Be leery of large optic cups when screening for pediatric glaucoma

By Benjamin P. Casella, OD, FAAO

Kids with big optic cups make me leery. They always have. I will say that, like most ODs, I have seen far more cases of pediatric physiologic cupping than I have of pediatric glaucoma.

For this reason, I feel better when I see a large optic cup in the presence of a large optic disc. A big disc should have a big cup because the number of ganglion cells (a million or so) that converge to the optic nerve head is not governed by the size of the disc.

In other words, a larger donut equates to a larger donut hole.

I had an experience as a young clinician at a school screening that drove home this concept. I was a fourth-year student working at an ophthalmoscopy station of an elementary school screening with my binocular indirect ophthalmoscope (BIO) in hand.

Knowing the clinical signs can aid diagnosis and treatment

By Mohammad Rafieetary, OD, FAAO, ABO

Toxoplasmosis is considered the most frequent etiology for “infectious” retinitis or, more appropriately, retinochoroiditis. The rationale for the nomenclature is that the infection begins in the superficial or “inner” retina and works its way toward the deeper “outer” retina, and eventually the choroid.

The organism responsible, Toxoplasma gondii, is a single-cell, obligate, intracellular protozoan parasite. Although a number of mammals, birds, and reptiles serve as a host for this organism, cats are the most definitive host and usually the cause of human infections. Its life cycle is in three infectious stages: tachyzoites (active infectious stage), bradyzoites (tissue cysts) and the sporozoites (oocysts in the soil).

Human exposure can be direct from cats (such as house pets), or indirect through ingestion of undercooked beef or pork from livestock infected by the cat’s feces. If a pregnant woman becomes infected, tachyzoites can infect the fetus via the placenta bloodstream. Although otherwise healthy adults or children of both sexes are at risk of this opportunistic infection, patients who are immunosuppressed from disease such as acquired immune deficiency syndrome (AIDS) or chemotherapeutic agents carry a higher risk.

I have recently seen two middle-aged male patients with toxoplasmosis retinochoroiditis who were being treated with immunosuppressive agents for psoriatic arthritis. The prevalence of toxoplasmosis infection can also increase with age.

Clinical presentation and diagnosis

Patients suffering from toxoplasmosis retinochoroiditis may be completely asymptomatic. The extent and quality of vision loss is related to the location of the retinal lesions and the degree of vitritis. Lesions involving the optic nerve and macula can cause immediate visual acuity loss (Figure 1), and smoky vision “headlights in the fog” can be caused by the vitritis (Figure 2).

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TOXOPLASMOSIS RETINOCHOROIDITIS

A: Active lesion involving the temporal disc margin and papillomacular bundle (PMB). B: In the inactive phase the retinochoroidal scar in the PMB region and temporal disc pallor is indicative of vision loss. C: In the bottom case, the active lesion partially involves the patient’s macula. D: Once inactive, a residual scar will be responsible for vision loss. Images courtesy Mohammed Rafieetary, OD, FAAO

Pictorial review

FIGURE 1.

Q&A | DR. SELINA MCGEE Ocular aesthetics injections, Irish whisky, optometric legislation, becoming a Master Gardener

CONTACT LENSES
How to master hybrid contact lenses

GLAUCOMA
Know what common glaucoma mistakes to avoid

OCULAR SURFACE DISEASE
Offer IPL as a treatment for MGD and dry eye disease

TECHNOLOGY
Light-adjustable IOL technology creates novel treatment window

REFRACTIVE
Surgical update 2019: What every OD needs to know

RETINA
How to determine treatment for a patient with a Roth spot

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Know that the clinical signs can aid diagnosis and treatment

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Toxoplasmosis retinochoroiditis

FIGURE 1.

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Pictorial review

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Know that the clinical signs can aid diagnosis and treatment

By Mohammad Rafieetary, OD, FAAO, ABO

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PUT YOUR PATIENTS WITH
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MANAGING THEIR DISEASE AND
SET THE COURSE FOR SUCCESS IN DR

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Educate your patients about the severity of DR, especially when left untreated3,4
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According to the AOA, you should refer patients with3:
- Severe nonproliferative DR (NPDR) within 2 to 4 weeks
- Proliferative DR (PDR) within 2 to 4 weeks
- High-risk PDR with or without macular edema within 24 to 48 hours

Ensure patients have followed up with a retina specialist who can treat DR.

Monitor your patients with DR3,4

The AOA recommends frequent monitoring of patients3
- At least every 6 to 8 months in patients with moderate NPDR and more frequently for patients with greater disease severity3.

Refer patients to a specialist who can treat DR3,4

Regeneron is committed to helping you partner with your patients for comprehensive care of DR, as well as for care of other retinal diseases.

AOA = American Optometric Association.

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### Chairman’s letter
**By Mike Hennessy, Sr**

It’s November, the beginning of the winter holiday season that inspires many to take stock of their lives and give thanks.

Our Chief Optometric Editor Ben Casella, OD, FAAO, waxes introspective with his own gratitude list, and we are grateful to partner with Dr. Casella to continue bringing you, our readers, great content.

In this issue—and every issue—we are honored to showcase the work of our authors. Whether recognizing the different types of blood-derived serum tears, how they helped his patient in a case study, and how the collection process takes place. Delve further into this issue to find: how to determine treatment for a patient with a Roth spot, recognize signs and treatment for patients with persistent surgical pain, and why ODs shouldn't shy away from steroid use for surgery patients.

Thanks for reading.
Optometry Times

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Optometry Times blogs

Every week, leading professionals in the optometric field write blogs for Optometry Times on eye care. If you haven’t read them, you’re missing out on the latest and greatest in glaucoma, retina, dry eye, refractive surgery, contact lenses and practice management, just to name a few topics. Head over to OptometryTimes.com/topic/blog to check it out for yourself and catch up on the best ideas in modern optometry.

ODs must swim in ‘deep end of the pool’ and avoid over referring

Over referring is not the most pressing challenge facing optometry, but it is a drag chute holding ODs back. Michael Brown, OD, MHS-CL, FAAO, has seen instances of it firsthand, he knows it’s still a concern.

OptometryTimes.com/SwimDeep

Optometry on fleek: Part II

Tracy Swartz, OD, FAAO, was tested by her son on new terms that the “cool kids” use. She wrote a blog titled “Optometry on fleek” to make sure all ODs continue to be cool (and understand what the cool kids say in their offices). Now read Part II.

OptometryTimes.com/Blog/OnFleek

TOP HEADLINES Check out what your colleagues are reading.

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OptometryTimes.com/Blog/EyeCareApps

2 A case of Demodex infestation with eyelash extensions
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3 Understand diabetes and nutrition
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OptometryTimes.com/DigitalStrain
Giving thanks, optometry style

By Benjamin P. Casella, OD, FAAO
Chief Optometric Editor

I’m thankful for that one CE lecture I attended where the speaker said you have to keep talk of fees out of the exam room because the exam room is for science only. That has been easy to implement!

Our content is now organized by topic! Turn to page 8 to start jumping into our core concept sections on popular clinical topics.

Giving thanks sounds like a great idea. The enterprise seems easy enough. However, the days come and the days go with me not exercising the giving of thanks nearly enough. So, here goes…

I’m incredibly thankful for my family. Without them, there simply is no me.

I’m thankful for my Optometry Times family, as well. Without it—I’m looking at you, Gretchyn—there simply is no publically editorial version of me.

I’m thankful for my staff. Without them, I wouldn’t get to actually examine people’s eyes every now and then.

I’m thankful for organized optometry. Without it, optometry as we know it would be over.

I’m thankful for dilating drops (and the ability to use them). Without them, the manufacturer- ers of mydriatic spectacles would likely go out of business.

I’m thankful for that one patient who referred something to argue about. Without them, I would be hard-pressed to find something to argue about.

I’m thankful for insurance copays. Without them, I’m incredibly thankful for my family. Without them, I would have far less material to work with.

I’m thankful for my staff. Without them, I would have far less material to work with.

I’m thankful for large multicenter longitudinal studies. Without them, we would still be blood-letting patients with leeches.

I’m thankful for those who support optometry. Without them, it wouldn’t be a doctoral level pro- fession—it would just be a job.

I’m thankful for that one patient who referred something to argue about.

I’m thankful for insurance copays. Without them, I would be hard-pressed to find something to argue about.

I’m thankful for my family. Without them, I would have far less material to work with.

I’m thankful for the giving of thanks nearly enough.

Giving thanks, optometry style

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NECO launches industry conversation about optometric education

By Gretchen M. Bailey, NCLC, FAAO
Editor in Chief, Content Channel Director

S
ome 65 people from optometric industry and media gathered in early November with New England College of Optometry (NECO) administration and trustees in Boston to discuss optometric education at the inaugural Industry & Employer Relations Meeting. The meeting was spearheaded by NECO President and CEO, Howard Purcell, OD, FAAO, who joined NECO in July 2018.

“T
I believed that I knew a lot about optometric education, so when I came in here I thought I understood the challenges,” he says. “I learned very quickly that I was not accurate in that assessment. For me, any partnership that you’re building, the more you can understand the challenges, the better the partnership can be.”

Meeting inception and structure
Gary Y. Chu, OD, MPH, FAAO, NECO vice president of professional affairs, says that when NECO administrators were considering holding the meeting, they realized that relationships between the school and industry partners had become stagnant.

“When we started fleshing it out, we realized that we say we have a partnership, but we have been doing the same things for 10 years,” he says. “Our students’ time is precious, there is so much in the curriculum for them, so how do we do this more thoughtfully? Partners want students to come to events they hold, but there are so many and it comes down to students picking and choosing. Let’s bring everyone together to have a good conversation about what education looks like and how to move forward for the betterment of the profession.”

The meeting took place over two days at NECO’s main campus and Center for Eye Care. Attendees gathered on the main campus for a late-afternoon welcome reception, opening remarks from Drs. Purcell and Chu, and dinner. The following morning, attendees toured NECO’s Center for Eye Care, heard faculty presentations about NECO’s program, and posed questions to student and faculty panels. Attendees then broke into smaller groups to discuss optometric student applicant pool, challenges facing students, partnering with industry colleagues, educating students on new technology, and the successes and challenges of optometric education.

Attendee and student feedback
NECO administration, faculty who were present, and students on the panel say they are delighted with the strong presence of industry representatives and the quality of the discussion. Attendees say they are happy that a larger conversation about optometric education is taking place.

Other attendees included representatives from the American Academy of Optometry (AAO) and Association of Schools and Colleges of Optometry (ASCO). Per NECO administrators, the National Board of Examiners in Optometry (NBEO) was not invited but should have been, and the American Optometric Association (AOA) was invited but did not respond to the invitation.

Third-year NECO student—and soon to be third-generation OD—Lauren Thamel says that she hopes one of the biggest takeaways is for industry to realize that optometric education is not the same as it was 30 years ago.

“There are different pressures now,” she says. “Students don’t get summers off anymore. You can’t work through school.”

She also says that her generation of ODs will better adapt to changes in the profession because change is their norm.

“I have grown up with optometry; I have seen it change in my time,” she says. “Even in our time in school, there is something new and our curriculum expands. We are able to change on the fly. When the auto refractor came out, that was the end of optometry. Then managed care and Warby Parker. I don’t think optometry is going anywhere. It will evolve as the needs of our patients evolve.”

Says AAO President Barbara Cafery, OD, PhD, FAAO: “We were strange bedfellows—Warby Parker, Luxottica, Johnson & Johnson Vision, National Vision, VSP, and CooperVision—disparate entities with goodwill and creative ideas. I was amazed and eager to understand what would follow.”

Fourth-year NECO student Jason Huang says he hopes industry leaders will now have a better idea of the needs of future students.

“As we graduate, we need to figure out how we can work together as a team in providing better care for patients as well as support students and help them learn what industry leaders can offer and utilize their products and resources,” he says.

Says Johnson & Johnson Vision Head of North America Professional Relations Carol L. Alexander, OD, FAAO: “The meeting showcased a novel approach in the engagement of thought leaders from all facets of industry with a college of optometry. The transparent approach to sharing the perspectives of students, faculty, and administrators was valuable in our collective understanding of both the opportunities and challenges they face in a rapidly changing healthcare system.”

