetry."

The OCT "stoplight colors"—red/yellow/green—are derived from a relatively small database, explains Danica Marrelli, OD, clinical professor and assistant dean of clinical education at the University of Houston College of Optometry. "The fact that an area shows up in 'red' does not necessarily mean that there is disease, it could just be anomalous or unusual. Furthermore, the 'green' that we consider 'good' has a huge range—the color doesn't let us know if the patient is close to the bottom of that 'green' or if they are close to the top of the range."

When evaluating RNFL OCT findings, Dr. Marrelli advises that optometrists should be looking at the TSNIT or NSTIN curve (whichever your device shows) for symmetry and good modulation (peaks in superior/inferior zones), which is much more valuable than red/yellow/green," she says. "We can both 'over-call' (false positive) and 'under-call' (false negative) glaucoma if we rely on the red/yellow/green."

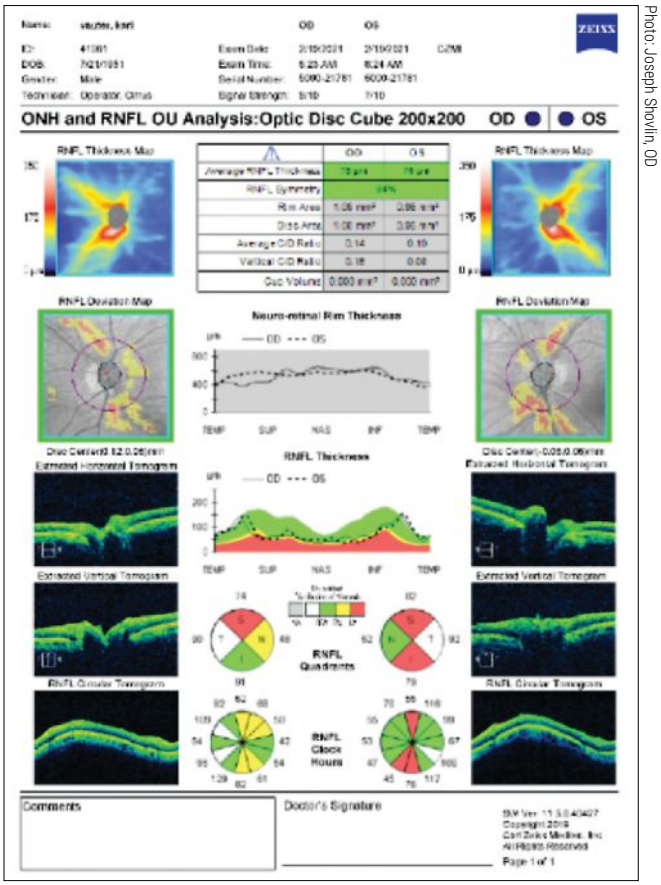


Photo: Joseph Shovlin, OD

OCT showing areas designated as being outside normal limits but is merely a myope with a temporization of the RNFL peak.

Disease Misclassification

Effective glaucoma management can be hindered due to misclassification, according to Andrew Rixon, OD, an attending optometrist and the residency coordinator at the Lt. Col. Luke Weathers, Jr. VA Medical Center in Memphis, who explains that this involves not only misclassifying the extent of the disease but also the form of the disease.

"Initial misclassification, especially in cases where patients are underclassified, may set up a false sense of security leading the OD to be insufficiently aggressive with their therapeutic approach," he says.

There tends to be an assumption that everyone has primary open-angle glaucoma (POAG), but doing so can lead to negative outcomes, notes Dr. Rixon. For instance, angle-closure glaucoma, although rarer, is underdetected in North America.

Disease misclassification can be mitigated with the use of gonioscopy, which is reported to be performed in only about 50% of cases, Dr. Rixon explains. "Hone your gonioscopy skills and use it on all glaucoma suspects to appropriately classify the form of disease you are working with," he recommends. "Angle closure spectrum of disease is more common than we think."

Leaving Tools in the Toolbox

The diagnosis, treatment and monitoring of glaucoma is multifaceted, and shouldn't be limited to a single approach. For instance, Dr. Marrelli emphasizes the importance of not relegating the clinical evaluation of the optic nerve and RNFL to an afterthought.

"We have become so reliant on OCT," she says. "This information is truly invaluable, but the clinical evaluation of the optic nerve, evaluating for diffuse or focal neuroretinal rim loss, notching, disc hemorrhage, beta zone peripapillary atrophy and RNFL dropout is really the first step in determining who has glaucoma. OCT provides excellent additional information but should not be the sole test for the diagnosis of glaucoma."

Macular scans are another example of a useful tool that shouldn't be forgotten. There is ample and compelling evidence that the macula can be damaged in early glaucoma, according to Dr. Marrelli, who notes that this is not visible on clinical exam.

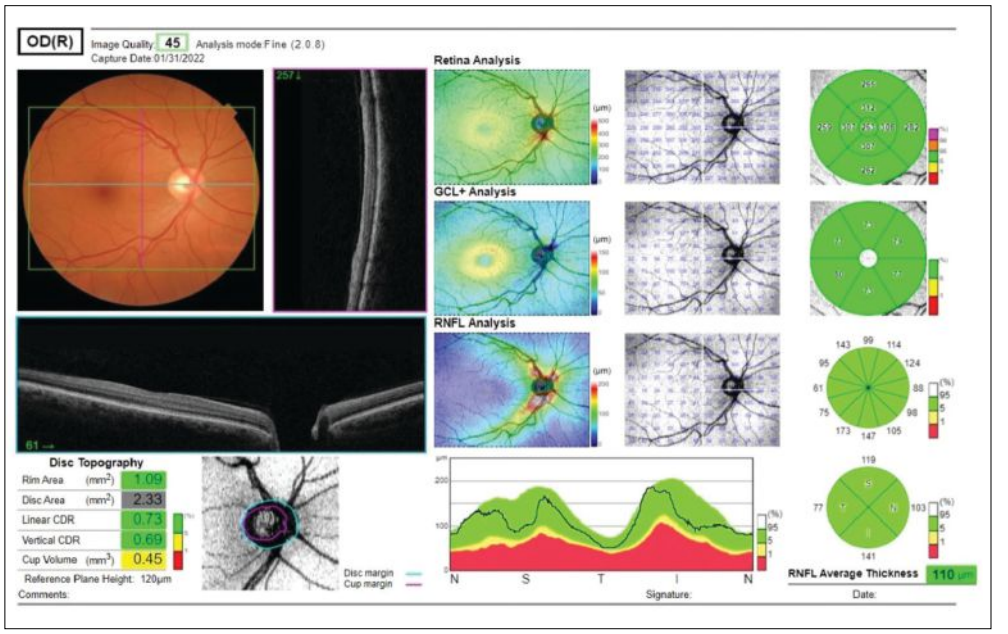
"We can't 'see' ganglion cell thinning in the same way that we can see nerve fiber layer or neuroretinal rim thinning, so the only way to observe this is by using OCT," she explains. "Every OCT has a glaucoma-specific macular protocol that provides excellent adjunct information to the RNFL/optic nerve scans. The American Academy of Ophthalmology Preferred Practice Patterns include macular imaging as part of the evaluation of glaucoma patients."

In terms of therapeutic management, there are also abundant options—including many that optometrists tend to overlook. Dr. Marrelli says, "The general tendency of ODs who manage glaucoma is to prescribe a prostaglandin analog, and if the patient needs escalation of therapy, they refer the patient to ophthalmology."

While she acknowledges that there are certainly exceptions to this pattern, Dr. Marrelli urges optometrists to consider the many new and efficacious treatments that are available before referral is necessary. This includes drugs like "latanoprostene bunod and netarsudil that target the trabecular outflow pathway—which we've not been targeting with drops for over 25 years—fixed combination drugs that help with adherence by reducing the complexity of the drug regimen."

It is also important to think about options such as selective laser trabeculoplasty as first-line therapy, new drug delivery systems (*i.e.*, sustained-release bimatoprost) and minimally

Photo: James Fanelli, OD



Several metrics are available for evaluation of a glaucoma suspect, including the ganglion cell layer analysis and the RNFL analysis. Also noted are disc topography metrics.

invasive glaucoma surgery, according to Dr. Marrelli. "Even if an OD lives in a state in which they cannot perform laser or injected medication, those treatment options should remain in play for their patient."

Dr. Shovlin underscores the value of working with a surgeon who is well-versed in the various MIGS procedures. "When any glaucoma patient requires cataract surgery, be certain to refer to someone eager to do MIGS," he says. "It's a great opportunity to lower intraocular pressure (IOP) at the time of surgery. Many cataract surgeons will forego that opportunity, so optometrists should take that into consideration at the time of referral."

Initiating Treatment Without a Complete Picture

Rushing to treat and/or not gathering enough baseline data is another misstep ODs should avoid in glaucoma care, suggests Dr. Marrelli.

"It is so important to obtain multiple IOP readings prior to initiation of treatment—even if you make the diagnosis of glaucoma on the first visit—in order to know where to set your target IOP," she recommends. "Glaucoma is generally a slow process and in almost all cases we have time to gather good reliable data from which to base our treatment."

When determining to treat vs. not treat patients for glaucoma, it is critical to avoid beginning intervention because of a single irregular factor, such as the patient having a large c/d ratio, notes Dr. Haynes.

"We have to consider numerous factors, including the size of the optic nerve, for example," she says. "The patient with a large c/d ratio may have a large optic nerve size that contributes to the larger c/d ratio. Their c/d may be large, but their neuroretinal rim tissue is entirely healthy, their RNFL is robust and their ganglion cell layer (GCL) is normal."

On the other hand, a patient could have glaucomatous cupping with a smaller c/d ratio because they have a smaller-sized optic nerve, explains Dr. Haynes. "When determining if glaucomatous structural damage is present, we have to consider the size of the optic disc, as well as the status of the neuroretinal rim, the RNFL and the GCL."

Dr. Shovlin also recommends using corneal hysteresis data when available. "It's a measure of the cornea's 'shock absorbing' biomechanical properties," he explains. "Overall, low hysteresis eyes tend to progress more quickly. Hysteresis and peak IOPs are the best predictors of who will progress fastest. It may help explain why some patients show little response to drops and have no progression or little progression over time."

For example, eyes with high hysteresis may show very little drop in pressures but not change on OCT or field assessments. In these cases, there may be a tendency to add more drops or surgical procedures when it might not be needed. On the other hand, low hysteresis eyes get a better response to drops but actually need it. This is why it is so important to continue to carefully monitor for field and OCT changes, Dr. Shovlin advises.

Too Much Emphasis on Static Target Pressure

While measuring IOP is a key component of glaucoma management, ODs should not base all of their decisions on a static target pressure, according to Dr. Rixon, who notes that this can result in robotic and non-personalized management. This, in turn, can cause under-treatment in some and over-treatment in others.

"Decision-making should involve assessing structural and functional biomarkers," he says. "We need to manage the disease, which involves adjusting therapeutic goals according to the disease behavior, not based on preconceived notions of IOP alone."

IOP susceptibility is key, he emphasizes. "Look at what the disease is doing. If the patient's IOP is higher than your initial target but their disease remains chronically stable, the nerve is unlikely to be susceptible to damage at the present level. In such a case, the initial target may have been unnecessarily aggressive, Dr. Rixon offers. "Target IOP is dynamic, and

it is adjustable based on current and projected disease status. Resetting the target throughout the lifetime of management should be expected and is part of personalizing care."

Progression Without Confirmation

A crucial aspect of glaucoma management is monitoring disease progression, and it is important not to jump to conclusions without adequate information. Therapy shouldn't be escalated without clear confirmation of progression.

Both visual fields and OCT data can vary, notes Dr. Marrelli, while recommending that a field that looks like it has progressed should be repeated—usually twice—to confirm that suspicion. "We tend to think of OCT data as objective and infallible, but it, too, can vary from visit to visit," she says. "The use of progression software is very helpful and can tell us not only if there is progression (using 'event' analysis), but also at what rate the progression is occurring. That rate of change is very important in deciding whether or not therapy needs to be enhanced."

Another mistake is not getting enough visual fields in the first two years, according to Dr. Marrelli. "It has been suggested that six visual fields in the first two years is the best number in order to identify the 'rapid progressors.'" While Dr. Marrelli knows this sounds like a lot of testing, she says, "it's really only one every six months plus one additional one relatively soon after the first—which also helps to establish a good baseline." After two years of visual fields, if the field looks relatively stable, you can "relax" a bit and back off on the frequency of the field testing, she advises.

When you have identified a patient as a fast progressor, you must be prepared to intervene accordingly. This may include, according to Dr. Rixon, earlier surgical intervention either in the optometric office where scope allows, or subspecialist referral.

ODs must also make sure that they are considering the rate of progression, notes Dr. Rixon. "Most POAG patients are not fast progressors, approximately only 10%," he says. "Fast progressors are >2µm/year on OCT and -1.5-2dB/year on visual fields. Fast progressors are much more likely to lose function than their slower counterparts—assuming equal life expectancy."

Skipping Re-Baselining

Once progression has been confirmed and treatment escalated, it is important to re-baseline. Without this step, it can be difficult to gauge success, says Dr. Rixon. "You need to be able to assess how the intervention modifies the rate of progression to ensure you are taking the right approach.

"Comparing post-treatment rate of progression to a previously untreated or less treated state can lead to misinterpretation, which could lead to avoidable side effects and increased burden on the patient," he continues.

Dr. Rixon recommends that ODs become familiar with how to re-baseline on the various visual field and OCT machines. "This should reduce the desire to intensive therapy soon after having just escalated it," he notes. "The general recommendation is to hold off on additional treatment for approximately 12 months after the last intervention. If a sufficient number of tests are performed in that year, it should be enough time to elicit whether the last intervention modified the disease meaningfully."

Failing to Consider Other Possibilities

It is important for optometrists to always consider masqueraders for neurologic and vascular diseases, conditions that might look like glaucoma, but aren't, according to Dr. Shovlin. "A one eye, diffuse, one quadrant loss is likely not early glaucoma. It's probably a deeper layer vascular cause such as central retinal vein occlusion or non-arteritic anterior ischemic optic neuropathy. Generally, early glaucoma will show a narrow one quadrant loss."

Dr. Shovlin also recommends paying particular attention to disc pallor, in addition to rim erosion and matching what you observe with field loss.

"Homonymous macular atrophy with ganglion cell complex (GCC) assessment often represents previous demyelination or optic tract damage from a traumatic brain injury. Bilateral nasal GCC loss may represent a chiasmal lesion," he says. "A right or left sided GCC may represent a posterior lesion. In glaucoma, the GCC loss should respect the horizontal midline on the temporal side. When things don't add up, neuroimaging is indicated. There's nothing more expensive than a missed/wrong neurologic diagnosis."

Photo: James Fanelli, OD

The reference database plots of a patient's RNFL circle scan in an NSTIN format. Metrics of the right optic nerve raised questions; namely, a larger cup-to-disc ratio than seen clinically.

10 Hacks and Tricks for OCT Interpretation in Glaucoma, *By Mark T. Dunbar, OD*

1. Make sure it is a reliable scan.
2. Perform three RNFL scans at a time.
3. GCC is valuable and often correlates with RNFL.
4. Can the RNFL/optic nerve of your patient be applied to the normative database?
5. Do the OCT findings fit with the clinical presentation?
6. Watch out for "red disease."
7. There is a large range of "normal" before the RNFL reaches a tipping point.
8. OCT can show glaucomatous change *before* it is seen on visual fields.
9. A change of >10µm from previous measurements is significant.
10. SD-OCT is not as sensitive with more severe glaucoma.

Clinical Pearls for Optimal Management

Mistakes like the ones discussed above can have a negative impact on both patients and optometrists. Keeping these missteps in mind while managing your glaucoma patients helps ensure optimal outcomes for all involved.

"These mistakes can lead to (1) non-glaucomatous patients being diagnosed and treated unnecessarily, causing potential undue burdens such as financial, emotional, time and development of adverse treatment effects, and (2) glaucomatous patients not being treated or not being treated aggressively enough which can lead to lifelong, permanent visual disability," says Dr. Haynes.

An easy first step, she notes, is ensuring that you are acquiring and looking at all the pieces of information necessary to make an appropriate diagnosis. At a minimum, this includes the following, according to Dr. Haynes: IOP, appropriate visual field testing, OCT imaging of the optic nerve showing both the RNFL thickness and GCL analysis, evaluation of the neuroretinal rim tissue—clinically and with OCT if available, determination of the optic nerve size—clinically or with OCT if available, pachymetry and gonioscopy.

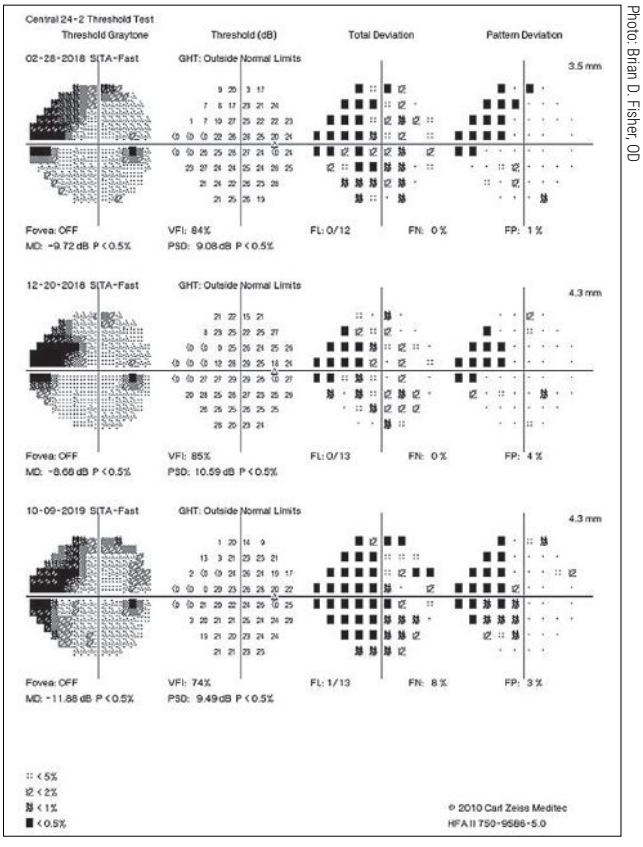


Photo: Brian D. Fisher, OD

Authors of a recent study advocate for better metrics to track and anticipate central visual field loss, owing to the high rate of progression seen in their research.

After gathering all of these metrics, the next step is to perfect your interpretation skills. "This may include doing work to better understand your OCT instrument: it's resolution capabilities, possible imaging errors that could occur, and how data can be visualized and analyzed including progression analysis," says Dr. Haynes. "Obtaining the data is a good start, but you have to put the time in to become proficient at interpreting that data."

When offering his advice for glaucoma management, Dr. Rixon emphasizes the importance of thoughtfulness and patience. "Don't make rash decisions, collect the information and increase the certainty of your decision-making process before each intervention," he urges.

Patient education is also a critical component of effective care and positive outcomes. Dr. Rixon recommends taking time to explain what glaucoma is, as well as why specific testing is needed and certain testing intervals are necessary.

"This should lead to increased buy-in and a shared decision-making approach," he says, while also encouraging ODs to "embrace interventional care, regardless of what method you use to gauge adherence; nonadherence is a reality that needs to be considered."

Effective glaucoma management is not one-size-fits-all and ODs must have the skills and knowledge to not only use the tools at their disposal, but also recognize the nuances of this condition.

"Although we can use the entire clinical picture to help predict outcomes and necessary interventions, none of us possess some magic formula, and therefore vigilant monitoring supplants any assumptions we might make," concludes Dr. Rixon. "Each case and patient is unique, and different strategies for success may be required. We, as clinicians, have to be prepared to adapt as needed." ■

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PROGRESSION IN GLAUCOMA: HOW TO RECOGNIZE AND REACT

We help guide you through the importance of clinical data usage in long-term monitoring.

BY HALIE COTTRILL, OD, SARAH MAXEY, OD, AND ANDREW RIXON, OD
MEMPHIS

Once the diagnosis of glaucoma is made and there is ultimately a decision to treat it, an entirely new set of decisions arise that can lead to uncertainty for the practitioner and patient alike. Primarily, we need to determine whether our initial intervention is successful or unsuccessful, and can gauge this by seeing if the patient has progressed. If so, what is the rate of progression? Working within the confines of available technology to streamline confirmation of progression, we can subsequently personalize additional care as much as possible in order to prevent loss of vision and reduced quality of life due to glaucoma.

Confirm There is Progression

Despite having intervened, clinicians should not be surprised or dismayed when further progression occurs.[1] Fortunately, when treated, most eyes will not progress at rates rapid enough to lead to vision loss. Although the majority of patients are not at risk of vision loss, there is still a minority (3% to 17%) that are.[2-6] A major goal in longitudinal glaucoma care is to determine the rate of progression and prioritize fast progressors who are more likely to have a worse prognosis than slow progressors. Keep in mind the course of glaucoma is not always linear, and patients that have historically progressed slowly may change gears and show more rapid advancement of their conditions along the management road.[7]

An abundance of data is acquired in longitudinal glaucoma care, and the sheer volume can confound the task of confirming progression if not captured or analyzed appropriately. Here, we will discuss some of the more relevant clinical data collected and how to apply it.

Long-term Monitoring

Given the chronic progressive nature of glaucoma, multiple variables must be frequently monitored on a customized, long-term basis. Important monitoring considerations are listed below.

Intraocular pressure (IOP). The statement that IOP is the only tangibly modifiable risk factor in glaucoma management is glaucoma dogma at this point. Although it's accurate, it can create the impression that lowering IOP to a certain predetermined level implies therapeutic success. More accurately, the stability of our patient's individual glaucomatous optic neuropathy should be used to gauge the success or failure of our interventions. Let's examine the relationship between IOP and progression and whether IOP levels have prognostic or confirmatory value in progression.