Says Tom Duchardt, FAAO, director of professional relations and academic development at Alcon: “I was pleased with the NECO leadership as they proactively work to change the narrative from ‘disruptive technology’ to ‘innovation adaptation.’ I look forward to next steps in the program.”

Dave Gibson, associate vice president of consumer eye care and customer development at Allergan, says it was great to see industry colleagues workshop topics from quality applicants and student debt to the knowledge needed to be successful in optometry in the years ahead.

“When it’s well known that there are many challenges for the profession, Drs. Purcell and Chu decided to start a conversation to do something about it,” he says. “Like all grand initiatives, success will be measured not just by starting the conversation, but on the actions taken from here. I have confidence in the leadership and tenacity of Dr. Purcell that this event was just the beginning.”

Next steps
NECO administration termed the meeting “inaugural”—and in fact NECO plans to make the gathering an annual event. But what the event will look like next year is not yet clear.

Dr. Purcell says he has heard from key opinion leaders who want to be part of the conversation. In the meantime, meeting organizers plan to stay in touch with attendees over the next 12 months via workshops on specific topics such as:

- Debt and cost of education
- Bias against corporate optometry/scope of practice
- Business of optometry
- Strategic partnerships with industry
Multifocal contact lenses are advancing fast in the contact lens market, and optometrists may be surprised at their applications. This topic was discussed at a rapid-fire session at the American Academy of Optometry 2019 annual meeting in Orlando.

**Speakers included:**
- Beth Kinoshita, OD, FAAO, at Pacific University College of Optometry
- Vinita Henry, OD, FAAO, at the University of Missouri-St. Louis College of Optometry
- Dawn Lam, OD, FAAO, at Southern California College of Optometry at Marshall B. Ketchum University
- Julie DeKinder, OD, FAAO, at the University of Missouri-St. Louis College of Optometry

### Soft multifocal considerations

A crucial aspect of fitting soft multifocal contact lenses, according to Dr. Kinoshita, is good centration. With single-vision (SV) contact lenses, there is some room for error in centration. But in multifocal lens designs, specific optics can help the lens center over the visual axis. Thus, centration is more important for a proper fit.

“Today’s off-the-shelf contact lenses provide many of these features,” she says.

Fitting considerations for multifocal contact lenses are anatomical, so ODs should take care to ensure good coverage and movement.

“I challenge ODs in practice to really start looking at the decentration, though slight, of their contact lens fits,” Dr. Kinoshita says.

She says that in her experience, many contact lens patients seen in previous evaluations appeared to be properly centered, but in actuality had temporal displacement. While challenges like centration are less of a concern for monovision fits, other aspects, such as pupil size, become more significant.

Dr. Kinoshita recommends that ODs perform topography over the contact lenses to determine centration.

“This is best achieved if ODs perform topography on the patient without a contact lens and repeat the topography while the patient is wearing the multifocal lenses,” she says.

### GP multifocals, aspherics, & translation

For both aspheric and translating gas permeable (GP) multifocal designs, a physical assessment is crucial to a proper fit.

“The lid position is going to be very important with these types of lenses,” Dr. Henry says.

She recommends that before fitting any GP lens, ODs take care to perform all necessary pre-fit evaluations, including:
- Physical exam of tears, cornea, lid
- Anterior and posterior health assessments
- Current refraction and add values
- Keratometry (K) values
- Dominant eye identification
- Pupil size measurements
- Horizontal visible iris diameter (HVID) measurements
- Lower lid position

Aspheric GP multifocals work best on patients with smaller pupils, though lower lid sizing is less of a factor.

“Typically, these will be a little more difficult if the patient requires critical near vision,” Dr. Henry says.

She recommends that ODs follow the GP laboratory’s fitting guide or manufacturer guidelines as references when using aspheric multifocals.

For translating designs, add power and pupil size are less of a concern, but ODs should note that the ideal patient will have a lid that is at or slightly above the lower limbus. Good lid tonicity helps as well.

Dr. Henry warns that ODs should be on the lookout for potential challenges like excessive lens rotation, poor translation, and near or distant blur.

### Multifocal lenses for myopia control

Projections estimate that by 2050, five billion people will have myopia.1

However, new lenses for myopia control have the potential to stem this tide. Research into optical correction shows that certain contact lens designs can slow myopia by 36 to 79 percent.2-4

While applicable to all patients, lenses that slow refractive progression may offer particular value to myopic children. Typically, children as young as age 8 may wear contact lenses, though Dr. Lam notes that this range depends on the patient.

“Look at the maturity level of the patient and cooperation among parent, guardian, and child,” she says.

She describes key considerations when fitting patients with reshaping contact lenses to control myopia progression.

- Choose spherical-equivalent distance power from the fitting set
- Choose the highest tolerable add power
- Look for patients with low levels of refractive astigmatism
- Choose among daily, two-week, and monthly wear schedules

Dr. Lam notes that while these myopia control lenses have produced results for slowing myopic progression, they are not approved by the U.S. Food & Drug Administration (FDA) for this purpose. Practitioners should make these distinctions clear to patients and establish expectations going in.

### Multifocal scleral fitting

Practitioners hoping to fit multifocal scleral lenses for patients have some obstacles.

“It’s a bit of a challenge,” Dr. DeKinder says.

Not all scleral lenses have a multifocal option, meaning that ODs need to think long-term when fitting patients in sclerals. In particular, they should consider the patient’s age and possible refractive progression.

“If you have a patient who is already presbyopic or may become presbyopic within the next few years, you need to make sure the lens you are selecting has the option for a multifocal design,” Dr. DeKinder says.

She also says that a well-fitting scleral lens will not move with blinking, so ODs must take care to ensure that the lens fits the pupil well. Scleral lenses, in general, will decenter when they are placed on the eye.

Again, Dr. DeKinder recommends that providers reference fitting guides to help make determinations.

Designs for these lenses can be concentric or aspheric, but it is possible to find combination lenses that offer more customization options.

“If you can get a lens with a center-distance or center-near design, you have more flexibility in the way you can manipulate those optics,” she says.

Overall, Dr. DeKinder recommends practitioners have a systematic approach and gain experience fitting different types of designs, one at a time.

“When you feel very good at fitting one, add a second lens design into your toolbox,” she says.

### References


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**By Greg Hill**
How to master hybrid contact lenses
Adding complex fitting to the toolbox helps patients achieve better vision

By Greg Hill and Marek Biernacinski

Hybrid contact lenses are an innovative yet challenging way to improve patient vision. At this year’s Vision Expo West in Las Vegas, Jason Miller, OD, MBA, FAAO, of Powell, OH, offered strategies to help ODs better understand the process.

Hybrid contact lenses
New hybrid lens options are opening up treatment possibilities for patients with unusual visual needs.

“There are some options that can make a big difference,” Dr. Miller says.

Options available to ODs include silicone hydrogel soft skirt lenses, gas permeable (GP) lenses, SynergEyes Duette progressives, and SynergEyes UltraHealth for irregular corneas.

Many of these lenses are designed to address several refraactive errors at once, such as presbyopia and astigmatism, while others are made to help patients address ocular conditions like keratoconus.

These options have the potential to make patients happier in their lenses while reducing dropout, Dr. Miller says.

“These patients are going to be lifelong patients—a big referral source for your practice,” he says.

The market for hybrid contact lenses
As the contact lens market grows, ODs can expect to see more patients coming in with complex visual needs.

“There is a big market for this underserved, undertreated optometric specialty,” Dr. Miller says.

Hybrid contact lenses may be particularly beneficial for patients with specific types of visual impairments, such as:

- Post-RK
- Keratoconus
- Corneal scarring or trauma
- Corneal transplants
- Irregular or high astigmatism
- Extreme dry eyes
- Those unhappy with vision of toric or multifocal contact lenses

“These patients don’t realize that potentially they could be wearing contact lenses,” Dr. Miller says.

Providing hybrid lens options to patients isn’t just a matter of staying at the forefront of technology, it’s about giving patients the options they need to improve visual outcomes. Lens selection is just one part of the process.

Fitting challenges
Many of the above ocular challenges can be managed with hybrid lenses. For problems that require more sophisticated solutions, however, ODs need a process in place to achieve proper fitting.

They can be successfully treated but it may take time, and ODs should have a process in place to account for the extra challenge.

Providing hybrid lens options to patients isn’t just a matter of staying at the forefront of technology, it’s about giving patients the options they need to improve visual outcomes. Lens selection is just one part of the process.

“You want to block out enough time to make sure you’re comfortable fitting these lenses,” he says.

Dr. Miller also recommends training optical technicians in both process and terminology. Getting staff excited about lenses helps them get patients excited and interested, he says.

ODs must also have the topographical imaging equipment necessary for proper assessment.

“If you don’t have a topographer, you honestly can’t do a lot of these fittings,” Dr. Miller says.

Other tools that may be helpful include a full set of diagnostic lenses, anterior segment cameras, and optical coherence tomography (OCT). ODs should start by assessing keratometry (K) values and physical characteristics to find a fitting start point for the hybrid contact lens.

When should hybrid lenses be avoided?
Despite their benefits, hybrid lenses are not suitable for everyone, Dr. Miller says.

In particular, those suffering from severe dry eye may need to avoid these lenses until symptoms are under control.

“Any ocular surface disease needs to be treated and addressed ahead of time,” he says.

Other disqualifying factors may include a lenticular cylinder in the patient’s prescription or patients who seek convenience above all else, according to Dr. Miller.

Kenneth Cole New York unveils winter 2019 eyewear collection
Kenneth Cole New York recently introduced its fall and winter design collection for 2019. This season’s designs promote relaxed and easy comfort infused with fashionable shapes like deeper B measurements for men and modern rectangles for women.

Model KCO299 features the new techni-cole style with a deeper B measurement and titanium construction, making it lightweight and flexible. The titanium temples are finished with an acetate endpiece detailed with the Kenneth Cole logo.

Model KC0300 is available in a matte finish as well as black matte. Crafted in acetate, this pair features a rectangle front in classic horn coloration. The frame’s temples are offered in contrasting finishes of shiny and matte.

Model KC0301 is features a soft and feminine cat-eye silhouette. This style is part of the new techni-cole optical collection. The titanium temples are finished with an acetate endpiece detailed with the Kenneth Cole logo.
Know the hidden links among glaucoma, contact lenses, and the cornea

By Greg Hill and Marek Biernacinski

Halting glaucoma progression can be challenging, but as it turns out, medication is not the only tool in an OD's toolbox.

Many factors influence glaucoma progression in patients, some of which may be unrelated to the disease itself.

ODs must be aware of the hidden links among glaucoma symptoms, medication, and contact lenses with respect to how ocular surface disease (OSD) affects patient outcomes.

Karen Lee, OD, FSLS, FAAO, and Jane Kuo, OD, FAAO, raised awareness to these links at the American Academy of Optometry 2019 meeting in Orlando.

Link between OSD and glaucoma

It is known that there is a higher prevalence of OSD in glaucoma patients, primarily related to decreased tear production and break up time. These symptoms may not be related to glaucoma proper, but instead, the medical drops patients use to manage their symptoms may sometimes produce side effects in patients that may reduce treatment compliance.

“When you have patients with dry eye, it really decreases the quality of life. Anti-glaucoma eye drops containing BAK compromise patient compliance,” Dr. Kuo says.

This molecule disrupts the corneal epithelium by damaging DNA and increasing inflammation. Such a disruption can create particularly challenging concerns when the patient is a contact lens wearer.

Certain contact lenses, particularly hydrogel lenses with high water content, absorb BAK molecules and release them slowly into the corneal epithelium over time. Prolonged exposure to BAK is known to increase symptoms.

Fortunately, ODs can mitigate these corneal/drug interactions through patient education.

“The big idea here is that corneal exposure time to BAK tends to be relatively short-lived,” Dr. Lee says.

The U.S. Food & Drug Administration (FDA) recommends that patients using both glaucoma drops and contact lenses wait at least 15 minutes after instilling drops before applying their contact lenses.

ODs should share this information with their patients to ensure they understand the possible interaction between their contact lenses and their medication.

Additionally, ODs who fit glaucoma patients in contact lenses can work these considerations into their lens selection.

“I might be reaching for a low water content hydrogel soft lens if I know the patient will abuse his drops with contact lens wear,” Dr. Lee says.

Glaucoma and postop lens wear

It is common for ODs to encounter patients interested in wearing contact lenses during or after surgical treatments. While there are no contraindications to contact lens wear after procedures like minimally invasive glaucoma surgery (MIGS), ODs need to assess the corneal health of each patient to determine the best approach.

“If the cornea or the sclera is not affected, then patients can potentially keep wearing what they are currently wearing,” Dr. Lee says.

However, if the cornea is affected, ODs will need to consider using gas permeable (GP) contact lenses that produce a new refractive surface. In these cases, soft contact lenses may not be enough.

“Think about other options. Maybe using scleral topography or some customized lens designs,” Dr. Lee says.

Corneal procedures and glaucoma

Glaucoma can cause corneal challenges, but what about corneal procedures that make glaucoma worse?

“As the techniques are getting more and more advanced, we are starting to see more partial thickness procedures,” Dr. Lee says.

While the link between corneal refractive surgery and intraocular spikes in pressure are not well understood, it is clear that such procedures can change the biomechanics of the cornea. For some patients with high refractive errors, this can produce a predisposition for glaucoma.

But new procedures are on the horizon, such as corneal cross-linking that can slow down or even halt progression of keratoconus without undoing corneal changes.

“We are really recommending our keratoconus patients go out and get this done,” Dr. Lee says.

However, changes to the physiology of the cornea may be unavoidable in some procedures, and ODs must be aware of these concerns before recommending a procedure.

“If your patient had glaucoma before a transplant, there is a 12 to 15 percent risk of glaucoma worsening afterward,” Dr. Lee says.

ODs must monitor and continue treating patients after invasive procedures, particularly helping patients manage their intraocular pressure (IOP) by testing via temporal sclera, Tono-Pen (Reichert), or globe palpation. This preventative care is a necessary part of managing patient symptoms and delivering a high standard of care.

“Try to get patients the best vision that you can in a healthy way,” Dr. Lee says.

IN BRIEF

CooperVision MiSight 1 Day myopia control soft lens gets FDA nod

SAN RAMON, CA—CooperVision has received U.S. Food and Drug Administration (FDA) approval of its MiSight 1 day contact lens. This daily wear, single-use contact lens is the first and only FDA-approved product clinically proven to slow the progression of myopia when initially prescribed for children 8 to 12 years old, according to the company.

Myopic progression has been linked to sight-threatening conditions later in life such as cataracts, retinal detachment, glaucoma, and myopic maculopathy.

Until now, traditional eyeglasses and contact lenses available in the U.S. have been developed to correct only blurred vision, while not approved to slow myopic progression.

CooperVision’s prospective, multi-center, double-masked, randomized multi-year study enrolled 144 myopic children aged 8 to 12 years from Singapore, Canada, the United Kingdom, and Portugal. Three-year peer-reviewed results published in Optometry and Vision Sciences in August 2019 indicated that use of MiSight 1 day was shown to slow myopia progression: 59 percent as measured by mean cycloplegic spherical equivalent (SE) and 52% as measured by mean axial elongation of the eye. The trial continued with encouraging results reported for years four and five, in which the original control group was refit into MiSight 1 day.

MiSight 1 day will launch in the U.S. as part of a CooperVision myopia management initiative beginning in March 2020. The lens is already being successfully worn by thousands of myopic children in other parts of the world, according to the company, including Canada, the United Kingdom, Spain and Australia, where age ranges for initial fitting may vary.

BAK, contact lens material, and post refractive surgery IOP spikes should be kept in mind

epilogue
Artificial intelligence can help discover laucoma, angle-closure disease, and diabetic retinopathy

By Greg Hill

Artificial intelligence (AI) may hold the answers to some of the biggest challenges in optometry, according to Nahida Akter, PhD; Jack Phu, OD, PhD, FAAO; and Christopher Clark, OD, PhD, at the 2019 American Academy of Optometry meeting in Orlando.

Deep learning for OCT glaucoma diagnoses

AI promises in ophthalmic applications of disease screening, image interpretation, and data synthesis. Research is exploring how modified convolutional neural networks (CNNs) can analyze patterns and data to classify glaucoma based on raw optical coherence tomography (OCT) images.

This process assessed 410 raw OCT images of temporal-superior-nasal-inferior-temporal (TSNIT) retina layers across both glaucoma and non-glaucoma patients.

“I think all of the layers have some benefits,” Dr. Akter says.

Each layer contributes to the transfer-learning based CNN, creating a more detailed profile of retinal layers that could aid ODs in clinical imaging.

Rethinking monitoring of angle closure

As ODs know, angle-closure glaucoma is a significant public health problem. Gonioscopy is the gold standard for assessing angle-closure spectrum disease, but the tool has its limitations.

“It is highly skill-intensive and highly subjective among doctors,” Dr. Phu says.

And while angle-closure glaucoma is the one form of glaucoma that can be prevented, success is contingent on an early diagnosis through gonioscopy grading.

But what if ODs could rely on anterior segment (AS) OCT imaging instead of gonioscopy? Dr. Phu detailed the research questions his team studied. He honed in on whether quantitative parameters obtained using OCT imaging could describe the spectrum of gonioscopic angle closures that ODs typically use in the clinic.

Although there is potential for further integration of artificial intelligence models for distinguishing between open and closed angles, gonioscopy is still an essential skill for ODs.

This involved reviews of gonioscopy and AS-OCT clinical data, including evaluations of nasal and temporal angles, gonioscopic grades, and the posterior trabecular meshwork.

Results showed that while AS-OCT evaluations were somewhat reliable for identifying the continuum of change in open angles to closure, there were significant errors when no prior gonioscopic information was available.

Although there is potential for further integration of artificial intelligence models for distinguishing between open and closed angles, gonioscopy is still an essential skill for ODs.

In brief

Aerie acquires Avizorex Pharma to advance dry eye portfolio

DURHAM, NC—Aerie Pharmaceuticals, Inc. announced the signing of an agreement for the acquisition of Avizorex Pharma, S.L. (AVX), a Spanish ophthalmic pharmaceutical company developing therapeutics for the treatment of dry eye disease.

AVX completed a Phase 2a study in dry eye subjects earlier this year with its lead product candidate, AVX-012. The active ingredient in AVX-012 is a selective agonist of the TRPM8 ion channel, a cold sensor and osmolarity sensor that regulates ocular surface wetness and blink rate, according to the company. By stimulating these processes, TRPM8 agonists have the potential to restore tear film stability and reduce discomfort in patients with dry eye.

Positive results from the Phase 2a study support the therapeutic potential of AVX-012 to treat signs and symptoms of dry eye, and Aerie is planning to initiate a larger Phase 2b study in late 2020.

Under the terms of the agreement, Aerie will acquire AVX Pharma in an all-cash transaction. Aerie will make an upfront payment of $10 million, subject to customary adjustments, and AVX Pharma shareholders will be eligible to receive additional payments subject to achievement of certain clinical and regulatory performance milestones, plus royalties on net sales of approved products from AVX Pharma’s development pipeline.

In addition to AVX-012, Aerie will also be acquiring rights to other compounds targeting TRPM8. The parties expect to close the acquisition before the end of the year pending the completion of certain pre-closing obligations.
Embrace new frame and lens technology

New advancements offer opticians more options to meet

By Greg Hill and Marek Biernacinski

ow many ODs embrace technology? Lens and frame technology has come a long way since the days of glass and metal, says Phernell Walker II, ABOM, NCLC, of Portland, OR, at Vision Expo West in Las Vegas. Today, lenses and frames aren’t mere aesthetic concerns. They are tools for improving the way opticians deliver eye care across lens quality, frame choice, and integrated health monitoring.

“The 21st century optician has to understand what’s new in technology. We have to understand what people want,” he says.

With advancements in material science, treatments, clarity, and shape, modern lenses have led to options that, 20 years ago, could never have been imagined.

Framing a solution

Frame materials, styles, and designs are expanding fast. Though certain standbys are still popular (and zylite isn’t going anywhere), opticians and optometrists can expect to see a broad spectrum of new materials to enter the scene such as translucent materials, nylon blends, wrapped frames, and laminates.

With new materials coming onto the market, it’s important for opticians to understand what options are available to them and make those choices clear to their patients.

“Some people need a lot of help, but unfor-
Light-adjustable IOL technology creates novel treatment window

By Laird Harrison

A light-adjustable intraocular lens (IOL; LAL, RxSight) can improve patient satisfaction by allowing ophthalmologists to fine-tune and customize the patient’s refractive outcome after cataract surgery, according to David Chang, MD, in a presentation at the American Academy of Ophthalmology 2019 meeting in San Francisco.

“It shifts the need to do all of our counseling and decision-making preoperatively more to postoperatively,” says Dr. Chang, clinical professor of ophthalmology at the University of California, San Francisco. “You can let the patient preview different refractive outcomes while he is pseudophakic.”

Light-adjustable IOL

The LAL is a three-piece silicone lens with diffusible monomers in the optic. Following a standard phacoemulsification procedure, the ophthalmologist uses a slit lamp equipped with a near-UV light to alter the IOL shape to adjust the patient’s refraction.

As the light hits the lens, it initiates polymerization, causing micron-level changes in the structure of the lens. This allows the surgeon to adjust both the sphere and cylinder, Dr. Chang says. An LAL precludes the need to perform intraoperative aberrometry or to mark the astigmatism axis prior to surgery because the refraction should be able to achieve better results with the LAL than the most experienced surgeons now get with the most advanced pre- and intraoperative technologies.

While patient refractive outcomes can be changed or enhanced with laser in situ keratomileusis (LASIK), many ophthalmologists do not perform keratorefractive surgery, requiring a patient who needs an enhancement to see a second surgeon.

Even then, the patient must wait a few months until the refraction is stable before undergoing LASIK or photorefractive keratectomy (PRK).

Patients can be overwhelmed by a bevy of unfamiliar terms and often intimidated by disclaimers that results of surgery may not meet their expectations

In addition to improving the refractive accuracy, Dr. Chang hopes that adjustability will improve the patient experience. Setting reasonable expectations and helping patients make decisions about their refractive goals during preoperative counseling can be difficult for both the patient and the eyecare practitioner.

“Patients can be overwhelmed by a bevy of unfamiliar terms and often intimidated by disclaimers that results of surgery may not meet their expectations. The ability to try different pseudophakic refractive states should reduce preoperative anxiety and confusion and improve patient satisfaction.”

Better patient experience

In addition to improving the refractive accuracy, Dr. Chang hopes that adjustability will improve the patient experience. Setting reasonable expectations and helping patients make decisions about their refractive goals during preoperative counseling can be difficult for both the patient and the eyecare practitioner.

“Patients can be overwhelmed by a bevy of unfamiliar terms and often intimidated by disclaimers that results of surgery may not meet their expectations. The ability to try different pseudophakic refractive states should reduce preoperative anxiety and confusion and improve patient satisfaction.”

If you wanted natural distance vision,” Dr. Chang says, “how would you know what the difference would be between plano and -0.75 D with an IOL? If you want to read without glasses, how could you appreciate the difference between being -1.50 D versus -2.50 D? With an adjustable IOL, you can preview these different refractive targets once you have the IOL, and then have your preferred target delivered with an adjustment.”

Light-adjustable IOLs will be a great way to deliver customized mini-monovision, Dr. Chang says. “In addition to achieving good distance vision in one eye, we can try out different amounts of myopia in the second eye,” he says. “We can let the patient decide postoperatively how much anisometropia is optimal for them, and how much they can comfortably tolerate. If they don’t like it, we can then reverse it.”

In theory, the ability to wait until after surgery to demonstrate different refractive options and targets should substantially reduce the amount of time that surgeons must spend preoperatively trying to describe these different options.