Major landmark studies have historically demonstrated that lowering IOP does, on average, reduce the percentage of patients who develop glaucoma and suffer progressive visual field loss.[8-12] The problem with these findings is that a substantial proportion of patients in each of those studies continued to have visual field

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progression and none provided a universal level of IOP reduction that specifically guides us on how low it needs to go to blunt progression on an individual basis.[13]

Recently, it was quantitatively substantiated for the first time that adhering to and meeting the European Glaucoma Society's severity of disease-based target IOP lowering guidelines resulted in decreasing the rate of visual field progression to that of normal age-related change (MD loss of -1.02dB/decade).[14]

A recent study examined the relationship between OCT structural measurements, level of average IOP lowering and progression. IOP was shown to significantly impact the rate of global RNFL, isolated ganglion cell layer (GCL) and ganglion cell-inner plexiform layer (GC-IPL) loss, with each additional 1mm Hg mean increase being associated with faster loss of 0.05µm/year of RNFL, 0.021µm/year GCL and 0.032µum/yr of GC-IPL thickness, respectively.[15,16] Notably, in the most aggressively managed group (those achieving an average IOP under 15mm Hg at all visits), 9% of patients continued to undergo rapidly progressing RNFL deterioration (>2µm/year).[15]

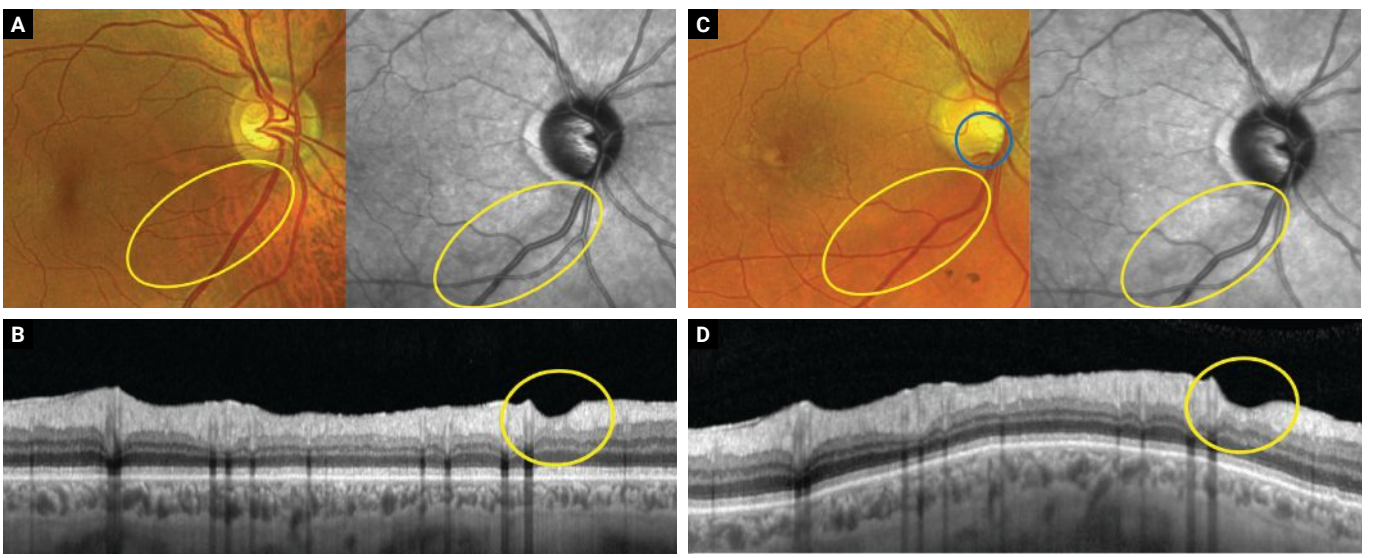
The above findings all align to support the contention that higher IOP results in more rapid progression while more aggressive IOP lowering delays progression, on average. However, simply lowering IOP in our individual patients does not substantiate that we, as practitioners, have slowed glaucoma, nor does an inability to show a lower IOP confirm that glaucoma has progressed.

Recently, it was suggested that using SD-OCT tissue measurements as structural biomarkers is a viable approach to determine how effective IOP lowering has been in altering the disease.[16] Essentially, if the tissue thickness isn't deteriorating over time, the level of IOP being achieved is likely sufficient, even if it is greater than initially desired. Conversely, if the tissue is continuing to atrophy in spite of meeting what was presumed to be a "safe" pressure, then the IOP level achieved is, in fact, insufficient. This concept is known as determining the patient's individual IOP susceptibility.[13,17]

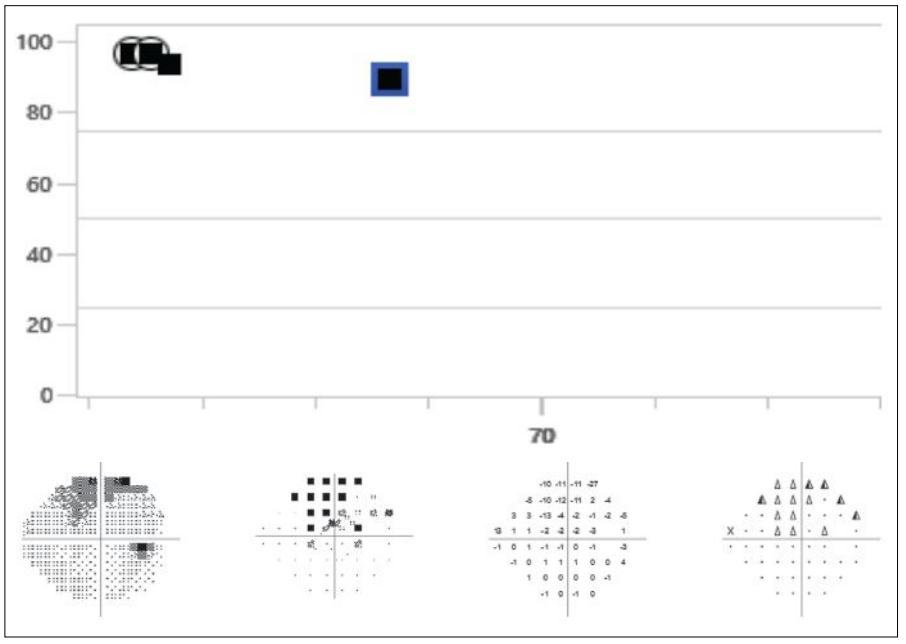
An additionally helpful concept is the use of a target rate of progression.[18] Much like with determining IOP susceptibility, this refocuses the emphasis on the severity of the disease state rather than obsessing over meeting a pre-determined target IOP to gauge success. Accordingly, a sounder approach to determine success is to consider whether the only tangibly modifiable risk factor, IOP, is in fact modifying the disease by achieving a target rate of progression that is unlikely to result in functional loss.

Fundus evaluation. Clinical funduscopic examination of the optic nerve remains integral in assessing disease stability and prognosis. Systematically assessing the optic nerve complex for rim erosion, formation of acquired pits of the optic nerve, evolution of parapapillary atrophy and presence of disc hemorrhages is a must, as all are negative prognostic progression indicators.

Disc hemorrhages are associated not only with OCT and visual field progression (on both 24-2 and 10-2 grids), but also with increased velocity of that progression when compared to glaucoma patients without.[19-22] It was found that the rate of RNFL progression was faster with post-disc hemorrhages than pre-disc hemorrhages, and intensifying treatment following hemorrhage slowed progression by an average of -0.50µm/year.[23]



Figures A and B show color, near IR and OCT-B scan images of a glaucomatous inferior temporal wedge (yellow circles) from September 2022. Figures C and D show the same images taken in April of 2023. Note how the disc hemorrhage (blue circle, C) arises within the already present area of tissue loss. This is consistent with the proposed theory that disc hemorrhages are part of the continuum of loss and may not be standalone inciting events.



A 68-year-old patient whose visual fields on both event and trend analysis may have progressed when compared to baselines. This patient's OCTs and clinical appearance do not show signs of progression. The event analysis displays "possible progression." It is recommended that the visual field be repeated an additional time to confirm progression.

These findings might suggest that disc hemorrhages should not only alert the practitioner to the presence of progression, but compel them to intensify IOP lowering upon disc hemorrhage detection. However, discovery of a hemorrhage may not warrant immediate intervention, as progression has actually been shown to precede disc hemorrhages, even if it often speeds up post-hemorrhage. In fact, it's been proposed that disc hemorrhages are part of the continuum of structural loss, not an isolated event that initiates tissue loss.[24,25] Hence, when a disc hemorrhage is observed, at minimum it's necessary to increase monitoring in the region where it occurred, as well as carefully scrutinizing associated visual fields to avoid overlooking deepening of existing defects or development of new defects. Remarkably, the lag time to confirm visual field changes post-disc hemorrhages has been shown to be 16.8±/-2 months, meaning that if you choose to maintain present course of therapy after isolating a disc hemorrhage, patience is required.[26]

Visual fields. Perimetry quantitatively assesses the function of retinal ganglion cells at various retinal locations susceptible to damage.[29] In deciding which perimetric testing algorithm to use in confirming progression and determining its rate, the decision will hinge on the baseline strategies that each clinician employed when making the initial diagnosis, whether it be 10-2, 24-2, 24-2c or a combination of those strategies. Earlier this year, Sullivan-Mee et al. discovered in their study cohort that having a baseline defect on 10-2 testing was an effective predictor of subsequent progression on 24-2 tests, implying that 10-2 has prognostic progression value and should be considered when establishing the aforementioned baseline.[30]

For reference, a fast rate of visual field progression is generally considered to be a mean deviation (MD) change of -1.5dB to -2dB per year.[31-34] In order to accurately detect rapid field loss, a significant number of visual fields need to be performed. The World Glaucoma Association recommendation is that in order to detect a change of -2dB/year, a minimum of three visual fields per year are required within the first two years, assuming the patients' fields have low variability.[34,35]

Unfortunately, these recommendations are often not followed in practice and many practitioners only perform one visual field per year, if that.[36] At that rate, it would take five years to exceed test-retest variability (assuming it is low) and confirm the patient is progressing at -2dB/year. Increasing the test frequency from one to two fields per year can be impactful and three per year can provide the managing doctor greater assurance that they are acting upon true progression.[37]

In detecting progression on perimetry, the various manufacturers have

TABLE 1. RATES OF PROGRESSION[1-4]

	Age-related	Slow	Moderate	Fast
Average circumpapillary RNFL	-0.54µm/year	<-1µm/year	Between -1 and -2µm/year	Between -2 and -4µm/year
Standard automated perimetry MD	-0.06dB/year	-0.5-1dB/year	-1-1.5dB/year	-1.5-2dB/year

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decision-support tools that can be categorized as either trend- or event-based analyses. Evaluating both analyses is compulsory in longitudinal glaucoma management.[38]

Trend analysis. This uses global metrics, either MD or visual field index from all the tests available during the relevant follow-up period time (in this case, the post-treatment period), to supply an estimated rate of progression, as well as providing a projection of remaining visual sensitivity in the future. The relevance of fast progressors and what is considered a fast rate on MD trend analysis is covered above.

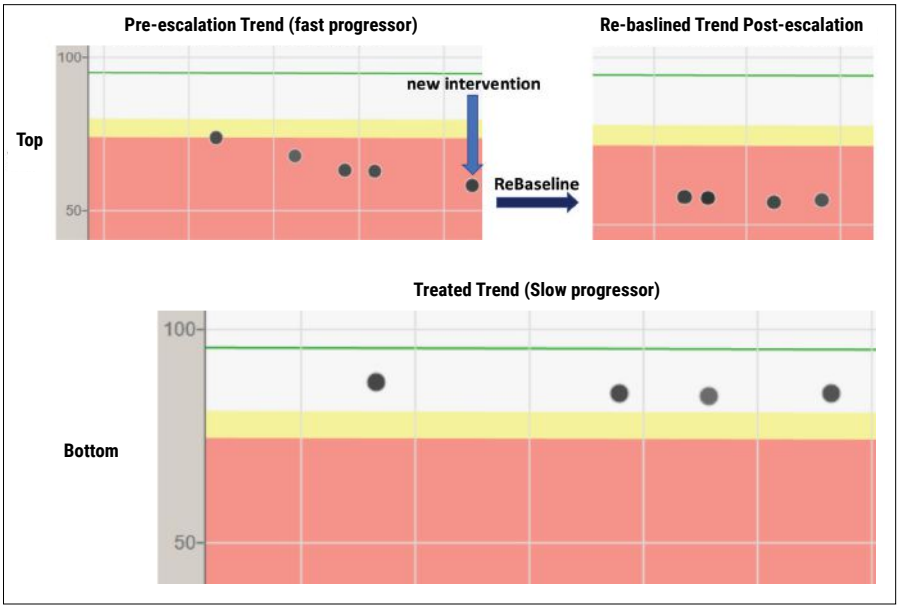
Event analysis. This assesses the most recent field and determines whether there are any statistically significant changes to the visual sensitivities in each test location when compared to the same test locations on two established baselines. If the changes exceed a certain threshold, the software will flag the abnormality and alert the clinician to the probability that the change indicates true progression. For instance, with guided progression analysis (GPA), three consecutive fields, having the same three test locations undergo statistically significant change will alert the clinician that progression is "likely."[39]

A 2012 study comparing GPA event analysis to manual progression analysis by five world-renowned glaucoma subspecialists showed fair agreement between the two groups, substantiating the value of GPA as a decision support tool.[40] Ultimately, regardless of how beneficial the software is, we as doctors must evaluate both trend and event analyses together and do our best to integrate them in our interventional decisions, when visual fields are the most compelling determinant of those decisions.

OCT. This allows the clinician to quantify circumpapillary RNFL, neuroretinal rim and macular tissue loss; in earlier stages of disease progression, it is a more sensitive and less variable technology than automated perimetry.[41] In progression analysis, OCT will supply event and trend analyses. These may be labeled differently by the various platforms, but the concept is the same. Event analysis compares each OCT taken to a minimum of two baseline OCTs, generally assessing neural tissue as global, quadrant, sector or clock hour averages. The various platforms will then present probabilities of whether the patient has progressed. Conversely, trend analysis takes an average of the tissue thickness over time and provides the rate at which the disease is progressing.[42]

The most researched optic nerve complex parameter from a progression trend and event analysis standpoint is global/average RNFL.[43,44] Confirmation of disease progression on OCT is limited by the need to exceed machine reproducibility tolerances. Longitudinal use of global/average RNFL is not immune from this limitation. Average RNFL test-retest variability is approximately 4.9µm (this may vary depending on the OCT platform). To compensate for this noise and reinforce the need to exceed it, the informal event analysis based "Rule of 5" has emerged. This rule states that if there is a repeatable 5µm or greater global RNFL loss on consecutive tests, that loss is evidence of progression and changing treatment might be justified.[45] The Rule of 5 has actually been shown to result in a 25% false positive rate when studied over five years of progression analysis. Longitudinally, RNFL trend analysis has been shown to be superior to event analysis and is the recommended go-to best progression on OCT.[46]

Capturing the rate of progression using trend analysis provides perspective on progression and should inform your next steps. For reference, normal age-related attrition of the RNFL is less than -1µm/year (an average of -0.54µm/year) and rates of



OCT trend analysis on a fast progressor with POAG that may have been detected earlier with more initial OCTs (top row). This patient progressed at a rapid rate (-5µm/year) despite intervention on the left image. Treatment was subsequently escalated (blue arrow) and the right image reflects that no additional RNFL tissue loss occurred on the re-baselined (dark arrow) trend analysis. Bottom image shows an extremely slow progressor (<-1µm/year) who was initially put on a second medication because of not meeting target IOP. After the trend analysis showed stability, the patient had the second medication removed and the tissue has remained stable on one medication—a good reminder that OCT biomarkers can guide decision-making.

loss are delineated within the Duke Glaucoma Registry as 1µm/year as slow, between 1µm to 2µm/year as moderate, 2µm to 4µm/year as fast and >4µm/year as a catastrophic rate of progression.[15,47]

Obviously, when discerning glaucoma from normal age-related change and in slower moving cases, more time and testing may be needed to separate normal from pathological results. Mahmoudinezhad et al. recently showed the time required to detect a slow change of -1µm per year was 6.3 years if only one OCT per year was run, five years with two scans per year and 4.2 years if three scans per year are performed.[48] For detecting fast progressors, Melchior et al. discovered that performing two quality OCT scans per year is reasonable and sufficient.[18]

Warning Signs

While both visual fields and OCT scans are helpful in monitoring for progression in glaucoma, artifacts in either method have the potential to lead to false assumptions regarding progression's validity. In visual field testing, prominent brows, misaligned corrective lenses, blepharoptosis, poor patient instruction and patient or perimetrist inattention all have the capacity to cause artifacts that may show false visual field defects.[39] Additionally, media opacities, retinal disease or other optic nerve disease may also cause visual field defects that can be falsely attributed to glaucoma.

OCT is also subject to artifacts and findings that may mimic glaucomatous change. Acquisition errors can be caused by machine, operator or anatomy-related issues and broadly result from the following:

- segmentation errors (leading to over- or underestimation of tissue)
- tear film abnormalities
- media opacities
- epiretinal membranes
- development of and release of vitreoretinal traction
- poor scan alignment
- increased axial length

It's critically important that the B-scans provided on OCT or the printouts are assessed for quality and utility prior to using them in analysis on the current state of the patient's condition.[49,50]

Wedge defects are often assumed to be secondary to glaucoma; however, this is not always the case. The Beijing Eye Study demonstrated that localized RNFL wedge defects were present in 15% of patients screened on OCT. These defects were, besides glaucoma, associated with increased axial length, diabetes and other vascular pathologies that resulted in RNFL infarct. Specifically, diabetic RNFL wedge defects have been shown to be smaller than those found in patients diagnosed with glaucoma and do not enlarge over time as glaucomatous wedges do.[53,54]

> **A major goal in longitudinal glaucoma care is to determine the rate of progression and prioritize fast progressors, who are more likely to have a worse prognosis than slow progressors.**

Branch retinal artery occlusions may also yield OCT findings consistent with glaucoma. Macular thickness maps have been shown to be valuable diagnostic tools that can accurately differentiate the loss of tissue from glaucoma in comparison to the more extreme loss expected from vascular events such as branch retinal artery occlusions. Increased intra-eye asymmetry and retinal thickness below 200µm is diagnostic of a previous artery occlusion.[55]

Once Progression is Confirmed, What's Next?

The decision to continue, modify or escalate treatment, coupled with alternating or maintaining a follow-up schedule once progression is confirmed, is multifactorial and should be individualized for each patient. A realistic treatment goal is not one that completely halts all glaucoma progression, but rather one that slows it enough to preserve function.[7,14] Visual impairment from glaucoma is linked to increased risk of falls, depressive symptoms and decreased overall self-reported QoL, so identifying patients at risk for additional progression is key.[56,57]

A silver lining in the glaucoma progression "change the treatment or hold steady?" conundrum is that most patients whose disease is identified early in its course and are treated will not experience visual impairment.[6,14,58] Nonetheless, rapid progressors are at a much higher risk of impairment than their slower progressing counterparts. Prognostically, faster visual deterioration is associated with more severe baseline visual field mean deviation levels, larger baseline C/D ratios (>0.7), and older age at initial diagnosis and worse QoL outcomes are associated with faster visual field decline in the better eye.[59]

The Progression Flow Process

Step 1: Seeing possible progression

Step 2: Confirming progression

Step 3: Ruling out nonadherence as the cause of ineffective treatment

Step 4: If progression has occurred and the patient is adherent, consider escalating therapy

Step 5: Once therapy is modified, re-baseline all imaging

Step 6: Restart the progression flow process

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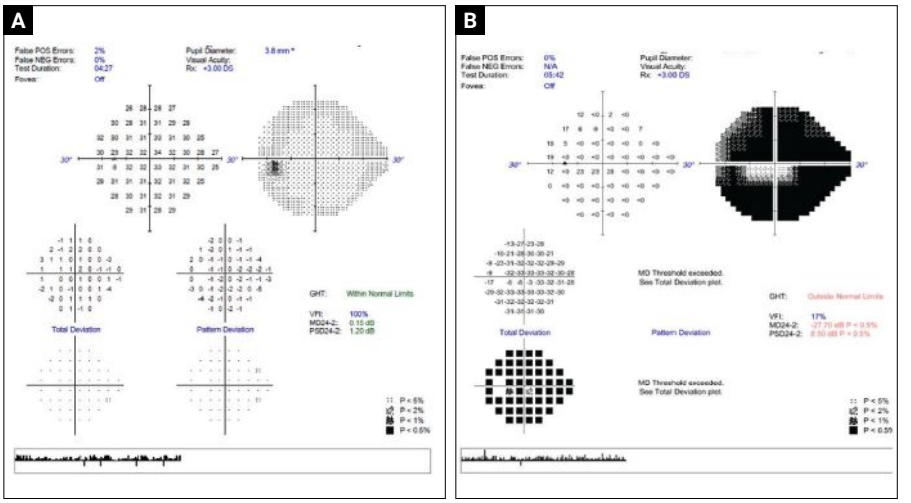

With the goal of preventing progression from Fig. A to Fig. B, a major emphasis is to identify those at greatest risk and knowing associated risk factors. For example, faster progressors are at greater risk of experiencing loss of vision and subsequently experience lower quality of life. Conversely, recognizing that slow progressors with longer expected life expectancy is also a risk for advanced disease progression is also vital.

Therefore, prospectively identifying signs consistent with the risk of rapid glaucomatous progression and then verifying it should lower the threshold for escalating treatment and adopting a more aggressive stance. Intervening with fast progressors is a necessity, but across the board the level of subsequent intervention after a patient has progressed is dependent on many factors, most importantly; current disease stage, rate of past progression, residual field and predicted remaining lifetime.[6,14,58]

Accordingly, and depending on the above risk stratification, abandonment of the initially prescribed intervention may not always be the correct reaction to progression. Although topical hypotensives have been a historical first-line therapeutic mainstay in glaucoma care, lack of adherence to these medications is notorious.[60-62] Poor treatment adherence can present the illusion that the patient is progressing due to therapeutic failure, when in reality the patient has self-discontinued the drops or was never using them in the first place.[60,62-64] Contributors to nonadherence are extensive and include but are not limited to:[65,66]

- lack of effective doctor-patient communication
- inaffordability of medications
- patient healthcare literacy
- inability to successfully instill drops
- preservative-induced side effects
- lack of self-efficacy (belief in one's ability to achieve goals)

Confirming treatment adherence provides greater assurance that progression is due to insufficient treatment vigor and additional treatments need to be added. Taking an interventional approach is a viable way to assure treatment is accomplished in nonadherent cases and those where additional treatment complexity is necessary to mitigate patient burden. Interventional options are vast and continue to expand with newer surgical and drug delivery innovations becoming available, as well renewed support for laser treatment in some situations.[67,68]

The decision to modify glaucoma treatment once progression is confirmed is an infinitely dynamic process and there are myriad combinations of treatments that can be paired to positively influence patient outcomes. Ultimately, the best approach is to attempt to tailor care as much as possible to the individual while acknowledging that treating glaucoma is never simple due to all the unique patient variables we encounter as physicians.[69]

Re-baselining After Intervening

Lastly, once the decision to further intervene is made, the reference point from which your progression determination was originally based needs to change. The new reference point originates with the newest treatment and is labeled the new baseline; this process is known as re-baselining. It is critical to re-baseline when enhancing therapy, as failure to do so may result in incorrectly interpreting that later progression is occurring post-treatment escalation, when in reality future testing is still being compared to past therapeutic regimens. Re-baselining reduces confusion and establishes whether the newest treatment works or not.

Takeaways

Undoubtedly, confirming progression and deciding how to intervene accordingly is an art and may need repeating multiple times throughout a patient's glaucoma lifecycle. Vigilance in capturing and analyzing longitudinal clinical data is the way and will enhance the soundness and certainty of our decision-making in chronic glaucoma care. ■

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MANAGING PATIENTS ACROSS THE NARROW-ANGLE SPECTRUM

Clinicans must perform the proper tests and consider all the evidence to make a confident diagnosis and reduce the risk of angle closure.

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Think about this patient scenario, which you've likely encountered before: You enter the exam room to assess a middle-aged, hyperopic female. While performing biomicroscopy, you notice that she has a narrow van Herick angle and an elevated intraocular pressure (IOP).

These types of cases present a clinical dilemma in which four critical questions must be answered:

1. Should we dilate?
2. Should we perform gonioscopy?
3. Should we perform or recommend a laser peripheral iridotomy (LPI)?
4. Should we refer for cataract surgery?

This article will attempt to answer these questions using two patient case examples and the findings of various clinical trials with the aim of clarifying some nuances of dealing with patients across the narrow-angle spectrum.

Case One: Patient with previously diagnosed narrow angles presents for exam 18 months after missing follow-up

A 60-year-old Hispanic male presented for an exam. He was previously diagnosed with anatomic narrow angles and instructed to return in six months for continued angle assessment. Unfortunately, he canceled that appointment and did not return until two years later, when he reported mild changes in his distance and near vision. His refraction was +2.00 -1.00x010 OD and +2.00 -0.75x125 OS, both correctable to 20/20 and both glare testing to 20/40. Corneal-corrected IOP (ccIOP) by Ocular Response Analyzer was 13.5mm Hg OD and 13.2mm Hg OS.

Should we dilate this patient? To help make this determination, we can look at the findings of the Zhongshan Angle-Closure Prevention (ZAP) study, where primary angle-closure suspects (PACS) were dilated with 1% tropicamide and 2.5% phenylephrine six to seven times throughout follow-up. The results showed that the risk of an angle-closure attack was uncommon (one in 1,587 dilations).[1] The study authors were concerned enough about potentially creating angle closure that they treated every patient with 250mg acetazolamide. For patients who had a post-dilation IOP increase of 8mm Hg or more, topical brimonidine and pilocarpine were also used. This may have altered the natural course of angle-closure disease resulting in underestimation.

It is worth noting that all the patients who closed in the ZAP study had all four quadrants closed at baseline and an average of +4D of hyperopia, while the mean was +2D. The Northern Ireland Diabetic Retinopathy Screening Program dilated all patients regardless of risk factors and found an incidence of angle closure of one in 31,755 patients.[2]

It is difficult to determine the appropriateness of dilation without first performing gonioscopy, which leads us to the next question:

Should we perform gonioscopy? This test should always be performed prior to dilation when narrow angles are suspected. A gonioscopy lens should be as ubiquitous as a 90D or 20D lens in

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optometric exam rooms. In our patient, gonioscopy showed posterior trabecular meshwork (TM) as the last structure seen, and there was greater than 180° of iridotrabecular contact. The amount of iridotrabecular contact was estimated to be around 270°. Anterior segment optical coherence tomography (AS-OCT) showed a narrow angle (*Figure 1A*). We also performed indentation gonioscopy, which involves applying pressure to the cornea using a small-footprint gonio lens to determine if peripheral anterior synechiae (PAS) exist, which they did not.

In our patient, even though the angle was quite narrow by gonioscopy and AS-OCT, we felt justified in dilating due to the need for a proper nerve and nerve fiber layer assessment. Clinicians should consider performing a post-dilation IOP measurement with special attention if the IOP increases 8mm Hg or more. It may also be reasonable to treat with 250mg acetazolamide, brimonidine and pilocarpine as in the ZAP protocol.

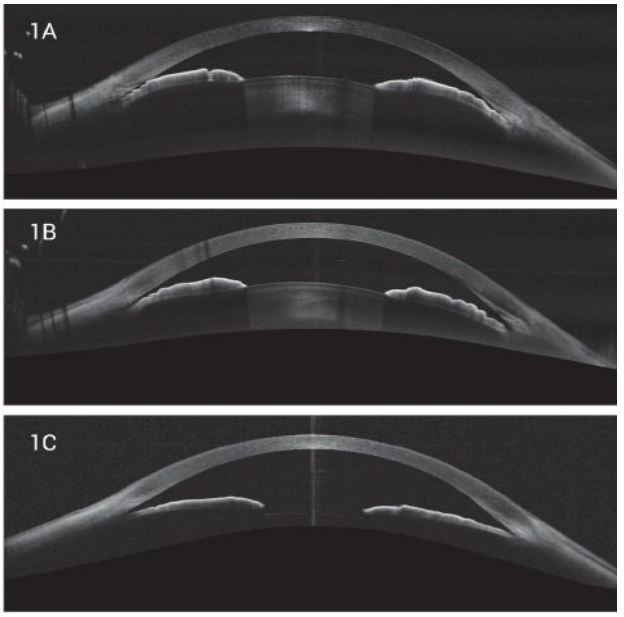

Fig. 1. (A) Edge-to-edge OCT image of narrow angle with iridotrabecular contact. (B) OCT image of same eye after LPI. Note the angle slightly more open. (C) OCT of same image after cataract extraction. Note the flattened iris position with significant angle opening.

We proceeded to dilate with 0.5% tropicamide and rechecked his IOPs by Goldmann applanation tonometry post-dilation, which measured 18mm Hg OD and 19mm Hg OS. His cup-to-disc ratios were graded at 0.4x0.4 OD and OS and his lenses were nuclear sclerosis grade 1. Visual fields and OCT were unremarkable with no evidence of glaucomatous conversion, leading to the diagnosis of PACS.

Based on findings of the ZAP study, we generally dilate all but the highest-risk individuals, including those with 360° iridotrabecular contact, extensive PAS, shallow anterior chamber depth and/or greater than +3D hyperopia. If the need is great that day, we will dilate even the high-risk patients but make sure to perform post-dilation tonometry. We also carefully discuss angle-closure symptoms as well as inform them about our 24-hour on-call service. If we determine that the patient will need frequent dilations in the future, we recommend LPI.

Should we perform or recommend LPI? Ever since the 1993 landmark study by Wilensky found that 6% of angle-closure suspects developed angle closure over a mean of 2.7 years, optometrists and ophthalmologists have viewed narrow angles as a problem best managed prophylactically with LPI.[3] However, recently released long-term data from the ZAP study presents evidence to suggest that LPI may be warranted specifically in patients at highest risk of conversion from PACS to primary angle closure (PAC).

The ZAP study—the largest single-center clinical trial for patients at risk of PAC—enrolled 889 patients and randomly treated one eye with LPI while the other acted as a control. The 14-year data showed that while eyes treated with LPI showed a 69% reduced risk of PAC occurrence, even after 14 years, the cumulative risk of progression to PAC was quite low.[1]

In the ZAP study cohort, the number needed to treat to stop one case of PACS from converting to PAC was 44 at year six and 12.35 at year 14. The number of patients needed to treat to prevent one case of PAC glaucoma (PACG) was 126 at year six. There were 6.3 acute PACs per 10,000 dilations. The study authors concluded, "prophylactic LPI should be recommended preferentially to those at the highest risk (higher IOP at baseline, shallower limbal anterior chamber depth and central anterior chamber depth) of angle closure because the annual incidence of PAC was low."[1]

A second study that examined the treatment efficacy of LPI in PACS was the Singapore Asymptomatic Narrow Angles Laser Iridotomy Study (ANA-LIS), which enrolled 480 patients. Similar to ZAP, ANA-LIS randomly treated one eye with LPI with the other being a control.[4] Results showed that PACS eyes with LPI had a 45% reduced risk of converting to PAC. The number needed to treat to prevent one case of PACS from becoming PAC was 22 at five years and 103.1 for PACG.[1] The authors also concluded that the overall incidence of PAC or PACG in PACS is low (10.21% over five years).

Both the ZAP and ANA-LIS studies focused on patients of Chinese ethnicity that typically have higher rates of angle closure than those from the United States. As it relates to the US, Yoo et al. presented a large retrospective case study to analyze the rate of conversion from anatomical narrow angle/PACS to PACG. The study analyzed conversion over a six-year period. The overall conversion rate as indicated by practitioners per ICD-10 code was 4.13% per year.[5] They found that likelihood of conversion particularly increased among the elderly.

Because the level of iridotrabecular contact in this patient was well over 180° and the angle OCT was ominous,

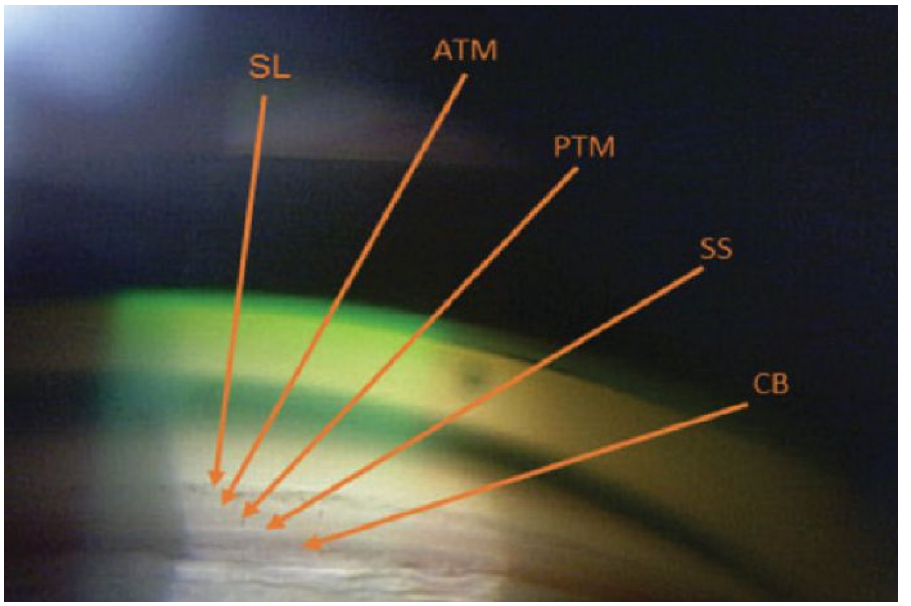

Fig. 2. The ciliary body is the most posterior structure visible, followed by the scleral spur, posterior TM, anterior TM and, finally, Schwalbe's line.

we scheduled him for LPI within a week. LPI had a positive effect on the angle opening, but less than expected (*Figure 1B*). We concluded that the mechanism was primarily phacomorphic.

While we approach each PACS patient individually, in our clinics we generally recommend LPI if the patient mentions symptoms of angle closure, has a family history of angle-closure disease, has at least +3.00D of hyperopia or needs frequent dilation. Family history is arguably even more important in angle-closure disease than in POAG, with standardized incidence rations being three times higher in angle-closure cases.[6] For the record, the patient in case one reported no family history of glaucoma or angle closure.

Should we proceed with cataract surgery? While LPI opened the angle slightly in the patient from case one, we decided to continue with careful monitoring. At the four-month post-LPI visit, the angle and IOP was unchanged, but the patient complained of increasing night glare, and we proceeded with cataract surgery. This flattened the iris configuration and opened the angle further (*Figure 1C*). We now monitor this patient yearly.

General Assessment Basics

It's important to first understand how we classify open vs. narrow angles so we can become better diagnosticians behind the gonioscopy lens. A "narrow angle" is that in which there is greater than 180° of iridocorneal contact. There are three angle closure subtypes: PACS, PAC and PACG.[7-8]

A PACS is defined as a subject with narrow angles (<180° of TM seen clinically) and the absence of PAS.[9-10] In PACS, IOP remains normotensive (<21mm Hg) without the presence of optic atrophy or visual field deficits.[11]

In PAC, there is appositional occlusion of the TM and peripheral iris.[12-13] The primary underlying mechanism in PAC is pupillary block. Pupillary block initially begins with increased interaction between the iris and anterior lens. As aqueous fluid attempts to flow anteriorly, resistance builds posteriorly resulting in an anterior bowed appearance (iris bombé). In the mid-dilated position, the flaccid peripheral iris moves laterally to connect to the TM and induce angle closure. Plateau iris is an anatomical variant in which the ciliary body is positioned more anteriorly, leading to mechanical contact with the TM.[14] Plateau iris is a leading cause of PAC in younger individuals.

Angle closure is rare in anterior chamber depths exceeding 2.5mm.[12] The average anterior chamber depth of eyes with PAC is approximately 1.8mm. This is 1mm shorter than normal eyes. Contributing factors include exaggerated lens vaulting or anterior lens positioning which accounts for approximately 0.65mm of anterior chamber depth shallowing. Increased lens thickness also plays a role, which induces roughly 0.35mm of anterior chamber depth shallowing. Average lens thickness in PAC eyes ranges from 4.24mm to 5.02mm vs. 4.04mm in non-PAC control eyes.[15] PAC may be acute or chronic.

During acute angle-closure attack, patients present with an acute rise in IOP (typically >30mm Hg). They also present with several key characteristics including two of the following: ocular or periocular pain, nausea or vomiting and/or visual halos, in addition to at least three of the following: conjunctival injection, a mid-dilated pupil, microcystic corneal edema and/or a shallow anterior chamber.[16]

In secondary angle-closure glaucoma, various mechanisms are responsible for angle closure and result from either an anterior "pulling" of the peripheral iris into the angle to occlude the TM (*e.g.*, neovascular membranes from ischemia, PAS secondary to inflammation, endothelial dystrophies, trauma) or a posterior "pushing" of the iris and ciliary body forward to occlude the angle (*e.g.*, pupillary block from PAS, lens displacement, vitreous displacement inducing secondary pupillary block, space-occupying lesions of the ciliary body or posterior segment, drug-induced choroidal effusion [topiramate, sulfonamides] or secondary to glaucoma surgery and/or ciliary block).[17]

PACG is classified by narrow angles (as noted previously, these are defined by greater than 180° of iridocorneal contact) with chronically elevated IOP >21mm Hg and evidence of glaucomatous optic neuropathy with corresponding visual field defects.[18] Comparatively, individuals with PACG tend to

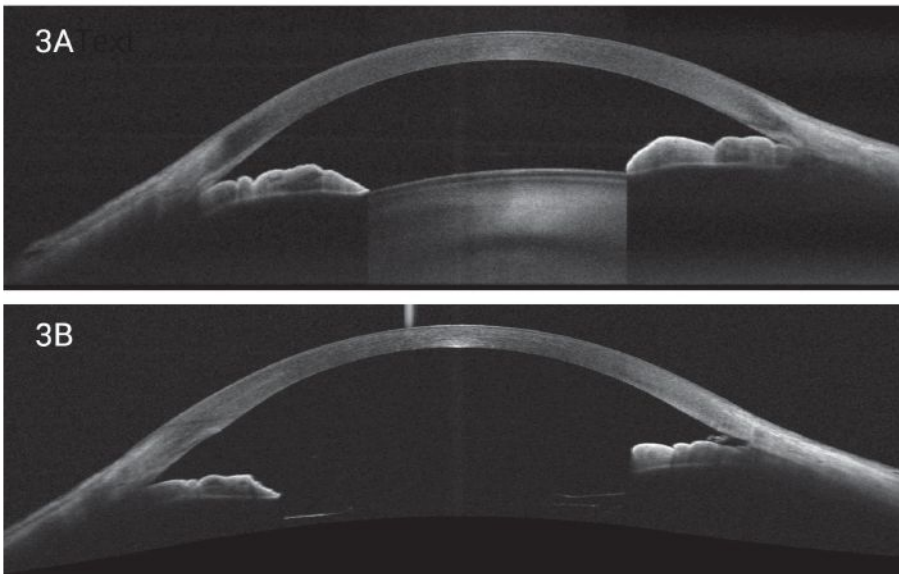

Fig. 3. (A) Edge-to-edge OCT image of chronic angle closure with iridotrabecular contact in the patient from case 2. (B) Same eye after cataract extraction, goniosynechialysis and goniotomy. Note the TM fragments in the angle on the right side.

have more diffuse visual field defects than those with POAG, while degrees of glaucomatous optic atrophy remain the same.[19] Like PAC, PACG may be acute or chronic.

PACG Prevalence

In 2020, a meta-analysis was performed including literature over the last 20 years as it related to global prevalence of PACG. It was determined that as of 2020, PACG affected approximately 17.14 million individuals older than 40 globally.[20] Predictive trends were updated to suggest 20 million will be affected by 2030 and 23 million by 2040, a comparatively lower trend than suggested in a previous study.[21] This may in part be due to improved methods of detection and management of PACS/PACG.

PACG Risk Factors

A patient's risk of developing PACG can increase from various factors such as age, female sex and South Asian populations.[20-21] As it relates to the pathogenesis of PACG, lenticular changes from aging contribute to crowding of the angle and pupillary block. Compared with male counterparts, female subjects presented with narrower angles and greater shallowing of the anterior chamber depth with age. Asian populations accounted for 70% of the PACG population worldwide. Several studies suggest South Asian irises are thicker and stickier, leading to PAS formation and enhanced iridocorneal contact.[22]

Angle Anatomy

Although underused in practice, gonioscopy remains the standard of care in angle assessment.[23] The most posterior structure visualized in an open angle is the ciliary body, which is found between the iris root and scleral spur. The next structure visualized anterior to the ciliary body is the scleral spur, which is typically white or gray and serves as the anchor for the ciliary muscle. Next up is the TM, which is subdivided into the anterior (nonfunctional) and posterior and filters aqueous into Schlemm's canal. Finally, the most anterior angle structure is Schwalbe's line, which represents the end of a clear cornea (*Figure 2*).

Grading Systems

There are three gonioscopy grading systems that exist to better understand the anatomy of the angle: Scheie, Shaffer and Spaeth.[24-25]

The Scheie classification system uses Roman numerals to describe angle depth based on visible structures in which the larger the number, the narrower the angle (*Table 1*).[24] With this system, grade 0 indicates all structures are visible, whereas grade 4 indicates only Schwalbe's line is visible. The Scheie grading system also provides information regarding angle pigmentation on a scale from 0 (no pigment) to IV (heavy pigment).

The Shaffer gonioscopy grading system attempts to describe the degree of the iris in relation to the TM (*Table 2*).[24] Therefore, a larger grading indicates a wider degree of openness. With this grading system a narrow angle is assigned a grade 2, indicating approximately 20° of opening.

The Spaeth grading system describes four clinical aspects of the angle: level of iris insertion, angular width, iris configuration and pigmentation (*Table 3*). Iris insertion is represented by letters A to E, in which A represents the iris inserting anterior to Schwalbe's line, B represents insertion

TABLE 1. THE SCHEIE GRADING SYSTEM[25]

Grade	Visibility	Interpretation
Wide	Wide	Open, all structures visible
I	Slightly narrowed	Ciliary body visible, but recess obscured by the last roll of the iris
II	Apex not visible	Ciliary body not visible
III	Posterior half of TM not visible	Ciliary body, scleral spurcase and posterior half of the TM not visible
IV	No angle structures visible	Ciliary body, scleral spur and TM not visible

TABLE 2. THE SHAFFER GRADING SYSTEM[25]

Angular Grade	Grade Width (in degrees)	Grade	Clinical Interpretation
Wide open angle	45 to 35	4	Angle closure impossible in both grades 3 and 4
	35 to 20	3	
Narrow angle	20	2	Angle closure possible
Narrow angle, extreme	10 or less	1	Angle closure probable, eventually
Narrow angle, slit	Critically narrowed angle, quite possibly against the TM beyond Schwalbe's line	-	-
Narrow angle, partial or complete closure	0	0	Angle closed in part or all of circumference

TABLE 3. THE SPAETH GRADING SYSTEM[24]

Iris Insertion	Angular Approach	Peripheral Iris		Pigmentation of Trabecular Meshwork
A: Anterior to Schwalbe's line	0° to 50°	r: regular	f: flat	0: no pigment
B: Between Schwalbe's line and scleral spur		s: steep	b: bowed anteriorly	1+: minimal
			p: plateau iris	2+: mild
C: Scleral spur visible		q: queer	c: concave	3+: moderate
D: Deep with ciliary body visible				4+: intense
E: Extremely deep with >1mm of ciliary body visible				

anterior to posterior TM, C is posterior to scleral spur, D is "deep" into the ciliary body and E is "extremely" deep with wide ciliary body visibility. The Spaeth grading system lends additional value in the assessment of narrow angles. It denotes parentheses to differentiate the optical insertion vs. the true anatomical insertion revealed by indentation gonioscopy. This technique can expose hidden anomalies that may otherwise be obscured in narrow angles such as angle recession or a plateau iris configuration.

In Spaeth grading, the angular width is more descriptive of the iris approach to the recess rather than the angle of the recess itself.[24-25] There are four iris configurations in the Spaeth grading system: "b" denotes a steep anterior bowing of the iris, which can further be broken down on a 1 to 4+ scale; "p" indicates a plateau configuration, which previous grading systems were unable to differentiate; "f" is for flat configurations; and "c" suggests a concave or posterior bowing more consistent in pigment dispersion syndrome. Pigmentation can also be denoted on a numerical scale from 0 (little pigment) to 4+ (heavy TM pigmentation).

Now that we've reviewed the basics of angle assessment and anatomy, PACG prevalence and risk factors and the three gonioscopy grading systems, let's apply this information to help determine the proper course of assessment and diagnosis in another patient case.

Case Two: Patient with high IOP referred for glaucoma evaluation

A 63-year-old Caucasian male was referred by his optometrist to the Glaucoma Institute of State College for management because of an IOP of 28mm Hg OD and 17mm Hg OS with nerve fiber layer thinning on OCT OD. He had a vitrectomy and epiretinal membrane peel six months prior OD. One month after the repair, he developed ocular hypertension and was treated with Cosopt BID OD by the retinal specialist. His corneal-compensated IOP by Ocular Response Analyzer was 24.2mm Hg OD and 20.3mm Hg OS. Corneal hysteresis was reduced at 9.3mm Hg and 9.5mm Hg, and his central corneal thicknesses measured 554µm and 548µm.

Should we dilate? Due to the importance of proper nerve and nerve fiber layer assessment, and because he was dilated numerous times by the retina specialist, we felt it was reasonable to dilate. As in case one, gonioscopy should be performed prior to dilation. Gonioscopy revealed minimal posterior TM OD with close to 360° of iridotrabecular contact, which was confirmed by angle OCT (*Figure 3A*). There were several areas of PAS. Gonioscopy OS showed greater than 180° of iridotrabecular contact with minimal PAS. Cup-to-disc ratios were estimated to be 0.7/0.8 OD and 0.5/0.5 OS, and there was an epiretinal membrane present OS. OCT showed severe glaucomatous thinning of the nerve fiber layer and ganglion cell complex OD (*Figure 4*).

Post-dilation IOPs measured 31.2mm Hg OD and 23.6mm Hg OS. The patient's visual fields revealed a superior arcuate defect OD, while OS had scattered nonspecific defects.