“The best thing is that patients will not have to understand concepts such as depth-of-focus, myopia, astigmatism, and anisometropia,” Dr. Chang says. “We can use trial lenses or even a soft contact lens trial to demonstrate postoperatively how increasing or decreasing myopia affects their uncorrected vision.”

The LAL is approved by the FDA and slated for commercial availability in the United States in late 2019.

This article was adapted from Dr. Chang’s presentation at the 2019 congress of the European Society of Cataract and Refractive Surgeons. Dr. Chang disclosed that he is a consultant at RxSight and Perfect Lens.

TAKE-HOME MESSAGE

The ability to fine-tune and customize patients’ refractive outcomes after cataract surgery could shift the need for physicians to do counseling and decision-making preoperatively more to postoperatively.

REFERENCE

Recognize signs and treatment for patients with persistent PSP

Significant difference from OSD apparent between period of time after surgery, lack of signs

I had surgery on my cervical spine a long time ago. Necessary for that surgery was harvesting an allograft from my hip. What I recall about the surgery is how painful my hip was and for how long it bothered me—not my neck.

The technical jargon is persistent post-surgical pain (PPSP). It turns out that PPSP is not at all uncommon, with the incidence up to 60 percent in some types of surgery.

It appears to be most common in breast surgery, amputation, and thoracotomy, and less common in arthroscopic knee surgery and dental implants.1-2

Looking at PPSP

PPSP is not well studied, and can be confounding, as the symptoms of pain closely mimic those of other ocular conditions—most commonly ocular surface disease (OSD). It is not until these symptoms persist past six months does PPSP begin to enter consideration for the clinician.

It is therefore important not to “jump” to a dry eye diagnosis too aggressively or too soon. It is also valuable to identify when a patient is better diagnosed and treated as PPSP.

Laser in-situ keratomileusis (LASIK) is a common procedure in the United States with a number of reported successful clinical outcomes and overall patient satisfaction.3

Nevertheless, there are side effects from the procedure, mostly in the immediate post-operative period. These can include burning, scratchiness, and discomfort on the ocular surface.4 Symptoms are common to see up to one-month post-LASIK but become far less common at three months after surgery.5

Corneal effects

Both corneal nerves are severed when making the LASIK flap and ablated when treating with the excimer laser.

Corneal sensitivity is decreased initially and returns to normal in most patients between three to 18 months.6 This decrease in corneal nerve firing can lead to decreased basal secretions along with hypoesthesia. This hypoesthesia is associated with an increase in both symptoms and signs of OSD.7

The prolonged corneal hypoesthesia has been correlated with an increase in symptom severity, often without corneal signs.8 This can lead to persistent pain similar to neuropathic pain syndromes that exit with other body parts.

The concept is called peripheral sensitization and is a result of a nociceptor firing secondary to injury or prolonged inflammation. This can lead to an alteration in the central nervous system called central sensitization. It is most commonly identified when there is pain but no input causing that pain.8

Patient base

A common complaint of these patients is their eyes hurting when putting in eye drops, including non-preserved artificial tears. They also tend to be sensitive to wind and cold climates.

Finally, every treatment seems to make them worse—never neutral or better. These patient types are rare (incidence is unknown).

They do not typically respond to traditional dry eye therapies and are most likely best managed by a pain management specialist in ocular pain or an eyecare provider who has experience working with the patient population.

A challenge of these patients is their tendency to self-refer to local corneal experts, who often dismisses their complaints.

This lack of concern from a “specialist” can further complicate treatment.

Corneal nerves are at the root of this problem. It therefore seems reasonable to evaluate different methods of corneal refractive surgery to determine if any create an increased risk for patients.

While there are several studies on hinge position, they have not revealed any differences.9 Femtosecond flaps appear to produce fewer dry eye symptoms and a faster recovery of corneal sensation.10

Further, since photorefractive keratectomy (PRK) does not utilize a corneal flap, it was theorized that there may be less dry eye. But studies comparing the incidence of dry eye in PRK versus LASIK are mixed at best.11

Comparison

Currently, my discussion with patients prior to LASIK is slightly different. I inform them that all patients experience pain immediately after the surgery.

However, if they go home and sleep for a few hours, they will sleep through the worst of the pain.

Next, I let them know that corneal nerves are damaged during the procedure and that those nerves take months to regain their full function.

Patients may experience corneal sensations similar to their eyes feeling dry during the post-operative period.

An OD will therefore have the patient take artificial tears during the first month to help the cornea heal.

Most often these symptoms are completely resolved by three months. On the rare instance the condition becomes more centralized, and OD has not necessarily inaccurately diagnosed the patient’s condition as “dry eye.”

It is therefore important not to “jump” to a dry eye diagnosis too aggressively or too soon

Cataract surgery

PPSP can also occur in cataract surgery. A study published in Clinical Ophthalmology added pain as end point and found that approximately 7 percent of patients had post-operative pain that persisted for six weeks.12

In a retrospective analysis of post-operative
Patients may experience corneal sensations similar to their eyes feeling dry during the post-operative period. Chronic postoperative pain (CPP) is a common symptom following cataract surgery and can be associated with dry eye symptoms. 

A study published in *Anesthesiology* found that gabapentinoids were successful in reducing chronic post-surgical pain for many surgeries, but cataract surgery was not studied. It is believed the effect of gabapentin on injured nerves is a reduction in discharge.

**Conclusion**

PPSP occurs in many surgeries—including both LASIK and cataract surgery. In both areas, the patient’s symptoms for PPSP are similar to those of OSD. The main distinction is the period of time after the surgery and the lack of clinical signs to support the symptoms.

If ODs listen carefully to this patient base, the symptoms they describe can be slightly differentiated from that of a patient with OSD.

Finally, consulting with a pain management doctor who specializes in ocular pain can be beneficial for both an optometrist and the patient.

**REFERENCES**


**Surgical update 2019: What every OD needs to know**

From IOLs to corneal and glaucoma procedures, stay up to date with the latest

By Greg Hill and Marek Biernacinski

Eye care is an ever-evolving field, and 2019 brought with it several advances in approach and technique that surgeons need to keep in mind as they adopt the latest best practices in glaucoma surgery.

Josh Johnston, OD, FAAO, in Atlanta and Justin Schweitzer, OD, FAAO in Sioux Falls, SD, offered an overview of what surgical updates have come to optometry in the past year, speaking at Vision Expo West 2019 in Las Vegas.

**New ways of looking at cataracts**

A primary shift in thinking has been focused on cataract surgery. ODs are seeing a paradigm shift where patients expect their cataract procedures to produce positive refractive outcomes, even in cases of astigmatism and presbyopia.

“Modern cataract surgery can do that,” Dr. Johnston says.

A new era of intraocular implants (IOLs) is here, with toric, multifocal, and presbyopic IOLs on the market offering better results than older generations of implants.

Also on the horizon are extended depth-of-focus diffractive IOL designs that elongate focus.

“That spacing and height variation here gives you a range of vision,” Dr. Johnston says.

**Future IOL technology**

The world of IOLs is about to see even more exciting advancements.

Light-adjustable lenses offer a new approach to IOL placement. The method uses ultraviolet (UV) light to lock in IOLs after surgery. This offers predictable correction of residual refractive error after lens implantation for optimal distance vision, and

the IOLs are customizable to control for monovision, near adds, and asphericity.

The advancements give more control to both ODs and patients.

“The ability to adjust that implant in the first month speeds up the process,” Dr. Schweitzer says.

Another emerging technology is a refractive capsule with potential applications for IOL exchanges and drug-emitting devices.

ODs can also expect to see more applications for femtosecond laser-assisted cataract procedures.

“The femtosecond laser is more accurate for treating astigmatism,” Dr. Johnston says.

Other strategies such as dropletless cataract surgery and laser fragmentation were also mentioned.

**MIGS can reduce the burden of medications, even if they don’t eliminate the need for them completely**

Since its infancy in 2012, many new options have launched to help patients manage their symptoms. Part of this demand is driven by poor patient adherence.

“More than 90 percent of patients are not adhering to their ocular dosing regimens,” he says.

MIGS can reduce the burden of medications, even if they don’t eliminate the need for them completely.

Options such as iStent inject (Glaukos), Hydrus Microstent (Ivantis), and tube shunts can offer minimally-invasive relief. Both iStent and Hydrus have been FDA approved to be implanted in conjunction with cataract surgery.

The ideal patient type for these devices are those with both cataracts and mild to moderate glaucoma, Dr. Johnston says.

“Even if they don’t eliminate the need for them completely, Options such as iStent inject (Glaukos), Hydrus Microstent (Ivantis), and tube shunts can offer minimally-invasive relief. Both iStent and Hydrus have been FDA approved to be implanted in conjunction with cataract surgery.”

**Corneal collagen cross-linking and refractive update**

According to Dr. Johnston, the keratoconus mantra that ODs are familiar with has changed. The treatment methodology used to involve diagnosis, application of special lenses, and an inevitable surgical procedure. Today, it is a process of early diagnosis, halting disease progression, and rehabilitating vision through lenses and tools.

There are also new strategies for topography-guided refractive correction, Dr. Johnston says.

“The goal with this is to be able to rehabilitate vision on people who, in the past, probably could not have had laser vision correction,” he says.

The objective of topography-guided correction is anterior surface normalization and vision rehabilitation. Topography-guided photorefractive keratectomy (PRK) offers benefits for normalizing the cornea, improving uncorrected vision, and improving image quality through glasses.

The small incision lenticule extraction (SMILE) procedure has been approved by the FDA with high rates of postoperative patient satisfaction. SMILE may offer comparable benefits to LASIK alongside possible improvements to dry eye.

**Endothelial keratoplasty (EK)**

Descemet’s membrane endothelial keratoplasty (DMEK) is the latest iteration of EK. Compared to penetrating keratoplasty (PKP), EK offers faster recovery and less risk of rejection.

“Much speedier visual recovery, optically much better, fewer higher-order aberrations,” Dr. Johnston says.

A key advantage comes from how DMEK avoids stroma-to-stroma interface and offers the thinnest possible graft. DMEK also has lower graft rejection rates compared to more conventional options, such as PKP or Descemet’s stripping automated endothelial keratoplasty (DSAEK).

**Minimally invasive glaucoma surgery (MIGS)**

ODs can expect increased demand for MIGS management in their practices, says Dr. Johnston.

“It is really the hot thing in surgical glaucoma right now. It is only going to continue to increase,” he says.
To note: I am more comfortable with a BIO and 20.00 D lens at a school screening than I am using a handheld ophthalmoscope because I do not really have to direct gaze all that much.

Even if the pediatric patients just want to follow the light around with their eyes, I can still get a decent view of the optic nerve head, arcade vessels, and macula all in one go.

During this particular screening, I had, for the first time, an opportunity to look at a number of optic nerve heads consecutively in a short period of time.

The concept of vast difference between optic nerve head sizes became readily apparent that day. Even now, I make a note of optic nerve size in a patient’s chart. I do not take exact measurements, but I do make a qualitative remark of the size: small, normal, or large.

**Scenario**

With this notion in mind, a new patient was referred to me a few weeks ago for suspicion of glaucoma.

Accompanied by his grandfather, this 14-year-old white male presented with no other complaints. His medical history was remarkable for attention-deficit/hyperactivity disorder (ADHD), which was managed with a methylphenidate extended-release tablet every morning.

His family history was remarkable for cataracts. There was no frank family history of glaucoma, although the grandfather could not be entirely sure.

Visual acuity through his conventional spectacles was 20/20 in each eye (he wore a low hyperopic correction on an as-needed basis). Pupil function was unremarkable for each eye, and confrontational visual fields were intact for each eye.

Anterior segment examination was unremarkable for each eye to include open angles. Intraocular pressures (IOP) by means of Goldmann applanation tonometry were 24 mm Hg in the right eye and 21 mm Hg in the left eye at 2:15 pm.

He was a little apprehensive with his lids, but I think I prevented any squeezing from affecting my measurements. The patient was dilated with the consent of his grandfather, and each eye’s posterior pole was photographed (see Figure 1).

I judged each vertical cup-to-disc ratio to be around 0.65. Each corresponding optic disc appeared to be a bit large. With the help of a pre-corneal lens and my slit lamp’s red-free filter, I judged each eye’s retinal fiber layer—as it approached the optic nerve head—to be frankly intact without defects.

Each optic nerve also appeared to respect the ISNT guideline (inferior neuroretinal rim thicker than its superior counterpart and so forth and so on).

**Findings**

At the conclusion of the examination, I informed the patient and his grandfather that his optic nerves looked interesting but not pathological. I went on...
Know what common glaucoma mistakes to avoid

Mistakes to avoid

- Not recognizing a neurologic field
- Thinking glaucoma causes optic disc pallor
- Diagnosing NAAION in glaucoma patients
- Not recognizing when the OCT is wrong
- Not treating real disease
- Changing therapy based upon one bad intraocular pressure (IOP) or field
- Not getting enough pre-treatment and post-treatment IOPs
- Not recognizing patients who will likely do well
- Not identifying patients who likely will not do well

By Greg Hill

Because glaucoma is one of the most prevalent eye diseases in the world, ODs are familiar with best practices for glaucoma management.

But do they really understand glaucoma care as well as they think?

As it turns out, maybe not.

That is according to Joseph Sowka, OD, FAAO, at Nova Southeastern University College of Optometry at the American Academy of Optometry 2019 annual meeting in Orlando.

In particular, optometrists should be aware of several pervasive mistakes in glaucoma management in order to deliver better care to their patients.

**Misdiagnosing non-arteritic anterior ischemic optic neuropathy**

More than anything else, ODs should avoid diagnosing non-arteritic anterior ischemic optic neuropathy (NAAION) in glaucoma patients.

“It just doesn’t happen,” Dr. Sowka says.

The danger lies in the fact that there is no clinical test to conclusively diagnose this condition, making it a common diagnosis of convenience.

A key differentiator for ODs to keep in mind is that glaucoma is a disease of cupping, while NAAION is a disease of non-cupping.

**Over-reliance on OCT**

Optical coherence tomography (OCT) is an indispensable tool for diagnosing glaucoma, but a common pitfall inexperienced providers face is over-reliance on this imaging.

“The overuse and overemphasis on imaging technology to the exclusion of the other clinical findings and assessment of risk factors is going to put yourself and the patient in some degree of peril,” Dr. Sowka says.

In particular, imaging concerns such as signal quality, blink rates, or segmentation errors can produce erroneous data.

So how much confidence should ODs have in their OCTs for diagnosing glaucoma?

According to Dr. Sowka, optometrists should trust their initial evaluations while factoring in the imaging results. In other words, they should ask themselves how certain they were the patient had glaucoma prior to looking at the OCT imaging results.

“Don’t make clinical decisions based on bad data,” Dr. Sowka says.

**Mismangement of red and green diseases**

When a disease state masquerades as another condition, it is common for testing values or imaging to fall outside of expected values.

But just because a value falls outside of a standard range, that does not necessarily mean a problem exists—this phenomenon is known as red disease.

Just because a value falls outside of a standard range, that does not necessarily mean a problem exists—this phenomenon is known as red disease.

ODs should ask themselves how certain they were the patient had glaucoma prior to looking at OCT results

Physical assessments are critical for analyzing these conditions.

“We still need to perform fields in the age of imaging because sometimes it is not glaucoma,” he says.

**Tools as such visual fields used in conjunction with nerve fiber analyses, medical histories, and physical assessments are critical for analyzing these conditions.**

**Mismangement of red and green diseases**

When a disease state masquerades as another condition, it is common for testing values or imaging to fall outside of expected values.

Just because a value falls outside of a standard range, that does not necessarily mean a problem exists. This phenomenon is known as red disease.

“Don’t make clinical decisions based on bad data,” Dr. Sowka says.

But just because a value falls outside of a standard range, that does not necessarily mean a problem exists. This phenomenon is known as red disease.

“This is a new clinical non-entity,” Dr. Sowka says.

Conversely, there may be glaucomatous processes in a patient masquerading as non-disease. This is known as green disease.

Both of these outcomes tend to increase in prevalence when optometrists place too much trust in imaging tools and machines to make diagnoses. Often, the data inputs that make these decisions may be fallacious.

“Don’t make clinical decisions based on bad data,” Dr. Sowka says.
to explain what so-called “normal” IOP is, and that clinically ODs measure it only by an indirect means.

I told them both not to be concerned about the findings and advised the patient to return for a follow-up visit to include additional testing of pachymetry, gonioscopy, spectral-domain optical coherence tomography (SD-OCT) studies of each optic nerve, retinal nerve fiber layer (RNFL) and ganglion cell complex (GCC), and consideration of a visual field study.

I also asked that they make time to have the patient’s follow-up visit during a morning so that I am able to get a feel for how his IOP behaves throughout the day.

My hope is that pachymetry will be the most useful piece of information, and that it will show thicker-than-average central corneal thickness values.

**Wrapping up**

This patient encounter reminds me how fortunate I am to be practicing optometry in this day and age. Even if I thought the patient’s retinal nerve fibers looked pristine, a young patient with big cups and slightly elevated IOP requires an OD’s close attention and access to ancillary testing technology available through a new generation OCT studies.

Although the normative database on my particular instrument does not include patients younger than 18 years of age, I can still receive qualitative information through such a study.

My hope is that pachymetry will be the most useful piece of information, and that it will show thicker-than-average central corneal thickness values.

I am still hoping that pachymetry will give ODs the most information, for kids with big optic cups make me leery.

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**InDispensable**

**Komono launches Anton snow goggles**

**THE ANTON,** Komono’s first foray into winter sports, is named after Komono founder and ex-professional snowboarder Anton Janssens.

Using enhanced lenses and anti-slip rubber straps, the Anton is the first goggle to combine a perfect fit and ample protection with a fierce attitude, according to the company. Staying true to Komono’s roots of going off-piste, it adds superior design and a touch of playfulness to the skiwear category.

Referencing the practice of personalizing your board, every pair will come with replaceable patches that can be added or removed according to the wearer’s state of mind.
Ocular surface disease

CASE STUDY

Blood-derived serum tears go beyond conventional therapy

Biochemical similarities exist between a patient’s serum and natural tears

By Richard B. Mangan, OD, FAAO

A recent patient’s experience highlights how autologous serum tears can help heal the ocular surface and provide relief of dry eye symptoms.

Case presentation

A 53-year-old female presents on referral from her rheumatologist for a dry eye consultation. She has been under the care of her rheumatologist for rheumatoid arthritis (RA) and Sjögren’s syndrome (SS). She reports that she has been under the care of another eye doctor for several years. However, despite trying a number of different dry eye treatments, she continues to struggle throughout the day. Extended hours on the computer exacerbate her symptoms.

Risk factors for her dry eye disease include:

• Post-menopausal female
• Medications with a known drying effect—Zoloft (sertraline, Pfizer) and Benadryl (diphenhydramine, eJohnson & Johnson)
• Autoimmune disease (RA and secondary SS)
• > 4 hours of electronic device use each day.

Her current treatment regimen includes preservative-free Systane Ultra (Alcon) q3h, Systane Gel (Alcon) qhs, Restasis (cyclosporin, Allergan) bid, FML (fluorometholone, Allergan) 0.1% bid, and six-month extended-duration plugs in the lower punctum OU inserted approximately four months ago. She reports trying several contact lenses in the past, but she was unable to wear them for any extended period of time. Insertion and removal was challenging, so she ultimately gave up on them.

She also reports being prescribed Xiidra (lifitegrast, Novartis), but she says it was cost prohibitive.

The patient’s entrance testing showed best-corrected visual acuity (BCVA) of 20/20 OU. Meibography exhibited mild tortuous gland morphology but no gland dropout. Tear osmolarity scores were abnormal (314 OD, 323 OS). The patient also had a positive Schirmer tear test without use of topical anesthetic.

Biomicroscopy revealed scant (con-cave) tear film in both eyes. Lissamine green staining was positive for both the nasal and temporal conjunctiva as well as the central cornea OU with grade 2 staining (Figure 1).

The patient has 2-3+ central punctate epithelial keratitis (PEK) OU which was most evident with fluorescein. Remnants of the extended-duration plugs were evident in lower puncta in both eyes. Blink reflex was complete in both eyes.

Discussion

After I completed my assessment, I explained the severity of her condition and educated her on my recommended treatment.

Based on Dry Eye Workshop (DEWS) II guidelines, on a severity scale of 1 to 4, she would be considered to have Grade 3 dry eye disease.

While her autoimmune disease is the primary underlying cause of her signs and symptoms, her dry eye is likely exacerbated—at least to some degree—by the use of Zoloft and Benadryl.

Given her past and current therapies, and given her persistent signs and symptoms, I felt that autologous or allogenic serum eye drops, otherwise known as “serum tears” may be a good next step for her. I explained how important our own natural tears are to our ocular surface and corneal health.

Our natural tears are composed of key components not found in artificial tear products, such as epidermal growth factor (EGF), fibronectin, and vitamin A, which support the proliferation, maturation, migration, and differentiation of corneal and conjunctival epithelia.

We also know that serum contains IgG, lysozymes and complement, which have bacteriostatic properties. If these factors are low or missing, there is increased risk of persistent epithelial defects, blurred vision, infection, and scarring.

I explained that serum is derived from whole blood after the blood is donated by the patient (autologous serum), a family member (allogenic serum), or a blood donor (fresh frozen plasma [FFP] or ABO-ready allogenic serum). Using a variety of methods of blood collection, storage, centrifugation, filtration, and dilution, we are able to formulate serum tears in which the serum components closely mimic our own natural tears.

Autologous serum has been used for ocular surface disease since the mid 1980s with a track record for a variety of different ocular surface conditions, including SS-related dry eye disease.

However, there is debate about whether patients with secondary SS should use their own serum. Some evidence suggests that pro-inflammatory cytokines may be re-introduced to the eye—higher amounts of serum inflammatory markers have been identified in patients with secondary SS as compared to those with primary SS or age-matched controls.

I explained that, in my experience, there have been many success stories with autologous serum
in secondary-SS patients, but there may be merit to considering allogeneic serum.

The patient indicated that she had no family members in the immediate vicinity, and the thought of asking one of them to donate blood for her serum tears every three months would be an unreasonable request. This led to discussing FFP allogeneic serum eye drops.

**TABLE 1**

<table>
<thead>
<tr>
<th></th>
<th>TEARS</th>
<th>SERUM</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>pH</strong></td>
<td>7.4</td>
<td>7.4</td>
</tr>
<tr>
<td><strong>OSMOLARITY</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>EPIDERMAL GROWTH FACTOR (EGF; ng/ml)</strong></td>
<td>0.2-3.0</td>
<td>0.5</td>
</tr>
<tr>
<td><strong>TRANSFORMING GROWTH FACTOR BETA (TGF-B; ng/ml)</strong></td>
<td>2.0-10</td>
<td>6.0-33</td>
</tr>
<tr>
<td><strong>VITAMIN A (mg/ml)</strong></td>
<td>0.02</td>
<td>46</td>
</tr>
<tr>
<td><strong>LYSOZYME (mg/ml)</strong></td>
<td>1.4 (0.2)</td>
<td>6</td>
</tr>
<tr>
<td><strong>SURFACE IMMUNOGLOBULIN A (SigA; ug/ml)</strong></td>
<td>1190 (804)</td>
<td>2</td>
</tr>
<tr>
<td><strong>FIBRONECTIN (ug/ml)</strong></td>
<td>21</td>
<td>205</td>
</tr>
</tbody>
</table>


FFP serum tears are formulated from whole blood that is acquired through general blood donations at a blood bank or center. Unlike autologous serum, each donor is required to complete a blood donor questionnaire, and each donation is typed, cross-matched, and tested for infection (See box).

Testing is negative prior to the product being shipped. There also must be no previously detected red blood cell antibodies.

While donors can be male or female, female donors must have no history of pregnancy or they must be HLA antibody negative. Donors must be medicated free, including aspirin.