Based on the clinical assessment, this patient was diagnosed with chronic moderate-stage PACG OD and PACS OS. We instilled one drop of brimonidine OU prior to sending him home. As in the previous case, we educated him on the symptoms of an angle-closure attack and gave him the number of our on-call service.

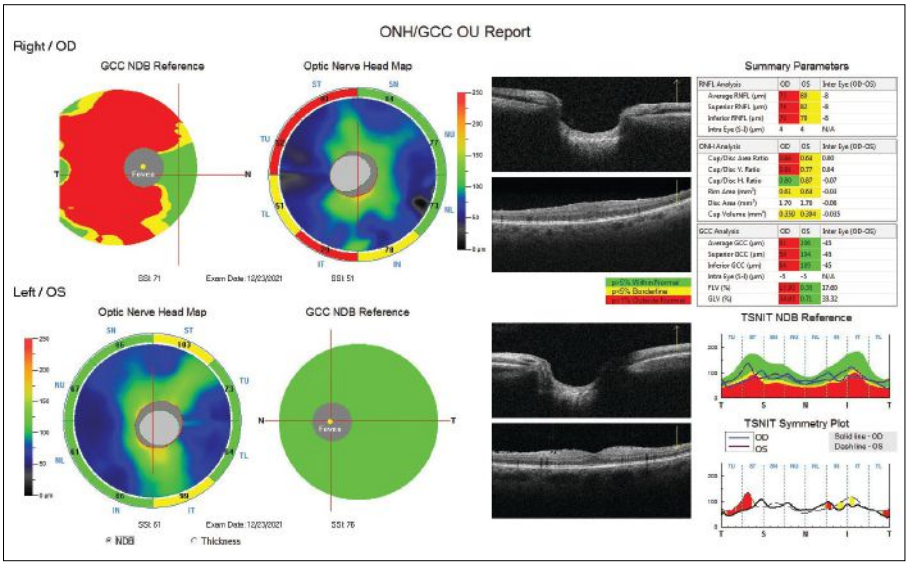

Fig. 4. OCT shows a reduced ganglion cell complex and nerve fiber layer in the patient from case 2. Note the significant asymmetry in the ST and IT sectors in the TSNIT Symmetry Plot.

Should we perform or recommend LPI or proceed directly to cataract extraction? To help answer this question, let's take a look at the data from the Effectiveness in Angle-closure Glaucoma of Lens Extraction (EAGLE) study, which recruited 419 patients. One eye was randomized to early lens replacement vs. conventional management in patients with mild to moderate PACG.[26] All PAC patients had IOPs above 30mm Hg, and the PACG patients had IOPs above 21mm Hg. While many had early cataracts, all were visually asymptomatic. The study found that patients who had early cataract surgery reduced the need for additional glaucoma surgeries or IOP-lowering medications. They also had a better quality of life and a high chance of being cost-effective at three years.[25]

Based on the EAGLE study findings and the unlikely success of LPI with PAS, we proceeded directly to cataract surgery and attempted goniosynechialysis and goniotomy on the patient in case one. Goniosynechialysis involves pushing down on the peripheral iris for the purpose of gently removing the iris from the TM, while goniotomy involves removing three to four clock hours of TM. The patient underwent successful cataract surgery with goniosynechialysis and goniotomy OD. Postoperative IOP on Combigan BID was 14.4mm Hg, and OCT showed a more open angle (*Figure 3B*).

Takeaways

Caring for patients across the angle-closure spectrum may seem challenging. Remember that gonioscopy should always be performed prior to dilation when narrow angles are suspected. Consider LPI if the patient mentions symptoms of angle closure, has a family history of angle-closure disease, has at least +3D of hyperopia or needs frequent dilation. Consider cataract surgery early in patients with PACG.

Having a thorough understanding of PACS, PAC and PACG helps clinicians to know when to recommend or perform dilation, gonioscopy, LPI and cataract surgery, leading to better patient outcomes. ■

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OPTIC NERVE DISORDERS: HOW THEY MANIFEST AND WHAT THEY MEAN

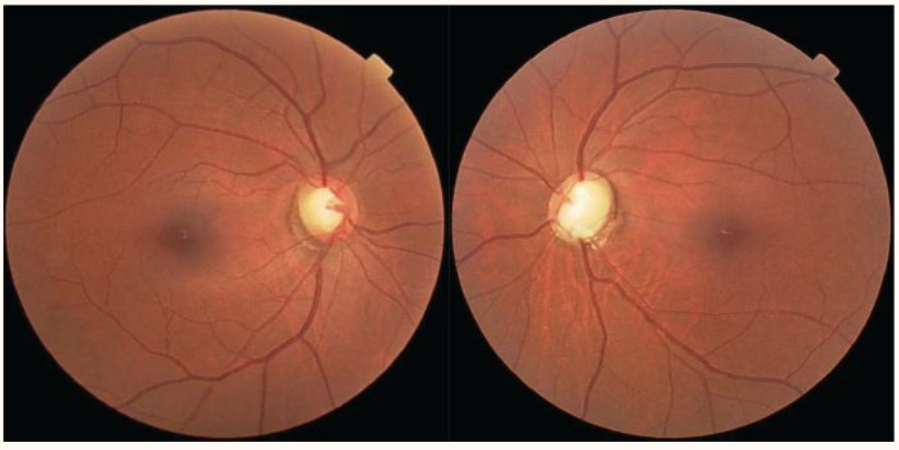
Understanding how to accurately identify, diagnose and manage these conditions is a key component of optometric care.

BY MARC D. MYERS, OD, AND ANDREW S. GURWOOD, OD
PENNSYLVANIA

There are a variety of disorders that can affect the optic nerve, and optometrists play a key role in the management of patients with these conditions. Effective treatment requires the ability to accurately identify optic nerve disorders and distinguish between the various diagnoses. This article will not only delve into how to recognize these conditions in clinical practice but will also discuss diagnostic tests and management approaches for comprehensive—and effective—patient care.

Congenital and Hereditary Optic Nerve Malformations

The optic nerve may be atypical and malformed with functional consequences at birth. Congenital optic nerve malformations are nonprogressive and have a broad spectrum of functional vision limitations.[3-7] Early diagnosis should include ruling out any association with neurologic or systemic disease.



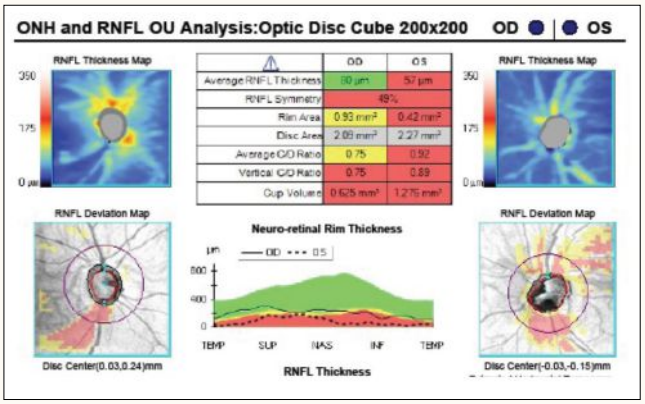


Fig. 1. Tilted discs with RNFL dropout OD and congenital optic pit OS. OCT reveals RNFL defects in the interior quadrant consistent with disc tilt.

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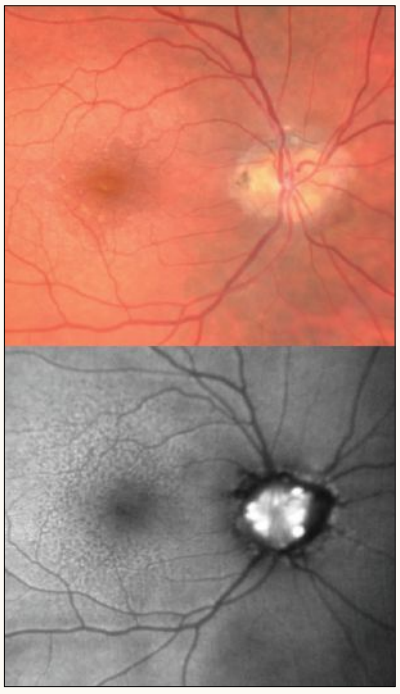

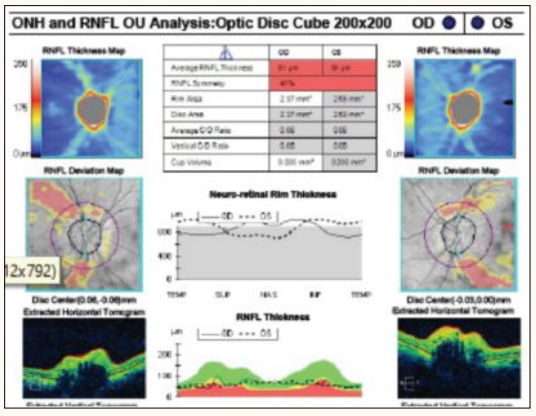

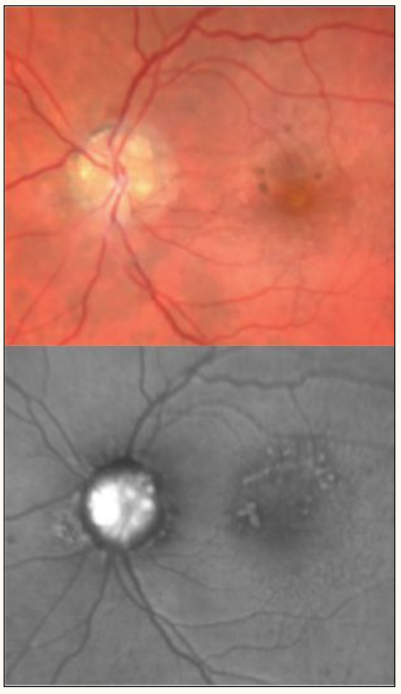

Fig. 2. Color and fundus autofluorescence images of optic disc drusen involving both the right and left eyes. OCT reveals RNFL thinning and elevated optic disc margins.

Congenital presentations, such as hypoplasia, tilted disc, optic pit and optic nerve head drusen, are common and frequently present with minor functional consequences (*Figures 1 and 2*).[3,4] Coloboma, peripapillary staphyloma and morning glory syndrome can have a greater bearing on both the structure and function of the optic nerve. In addition, Aicardi syndrome (in which all or part of the corpus callosum is missing) and papillorenal syndrome (optic nerve dysplasia and renal hypoplasia) can occur with more significant visual and systemic consequences.[3,4]

Hereditary optic neuropathies are associated with progressive visual decline.[4] Noteworthy are dominant optic atrophy, Leber's hereditary optic neuropathy, optic atrophy with neurologic or systemic disease, Wolfram syndrome (juvenile-onset diabetes mellitus, optic nerve atrophy, hearing loss, neurodegeneration) and Costeff syndrome (optic nerve atrophy, delayed development, movement disorders). Vision loss in these cases is often profound and associated with neurologic and/or systemic disease.[4]

Optic Nerve Disorders: How They Manifest and What They Mean

Jointly provided by the Postgraduate Institute for Medicine (PIM) and the Review Education Group

Release Date: July 15, 2023

Expiration Date: July 15, 2026

Estimated Time to Complete Activity: two hours

Target Audience: This activity is intended for optometrists engaged in optic nerve disorder management.

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Educational Objectives: After completing this activity, participants should be better able to:

- Accurately identify optic nerve disorders.
- Distinguish between various differential diagnoses.
- Perform the necessary diagnostic tests to properly diagnose these conditions.
- Manage patients with optic nerve disorders.

Faculty: Marc D. Myers, OD, and Andrew S. Gurwood, OD

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A Closer Look at the Optic Nerve

Cranial nerve II, the optic nerve, is formed by the axons of approximately 1.2 million retinal ganglion cells.[1,2] As the most anterior structure of the visual pathway, it contributes to the transmission of the electrical impulses from the retina to the brain. Disorders of the optic nerve often have devastating visual consequences and can be the result of congenital, hereditary or acquired diseases.

Measuring approximately 6cm in length, the optic nerve is divided into four segments based on anatomical location.[1,2] The intraocular section of the optic nerve consists of prelaminar and postlaminar sections, measuring approximately 1mm. The intraorbital, or postlaminar, section is approximately 3cm in length and courses from the globe to the apex of the orbit. The intraorbital segment is surrounded by orbital contents, including the recti muscles.[1,2] The sheath of the superior and medial recti adhere to the sheath of the optic nerve, attributing to the pain associated with eye movements in a diagnosis such as ON.[2]

Continuous with the meningeal coverings of the brain, the dura, arachnoid and pia mater surround the intraorbital optic nerve. The outermost dura mater consists of dense connective tissue containing elastic fibers. The inner arachnoid layer is next to the dura. The subarachnoid space is continuous with the intracranial subarachnoid space and contains CSF. The pia mater sends blood vessels and connective tissue septa into the nerve.[1,2]

The intracanalicular portion of the optic nerve measures approximately 1cm and passes along the ophthalmic artery through the optic canal. The intracranial segment measures 1.6cm and travels within the suprasellar cistern. The right and left intracranial segments join to form the optic chiasm.[1,2]

The function of the optic nerve is purely sensory, as it contains only afferent fibers. Its functional capabilities include VA, perception of brightness, color and contrast, as well as both light and accommodation reflexes.[1,2]

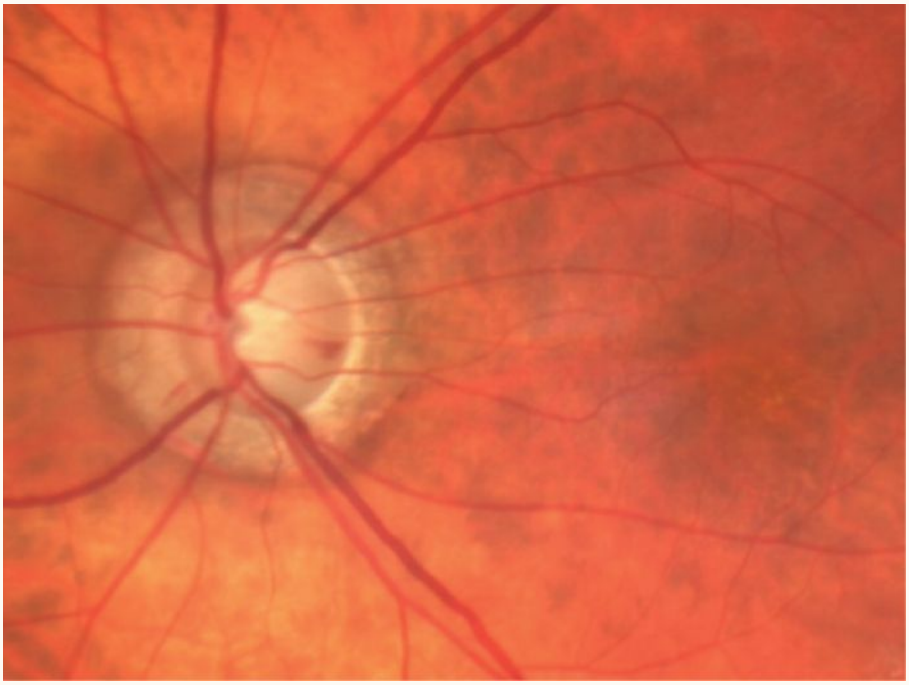


Fig. 3. Glaucomatous optic disc cupping, optic disc hemorrhage and atrophy surrounding the nerve.

Acquired Optic Nerve Disorders

Beyond congenital and hereditary malformations, disease of the optic nerve can be the result of many etiologies. Glaucoma is a progressive optic neuropathy of a mixed mechanism. Non-glaucomatous optic nerve damage may be the result of compressive, toxic/nutritional, traumatic, vascular and inflammatory causes, as well as intracranial space-occupying lesions.

Glaucoma

Glaucomatous optic neuropathy (GON) occurs in the setting of chronic, painless vision loss associated with variable optic atrophy.[5-10] "Cupping," a form of optic nerve atrophy, describes the enlargement of the cup-to-disc ratio. Optic nerve cupping in glaucoma is thought to result from the loss of ganglion cell axon fibers and the thinning and posterior displacement of the lamina cribrosa (*Figure 3*).[8,9] Clinical characteristics of glaucoma include elevated intraocular pressure (IOP), cupping, spared central visual acuity (VA) and color vision (until late stages) and characteristic visual field defects (nasal step, arcuate pattern).

Treatment of GON is aimed at limiting the progression of damage to the optic nerve by reducing IOP by either medical or surgical means.[8-10] Numerous efficacious topical and oral medications are available that target aqueous humor suppression, aqueous outflow through both the trabecular meshwork and uveoscleral pathway and reduced resistance from episcleral venous pressure. Surgical procedures, both laser and traditional, remain options in both early and advanced stages of glaucoma.[8-10]

In the setting of normal IOP and in early disease when structural and functional findings are not as obvious, consider other causes of optic nerve atrophy, including compressive optic neuropathy (CON), hereditary optic neuropathy and arteritic anterior ischemic optic neuropathy (AION).[4-11,15,29]

Compared with GON, patients with CON are often younger with worse VA and visual defects that may respect the vertical meridian. Also, pallor of the neuroretinal rim (vs. thinning) is more common in non-glaucomatous cupping.[5-10] OCT provides structural information about the optic nerve head, RNFL and

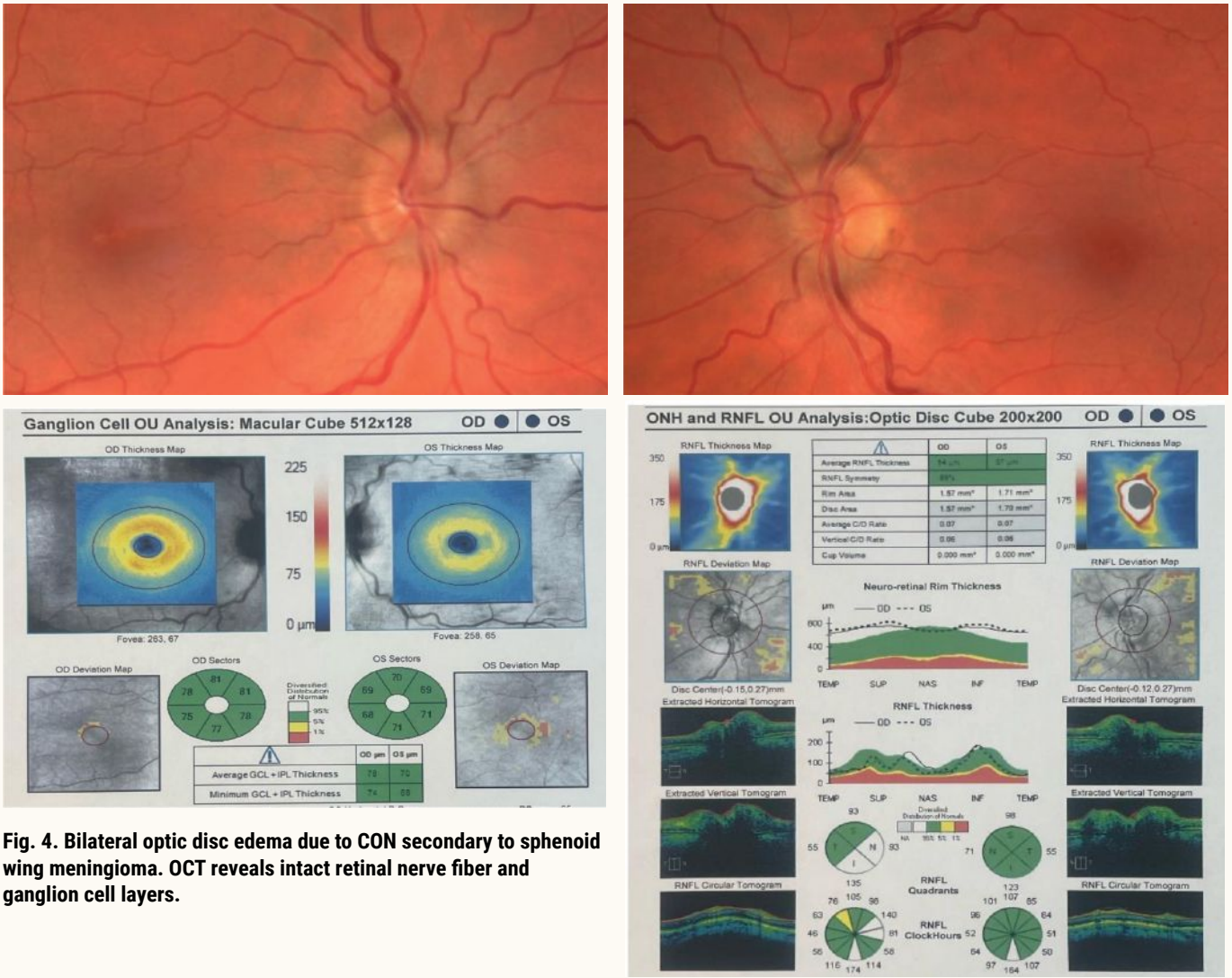


Fig. 4. Bilateral optic disc edema due to CON secondary to sphenoid wing meningioma. OCT reveals intact retinal nerve fiber and ganglion cell layers.

ganglion cell complex (GCC). OCT angiography assesses the peripapillary and macular microcirculation. Studies have revealed decreased retinal vessel density in CON.[5,6]

Non-Glaucomatous Causes

Accurate identification and diagnosis of optic nerve disorders requires the ability to distinguish between glaucomatous and non-glaucomatous optic neuropathies, which can be challenging. Next, we will discuss the various manifestations of these conditions and how to recognize and approach each.

Compressive Optic Neuropathies

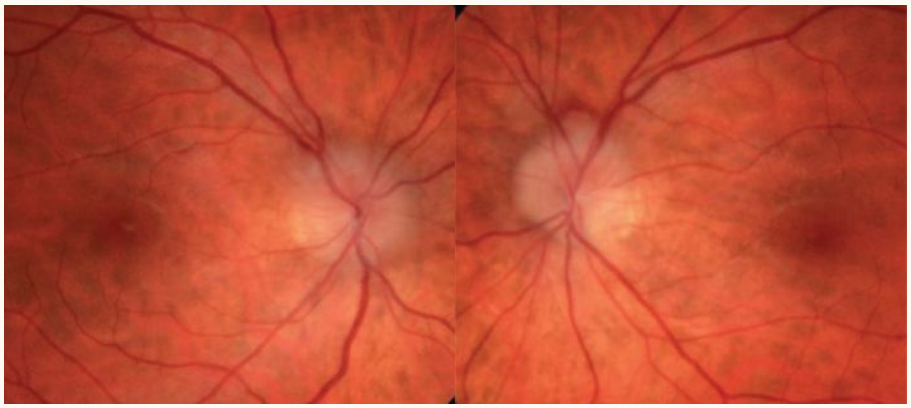
These conditions are the result of space-occupying lesions that disrupt the physiology of both the optic nerve and retinal ganglion cells.[11,15-17] Common neoplasias that may cause CON include glioma, meningioma, hemangioma, craniopharyngioma and pituitary adenoma (*Figure 4*).

Thyroid eye disease, aneurysms and ethmoid or sphenoid sinus mucocele are non-neoplastic causes of CON.[15-17] Compression may occur along the course of the four segments of the nerve, resulting in unilateral or bilateral nerve involvement in the event of a chiasmal lesion.[15-17]

In a recent population-based study, compressive optic neuropathy was found to occur at an incidence of 1.14 per 100,000 people per year. The median age at diagnosis was 55, with 61% of patients being female.[15]

Pituitary adenoma was the most common cause of CON, accounting for 35% of all cases.[15] Presenting symptoms included visual field loss, loss of color perception and decreased visual acuity. Diplopia may be the result of ocular motor nerve compression or mechanical restriction of the extraocular muscles due to orbital tumor or thyroid myopathy. Progression of symptoms is typically gradual but may be acute and dramatic in cases of intracranial aneurysm in close proximity to the optic nerve or in pituitary apoplexy.[11,15-17]

Clinical assessment is variable, as early cases may present with subtle signs of optic nerve impairment. Acuity may range from normal to acutely reduced. A relative afferent pupillary



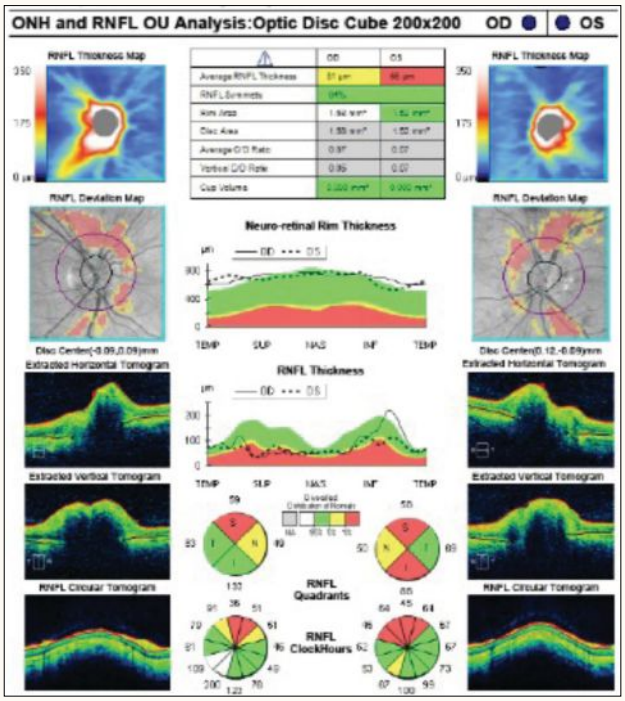


Fig. 5. Bilateral optic disc edema associated with IIH. OCT confirms the presence of optic disc edema and RNFL thinning.

defect (RAPD) will be present in unilateral optic neuropathy. Color testing is also often impaired. Assessment of the optic disc may vary when presenting as normal, swollen, pale or cupped. Eye pain and headaches can be symptoms of CON.[15-17]

Visual field analysis in patients with pituitary adenoma will show bitemporal hemianopsia that is denser superiorly or a junctional scotoma. Craniopharyngiomas most typically present with bitemporal hemianopsia, denser inferiorly.[15-17] Other causes of CON display a variety of patterns of visual field defects, such as cecocentral scotomas or generalized depression, depending on the location of the lesion.[15-17] In cases of early detection and successful treatment, visual field defects may improve over time.

Inner retinal layers, including the RNFL, GCC and inner plexiform layer, are of particular interest in cases of neuro-ophthalmologic disease.[14-17] The GCC is where the bodies of the ganglion cells are found. The RNFL is made up of axons of retinal ganglion cells that course out of the eye via the optic nerve, chiasm and tract, eventually synapsing in the lateral geniculate body.[14]

Compressive lesions may manifest as thinning of the RNFL and GCC because of the damage to retinal ganglion cell axons in the optic nerve, chiasm or tract. OCT of the RNFL and GCC is a method to quantify anatomic changes associated with pathology involving the anterior visual pathway.[15] Thinning of the RNFL and GCC may proceed vision loss, allowing for earlier diagnosis of CON. Early diagnosis can be a key element in preserving structure(s), in this case the RNFL and GCC, and may help limit visual impairment.[15-17]

Signs of CON accompanied by impairment of ocular motility, decreased corneal sensitivity or ptosis serve as an indication of multiple cranial nerve involvement.[15] Confirmation of a diagnosis involving a compressive lesion is made most frequently using MRI and CT.[12,13,15]

Management of compressive optic neuropathy ranges from observation to intracranial surgery. If a benign mass that is not threatening an adjacent structure proves to be stable in size and has no association with visual function, clinical observation with serial diagnostic testing may be recommended.[15-17] Pharmacologic agents are used in the treatment of hormonally active pituitary tumors. Modern treatment plans have great success, as they include some combination of surgery (craniotomy, endoscopy), chemotherapy and radiation.[15-17]

Elevated Intracranial Pressure and Papilledema

Optic nerve disorders may be associated with elevated intracranial pressure (ICP).[18-24] Papilledema refers to bilateral optic disc swelling secondary to elevated ICP (*Figure 5*). The most common cause of elevated ICP is idiopathic intracranial hypertension (IIH). As the name implies, in IIH there is no identifiable cause for elevated ICP.[21-23]

Other non-idiopathic etiologies that can cause either an increase in cerebrospinal fluid (CSF) production, decrease in CSF resorption and/or obstruction of CSF flow include space-occupying lesions, venous sinus thrombosis, diffuse cerebral edema, spinal cord masses, meningi-

tis, malignant hypertension and toxic pharmacologic effects.[11,18-24]

Electron microscopy demonstrates that the optic disc edema of papilledema is primarily intra-axonal, influencing energy-dependent axoplasmic transport.[11,19,20] It is the stasis of the intra-axonal fluid, swelling of axons and leakage of cellular contents into the extracellular space of the optic disc that gives rise to optic disc edema. Further, the reduced perfusion of axons may result in a secondary phenomenon of venous obstruction and dilation, nerve ischemia and vascular telangiectasia.[11,19,20]

Papilledema may occur in all ages, races and ethnic groups, as well as both genders. However, in papilledema specific to IIH, 90% of patients are female with an average age of 29, Caucasian predilection and average BMI of 39.9.[19-21]

In the setting of elevated ICP, regardless of the etiology, patients typically complain of headache, nausea, vomiting and visual symptoms, including blurred vision, transient visual obscurations (TVO), photopsias and diplopia.[19-21] In the Idiopathic Intracranial Hypertension Treatment Trial, 84% of patients reported headache, with 68% describing features similar to migraine. The second most common complaint was TVO, occurring in 68% to 72% of patients. Other symptoms include pulsatile tinnitus, back pain, dizziness, photophobia, neck pain, vision loss and diplopia.[21,22]

Clinical examination will reveal optic disc edema that is bilateral and may be asymmetric. Bilateral or unilateral cranial nerve VI (abducens) palsy may also be present. In cases of IIH, the clinical examination must be otherwise normal.[18-22] The Modified Dandy Criteria must be met in order to make the diagnosis of IIH (*see sidebar*). Beyond the identification of ophthalmic and systemic signs and symptoms, management criteria includes the assessment of CSF via lumbar puncture (evaluating both ICP and CSF cytology) and neuroimaging (completed prior to lumbar puncture) to rule out any potential underlying diagnosis that could cause increased ICP.[24]

If papilledema is the result of a mass, surgical resection may be indicated depending on the location. Anticoagulation and/or endovascular stenting is indicated to treat venous sinus thrombosis, a less common cause of papilledema. In cases of papilledema due to IIH, the severity of symptoms guides nonsurgical and surgical options.[11,18-24]

When visual changes have a gradual onset and are mild, a weight loss goal of between 5% to 10% of total body weight is associated with improvement of signs and symptoms.[21-23] Acetazolamide combined with weight loss has proven effective in benefiting symptomatic patients. Topiramate reduces the symptoms of headache and aids in weight loss.[21-23]

When conservative management does not improve symptoms or makes them worse, surgical intervention is indicated. Optic nerve sheath fenestration involves surgically decompressing the optic nerve by creating a slit or window in the dura mater of the optic nerve, allowing the egress of the CSF from the subarachnoid space.[22,23] Fenestration is used in cases of visual symptoms of an acute onset. It proves to be less effective in improving visual symptoms in cases where papilledema is chronic. Also, it is less effective at relieving headache symptoms when compared with CSF diversion procedures.[22,23]

If the predominant symptom associated with papilledema is headache, CSF diversion procedures such as ventriculoperitoneal shunt or lumbar peritoneal shunt are the more efficacious treatment options.[22,23] If these interventions fail, endovascular venous sinus stenting (EVSS) can be considered when diagnostic imaging confirms stenosis of the transverse sinus. EVSS may result in symptomatic improvement in visual symptoms.[22,23]

When papilledema is caused by IIH, permanent vision loss is the most feared outcome.[21,22] Hypertension is one of the greatest risk factors associated with a poor visual prognosis. Other contributors to poor prognosis include rapid symptom onset, progression, the severity of the presenting visual symptoms and the rate at which those symptoms deteriorate.[11,21-24]

Inflammatory Optic Neuropathy

Optic neuritis (ON) is a generic term used to describe an acute inflammatory syndrome of the central nervous system that affects the optic nerve.[11,25-27] Demyelinating ON is caused by an inflammatory attack that results in axonal injury and retinal ganglion cell apoptosis. It is the most common type of inflammatory disorder of the optic nerve. Typical demyelinating ON carries an increased future risk of multiple sclerosis (MS). This condition also frequently causes optic neuritis. The Optic Neuritis Treatment Trial showed that approximately 50% of ON patients had converted to MS after a 15-year follow-up period.[25-27]

It is important to note that MS is not the only demyelinating condition that can cause ON. Neuromyelitis optica (NMO) is a rare demyelinating autoimmune inflammatory disease that affects the central nervous system, causing ON and myelitis.[25-27] The frequency of NMO is low when compared with MS, with 1/100 cases in North America. Like MS, NMO initial ophthalmic presentations are common, but NMO has more severe bilateral visual disability and optic nerve damage with a guarded visual prognosis. OCT, brain and spinal cord MRI and the titer of anti-aquaporin 4 antibodies are the tests used to distinguish MS from NMO.[21-27]

Even less common is a recently defined inflammatory demyelinating disease of the central nervous system called myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD). This autoimmune

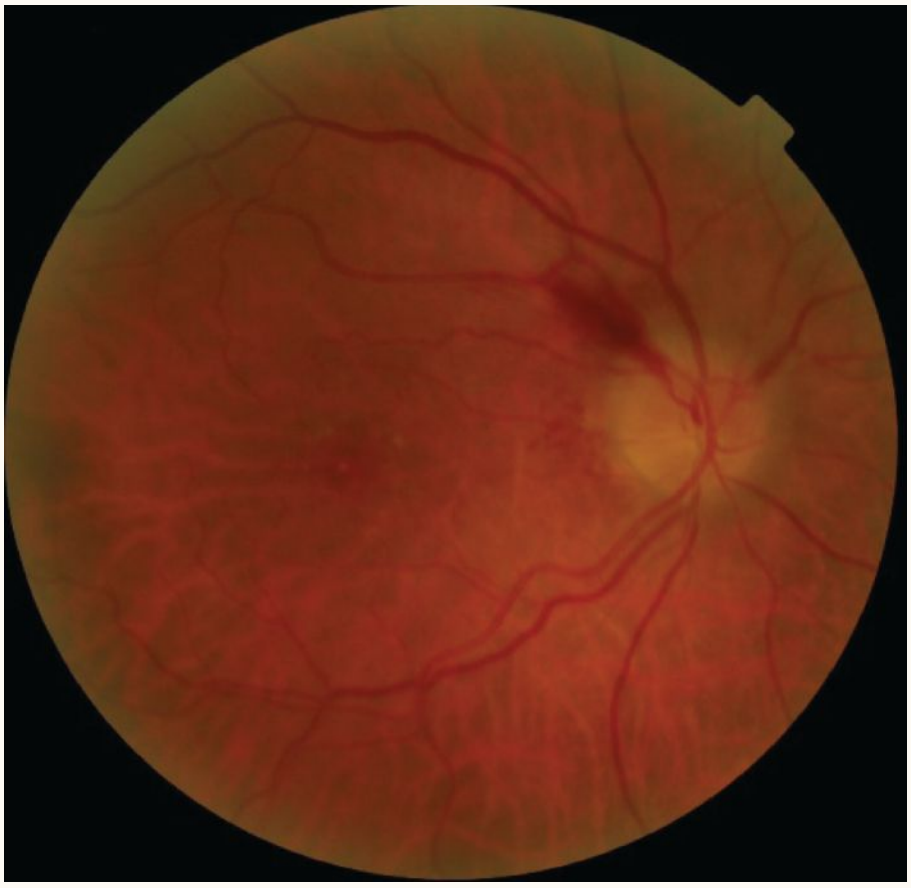


Fig. 6. Blurred disc margins with associated hemorrhage secondary to arteritic AION.

disorder is associated with antibodies directed against the myelin of the brain, spinal cord and optic nerves.[28] MOGAD may cause ON, transverse myelitis and, in children, acute disseminated encephalomyelitis. Diagnosis is confirmed when the protein's antibody is found in serum and/or CSF and the presence of MRI phenotype is consistent with MOGAD.[28]

In acute demyelinating ON, patients present with vision loss in one eye that rapidly worsens for up to two weeks. Periocular and retrobulbar pain occurs in 90% of patients and reportedly worsens with eye movement. Most patients have reduced contrast sensitivity, dyschromatopsia and a visual field defect.[25-27] At times, no other neurologic symptoms may exist on presentation. Taking a thorough medical history may uncover past transient, spontaneous-resolving episodes of neurologic dysfunction. For example, a patient may report limb weakness that lasts for days or weeks then resolves or episodic unexplained vertigo or balance loss.[25-27]

Signs include a variable decrease in VA, contrast sensitivity and color vision. Central scotomas and diffuse visual field loss are common. In unilateral cases, the symptomatic eye has an RAPD. Assessment of the optic nerve, in the minority of cases, will reveal mild to moderate hyperemic disc swelling. Depending on the underlying etiology, peripheral retinal assessment may show signs of intraocular inflammation that include peripheral sheathing of retinal veins and "snow banking," the accumulation of vitreous exudates over the pars plana.[11,25-27]

The standard treatment of typical ON is based on results from the Optic Neuritis Treatment Trial, which found that one gram of intravenous (IV) methylprednisolone daily for three days followed by oral prednisolone (1mg/kg/day) for 11 days often sped up visual recovery.[25-27] Although the recovery of acute visual loss was sped up, final recovery was the same whether or not steroids were used. A benefit of this regimen of care was that the onset of MS was delayed for up to two years; however, at two years, equal numbers of treated and untreated cases developed MS.[25-27]

The Controlled High Risk Avonex Multiple Sclerosis Study found that cases of first-episode typical ON with two or more white matter lesions on a brain MRI, when treated with weekly intramuscular beta-interferon injections, had a decreased risk of developing symptoms of MS by three years. Study patients also received the protocol of IV and oral steroids.[25-27]

Monoclonal antibody agents have been approved by the FDA for adults with demyelinating disease. Those to treat MS include alemtuzumab, natalizumab, ocrelizumab, ofatumumab and rituximab. Approved to treat NMO are eculizumab, inebilizumab and satralizumab, all of which display the ability to significantly reduce the risk of NMO relapse.[26,27]

Vascular Optic Neuropathy

One such condition—ischemic optic neuropathy (ION)—is the result of a transient or permanent interruption of blood supply to any portion of the optic nerve.[11,29-31] Anterior ION (AION) involves ischemia of the optic nerve head while posterior ION (PION) involves ischemia of the posterior optic nerve. Further, ION is classified as arteritic or non-arteritic.

The postulated pathophysiologic mechanism of non-arteritic AION (NAION) involves the prelaminar portion of the optic nerve head.[29,31] The short posterior ciliary arteries (PCAs) are thought to be a component of a compartment syndrome of the prelaminar nerve. A structurally predisposed, crowded optic nerve head with a small cup-to-disc ratio,

referred to as "a disc at risk," may lead to the death of ganglion cells. Vascular insufficiency is thought to play a role in the pathophysiology of NAION, as vascular diseases such as hypertension, diabetes and obstructive sleep apnea impair autoregulation of the optic nerve head blood flow.[29,31]

NAION is the most common cause of acute optic nerve disease in patients over 50.[29-31] The annual incidence of NAION is 10.3 per 100,00 individuals. The median age of onset is 72, and the condition disproportionately affects those of Caucasian descent.[31,32] Clinical features include the sudden onset of rapidly-progressive, painless loss of vision in one eye. Vision loss may be diffusely blurred or in a vertical hemifield distribution, commonly inferiorly. VA loss may vary, with approximately half of patients seeing better than 20/64 and one in three seeing less than 20/200.[29-32] Color vision impairment is proportionate to the level of acuity loss. Optic disc swelling may be diffuse or sectoral and accompanied by peripapillary flame hemorrhages. An RAPD is expected in optic neuropathy that is unilateral.[31,32]

Non-arteritic PION is a rare entity that presents with optic nerve signs and symptoms in the absence of disc edema. A diagnosis of exclusion, non-arteritic PION can only be diagnosed in the context of a normal MRI of the orbits, ruling out a compressive cause, and when giant cell arteritis (GCA) is excluded in patients over 50.[11,29-31]

Treatment of NAION, in theory, would reduce the optic nerve compartment syndrome via surgical decompression or by reducing disc edema. The Ischemic Optic Neuropathy Decompression Trial ceased recruitment when preliminary findings suggested no benefit and potential harm related to surgery.[33] Further investigations included the use of intravitreal bevacizumab, oral prednisolone and aspirin, all of which proved to be of no benefit in the recovery of VA.[29,31,33] An advised strategy to reduce the lifetime risk of further episodes of NAION includes the treatment of vascular risk factors, including hypertension, diabetes and obstructive sleep apnea, as well as smoking cessation.[29,31,33]

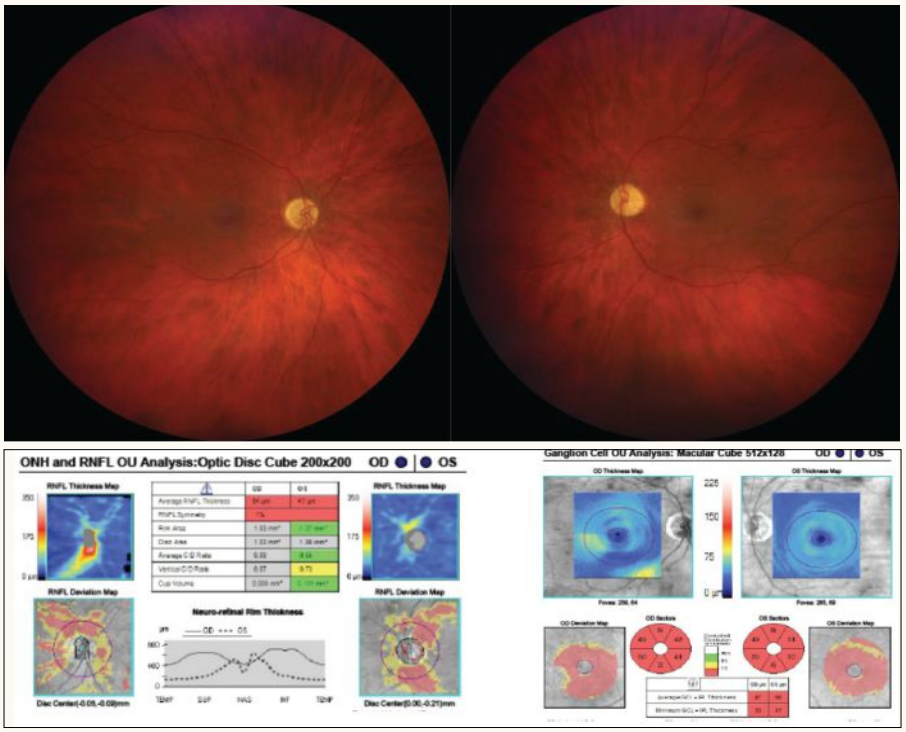


Fig. 7. Bilateral optic disc pallor secondary to toxic optic neuropathy due to rheumatologic medication. Discs are pale, and OCT confirms RNFL and GCC defects.