Once a request is submitted for serum, which must include the patient’s blood type (A, B, AB, or O), a match is made and serum tears are shipped to the patient’s regional collection facility for dispensing. This takes on average about two weeks. Approximately 650 single-use ampules will arrive packed in dry ice. Each ampule holds approximately six drops of serum.

According to Harritshøj and colleagues: “The eye is an immunologically privileged site, and ABO substances and HLA antigens are present on the cornea and conjunctiva. In this context, serum may contain high amounts of clinically relevant antibodies, such as ABO and HLA antibodies, which upon immune complex formation might activate complement and initiate inflammation. Furthermore, serum may contain high amounts of ABO substances that again might act as antigens and initiate immune complex-mediated inflammation. Therefore, we decided to produce allogeneic serum drops covering all four ABO types and providing patients with ABO-identical eye drops.”

I explained to the patient that the cost of FFP serum is about twice the cost of autologous serum for a three-month supply of tears. The advantage to allogeneic serum is that she would not have to personally give blood every three months.

After weighing the risks, benefits, and alternatives, we mutually agreed to start with 25 percent autologous serum eye drops (ASEDs) and re-assess after three months. Initial dosing will be QID, but I may need to increase it to Q2 to three hours, or switch to 50 percent ASEDs. If we determine serum tears are beneficial and worth staying on for an extended period of time, we can revisit the idea of FFP allogeneic serum tears.

The patient can expect to receive approximately 10 5mL bottles (3 to 4 mL fill) of ASEDs. Each bottle should last for seven to 10 days depending on the dosing regimen.

She was instructed on the importance of keeping her unused ASEDs stored in the freezer and keeping her active bottle stored in the refrigerator to reduce the risk of contamination. Under no circumstances is she allowed to share her ASEDs with others.

Once she starts ASEDs, she can discontinue Systane Ultra and Restasis. She can use her Systane Ultra, however, if she is traveling for a short period of time or if she runs out of serum. She was asked to decrease FML to once a day and continue Systane Ultra at bedtime.

While she was not asked to stop Zoloft or Benadryl use, she was educated on the adverse effects of antidepressants/anxiety agents and oral antihistamines can have on the ocular surface. She will discuss alternatives with her primary-care physician.

Follow-up visit was scheduled for six weeks.

**Follow-up**

The patient presented for follow-up as directed. She indicates that her blood draw and collection of serum tears went smoothly. She started the ASEDs approximately one month prior to the follow-up visit. She says that she takes one bottle...
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- Correlated Color Temperature, the temperature of a black body light source that would produce similar shade of white to the measurement—how blue or red a white light appears.
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Ocular surface disease

Autologous tears

Continued from page 21

to work with her and stores it in the refrigerator there. She uses the drops about every three hours because they are soothing to her eyes.

She says that she can already tell a difference in her comfort level and for the first time in a long time, she is “less aware of her eyes” than before. Her eyes still feel dry, but it is more tolerable.

Slit-lamp biomicroscopy showed modest improvement in surface staining of the conjunctiva and cornea. However, at her three-month follow-up visit, there was marked improvement in surface staining OU. While she still exhibited some central corneal staining, there was at least a 30 to 40 percent improvement OU.

The patient reported an improvement in the quality of her vision and says it does not fluctuate as much. Given this, the patient elected to stay the course with her current treatment regimen, including another round of 25 percent autologous serum.

Conclusion

Human serum contains a plethora of bioactive elements naturally released by activated platelets, which has been shown to offer a regenerative effect on the understanding that there are biochemical similarities between an individual’s serum and natural tears.

More studies are being conducted in an effort to standardize protocols in procurement and compounding of these products.

Access to serum tears also continues to evolve. While more compounding pharmacies are working with blood centers to efficiently produce serum tears, companies such as Vital Tears have mobile blood units that cover just about every ZIP code in the United States. In some cases, Vital Tears can arrange to collect blood at the patient’s home residence, then ship or deliver the final product within one to two weeks.

Who knows where we will be 10 years from now with blood-derived products in the fight against dry eye disease. What we do know is that currently, despite variability in how serum is derived or prepared, most clinical studies on autologous or allogenic serum confirm that serum eye drop therapy is effective in corneal healing and reducing ocular symptoms. When conventional therapy has not met expectations for moderate to advanced dry eye patients, serum tears may make the difference.

REFERENCES


Toxoplasmosis retinochoroiditis: A pictorial review

Continued from page 1

Clinical signs of the condition include localized area(s) of retinal whitening in acute phase, with overlying vitreous cells.6-7 (Figures 1-3). Retinal vasculitis can be seen typically near the infected region(s) (Figure 3). Retinal arterial occlusion is among the possible findings8 (Figure 4). In inactive or recurrent cases, pigmented retinochoroidal lesion(s) can have overlying and diffuse vitreous opacification (Figure 5).6,7 In recalcitrant cases, multiple satellite active and inactive lesions with variable degrees of vitreous involvement are seen (Figure 5). Kyrielleis plaques (Figure 4) are a rare inflammatory component, although they are most often associated with active toxoplasmosis retinochoroiditis and have also been associated with tuberculosis, treponema pallidum, cytomegalovirus, and varicella-zoster virus infections.8

Clinical signs and symptoms of usually non-granulomatous iridocyclitis can be present as well. Differential diagnosis of toxoplasmosis retinitis versus other infectious etiologies, such as herpes or cytomegalovirus, is crucial. Whereas toxoplasmosis may be a slowly progressive disease, conditions such as acute retinal necrosis (ARN), which is speculated to be caused by herpes viruses, is a rapidly progressive condition with a much more devastating visual outcome.

In addition to history and physical and retinal diagnostic imaging, serological testing to detect
Offer IPL as a treatment for MGD and dry eye disease

This option treats six conditions related to development of MGD

By Greg Hill

Intense pulsed light (IPL) technology has the potential to revolutionize dry eye management and ocular surface disease. Selina McGee, OD, FAAO, of Edmond, OK, explored the emerging world of IPL and its implications for ocular healthcare delivery at the 2019 American Academy of Optometry meeting in Orlando.

Optometric applications of IPL

IPL is one of the most popular cosmetic procedures for treating facial skin conditions, but new applications of the technology are emerging in optometry. Chief among these is the use of IPL to treat meibomian gland dysfunction (MGD), dry eye disease (DED), and rosacea.

IPL stimulates facial tissue through controlled light pulses, usually used to target chromophores in the melanin or blood. The light emitted during an IPL procedure is absorbed by the oxyhemoglobin, creating heat and coagulating the vessel to reduce its appearance below the skin.

“IPL is broad spectrum; it’s non-monochromatic, non-coherent,” Dr. McGee says.

Modern IPL devices offer light therapies at wavelengths from 450 nm up to nearly 1200 nm to treat various skin types and medical conditions.

Given that there are over 80 million Americans living with some type of venous disorder, 80 percent of which are cosmetic, it is clear why IPL has seen so much success in cosmetic dermatology.

According to Dr. McGee, IPL shows promise in the treatment of more confounding optometric conditions—such as MGD and DED.

Managing dry eye with IPL

As ODs know, MGD is a chronic, diffuse abnormality of the meibomian glands resulting in reduced tear film quality, inflammation, and ocular surface disease.

“It is a progressive disease,” Dr. McGee says.

The link between rosacea and MGD is well established, with 80 percent of rosacea patients suffering from symptoms of MGD. 1,2

Although MGD is complex and multifactorial, MGD arises from a combination of these conditions:

- Primary obstructive hyperkeratinisation
- Abnormal meibomian secretion
- Eyelid inflammation
- Corneal conjunctival inflammation
- Epithelial damage
- Ocular bacteria

“It’s a vicious cycle,” Dr. McGee says.

When one of these symptoms appears, it tends to create additional complications that make the overall condition harder to treat. However, IPL offers a comprehensive approach.

“When you look at intense pulsed light, it hits all six,” she says.

IPL treatment

Although IPL has applications in optometry, it is a new treatment modality that ODs need to explore and understand. IPL’s light stimulation can produce unintended side effects when handled improperly.

The primary concern is selecting the appropriate wavelength of light to adequately treat the patient.

“When we are performing IPL, we have to look at how to type the skin,” Dr. McGee says.

ODs should use the Fitzpatrick Scale to determine which level of light energy is safe for various skin types. IPL treatment can be adjusted for light energy, wavelength, pulse rate, and pulse duration to account for the patient’s condition.

While patients usually experience itching and irritation at the treatment site after therapy, the tools themselves contain safeguards to prevent undue exposure.

“Different filters block anything below a particular wavelength,” Dr. McGee says.

However, light energy isn’t the only concern. Dr. McGee says that other contraindications may make a patient unsuitable for an IPL treatment.

- Presence of visible lesions, cold sores, or dysplastic nevi
- Melasma
- Active infections
- Certain drugs (such as Accutane [isotretinoin])
- Visible tan or excess melanin

Pre-treatment education

Part of managing MGD, both with IPL and through traditional therapies, involves educating the patient and establishing expectations.

“You have to teach your patients that this is a chronic disease,” Dr. McGee says.

Treatment of MGD is a step-by-step approach that will, ideally, result in returning the front surface of the eye back to a state of homeostasis. This process always takes time, even with more modern therapies like IPL.

Dr. McGee says that IPL therapies are usually performed in three to five sessions spaced across weeks or months. Six-month or annual maintenance appointments may be necessary for continued results, depending on the patient.

There is no silver bullet solution for curing MGD or dry eye, but IPL marks an important milestone in treatment opportunities.

“To have another tool in our arsenal that treats all six of those pieces is exciting,” Dr. McGee says.

Diagnosing dry eye

Before IPL treatment can begin, ODs must make sure that they know what they are treating and the extent of the condition, when possible. What may appear to be DED may be something else entirely.

“A lot of things can mimic dry eye,” Dr. McGee says. “Not everything is dry eye.”

She advises that ODs take a methodical, step-by-step approach to uncovering potential challenges during the early stages of the patient’s examination.

Generally, it is to the benefit of both the provider and patient to keep things simple and straightforward. Dr. McGee recommends several tools to use when making an assessment:

- Standardized Patient Evaluation of Eye Dryness (SPEED) questionnaire
- Ocular Surface Disease Index (OSDI) questionnaire
- Medical history/medication use
- History of contact lens wear
- Lid seal and physical assessment
- Makeup use and composition

A system that uncovers which patients may have MGD or dry eye symptoms—even when they are seen for other complaints—is crucial, Dr. McGee says.

“Keep it simple, ask the right questions, look at a risk factor analysis, get through diagnostics, then classify and treat the disease,” she says.

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How to determine treatment for a patient with a Roth spot

Discovering the underlying cause of a white-centered hemorrhage is key to management

By Steven Ferrucci, OD, FAAO; Carol Fong, OD; and Brenda Yeh, OD, FAAO

Occasionally, the primary-care OD may encounter a Roth spot, or a white centered hemorrhage. Classically associated with bacterial endocarditis, leukemia and anemia, these lesions are actually linked to a myriad of systemic conditions, often leaving the provider wondering what tests should be ordered or what systemic work-up is needed.

The following is a case of a patient who presented with a Roth spot and the subsequent management.

Case report

A 55-year-old male presented to the clinic for a comprehensive eye exam with a chief complaint of blurry vision at distance and near with his habitual bifocal glasses.

His pertinent medical history included hypertension and type 2 diabetes mellitus for approximately 10 years. He had been on medications for his diabetes previously but was taken off a few years ago; he now controlled his diabetes with diet and exercise.

His blood pressure was measured as 131/84 mm Hg. The patient had a recent echocardiogram, performed approximately six months previously, which was normal per physician note. The patient was referred back to his primary-care physician who re-initiated oral treatment for his diabetes and discussed ways to lower the patient’s blood pressure.

The patient returned for diluted fundus examination (DFE) follow-up visit three months later with no subjective complaints. Upon dilated examination, the white centered hemorrhage had completely resolved. The patient also continued to deny fever, shortness of breath, or recent infections.