Arteritic AION is almost always caused by GCA, a large-vessel vasculitis affecting people over the age of 50.[11,29-31] Up to 20% of patients with giant cell arteritis have AION, a form of end-organ ischemia. Thrombotic occlusion of the short PCAs because of large-vessel vasculitis causes the optic nerve head infarction seen in AION (*Figures 6 and 7*). The diagnosis of GCA may be confirmed by erythrocyte sedimentation rate, C-reactive protein and temporal artery biopsy.[29-31]

Signs are commonly preceded by transient monocular vision loss resulting from optic nerve or choroidal ischemia. Transient monocular vision loss is a medical emergency warranting medical workup to rule out, among others, GCA and cerebral vascular accident.[29-31] Transient diplopia due to extraocular muscle or cranial nerve ischemia may be reported. The large-vessel vasculitis associated with GCA may cause symptoms of jaw claudication, scalp tenderness, headache, fever, malaise and weight loss.[29-31]

Clinical findings associated with arteritic AION include severe visual acuity loss of worse than 20/200 in over 60% of patients with a relative afferent pupillary defect. Posterior segment assessment may reveal signs of ocular ischemia in the form of pallid or chalky white disc edema and retinal cotton wool spots.[11,29-33]

Acute management of anterior ischemic optic neuropathy includes high-dose glucocorticoids, including prednisolone or IV methylprednisolone.[27-30] Specific to GCA, IV steroids are indicated based on improved visual outcomes, potential evolution of systemic complications and prevention of second-eye involvement.[27,29] Tocilizumab is a monoclonal antibody agent that is used in conjunction with corticosteroids, providing a

Modified Dandy Criteria to Identify IIH

- Signs and symptoms of increased ICP
- Absence of localized findings on neurologic examination
- Absence of deformity, displacement or obstruction of the ventricular system and otherwise normal neurodiagnostic studies except for evidence of increased CSF pressure >200mm H_2O. Abnormal neuroimaging except for empty sella turcica, optic nerve sheath with filled-out CSF spaces and smooth-walled, non-flow-related venous sinus stenosis or collapse should lead to another diagnosis.
- Awake and alert
- No other known cause of increased ICP, opening CSF pressure of 200mm H_2O to 250mm H_2O and at least one of the following:
  - Pulse synchronous tinnitus
  - Cranial nerve VI palsy
  - Frisen grade 2 papilledema
  - Echography negative for drusen and no other disc anomalies mimicking disc drusen
  - Magnetic resonance venography with lateral sinus collapse or stenosis
  - Partially empty sella on coronal or sagital views and optic nerve sheaths with filled-out CSF spaces next to the globe on T2-weighted axial scans

higher probability of sustained GCA remission and vision preservation.[34]

Infectious Optic Neuropathy

Numerous infectious agents have been identified as known causes of optic neuropathy. Bacteria, spirochetes, fungi and viruses may directly and indirectly cause inflammatory, degenerative or vascular compromise of the optic nerve.[11,35,36] Infectious optic neuropathy may present as an anterior optic neuritis (papillitis), retrobulbar optic neuritis (optic disc is normal in appearance), neuroretinitis (optic disc edema with macular star of exudate), anterior ischemic optic neuropathy or a perineuritis (infection affects the sheath of the optic nerve causing optic disc swelling).[35,36]

The most common bacteria include *Bartonella henselae* (cat scratch disease), *Mycobacterium tuberculosis* (tuberculosis), *Treponema pallidum* (syphilis) and *Borrelia burgdorferi* (Lyme disease).[35,36] Viral causes include herpes simplex virus types 1 and 2, varicella zoster virus (that includes both varicella and herpes zoster), cytomegalovirus, Epstein-Barr virus (mononucleosis) and human immunodeficiency virus.[35,36] Other infections due to parasitic vectors, toxoplasmosis and toxocariasis, and fungal vectors, histoplasmosis, may also cause optic neuropathy.[35,36]

The prognosis for recovery of visual function is largely dependent on timely assessment, ordering proper diagnostic tests and providing targeted medical treatments. In cases of infectious optic neuropathy, OCT test results may reveal damage incurred at the retinal nerve fiber and ganglion cell layers, limiting potential recovery of visual function.[35,36]

Toxic, Nutritional Optic Neuropathy

These disorders occur from persistent exposure to a toxic substance or a sustained nutrient deficiency.[11,37] Toxic neuropathy occurs due to the use of toxic medications, as well as ingestion or inhalation of toxic substances. Medication toxicity is both dose-dependent and duration-dependent. The antimycobacterial drug, ethambutol, is the most encountered cause of toxic optic neuropathy.[37] Methanol optic neuropathy has an acute clinical picture when ethanol is injected. More commonly, neuropathy occurs when ethanol in home-distilled alcoholic beverages is inadvertently ingested. The antiarrhythmic drug, amiodarone, has been associated with optic neuropathy mimicking NAION.[37-39]

Nutritional optic neuropathy has a well-established association with vitamin B12, folic acid and copper deficiencies.[37-39] Pernicious anemia, nitrous oxide toxicity and gastric maladies like atrophic gastritis, history of gastric surgery, gastric malabsorption and treatment of gastroesophageal reflux are all potential causes of B12 deficiencies. Folate deficiency is the result of decreased uptake, increased demand, malabsorption or suppression due to a folate antagonist, such as methotrexate. Copper deficiency is most commonly caused by gastric surgery and the associated malabsorption syndrome.[37-39]

Tobacco and alcohol use have been considered to have an association with toxic optic neuropathy.[37-39] Alcohol is not considered to be a direct cause of toxic optic neuropathy. Alcoholism and its association with a higher incidence of nutritional deficiencies and gastric malabsorption can result in optic neuropathy. Toxic optic neuropathy attributed to smoking is a diagnosis of exclusion.[37,39]

Early in the development of toxic and nutritional optic neuropathy, the optic nerves may have a normal appearance or may be slightly hyperemic.[38,39] If the exposure or deficiency persists, bilateral temporal optic disc pallor develops from injury of the ganglion cell axons in the papillomacular bundle. Visual field testing results in bilateral central and cecocentral defects. Progressive, bilateral vision loss, decreased color vision and normal pupil assessment (due to symmetry of optic nerve damage) may be present.[38,39]

Treatment is based on removing or discontinuing the offending agent, supplementing nutritional deficien-

cies and limiting or discontinuing the use of alcohol or tobacco.[38,39] The visual prognosis is variable depending on the offending agent and the severity of the resultant damage and may take months to resolve. It is important to educate patients as to how they should avoid exposure to toxins and potentially make necessary lifestyle changes.[38,39]

Traumatic Optic Neuropathy

This form of optic neuropathy is caused by injury to the optic nerves. The degree of vision loss depends on the portion of the optic nerve affected by the injury.[11,40-42] The classification of traumatic optic neuropathy can be described as either primary or secondary. Primary lesions may be further described as direct (penetrating) or indirect (non-penetrating, blunt trauma). Direct injuries are less common because of the protection provided by the orbit. When they do occur, direct injuries result in immediate and often irreversible damage to the affected nerve.[40-42]

The mechanism by which indirect injury may occur includes transmission of concussive forces directly to the nerve, as in cases involving the portion of the nerve within the optic canal.[40-42] These forces may also induce the transmission of energy away from the point of impact, generating rotational or translational movement of the globe or brain.[40-42]

A secondary traumatic optic neuropathy is due to damage to the optic nerve that occurs after the traumatic event. In these cases, visual loss is delayed.[32-34] There are several proposed mechanisms of how secondary injury may occur, including vasospasm, edema, hemorrhage and compression of vessels causing circulatory insufficiency and resulting in necrosis of the nerve.[40-42]

Takeaways

Optic nerve disorders are a relatively common clinical finding and are the result of many congenital, hereditary and acquired diagnoses. In cases of acquired optic neuropathy, it is important to distinguish between glaucomatous and non-glaucomatous etiologies. Awareness of a chronic or acute pattern of presentation, along with a detailed history, constellation of clinical findings and results of structural and functional diagnostic studies, allow for proper diagnosis and treatment.

Properly identifying optic neuropathies can not only save vision but also lives. ■

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OPTOMETRIC STUDY CENTER QUIZ

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1. What segment of the optic nerve courses from the globe to the apex of the orbit?
a. Intraocular.
b. Intraorbital.
c. Intracanalicular.
d. Intrachiasmal.

2. What statement is false regarding the optic nerve?
a. Its function is purely sensory.
b. It measures approximately 6cm in length.
c. It contains only efferent fibers.
d. The right and left segments of the optic nerve join to form the optic chiasm.

3. What statement is false regarding congenital optic nerve malformations?
a. May have findings that are progressive and are always unilateral.
b. May be associated with neurologic disorders.
c. May be associated with systemic disorders.
d. May present as optic nerve hypoplasia.

4. What statement is true regarding hereditary optic neuropathies?
a. May present as an optic pit.
b. Presentation is associated with visual disorders that are stable.
c. Presentation is associated with progressive visual decline.
d. Vision loss is isolated from systemic and/or neurologic disease.

5. Which of the following is not a neoplasia associated with CON?
a. Sphenoid sinus mucocele.
b. Pituitary adenoma.
c. Meningioma.
d. Hemangioma.

6. Compressive lesions may manifest as thinning of what retinal layer(s)?
a. Retinal pigment epithelium and external limiting membrane.
b. Internal limiting membrane.
c. Retinal nerve fiber and ganglion cell layers.
d. Outer nuclear layer.

7. What term is used to refer to bilateral optic disc swelling secondary to elevated ICP?
a. Cerebral edema.
b. Coloboma.
c. Optic nerve hypoplasia.
d. Papilledema.

8. What most commonly causes elevated ICP?
a. Meningioma.
b. Pituitary adenoma.
c. IIH.
d. Craniopharyngioma.

9. What term is used to describe an acute inflammatory syndrome of the central nervous system that affects the optic nerve?
a. Choroidopathy.
b. ON.
c. IIH.
d. Aneurysm.

10. What term describes a transient or permanent interruption of blood supply to any portion of the optic nerve?
a. Papilledema.
b. CON.
c. ON.
d. ION.

11. What statement is true about NAION?
a. It most often affects Caucasian people.
b. It rarely affects people over the age of 72.
c. It is usually caused by GCA.
d. The intraorbital optic nerve is primarily involved.

12. What statement is true regarding infectious optic neuropathy?
a. It only presents as an anterior ON.
b. It only presents as a retrobulbar ON.
c. It only presents as a neuroretinitis.
d. It may involve any part of the optic nerve.

13. Which of the following statements is false regarding nutritional optic neuropathy due to folate deficiency?
a. Folate deficiency may be the direct result of smoking and alcohol consumption.
b. Folate deficiency may be the result of reduced uptake of folate.
c. Folate deficiency may be the result of an increased demand of folate.
d. Folate deficiency may be the result of a malabsorption of folate.

14. What term is used to describe traumatic optic neuropathy that is due to damage of the optic nerve after a traumatic event?
a. Direct traumatic optic neuropathy.
b. Indirect traumatic optic neuropathy.
c. Primary traumatic optic neuropathy.
d. Secondary optic neuropathy.

15. What term is used to describe the loss of ganglion cell axon fibers and the thinning and posterior displacement of the lamina cribrosa associated with GON?
a. Disc pallor.
b. Cupping.
c. Optic pit.
d. Coloboma.

16. What statement is most true when comparing patients with GON to those with CON?
a. GON patients are often younger.
b. CON patients are often younger.
c. GON patients have worse VA in early disease stages.
d. CON patients rarely present with reduced VA.

17. Treatment modalities used in the management of GON have the main goal of which of the following?
a. Increasing profusion of the optic nerve.
b. Ensuring nutritional deficiencies are eliminated.
c. Lowering IOP.
d. Smoking cessation.

18. Confirmation of a diagnosis of CON is most frequently made with what diagnostic test?
a. Complete blood count.
b. X-ray.
c. Spinal tap.
d. MRI or CT.

19. What was the main outcome of the Ischemic Optic Neuropathy Decompression Trial?
a. Clinically significant benefit result from optic nerve decompression.
b. No clinically significant benefit result from optic nerve decompression.
c. Intravitreal bevacizumab is beneficial in the treatment of ION.
d. Oral steroid is beneficial in the treatment of ION.

20. The diagnosis of GCA may be made with which of the following tests?
a. Temporal artery biopsy.
b. Complete blood count.
c. OCT.
d. X-ray.

Examination Answer Sheet

Optic Nerve Disorders: How They Manifest and What They Mean

Valid for credit through July 15, 2026

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

Post-activity evaluation questions:

Rate how well the activity supported your achievement of these learning objectives. *1=Poor, 2=Fair, 3=Neutral, 4=Good, 5=Excellent*

21. Accurately identify optic nerve disorders. ① ② ③ ④ ⑤
22. Distinguish between various differential diagnoses. ① ② ③ ④ ⑤
23. Perform the necessary diagnostic tests to properly diagnose these conditions. ① ② ③ ④ ⑤
24. Manage patients with optic nerve disorders. ① ② ③ ④ ⑤

25. Based upon your participation in this activity, do you intend to change your practice behavior? (Choose only one of the following options.)

Ⓐ I do plan to implement changes in my practice based on the information presented.

Ⓑ My current practice has been reinforced by the information presented.

Ⓒ I need more information before I will change my practice.

26. Thinking about how your participation in this activity will influence your patient care, how many of your patients are likely to benefit? (please use a number): ☐

27. If you plan to change your practice behavior, what type of changes do you plan to implement? (Check all that apply.)

Ⓐ Apply latest guidelines
Ⓑ Change in diagnostic methods
Ⓒ Choice of management approach
Ⓓ Change in current practice for referral
Ⓔ Change in vision correction offerings
Ⓕ Change in differential diagnosis
Ⓖ More active monitoring and counseling
Ⓗ Other, please specify: _____

28. How confident are you that you will be able to make your intended changes?

Ⓐ Very confident Ⓑ Somewhat confident Ⓒ Unsure Ⓓ Not confident

29. Which of the following do you anticipate will be the primary barrier to implementing these changes?

Ⓐ Formulary restrictions
Ⓑ Time constraints
Ⓒ System constraints
Ⓓ Insurance/financial issues
Ⓔ Lack of interprofessional team support
Ⓕ Treatment related adverse events
Ⓖ Patient adherence/compliance
Ⓗ Other, please specify: _____

30. Additional comments on this course: _____

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Rate the quality of the material provided:

1=Strongly disagree, 2=Somewhat disagree, 3=Neutral, 4=Somewhat agree, 5=Strongly agree

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

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

Signature _____ Date _____ Lesson 124003 RO-OSC-0723

How to Stop Hydrops

With no standard for potential contributing factors, ODs can at least look out for these observed relationships.

Q I recently had a keratoconus patient develop corneal hydrops. What are the risk factors? I can't identify any except for his corneal thinning.

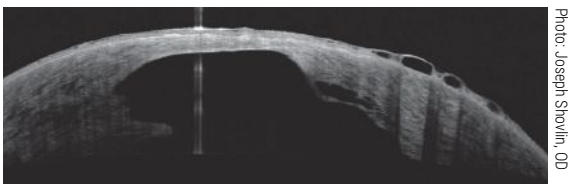

Photo: Joseph Shovlin, OD

Decreased corneal thickness is the strongest predictor risk for developing hydrops.

A Hydrops can be very difficult to predict, especially because there are no universally agreed upon risk factors for its development.[1] There are many different cases of hydrops with patients of differing demographics and even corneal thicknesses, explains Julie Song, OD, a Cornea and Contact Lens resident at SUNY's College of Optometry. At this point, decreased corneal thickness is considered a risk factor, but there is no agreed-upon minimum thickness that would indicate that a patient will develop corneal hydrops.

Risks

Literature points to several potential risk factors. One such factor is vernal keratoconjunctivitis, which can potentially cause patients who have keratoconus to rub their eyes more than usual and exacerbate their condition and corneal thinning, Dr. Song notes.[2-5] Other potential risk factors include asthma and atopic dermatitis.[2-5]

The associated conditions of dry eye disease and ocular allergies with comorbid asthma or atopic dermatitis can also exacerbate keratoconus if not properly treated, she continues. Such patients are more likely to develop hydrops from constant eye rubbing, which further increases the severity of keratoconus by thinning the cornea. Decreased best-corrected acuity associated with corneal thinning is another prevalent risk factor commonly seen in patients who develop corneal hydrops.[6]

Furthermore, patients with developmental disabilities are also potentially more likely to develop hydrops.[2-5] This risk factor is difficult to measure but can be correlated with the prevalence of keratoconus in this population.

For keratoconic patients diagnosed at an young age, their condition tends to be more aggressive and can exhibit an increased likelihood of developing hydrops.[3-5] In a study that evaluated the ethnic associations of developing acute corneal hydrops, it was reported that Pacific ancestry raised a patient's risk and New Zealand European ethnicity decreased it.[7] Ultimately, the literature suggests that the presence of advanced keratoconus is at the very least associated with the development of corneal hydrops, Dr. Song elucidates.

Treatment

Once hydrops has developed, the results after healing also vary patient to patient. Some patients can potentially gain improved visual acuity due to the flattening effect on the cornea, while in others acuity can decrease if central corneal scarring is severe. Hydrops heals at different rates for all patients (weeks to months), depending on the severity and patient's comorbidities. Some will develop hydrops in one eye, with a subset of these developing hydrops in the fellow eye later on.

Due to the unpredictable nature of corneal hydrops and the lack of concrete evidence as to what definite risk factors exist, the best we can do as eyecare practitioners is to treat corneal hydrops when it does occur and advise patients to undergo corneal crosslinking or other preventative treatment early after their initial keratoconus diagnosis, advises Dr. Song. For patients who have not yet had corneal crosslinking, a conversation about its necessity should occur soon after the detection of keratoconus. Pertaining to individuals who possess any form of ocular allergies and who are also prone to rubbing their eyes, adequate patient education and treatment for the allergies must happen at the onset of their diagnosis and not once the patient has already progressed to the stage of advanced keratoconus.

"In general, it is on eyecare practitioners to work toward detecting keratoconus in a timely fashion and to recommend appropriate preventative treatment(s) before patients develop severe corneal thinning. This will result in preventing corneal hydrops as well as loss of visual acuity," posits Dr. Song. ■

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About Dr. Shovlin

Dr. Shovlin, a senior optometrist at Northeastern Eye Institute in Scranton, PA, is a fellow and past president of the American Academy of Optometry. He consults for Kala, Aerie, AbbVie, Novartis, Hubble and Bausch + Lomb and is on the medical advisory panel for Lentechs.

COMING IN AUGUST

SECOND ANNUAL

Supplement to *Review of Optometry*

Practical Matters in Myopia Management

Proven strategies from experts to help you build confidence and improve your success rate.

As optometrists continue to embrace myopia interventions, they need concrete guidance on best practices for this new area of care. Questions of patient selection, treatment efficacy, parent "buy-in" and the practice's equipment needs can be a deterrent to enthusiasm among ODs. This supplement will guide optometrists through many of the practical challenges that might otherwise prevent them from pursuing myopia management.

Topics:

- **Myopia Management: What Does Success Look Like?**
- **All About Atropine: Do's, Don'ts and Debates**
- **Curtailing Myopia Progression with Corrective Lenses**
- **Anti-Myopia Efforts Patients and Parents Can Try Today**

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Cut Out For Cuts

Eyelid lacerations are caused by various sources of facial trauma and usually require prompt intervention.

BY JENA MEYER, OD
MIAMI

A 48-year-old Hispanic male was referred to our ophthalmic emergency department from an outside trauma center with notable pain, tearing and bleeding due to a cut on his left lower eyelid. The night prior, he was involved in a motor vehicle injury, during which he recalled hitting the front windshield upon impact.

Case

The outside trauma center performed a CT scan, which was remarkable for mild left periorbital soft tissue swelling. There was a suspected associated nondisplaced fracture of the left lamina papyracea without any intracranial or retrobulbar hematomas. CT angiography of the neck was unrevealing. He had an ocular history of keratoconus and contact lens use. His surgical history included a cholecystectomy.

His visual acuity with pinhole on presentation was 20/50 OD and 20/30 OS. The pupils were equally round and reactive in both eyes with no relative afferent pupillary defect. Extraocular motilities had full range of motion OU without evidence of proptosis or enophthalmos. Intraocular pressures measured 17mm Hg OD and 15mm Hg OS.

The external and anterior segment exam OD was unremarkable. On the left side, there was significant ecchymosis and erythema periorbitally with an inferior periorbital laceration. Upon closer observation, the left lower eyelid had a full-thickness tear medially to the puncta which involved the inferior canaliculus. The puncta was temporally displaced. A subconjunctival hemorrhage was present without conjunctival or corneal laceration. The dilated fundus exam was unremarkable.

External photo on initial presentation to our ophthalmic emergency room.

The patient was diagnosed with a canaliculus-involving marginal laceration of the left lower lid. He was treated that day in the minor operating room for emergent repair.

Discussion

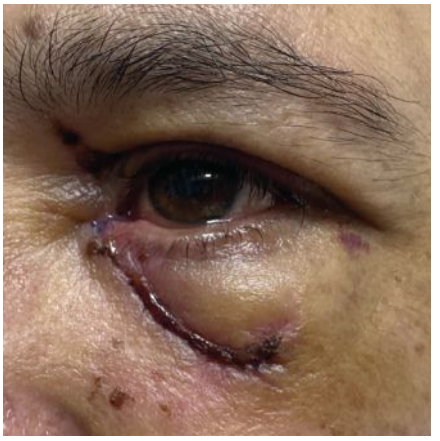
Partial- or full-thickness lid lacerations are precipitated by various causes of facial trauma and often concomitant with corneal or conjunctival lacerations, intraocular or intraorbital foreign bodies, open-globe injuries, orbital fractures, canthal tendon avulsion or disruption to the lacrimal system. The highest incidence of eyelid lacerations is found within the pediatric population and is frequently due to insults from bike handlebars, collisions with sharp objects, dog bites and falls.[1] The most common insults in the adult population include trauma from physical altercations, motor vehicle accidents and sports balls.[1]

A methodical approach must be followed in evaluating an eyelid laceration. First, it is paramount to obtain a full detailed history, analyzing for the involvement of any bug or dog bites and organic or metallic material. A CT scan in 1mm or 2mm cuts, or an MRI if a non-metallic injury took place, may be an imperative ancillary test for an open globe injury, retained foreign material, fracture or intracranial injury. In these instances, prompt attention to and treatment of these findings is necessary before any external repair, such as that for an eyelid laceration. Further, a tetanus booster shot or systemic antimicrobial coverage may be of urgent need.

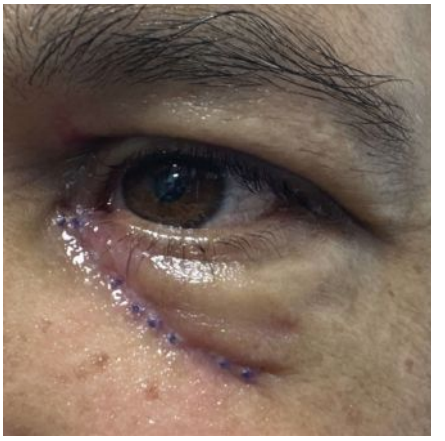
The next step is to perform wound irrigation with copious amounts of sterile saline. This may be followed by the removal of foreign particles and fibrin clots at the wound edges, reducing risk of infection or inflammation and promoting healing. Then, it is necessary to explore the wound's depth and width of penetration to classify the cut. Gloves and a sterile cotton tip applicator can be used to analyze and explore the eyelid involvement. Topical anesthetics can aid in desensitizing the area.

About Dr. Bozung

Dr. Bozung works in the Ophthalmic Emergency Department of the Bascom Palmer Eye Institute (BPEI) in Miami and serves as the clinical site director of the Optometric Student Externship Program as well as the associate director of the Optometric Residence Program at BPEI. She has no financial interests to disclose.



Five-day follow-up visit to evaluate the canalicular shunt sutures.



Eighteen days after the insult following removal of the sutures.

Eyelid lacerations can be classified into three groups: lacerations without eyelid margin involvement, with eyelid margin involvement or with nasolacrimal system involvement.[1,2] Any lid margin involvement, visible orbital fat or damage to the lacrimal system, as confirmed by dilation and irrigation or probing, should raise immediate concern for an oculoplastic referral. Sudden-onset ectropion or ptosis, tissue disruption, orbital paresthesia or eyelid notching are all possible signs of eyelid margin involvement. Laxity, displacement, rounding or pouting of the medial canthus or puncta can signify lacrimal system involvement.

Surgical repair includes direct laceration closure via sutures, canthal release, a transitional flap, grafts and a variety of lacrimal stents to repair canalicular lacerations and avulsions.[1-4] A referral within 24 hours is recommended to return drainage physiology to normal, reduce the risk of chronic epiphora and obtain good eyelid positioning postoperatively. However, one retrospective study of 334 patients divided into repair before and after 48 hours found no statistical difference in the treatment of canalicular lesions and suggested that surgery can be performed within six days of injury for confined cases.[3]

For patients with an eyelid laceration without margin involvement or visualization of orbital fat, understanding the eyelid anatomy and physiology is important for proper care. The eyelid skin is very thin and lacks subcutaneous fat, easily allowing for pockets of subepithelial edema.

The orbicularis oculi plays a key role in involuntary lid closure and may result in lagophthalmos with damage. This muscle is anterior to the orbital septum and orbital fat, which serve as important landmarks for the posteriorly placed levator aponeurosis. Therefore, as the injury deepens, orbital fat prolapse, septal perforation and ptosis may occur, all respective to their anatomical landmark.[2] Structural damage to the eyelid may result in eyelid notching, irregular contour, shortening of the fornixes or entropion. Sequelae of anatomical changes include damage to the meibomian glands, exposure keratopathy or trichiasis. Further complications of eyelid lacerations include missed injury and infection.

Superficial lacerations involving less than 25% of the lid may be managed by tissue adhesives, antibiotics and monitoring alone.[4] Broad-spectrum oral antibiotics can be prescribed, and topical antibiotics should be applied to the wound. A rabies prophylaxis shot may be used for patients who present with an animal bite. During follow-up, monitor for worsening edema or erythema, either of which would signify a possible infection.

Outcome

Our patient underwent same-day surgical repair and received a Mini-Monoka (FCI Ophthalmics) stent to aid in the repair of the left lower monocanalicular laceration. The distal edge of the stent was approximated near the lacrimal sac. Buried and superficial sutures were placed throughout the inferior periorbital dermal layers to approximate the epidermis and to appose the lid to the globe.

The patient was placed on amoxicillin-clavulanate 875mg-125mg by mouth twice daily for 10 days and bacitracin zinc/polymyxin B ointment twice daily.

At the patient's five-day follow-up visit, the eyelid and stent appeared properly positioned. However, copious swelling and a high tear lake did not allow for clear distinction of a patent puncta at that time. He was instructed that the oral antibiotics were to be continued for five more days.

Eighteen days after initial insult, with decreased edema and improved ecchymosis, a clear indication of a patent puncta and a well-approximated lid allowed for the removal of sutures. The bacitracin zinc/polymyxin B regimen was continued for five more days following sutural removal.

The lacrimal system and periorbital skin continue to be monitored for drainage, epiphora and hyperpigmented scarring. ■

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ABOUT THE AUTHOR

Dr. Meyer is an ocular disease resident at Bascom Palmer Eye Institute in Miami. She graduated from the University of Houston College of Optometry in 2022.

BY NATE LIGHTHIZER, OD

Vacation Plans

Intracameral injection of Durysta gives patients a break from the daily drudgery of topical medication use. Here's how to do it.

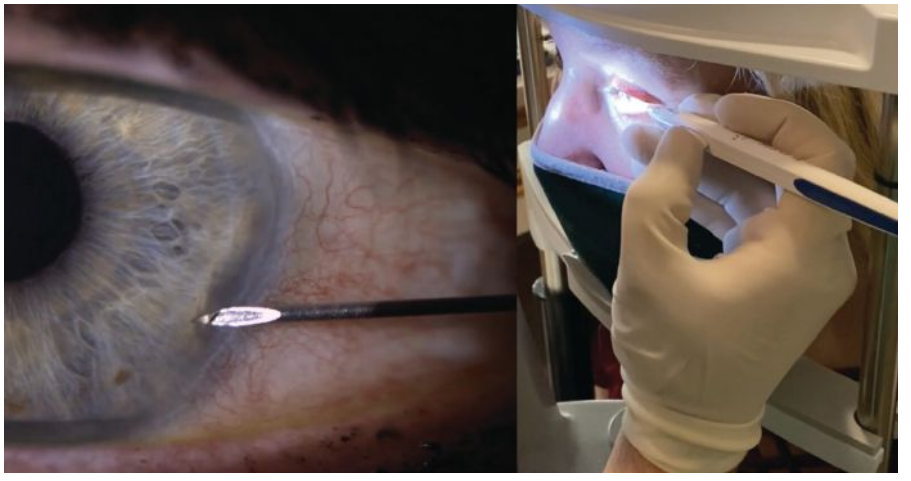

Fig. 1. Proper approach entry of the needle through the cornea. Notice the needle enters through the cornea at approximately the four to five o'clock position in this left eye. Proper hand placement showing stabilization of the hand and fingers on the patient's face (at right).

There has been a paradigm shift in the management of glaucoma over the last decade. With the introduction of the iStent (Glaukos) back in 2012, along with the renewed interest in first-line selective laser trabeculoplasty (SLT), and now drug delivery in the form of Durysta (intracameral bimatoprost, Allergan), clinicians are appreciating the importance of earlier intervention and the impact of compliance on long-term glaucoma control. In our practice, compliance with topical glaucoma medications has been the most significant barrier to preventing glaucoma progression.

The Burden

A 2015 study of over 1,200 newly diagnosed glaucoma patients who were started on topical drug monotherapy found only 20% had good treatment adherence at one year.[1] Studies have found up to 60% of glaucoma patients had a concomitant dry eye, which has also been related to the number of topical glaucoma medications.[2-4] Due to the symptoms of dry eye and ocular surface disease (OSD) such as tearing, burning, pain and fluctuating vision, patients often blame their glaucoma drops and then reduce or even stop using them. Addressing compliance is crucial since poor compliance can lead to fluctuating intraocular pressure (IOP).

With the importance of reducing the topical drop burden for patients known, where do anterior chamber implants, in the form of sustained-release glaucoma medications, fit into the glaucoma treatment paradigm? Since June 2020, eyecare providers have had access to the Durysta intracameral implant, which has allowed us to decrease the drop burden in a variety of patients in multiple situations. Durysta is a 1mm preservative-free implant infused with 10µg of bimatoprost, which actively releases medication 24 hours per day for approximately four months. It is a preloaded device with an ergonomic injector system.

This procedure is within the scope of practice of optometrists in a few states. Regardless of whether you are in a state where ODs can perform the actual injection or you are comanaging Durysta with your local ophthalmologist, it is imperative that optometrists be familiar with the ins and outs of this procedure that can ease the drop burden for your patients.

The Data

The ARTEMIS 1 and ARTEMIS 2 Phase III clinical trials were two multicenter, randomized, parallel-group, controlled studies comparing the 10µg

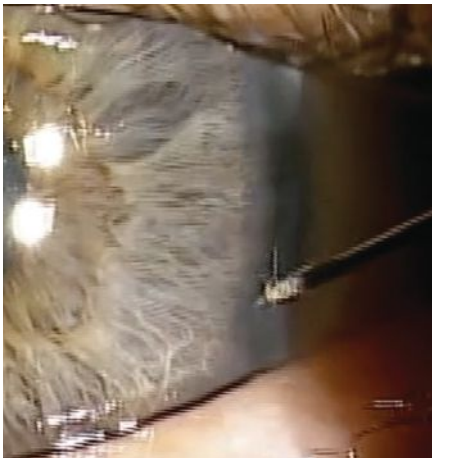

Fig. 2. A secondary device, a cotton-tipped applicator, is being used to apply a little countertraction opposite the needle as the procedure is about to be performed.

About Dr. Lighthizer

Dr. Lighthizer is the associate dean, director of continuing education and chief of specialty care clinics at the NSU Oklahoma College of Optometry. He is a founding member and immediate past president of the Intrepid Eye Society. Dr. Lighthizer's full disclosure list can be found in the online version of this article at www.reviewofoptometry.com.

bimatoprost implant to twice-daily timolol 0.5% topical drops.

Parallel groups of patients diagnosed with OAG or ocular hypertension (OHT; with a baseline IOP of 22mm Hg to 32mm Hg) were followed for a period of 20 months, including an eight-month extended follow-up. Durysta lowered mean IOP by 30% to 33% from baseline over the 12-week primary efficacy period. This works out to be about 5mm Hg to 8mm Hg of reduction from the mean baseline IOP of 24.5mm Hg.[5] The bimatoprost implant met predefined criteria for non-inferiority compared with timolol.

Patient Selection and Pre-op Considerations

The indication for Durysta is very broad. It is FDA-cleared as a single implant for patients with OAG or OHT. This includes primary open-angle glaucoma (POAG) and even secondary open-angle glaucomas such as pigmentary, pseudoexfoliation, angle recession or steroid-induced glaucoma. It can be considered in these selected patients regardless of stage of disease, be it mild, moderate or severe.

Gonioscopy is critical in the evaluation for consideration of Durysta. An open angle needs to be confirmed to ensure there is enough room in the space for the bimatoprost implant to sit in the inferior angle without touching or rubbing up on the cornea.

Talking to the patient regarding their struggles with eyedrops—whether it be side effects, cost, convenience, forgetting to administer or physical limitations to instillation—is important to gauge their motivation for alternative options such as Durysta.

It is critical that patients understand the nature of the procedure, how it is done, and the benefits and limitations (such as the effectiveness will not last forever, and currently it is FDA approved for a single implant only). So, how do we discuss this anterior chamber implant with our patients? Once you have identified a compliance-related issue, use the idea of "compliance" as the rationale to discuss the implant. You are offering a solution to their problem.

A consent form that details the nature of the procedure, single administration of the procedure, temporary nature of the effect of the IOP lowering (typically four months to two years), risks and potential complications and alternative treatments, should be thoroughly reviewed with the patient and the consent form signed.

Preoperative drops on the day of the procedure include:

- One to two drops of a topical ophthalmic anesthetic (proparacaine) in both eyes to minimize the blink reflex.
- One to two drops of a topical ophthalmic antibiotic in the procedure eye.
- One to two drops of 5% ophthalmic povidone-iodine (Betadine) to ensure proper asepsis.

The Procedure

Durysta implantation can be performed in the office at the slit lamp or in a minor procedure room with the patient in the supine position. It can also be done at the ambulatory surgical center or hospital operating suite.

Regardless of where the procedure is performed, it is important to follow three important principles:

1. Use good magnification, whether loops, a slit lamp or a microscope.
2. Provide good patient head stabilization, *i.e.*, having a technician hold the patient's head still if performed at the slit lamp.
3. Follow good aseptic sterile technique, using 5% povidone iodine prep, sterile gloves and the option of periprocedural topical antibiotics.

Below are basic steps to guide the practitioner on the slit lamp implantation technique:

- Anesthetize the nonprocedure eye as well. This will prevent the patient from blinking either eye.
- Have the patient and the slit lamp in proper position before removing the device from the packaging.

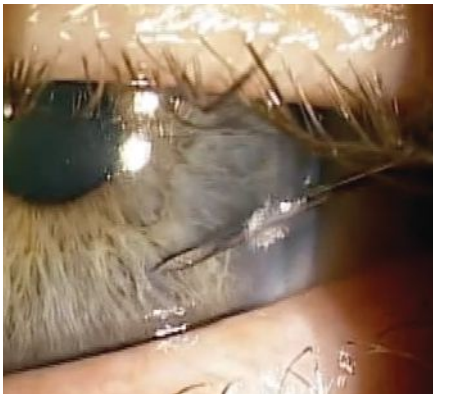

Fig. 3. The needle is now in the anterior chamber at the proper position for insertion of the pellet, about two bevel lengths into the anterior chamber. Notice how the needle is properly placed in front of the iris.

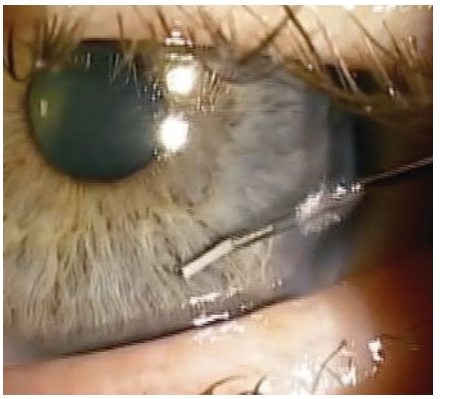

Fig. 4. The actuator button is being depressed, and the implant is starting to be released from the device.

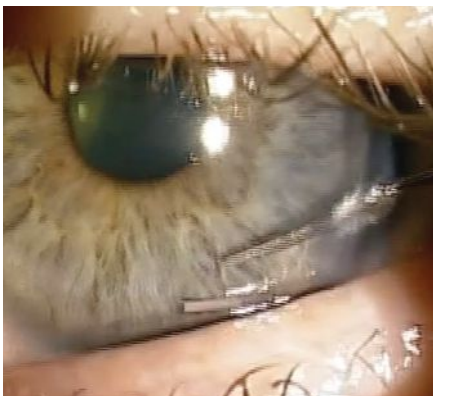

Fig. 5. The actuator button has been fully depressed, and the implant has been released and immediately falls towards the inferior angle.

- Once you have removed the device from the packaging, remove the safety tabs of the device.

• Rest your hand on the cheek of the patient to stabilize the device. Using an elbow rest is also encouraged (*Figure 1*).

• Have the patient focus on one part of the slit lamp or its fixation target. This will provide natural countertraction. Additionally, you may want to use a second instrument (cotton tipped applicator or 0.12mm forceps) to stabilize the eye. You can apply a little countertraction using a soft cotton tip swab positioned 180° away from where you enter with the device needle. The second instrument can help to generate enough counterforce for a straightforward entry into the anterior chamber (AC) (*Figure 2*).

Fig. 6. Gonio view of the inferior angle showing perfect position of the Durysta pellet a few minutes after the procedure was completed.

• The insertion is performed by entering the AC via the loader's 28-gauge needle through the clear cornea, engaging just anterior to the limbal vessels.

• The goal is to enter the AC parallel to the iris and maintain the needle over the iris for the entire procedure.

• One should enter at the clock hour that is most convenient for your hand position and the anatomy of the orbit and eye. I tend to enter around seven or eight o'clock for the right eye and four or five o'clock for the left eye (*Figure 3*).

• It is recommended when inserting Durysta in the right eye to use your left hand to hold the device, which allows you to enter temporally near the seven or eight o'clock position, whereas for the left eye you will want to use your right hand to enter near the four to five o'clock position. Entering at these clock hour positions will allow you to enter directly perpendicular to the cornea and maximize the area over the iris.

• After entering and ensuring you are approximately two needle bevel lengths into the AC, press the posterior aspect of the actuator button, which is located on the device, to release the implant. Once the implant is released (*Figures 4 and 5*), come straight back out of the eye. It is important to remove the needle straight back out of the track to avoid tangential forces on the wound, which could cause aqueous to escape and the implant to migrate back to the wound. Also, make sure your thumb is already on the actuator button so you can press it without having to take your eyes away from the slit lamp oculars. One pearl: press the oval button with conviction, for if you are too slow, the implant may get stuck to the needle.

• Check the wound using a surgical spear sponge or cotton-tipped swab to check for a wound leak. Place a drop of antibiotic in the eye after the procedure in-office. An antibiotic prescription for the patient to take home is not necessary.

• With gravity, the implant sinks to the inferior angle, where it resides (*Figure 6*) and slowly releases the bimatoprost over the course of the next four months.

• The majority of clinicians implant Durysta in one eye, then have the patient come back one to two weeks later for implantation of Durysta in the fellow eye.

Key Post-op Considerations

• Topical ophthalmic antibiotic eyedrop instilled in office immediately after the procedure.

• Patient education to teach them to:
–Keep head elevated for the first day.
– Not rub the eyes for the first 48 to 72 hours.

• Return to clinic in four to six weeks for an IOP check and gonioscopy to check positioning of the implant.

Proper management of glaucoma with IOP readings within our target ranges is key to providing the best possible long-term outcomes for our patients. Noncompliance with eye drops is one of most significant barriers patients and eye care practitioners face in glaucoma.

Administration of intracameral bimatoprost into the anterior chamber has provided relief and eased the burden for many patients. The idea of interventional glaucoma, where noncompliance is less of an issue and IOP is more controlled with procedures such as SLT, MIGS or Durysta implants, is only just gaining steam and will likely continue to evolve as a bigger part of our glaucoma treatment armamentarium.

All eyecare practitioners, whether you plan to do the procedure in the future or refer to another provider, are encouraged to consider the benefits of sustained drug delivery for your patient. Everyone likes a holiday, and glaucoma patients have been thrilled to have an eyedrop vacation! ■

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- Contact Lens Prescribers
- Years in Practice (1-15 and 15+)
- Among Key Opinion Leaders

***To our readers:* Thank you for your loyalty, time and trust. We'll keep working hard to earn your support.**

BY RAMI ABOUMOURAD, OD

RETINA QUIZ

Don't Get Abscessed

Can you identify this rare but deadly disease?

A 40-year-old Hispanic male presented with acute vision loss, redness, pain and photophobia in the left eye. Review of systems revealed that he had been febrile with myalgias and malaise for five days. Prior to presentation, the patient was seen via telemedicine by his general physician, who empirically diagnosed him with influenza and prescribed oseltamivir and acetaminophen, which were not improving his symptoms. He was in otherwise good systemic health with no history of systemic malignancy, human immunodeficiency virus (HIV) infection, intravenous (IV) drug use, prior ocular surgeries or trauma.

Visual acuity (VA) was 20/25 OD and 20/70 OS. Extraocular motilities were full, confrontation visual fields were full and there was no relative afferent pupillary defect. IOP was 12mm Hg OD and 9mm Hg OS by applanation. Anterior and posterior segments were normal OD. Anterior segment examination revealed 1+ diffuse conjunctival hyperemia and 2+ anterior chamber cell and flare OS. Posterior segment imaging is included for review.

Take the Retina Quiz

1. Which of the following is true of the fundus photo (Figure 1)?

a. There is a solitary mass in the temporal macula.
b. There is extensive retinal vasculitis.
c. There are multifocal Roth spots and intralesional hemorrhages.
d. All of the above.

2. Which is true of the OCT in Figure 2?

a. There are sub-ILM and intraretinal cells.
b. There are vitreous cells.
c. There is a subretinal mass.
d. All of the above.

3. What is the most likely diagnosis?

a. Amelanotic choroidal melanoma.
b. Eales' disease.
c. Endophthalmitis.
d. Retinoblastoma.

4. Appropriate management includes all of the following except:

a. Hospital admission for blood cultures.
b. Hospital admission for extensive whole-body imaging.
c. Topical antibiotics with one week follow-up in clinic.
d. Vitreous aspiration and intravitreal antibiotics.

5. Which of the following regarding prognosis is true?

a. Visual outcome better than 20/400 is common.
b. Visual outcome of 20/20 is common.
c. Visual outcome of counting fingers or worse is common.
d. This ophthalmic condition carries a 50% risk of mortality.

For answers to the quiz, see page 114.

Diagnosis

Fundus examination OS revealed 1+ vitritis with a large, solitary, dome-shaped, yellow subretinal abscess in the temporal macula with retinal vasculitis, preretinal hypopyon along the inferotemporal arcade, Roth spots and intralesional hemorrhage (*Figure 1*). OCT depicted vitreous cells, sub-ILM cells, intraretinal cells and partially captured the large subretinal hyperreflective mass in the temporal macula (*Figure 2*).

Further questioning revealed recent onset chest pain with deep inspiration and abdominal tenderness. The constellation of findings

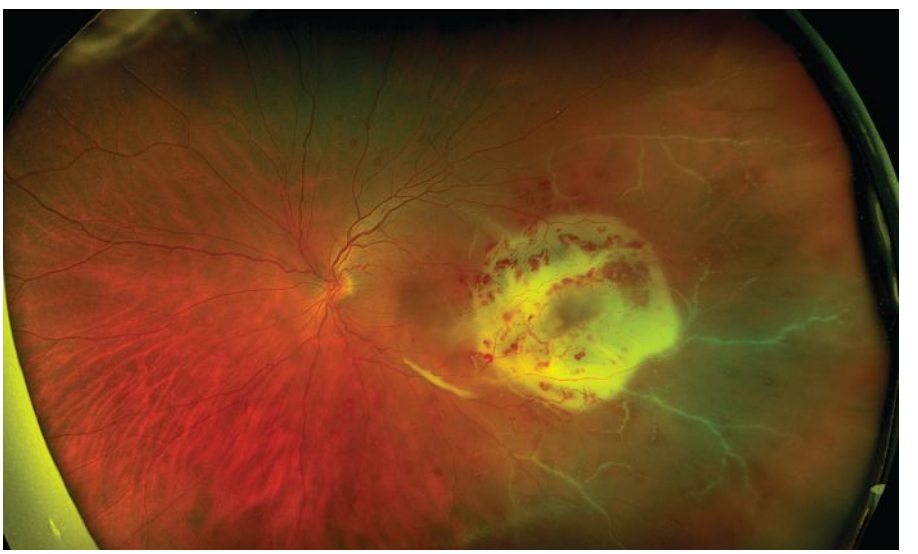

Fig. 1. Optos widefield fundus photography of the left eye at presentation.

About Dr. Aboumourad **Dr. Aboumourad** currently practices at Bascom Palmer Eye Institute in Miami. He has no financial disclosures.

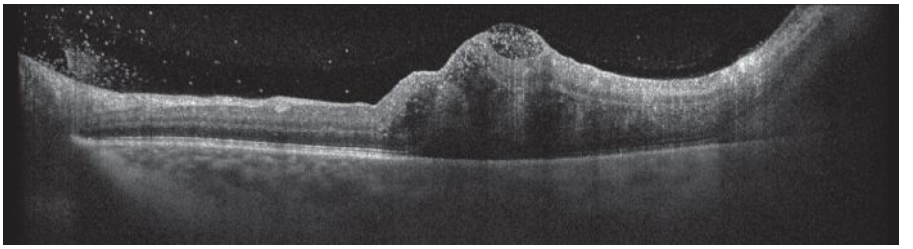

Fig. 2. Heidelberg Spectralis OCT of the left macula at presentation.

was highly concerning for endogenous endophthalmitis in the absence of exogenous risk factors. Vitreous aspiration was performed, and the patient was administered intravitreal vancomycin (1mg/0.1mL) and ceftazidime (2.25mg/0.1mL) before being transferred to the general hospital for systemic workup to search for an occult infectious source.

The patient underwent extensive full body imaging and blood cultures and a 7.3 x 4.5 x 4.5cm lesion was identified within the right lobe of his liver, consistent with a pyogenic liver abscess (PLA). Interventional radiology proceeded with image-guided percutaneous drainage of the PLA. The PLA and blood cultures both grew *Klebsiella pneumoniae* (K. pneumoniae).