Based on the review of systems, lack of acute symptomology, medical history, and lab test results, it was determined the isolated white centered hemorrhage was likely associated with the patient’s diabetes. The patient was scheduled for a six-month return visit.

Discussion

A Roth spot is any round to slightly oval hemorrhage with a solitary, homogenous, paler, round center completely surrounded by the hemorrhage.1

Background

Early investigators thought the white centers represented infected embolic foci of septic infarites or represented a concentration of leukocytes, which is true in cases of leukemia and in some cases of bacterial endocarditis.2 However, the white center actually represents a fibrin-platelet thrombus.3 It typically results from the rupture of retinal capillaries and the extrusion of whole blood.

Under normal circumstances, retinal capillary endothelium is impermeable to the transmission of whole blood, but with any anoxic event or sudden elevation in venous pressure, or both, the capillaries rupture and whole blood is extruded.4

Subsequent reparation leads to platelet adhesion and coagulation cascade at the site of the damaged endothelium and results in the formation of a fibrin-platelet thrombus.5 Morphologically, this thrombus appears as a pale white lesion in the center of the hemorrhage.

A diverse list of conditions can lead to retinal capillary rupture and result in white-centered hemorrhages (see box). They can be subclassified according to underlying mechanism, such as thrombocytopenia, elevated venous pressure (Valsalva phenomenon), ischemia, or capillary fragility.6,7

Thrombocytopenia is often associated with subacute bacterial endocarditis and acute leukemia, in which the body cannot produce ample platelets and leads to internal and external bleeding.8 Elevated venous pressure is seen with mothers who have undergone traumatic deliveries, neonatal birth trauma, battered children/shaken baby syndrome, intracranial hemorrhage from arteriovenous malformation, or prolonged intubation during anesthesia.9

Ischemic events can include anemia, anoxia, or carbon monoxide poisoning.10 Capillary fragility, as is the case with our patient, is often associated with diabetic retinopathy, hypertensive retinopathy, oral contraceptives, or idiopathic cases.2

Incidence with diabetes

White-centered hemorrhages are relatively common to see in cases associated with diabetes.

In one particular study, 215 diabetic patients (430 eyes) with early proliferative retinopathy, moderate to severe non-proliferative retinopathy, and/or diabetic macular edema in each eye were...
evaluated for the presence of such white-centered hemorrhages. 7

The study found that 15.6 percent of these eyes demonstrated at least one white-centered hemorrhage, and 4.9 percent of the eyes showed five or more white-centered hemorrhages. In addition, there was no statistically significant difference in incidence of macular capillary injury between those with and without concurrent white-centered hemorrhages. 7

The study also found that there was no significantly higher prevalence of systemic or hematologic disorders in patients with diabetic retinopathy and white-centered hemorrhages. 7

More specifically, there was no statistically significant difference between patients with and without white-centered hemorrhages in regard to the presence of increased systolic or diastolic pressure, hemoglobin levels, leukocyte counts, platelet numbers, increased serum creatinine values, or abnormal coagulation profiles. 7

**Differential diagnosis**

Even though our patient’s Roth spot presented other retinal findings consistent with diabetic retinopathy, it is still imperative to rule out all other possible etiologies for the isolated white-centered hemorrhage before concluding capillary fragility as a result of diabetes mellitus as the most likely culprit. Owing to the plethora of possible etiologies for the white-centered hemorrhage, it is imperative to match symptomatology, ocular signs, laboratory tests, and confirmatory results in order to reach a proper underlying diagnosis. For example, symptoms including fever, weakness, ecchymosis, hematuria, and/or infections along with ocular signs of white-centered hemorrhages, tortuous engorged vessels, vitreous hemorrhage, retinal detachment, retinal edema, and cotton wool spots, would indicate necessary lab testing with CBC with white blood cell (WBC) differential to rule out acute leukemia. A normal or decreased WBC count and WBC differential showings of predominantly immature cells would definitively confirm such diagnosis. 1

Common diabetes symptoms include weakness, weight loss, polyphagia, polydipsia, and/or polyuria. Ocular signs include diabetic retinopathy, fluctuations in refractive error, diplopia, optic atrophy, optic neuritis, and white-centered hemorrhages. Lab tests imperative to perform include fasting blood sugar and glucose tolerance test. 1

**Management**

Given our patient’s lab results of elevated blood glucose, personal medical history, and lack of acute infectious symptoms, it was appropriate to assume the underlying etiology was diabetes mellitus for the isolated white-centered hemorrhage.

The primary-care physician was notified of this retinal finding to consider the possibility of re-initiating medication for his diabetes, which is what ultimately happened.

Management for Roth spots is influenced by their underlying cause. The optometrist should refer patients to the appropriate physician in order to treat the underlying disease process. However, there is no specific treatment for the white-centered hemorrhage itself; it usually self-resolves within six weeks. 8 Patients who present with these non-specific lesions require a prompt comprehensive evaluation to determine the cause. Once it is determined, treatment for the underlying etiology is the priority. 9

**Conclusion**

Our patient’s isolated presentation of a Roth spot showcases the strong link between ocular and systemic health. Although there is no specific treatment for the lesion itself, it is of paramount importance that the clinician promptly performs a thorough review of systems and orders the appropriate lab testing to determine the lesion’s underlying etiology and initiate treatment for that condition. 10
Determine risk for hydroxychloroquine retinal toxicity

Guidelines highlight the need for screening for harm from a commonly used drug

By Selina R. McGee, OD, FAAO

A 57-year-old Caucasian female presented for exam with the complaint of blurry vision. She reported that the blurriness was in both eyes, and it was slowly progressive over the past few months.

She had a medical history of high blood pressure, high cholesterol, and rheumatoid arthritis.

She was currently taking 81 mg aspirin (Lipitor, Pfizer), Centrum Silver multivitamin, fish oil, hydroxychloroquine (Plaquenil, Concordia) 200 mg OD, isosorbide mononitrate (Indur, Hokma), levetiracetam (Keppra, Pfizer), Nitrostat (nitroglycerin, Pfizer), Restasis (cyclosporin, Allergan), Ranexa (ranolazine, Gilead), Trexall (methotrexate, Teva), citalopram (Cipralex, Forest Labs), losartan/hydrochlorothiazide (Hyzaar, Merck), sulfamethoxazole/trimethoprim (Bactrim DS, , and topiramate (Trokodendri XR, Ortho-McNeil).

Her visual acuity with habitual Rx at distance was 20/40 OD and 20/50 OS, while at near was 20/40. Pinhole showed no improvement OD with OS improving to 20/40. Pupils were equal, round, and reactive to light; no afferent pupil defect was noted OU. Extraocular motility was full with no restrictions OU. Intraocular pressures (IOP) by Goldmann tonometry were 14 mm Hg OD and 13 mm Hg OS at 15:01 pm. Slit-lamp biomicroscopy revealed dermatochalasia. The cornea in both eyes was clear and anterior chambers were deep and quiet OU. Angles were 4×4 using the Von Herrick method.

Pupils were dilated with one drop 1% tropicamide and one drop 2.5% phenylephrine. Posterior exam showed 1+ nuclear sclerotic of the lenses OU. Vitreous was clear of cell OU. Fundus exam showed OD and OS optic nerves were pink and distinct with a 0.15/0.15 cup-to-disc ratio. The macula in each eye exhibited a flat appearance with absent foveal reflexes. Peripheral retina was unremarkable OU. Fundus photos, visual field 10-2 were ordered as well as a spectral domain ocular coherence tomography (SD-OCT) (see Figures 1-3).

The appearance of disruption of the photoreceptor integrity line, perifoveal thinning, and paracentral scotomas confirmed a high likelihood of toxicity in this patient. She was asked to stop the medication immediately, which she did. The patient was educated that her vision could worsen until the medication was completely washed out of her system. A referral for a fluorescein angiography (FA) for confirmation of bull’s-eye maculopathy was ordered.

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Follow up

The patient was seen three weeks later for the consult and FA.

Uncorrected distance acuity OD and OS was 20/70, and pinhole was 20/50 OD and OS. IOP was measured at 14 and 12 mm Hg in OD and OS. Anterior segment examination was normal OU.

The patient was again dilated with 1% tropicamide and 2.5% phenylephrine. Vitreous and optic nerve were normal. Macula showed very slight bull’s-eye macular changes. FA showed subtle bull’s-eye maculopathy, and the repeated OCT showed slight parafoveal OCT ellipsoid zone (EZ) loss consistent with Plaquenil toxicity.

She had already stopped the medication and was again educated that further progression and vision loss could happen. Vision loss did indeed stabilize at 20/50 about six months later.

Discussion

Hydroxychloroquine is a commonly used medication for rheumatoid arthritis, systemic lupus erythematosus, discoid lupus, Sjögren syndrome, juvenile idiopathic arthritis, other mixed connective tissue autoimmune conditions, non-small cell lung cancer, and graft-versus-host disease (GVHD), to name a few.

In 2011, guidelines warned about toxicity risk at a cumulative dose of 1000 g or exceeding 6.5 mg/kg body weight/day. For a typical patient, most critical determinant of risk equals current dose and duration of use varied widely. The new guidelines that came out in 2016 illustrated the most critical determinant of risk equals current excessive daily dose by actual weight in the following manner: Under 5 mg/kg= 2 percent risk over 10 years with an increase sharply to 20 percent at 20 years. Furthermore, at 800 mg dosing, the daily risk would be 25 to 40 percent in one to two years.

Who else is at high risk? Patients who experience chronic renal disease with concomitant use of Plaquenil often are at high risk for toxicity.

TAKE-HOME MESSAGE. New guidelines provide information on how to decipher the likelihood of hydroxychloroquine toxicity in order to prevent disease onset and progression.

See Toxicity on page 31
positive titers for these conditions is important for confirmation of diagnosis and appropriate treatment. Serology for pathogens such as *T. gondii* includes testing for immunoglobulins. Positive and abnormally high IgM suggests recent infection and levels may return to normal soon after, while IgG appears soon after infection and remains positive throughout life. IgA may be helpful to distinguish congenital cases.3,6

**Treatment**
Small lesions not involving the macula or optic nerve with minimal vitritis may not require treatment. Traditional treatment for toxoplasmosis retinochoroiditis is a combination of sulfonamides such as sulfadiazine and pyrimethamine, an antiparasitic agent also used for malaria. There is a commercially available combination of pyrimethamine/sulfadoxine (Fansidar).6,7,9 Folinic acid is given concurrently to reduce pyrimethamine-related hematologic adverse reactions. This regimen is sometimes cumbersome and not always commercially readily available; therefore, alternatively, sulfamethoxazole/trimethoprim 800/160 mg (Bactrim DS) can be prescribed; azithromycin can be added to this regimen for better coverage.24 Long-term sulfamethoxazole/trimethoprim can be used for prophylaxis and/or to reduce recurrence of toxoplasmosis retinochoroiditis.11 Prescribers must bear in mind that long-term use of antibiotics may result in *Clostridium difficile* (*C. diff*) infection, a serious and potentially deadly gastrointestinal condition.12 For patients allergic to sulfonamides or non-responsive to the above oral medications, alternative therapy is oral and/or intravitreal clindamycin injections.13

Topical, systemic, or periocular steroids in conjunction with antimicrobial therapy can reduce the inflammatory component, improving patients’ symptoms while reducing inflammatory tissue scarring.9 In severe cases, with excessive retinal and particularly optic nerve involvement, presence of epiretinal membrane or excessive vitritis, pars plana vitrectomy (PPV) with membrane peel and intraoperative antimicrobial injection is a viable option. However, reactivation of toxoplasmosis after PPV has also been reported in the literature.14

**Conclusion**
*Toxoplasmosis gondii* is a widely prevalent human infection2 and a common cause of infectious retinal involvement of *Toxoplasmosis gondii* infection can be the cause of considerable vision loss. Prompt diagnosis and proper treatment can significantly improve the patient’s outcome.

**Figures**

**Figure 3.**
A: An active lesion is noted in the inferonasal mid-retinal periphery. Vascular sheathing in the region is indicative of diffuse vasculitis in the nasal retina. B: Involvement of the superficial retina is noted via optical coherence topography (OCT) with overlying vitreous cells.