Discussion

Endophthalmitis is a rare but devastating ocular infection that can involve the entire globe, and its source can be exogenous or endogenous.[1] Exogenous endophthalmitis is far more common (more than 90% of endophthalmitis cases), and typical risk factors include recent ocular surgery, open-globe injury and recent intravitreal injection.[1,2] Endogenous endophthalmitis occurs via hematogenous dissemination of a systemic infectious source.[1-3] Typical risk factors include diabetes mellitus, immunosuppression/compromise (*e.g.*, chemotherapy or HIV infection), indwelling catheters and IV drug use.[1,4,5]

Klebsiella species are gram-negative, encapsulated anaerobic bacteria commonly found in nasopharyngeal and gastrointestinal flora.[2,6] *K. pneumonia* is capable of producing pneumonia, urinary tract infections, PLA, meningitis and endophthalmitis (known as KPEE).[7] The presence of *K. pneumoniae* PLA portends a poorer visual prognosis, as well as up to 10% risk of mortality.[5,8]

The infectious source for KPEE is most frequently found in the hepatobiliary tract, with *K. pneumoniae* PLA present in greater than 75% of patients, followed by pneumonia and urinary tract infections.[9] Furthermore, nearly one in 12 patients with *K. pneumoniae* PLA will develop KPEE, and the risk increases fourfold for *K. pneumoniae* PLA measuring greater than 5cm.[10] While KPEE is most prevalent in Asian countries and in patients of Asian descent, there are increasing reports of cases in the United States and in non-Asian patients.[11]

PASSING THE BATON

My very first Retina Quiz column was published 24 years ago in the May 1999 issue of *Review of Optometry*—wow! What an incredible journey and privilege it has been being able to write the monthly Retina Quiz for so long. I am so grateful to Jobson and all those who I had the opportunity to work with at RO over the years, including Rick Bay, Jim Henne, Jack Persico and Mike Hoster, who was my editor when he first started with RO. I am so thankful to Mike and all the other editors who made the column far better than I ever could have. It really was an opportunity of a lifetime!

I have many great memories writing this column. In the early days, I decided to take some creative liberties with some of the case histories, like the semi-retired British secret service agent who started to notice blurry vision on a high-speed chase down the busy streets of Paris or the elderly lady who was training to climb Mount Everest with a macular hole in one eye and had the incredible misfortune of developing a macular hole in her fellow eye. There was even a professional mourner (somebody who gets paid to cry at funerals) and a Miami Dolphins quarterback, who started to have blurry vision in training camp from a retina problem. It's funny how nobody seemed to notice until one day I got a call from the Miami Dolphins wondering if one of their quarterbacks had an eye problem they didn't know about; even *they* read the column! After some groveling, I explained that it really wasn't a Miami Dolphins QB but instead a retired schoolteacher. That, by the way, put an end to my creative liberties with the cases.

Before I wrote the column, it was Jerry Sherman from SUNY, who really set the standard for excellence as the original author for Retina Quiz. In fact, my earliest memory when I started in optometry in the late '80s was reading Jerry's column. Never did I imagine that I would get the chance to take it over, let alone be able to write the column for over 24 years. I hope that between the two of us, we created a lasting legacy.

Now, it's time for somebody else to take over the column and inspire the next generation of optometrists.

I am pleased to introduce to you Rami Aboumourad, who I have relied upon more and more over the past few years to write some of the Retina Quiz columns. Rami was a resident with us several years ago and joined the staff at the Department of Ophthalmology at Baylor College of Medicine after his residency. Even at Baylor, Rami would reach out to me with an interesting retina case that he thought would be great for the Retina Quiz. When Rami came back to Bascom Palmer a few years ago, he became even more involved, and I realized very quickly he would be the perfect choice to continue the legacy. Rami is a great teacher and educator, and has already written some incredible columns. The Retina Quiz is certainly in great hands!

To the readers who read my column every month: thank you all for your support and for making the Retina Quiz one of the most-read columns in *Review of Optometry*!

—Mark Dunbar

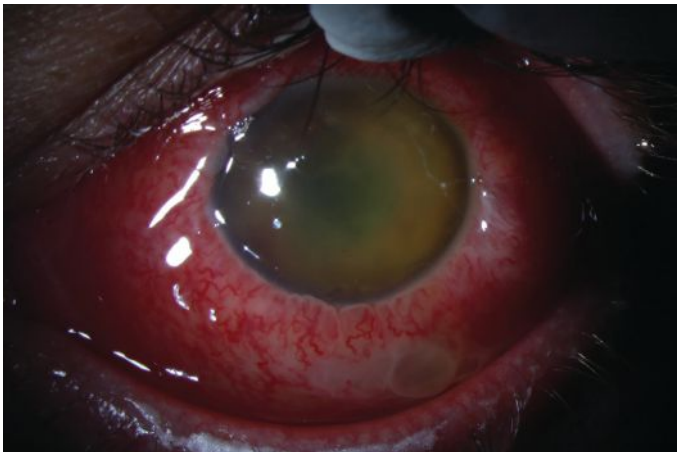

Fig. 3. Slit lamp photograph of the left eye at follow-up after 13 days.

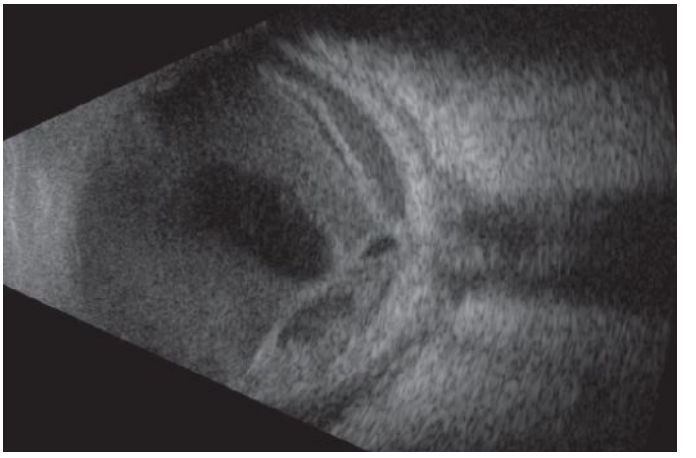

Fig. 4. Vertical axial B-scan over the posterior pole at follow-up after 13 days.

Presently, capsular phenotyping of *K. pneumonia* is available but not routinely performed in the US.[11,12] Capsular serotypes K1 and K2 are most virulent due to increased resistance/decreased susceptibility to neutrophil phagocytosis; as such, they are deemed hypervirulent strains, and the association with *K. pneumonia* hypervirulent K1 and K2 serotype bacteremia and KPEE is well-established.[5,11,12]

The most frequent symptoms seen in patients of a recent study with subretinal abscess secondary to endogenous endophthalmitis were vision loss (70%), pain (65%) and redness (35%).[3] Anterior chamber reaction, conjunctival hyperemia and hypopyon were seen in less than 75% of patients presenting with subretinal abscess, emphasizing the need for dilated fundus examination of every patient presenting with intraocular anterior segment inflammation.[3]

There is a broad differential diagnosis that includes other infectious (tuberculosis, viral, toxoplasmosis, syphilis) and inflammatory (sarcoidosis) entities, as well as neoplastic processes such as intraocular lymphoma, leukemic infiltration, retinoblastoma and primary and metastatic tumors to the uvea or vitreous.[1] When the clinical presentation and/or review of systems is suggestive of endogenous endophthalmitis or septicemia in the absence of known systemic illness, emergent systemic workup and infectious disease consultation is necessary to identify the source.[1] Some reports suggest final VA in patients with KPEE is correlated directly with initial VA; however, the vast majority of patients with KPEE develop final VA of counting fingers or worse.[2,10,13]

Treatment

Our patient received intravitreal vancomycin and ceftazidime prior to and during hospital admission, as well as IV antibiotics. Despite prompt recognition of the disease and detection of the systemic source, his vision rapidly declined to light perception within days. Systemically, the bacteremia was treated to resolution with systemic antimicrobial therapy. Upon discharge 13 days later, the patient returned with a significant fibrinous anterior chamber reaction and dense membranous vitritis with total retinal detachment (*Figures 3 & 4*). Observation was recommended, and comfort was achieved with topical difluprednate and atropine.

Though endophthalmitis is rare, optometrists must maintain a high index of suspicion for both exogenous and endogenous forms, as patients may initially present with acute or subacute vision loss. Clinical presentation can be variable, and the implication of delayed recognition carries risk of severe vision loss and mortality.

Finally, optometrists taking call at general hospitals for inpatient consultations must recognize the important association between *K. pneumoniae* septicemia, PLA and KPEE, and careful dilated fundus examination must be performed on all patients to rule out intraocular involvement. ■

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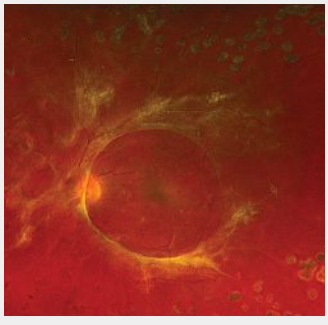

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REVIEW Education GROUP

BY PAUL M. KARPECKI, OD
CHIEF CLINICAL EDITOR

First of Its Kind

Miebo now gives us a medication option that targets MGD and evaporative DED.

The anticipation has been brewing and it's finally here after years of clinical trials—Miebo (perfluorohexyloctane ophthalmic solution, Novaliq, Bausch + Lomb). Formerly known as NOV03, the drop is indicated to treat the signs and symptoms of dry eye disease (DED). More notably, this therapeutic is the first on the market to directly target tear evaporation, which is a common culprit of DED.

Miebo is expected to be available in the second half of this year and should make a significant impact on the numerous patients with DED, especially those with evaporative eye disease. Let's get to know this potentially game-changing therapeutic.

Evaporative Dry Eye

This is the most common subtype of DED, with 86% of patients having either the evaporative form alone or a mixed presentation of both evaporative and aqueous-deficient dry eye. Evaporative dry eye, caused by meibomian gland dysfunction (MGD), tends to have symptoms that worsen later in the day or with prolonged reading or digital device use.[1,2] To date, we haven't had a therapeutic agent that has targeted MGD or evaporative dry eye.

Miebo's Mechanisms

This drug is a water-free, single-component, preservative-free topical drop. Perfluorohexyloctane (PFHO) ophthalmic solution is a semi-fluorinated alkane. What exactly is that? Alkanes have been used in the eye previously in complex retinal detachment surgery primarily for inferior retinal detachments. The molecule has a lipophobic fluorinated component that quickly evaporates in the air, plus an alkane base that easily mixes with the lipid layer to ground the molecule. This combination creates a monolayer within the lipid-to-air interface.[3] It also allows for extremely fast spreading of the drop across the ocular surface. The agent was found to remain in the tear film for six hours and the meibomian glands for over 24 hours.

The research in question is the first FDA study where all patients had MGD and the first approval of a drug requiring only two pivotal trials to reach statistical significance in signs and symptoms.

Photo: Bausch + Lomb

Miebo may particularly benefit those with dry eye related to MGD, as it targets evaporative DED.

Unique Properties

The extremely low surface tension of this molecule allows Miebo to have a small drop size of about 11µL. Compared with typical eye drops at 30µL to 50 µL, it is barely noticeable on the eye.[4,5] Unlike other preservative-free, multidose bottles, it comes in a normal, easy-to-squeeze 5mL bottle. Each bottle contains 3mL of PFHO or about 280 drops. It has a refractive index similar to that of water, helping minimize vision blur after instillation.[6]

In the Phase III FDA clinical trials, the most common adverse event experienced was blurred vision, but only at a rate of 2.1%. Burning and stinging—common side effects of many dry eye medications—were extremely low at 0.5% or three out of 614 patients, and most telling regarding this drop's comfort was the discontinuation rate secondary to an adverse event, at only 0.2% or one patient out of 614, due to mild irritation. The safety/comfort profile of this product is unheard of in the dry eye space.

Regarding the PFHO mechanism of action, data suggests that PFHO penetrates the meibum, potentially acting as a surrogate of the lipid layer.[7] In 48 dry eye patients, PFHO significantly increased tear film thickness and lipid layer thickness over four weeks compared to the control group.[8]

PFHO helps inhibit evaporation, based on a study comparing its use with hypotonic saline.[9] Evaporation rates were measured where 100µL PFHO alone inhibited saline evaporation by 88%, and adding PFHO to meibum lipids significantly inhibited evaporation even greater.

About Dr. Karpecki

Dr. Karpecki is medical director for Keplr Vision and the Dry Eye Institutes of Kentucky and Indiana. He is the Chief Clinical Editor for *Review of Optometry* and chair of the New Technologies & Treatments conferences. A fixture in optometric clinical education, he consults for a wide array of ophthalmic clients, including ones discussed in this article. Dr. Karpecki's full disclosure list can be found in the online version of this article at www.reviewofoptometry.com.

Corneal Staining and Symptoms

Although this medication has been shown to inhibit evaporation significantly, it also quickly improves signs of corneal staining. In fact, the primary endpoints for the Phase III clinical trials were changes in complete corneal staining as well as improvements in the Visual Analog Scale for eye dryness.

Miebo was able to achieve a clinical statistical improvement in total corneal staining scores and symptoms of eye dryness as soon as day 15 and also the primary endpoint at day 57 vs. the control group. The repeatability of the data is most impressive, as these were similar results to the Phase II trials. The approved dosing is QID based on the testing in Phase III clinical trials.

Fitting in to the Therapeutic Landscape

Miebo targets the most critical component of dry eye—the lipid layer—by preventing evaporation. Target patients are those with MGD, given that the clinical trial involved 100% of patients with this condition, but even patients with aqueous-deficient dry eye would benefit from a decrease in evaporation and improvement in ocular surface staining.

Miebo appears to work best when it can stabilize existing meibum as opposed to patients with severely thin lipid layers or significant meibomian gland atrophy such as those with severe ocular rosacea or previously taking Accutane (isotretinoin). It can also affect contact lenses, so it's recommended that Miebo be placed in the eye 30 minutes prior to insertion and not used on a contact lens. It should be compatible with anti-inflammatory drops, if inflammation is present.

Having a new therapeutic that targets evaporation is a first in many aspects, including the speed to FDA approval, consistency of data, quick response and especially the low side effect profile. Miebo is a welcome addition to our dry eye treatment options. ■

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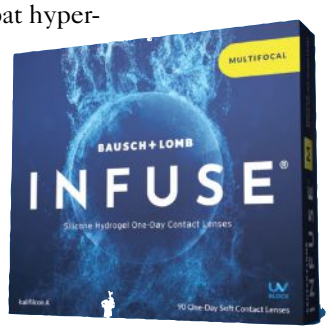
▶ CONTACT LENSES AND LENS CARE

B+L Launches Infuse Multifocal Contact Lenses

Last month, Bausch + Lomb introduced a multifocal version of its popular Infuse lens for presbyopes interested in a daily disposable. The silicone hydrogel lenses are made with a new low-modulus, high-moisture material—kalifilcon A—which the company says can maintain 96% of its moisture for 16 hours.

The contact lenses feature what B+L calls "probalance technology," which means they contain ingredients inspired by the TFOS DEWS II report to help maintain ocular surface homeostasis. This includes erythritol and glycerin (osmoprotectants to help combat hyperosmotic stress), potassium (an electrolyte to promote ocular homeostasis) and poloxamine 1107 and poloxamer 181 (moisturizers that help the lens retain hydration and maintain tear proteins).



Infuse multifocal lenses are also made with the company's three-zone progressive design, which B+L says helps to promote seamless transitions across near, intermediate and distance vision.

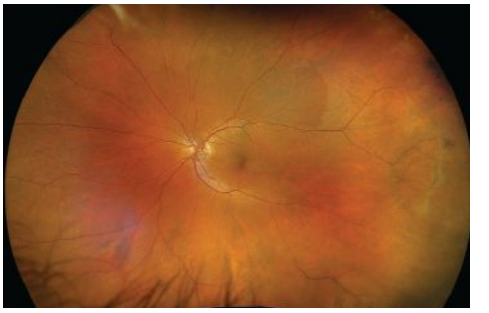
Hydration Boost Rewetting Drops Now Available

For contact lens wearers whose lenses don't stay moist throughout the day, rehydrating drops are a potential remedy. Bausch + Lomb recently added a new product to this market called Biotrue Hydration Boost Contact Lens Rehydrating Drops, which received FDA clearance in December and is now available for purchase. The company says that the drops are indicated to lubricate and rewet soft contact lenses, including daily disposables and rigid GPs, and provide wearers with up to eight hours of moisture.

The rehydrating drops have no preservatives and contain only natural ingredients informed by the TFOS DEWS II report, B+L says. These include glycerin (active ingredient), hyaluronan (a moisturizer naturally found in the eye), an electrolyte and an antioxidant to help protect hyaluronan against free radicals. The company adds that the solution's pH matches that of healthy tears to optimize lubrication and comfort.

▶ IMAGING EQUIPMENT

New AREDS 2 Vitamin with CoQ10 for Heart Health



If you use the California ultra-widefield (UWF) imaging device from Optos—or are in the market for one—note that the company has announced that it is expanding the modalities available to include red/green/blue (RGB) capabilities, a first for UWF. Previously, the device only captured color images in red/green wavelengths. California can also perform red-free, choroidal, autofluorescence, fluorescein angiography and indocyanine green angiography imaging.

A company press release cites retina specialists who point out that the RGB mode will improve discernment of holes in peripheral lattice degeneration and retinoschisis, yield more detail of drusen in intermediate AMD patients, allow better visualization of a macular epiretinal membrane and refine the grading of diabetic retinopathy.

▶ DIETARY SUPPLEMENTS

New AREDS 2 Vitamin with CoQ10 for Heart Health

Considering that heart disease is a prevalent concern in AMD patients, Bausch + Lomb recently launched a supplement that combines the proven AREDS 2 formula with CoQ10 to offer the added benefit of heart health support. B+L calls the two-in-one vitamin "PreserVision AREDS 2 Formula Soft Gels Plus CoQ10." The company explained in its press release that CoQ10 is an antioxidant naturally produced by the body that helps support healthy cell function. Its levels also decrease with age and are lower in patients with conditions like heart disease or in those taking statins.

The product is the first on the market to combine the AREDS 2 formula with CoQ10, the company says, and serves as an alternative to traditional AREDS 2 vitamins for AMD patients with risk factors of heart disease or those concerned about preserving their heart health. ■

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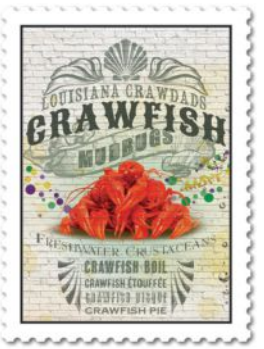

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BY ANDREW S. GURWOOD, OD

DIAGNOSTIC QUIZ

Battle of the Bulge

Is the puffiness shown here a sign of something more concerning? If so, how would you proceed?

A 74-year-old man presented to the office with a chief complaint of a red and swollen eye of six days' duration. He was pseudophakic OU. He reported some pain upon moving his eyes and mild tenderness upon palpation. He was not symptomatic for vision changes or diplopia. He denied any trauma. He was properly medicated for hypertension and diabetes and denied allergies of any kind.

Clinical Findings

His best-corrected entering visual acuities were 20/25 OD and 20/25 OS. His external examination is demonstrated in the photograph below. There was no evidence of afferent pupillary defect. His confrontation visual fields were full. His anterior segment examination revealed a normal OD and injected slightly proptotic OS. Goldmann applanation tonometry measured 17mm Hg OU.

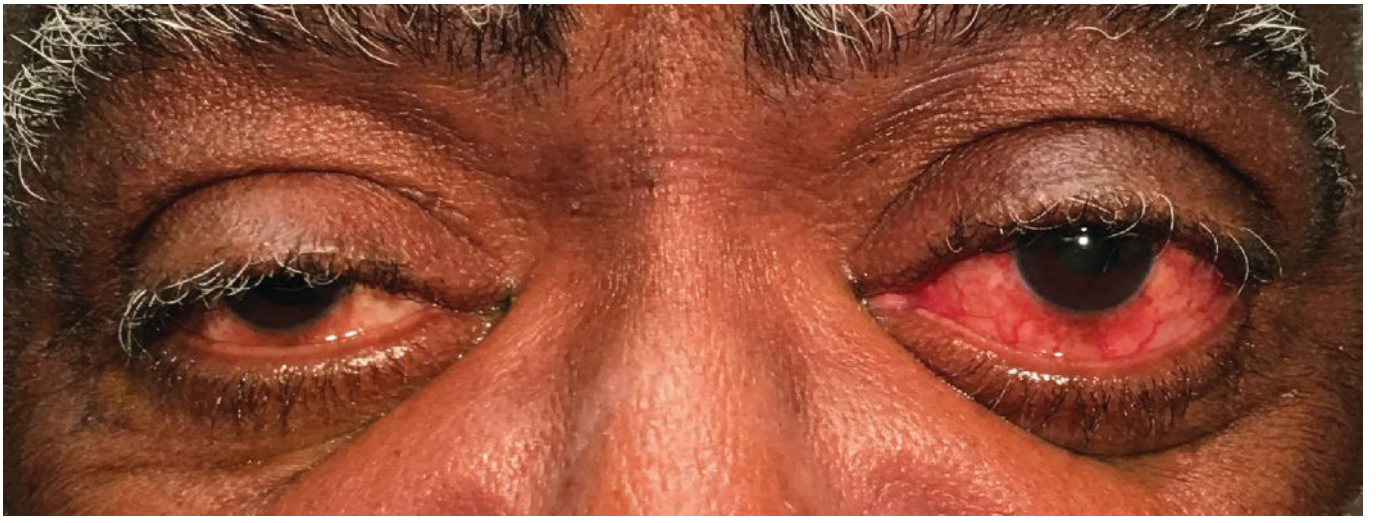
Dilated fundus exam demonstrated no posterior pole or no peripheral pathologies with cup/disc ratios of 0.3/0.3, with sharp and pink margins.

Other Testing

Additional studies included Hertel exophthalmometry, manual retropulsion of the left globe, binocular exam of the fundi to look for disc edema and choroidal folds, as well as neuroimaging, which included fat suppression MRI, venography and arteriography.

Your Diagnosis

What condition is this? What's the likely prognosis? To find out, read the online version of this article at www.reviewofoptometry.com. ■



Our patient presented to the clinic with the presentation seen here. He reported no visual changes but some pain upon movement.

About Dr. Gurwood Dr. Gurwood is a professor of clinical sciences at The Eye Institute of the Pennsylvania College of Optometry at Salus University. He is a co-chief of Primary Care Suite 3. He is attending medical staff in the department of ophthalmology at Albert Einstein Medical Center, Philadelphia. He has no financial interests to disclose.

Retina Quiz Answers (from page 104)—Q1: d, Q2: d, Q3: c, Q4: c, Q5: c

NEXT MONTH IN THE MAG

In August, we present our annual issue devoted to contact lenses. Articles will include:

- How to Improve Your First-Fit Success Rates
- Understanding the Influence of soft Lens Water Content
- Know These Custom Soft Contact Lens Uses for Irregular Corneas

Also in this issue:

- 2023 Office Design Contest: The 'Wow' Starts Now
- What to Think When the Patient Says They Have Ocular Migraine

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[1]Compared to Biotrue Multi-Purpose Solution.
[2]Based on a laboratory study.
[3]Antioxidant protects hyaluronan against free radicals.
[4]For 12 hours compared to Biotrue Multi-Purpose Solution, based on a laboratory study.
[5]Data on file. Bausch & Lomb Incorporated. Rochester, NY.
[6]Standardized Testing (ISO 14729) against *S. aureus, P. aeruginosa, S. marcescens, C. albicans, F. solani.*

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