**Figure 4.**
A: The patient is seropositive for alive toxoplasmosis with a large active lesion and diffuse arterial occlusion. B,C: Kyrieleis plaques are seen (B) in these lesions and the arterial occlusion is also notable on fluorescein angiography (C).
Toxoplasmosis

Continued from page 29

Ocular involvement of this infection can be the cause of considerable vision loss. Prompt diagnosis and proper treatment can significantly improve the patient’s outcome.1,2

REFERENCES

Differential diagnosis of toxoplasmosis retinitis versus other infectious etiologies, such as herpes or cytomegalovirus, is crucial.

Prompt diagnosis and proper treatment can significantly improve the patient’s outcome.3,4

FIGURE 5. Initial presentation typical solitary lesion (A1) superficial retinal involvement and retinal edema on OCT (A2), while fluorescein angiography (A3) reveals diffuse leakage and regional vasculitis. The initial lesion becomes inactive (B1, B2) with sulfamethoxazole/trimethoprim oral treatment and remained inactive for seven years. The second lesion (C1, C2) was treated successfully with same regimen for a longer duration after remission (D1, D2). Within one year a satellite lesion presented while the patient developed intolerance and subsequently treated with multiple doses of intravitreal clindamycin. As the lesion undergoes remission (E), a number of residual vitreous opacities persist (arrows).
Toxicity
Continued from page 28

of tamoxifen have a five-fold increase in toxicity. Additionally, patients who already have retinal and macular disease may masquerade or be subclinical simply because it can be very difficult to follow these patients with current testing strategies. It is prudent to take notice of these additional risk factors carefully when screening patients.

Appropriate screen testing for patients is imperative since, once vision is lost, it is not reversible and may progress even after the medication has been discontinued. A baseline exam should be performed within the first year of starting therapy, and SD-OCT with visual fields would offer clinical utility as a screening technique. While we naturally would use a 10-2 visual field for most cases, the exception would be Asian patients because the condition can manifest beyond the macula, necessitating wider-range test strategies (24-2 or 30-2 visual fields).

Screening frequency can be performed on a five-year basis unless there are heightened risk factors, in which case visual fields should be performed every year. Other useful screening tests are multifocal electroretinogram (mERG) and fundus autofluorescence (FAF). It is not advised and/or is no longer standard of care to order fundus photos, time-domain OCT, FA, full-field ERG, Amsler grids, color vision testing, or electrooculography (EOG) to screen for Plaquenil toxicity. Some of these tests can show photoreceptor damage, but only in the late stages of the disease.

REFERENCES
A 62-year-old male came to my office recently complaining of blurred vision for the last two weeks.

Earlier that day, he had been diagnosed with atrial fibrillation by his primary-care practitioner (PCP), and was prescribed a systemic beta blocker (carvedilol, Coreg) and was referred to a cardiologist.

His thyroid function studies had also been “slightly abnormal”—a longstanding issue. He complained about the blurry vision to his PCP, who told him it was likely due to hypothyroidism.

The patient’s previous medical history included having been treated for prostate cancer two years ago as well as a recent prostate specific antigen (PSA) value of zero.

Upon questioning, he noted that he had been under great stress during the holidays, and had been losing weight despite excess consumption of calories.

He also said that he had been drinking more water than usual. I asked him if his blood glucose had been measured earlier that day, and he was not sure.

With his most recent glasses (updated months earlier), the patient was 20/200 in each eye, which was easily corrected to 20/20 with a 3.00 D increase in myopic correction.

The patient is 73 inches tall and weighs 165 lbs, giving him a body mass index (BMI) of 21.77 kg/m².

I checked his blood glucose in-office, which measured 515 mg/dl. A point-of-care glycosylated hemoglobin (A1C) was completed (measuring 14 percent, equivalent to an estimated mean glucose of 250 mg/dl over the last eight to 12 weeks). Clearly, this patient has diabetes.

Game over—right? Nothing more to do but refer the patient back to the PCP and get started on treatment, right?

Wrong.

Diagnosis reveals ODs’ key role in diabetes identification

Extensive testing, consultation with primary-care doctor key to proper treatment

LADA

It is estimated that around 10 percent of adults diagnosed with type 2 diabetes actually have LADA. The disease is characterized by a relatively slower autoimmune destruction of insulin-producing pancreatic beta cells than in “classic” type 1 diabetes seen in younger patients.1

Recent analysis has suggested that half of all type 1 diabetes cases are diagnosed after the age of 30, rendering the moniker “juvenile-onset diabetes” obsolete.2

C-peptide is a by-product of pro-insulin cleavage and, as such, is an insensitive marker of patients’ ability to produce their own insulin. It also serves as an outstanding discriminator between type 1 and type 2 diabetes when the exact diagnosis is in doubt.3

GAD

GAD is an enzyme that catalyzes the conversion of glutamate to the neurotransmitter, gamma-aminobutyric acid (GABA) and carbon dioxide. In mammals, GAD has two isoforms: GAD65 and GAD67.

In both type 1 diabetes and LADA, GAD65 and GAD67 are known to be targeted by autoantibodies—which, when positive in tandem with a lower or non-existent C-peptide, is diagnostic of autoimmune diabetes.

Other autoantibodies may also be found, including those to pancreatic islet-cell antibodies (ICA). Of note, autoimmune thyroid disease is also associated with GAD autoantibodies and might account for hypothyroidism in this particular patient.4

Pancreatic cancer is a known cause of secondary diabetes resulting from localized destruction of beta cells. It may manifest as profound hyperglycemia and weight loss with classic diabetes symptoms (excessive thirst and frequent urination), just as in type 1 diabetes and LADA.5

Had this patient’s GAD65 results been normal, he would have been referred immediately to oncology.

REFERENCES

Don’t shy away from steroid use for surgery patients

Treating inflammation on anterior surface proves to be effective post-surgery

Hold your breath, I am about to show my age—not that my follicle sparse dome is not enough of an indicator. In 1994 while I was doing my residency at a secondary ophthalmic surgery center, I worked in a surgical center.

This center was on the cutting edge of all refractive and cataract surgical procedures, either from a clinical trial avenue or as the first to implement. Being that the clinic was in Arizona, a likely office location was in the Sun City area.

There was an established ophthalmologist with a large following in the Sun City locale. This MD would actually fly in one week a month from Chicago to continue his practice in Arizona.

Although my interactions with him were limited, I recall one conversation that has resonated in my clinical acumen.

Sound advice
He boldly expressed, through a mouth full of sugar cookie and coffee, “What is with you and your optometry colleagues being so afraid to use steroids?”

Boom. Life changer.

As this was 25 years ago, the notion of using steroids was considered high-risk and taboo—a sacrament unless an OD absolutely knew there was inflammation.

Rule out everything first, start an antibiotic, take a blood test, count backwards from 1,000, and then ask: Should I really?

Moreover, this was prior to any real advancements (in the U.S.) in the corneal refractive surgery area.

The steroid of choice back then was prednisolone acetate (Pred Forte, Allergan) and loteprednol (Lotemax, Alrex; Baush + Lomb). The steroid of choice back then was prednisolone acetate (Pred Forte, Allergan) and loteprednol (Lotemax, Alrex; Baush + Lomb).

However, it is known that subclinical and clinical inflammation can limit visual acuity potential or have transient effects on the cornea, steroids are a necessity.

Surgical patients
Another area where steroids have made an impact is in the way refractive and cataract refractive surgical patients are managed.

In the late 1990s—when photorefractive keratectomy (PRK) and laser-assisted in situ keratomileusis (LASIK) were a burgeoning surgery—ODs relied on prednisolone acetate to be the workhorse.

Yet, for patients who developed corneal haze secondary to PRK/epi-LASIK, ODs also had to work with an increased intraocular pressure (IOP) and potential glaucomatous damage.

LASIK is also prone to the sequelae of steroids. In fact, there have been cases of secondary glaucoma reported due to an increase in IOP from a steroid.

Extreme elevation induced fluid to fill under the flap. Subsequently, these patients had IOP measurements within normal limits, since the tonometer was bouncing off the fluid under the flap.

The Ocular Response Analyzer ([ORA] Reichert) can be used to avoid mistaking IOP post-surgery. This tightrope was balanced by the addition of loteprednol (Lotemax, Alrex; Bausch + Lomb). The ester-based steroid was able to be broken down faster and showed fewer IOP spikes.

Because refractive surgery induces inflammation that can limit visual acuity potential or have transient effects on the cornea, steroids are a necessity.

Steroids today
This is also true of modern-day cataract surgery. The use of the femtosecond laser has placed a safety net of predictability for cataract patients—particularly those with a more dense lens. The laser takes away unnecessary phacoemulsification that can induce a greater internal inflammation.

Yet ODs continue to look for opportunities to make this healing process faster and safer. Bausch + Lomb took loteprednol to submicron particle size and put Lotemax SM (loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension) on the market.

Lotemax SM was also designed to be patient-friendly with the moisturizing ingredients glycerin and propylene glycol, a pH close to that of human tears and the lowest preservative percentage (0.003% benzalkonium chloride), in a loteprednol etabonate formulation.

The same was done by Kala Pharmaceuticals with the introduction of its steroid Inveltys (loteprednol etabonate ophthalmic suspension 1%), which utilized Kala’s proprietary AMPLIFY Drug Delivery Technology to enhance penetration into target tissues of the eye.

Inveltys boasts a bid dosing, which can be a benefit for patient compliance. This does not take into account tried-and-true steroids such as Pred Forte and Durezol (difuroprednate ophthalmic emulsion, Novartis).

LASIK is also prone to the sequelae of steroids. In fact, there have been cases of secondary glaucoma reported due to an increase in IOP from a steroid.

Conclusion
There are now more drugs to personalize the anti-inflammatory drop of choice. This is exemplified when looking at a procedure such as the Kamra Inlay (CorneaGen). This inlay works best when the cornea is free of edema or inflammation.

However, it is known that subclinical and clinical inflammation follows patients in their daily activities, especially after surgery. ODs can now use effective penetrating steroids, less IOP spiking, and better dosing for these patients for a more prolonged taper.

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Selina McGee, OD, FAAO  President of the Oklahoma Association of Optometric Physicians

Aesthetics, Irish whisky, legislation, Master Gardener

Why don’t more ODs get involved in legislative changes?

I had a mentor when I started optometry school—Dr. George Foster was our dean. The first day of optometry school the conversation was around how important it was to be involved. If anyone has ever heard Dr. Foster’s three-legged stool talk, the school consists of our school and our state, the association and the members, and then the Board of Examiners. If any part of the three-legged stool teeters, the stool falls over. I had no idea optometry was such a heavily legislated profession. I learned very quickly because in 1998 we went to battle over our laser law. I hit the ground running with that knowledge, and I have never looked back. The fact that I’m president of our association and I spend as much time lobbying as I do anything else has been an interesting journey.

What prompted you to become a Master Gardener? My grandmother and my mother have heavily green thumbs, so growing up we always had a huge garden and a beautiful yard. It was certainly passed down. My oldest daughter, and I thought, “If I don’t do this now, I’ll never get this done.” I do a lot of woody ornamentals. We have a huge herb garden and tomatoes. Certification is a four-month long class session, one day a week. You spend another 60 hours at their phone bank and answer questions that people call in about it. It’s community service, but once you get through it you are considered a Master Gardener.

What’s something about optometry you’d like to change? Optometry historically has not done a good enough job about how comprehensive eye care is. That is one thing we have to change in the public space. The second piece is there is going to be a huge gap in care over the next 10 years that optometry has to fill. If we don’t step up to the plate, someone’s going to fill it for us. We have to continue legislative battles with ophthalmology so those symbiotic relationships are truly symbiotic. You have to build that trust, and there are too many instances of trust breaking over the years because of turf wars. It’s going to have to come one-on-one with the surgeons that you work with.

How do you see your role as an optometrist changing in the next 10 years? I think we are going to build on what we have done. I see stronger pillars on the medical side because of the way patient demographics are changing. The days of selling glasses and doing refractions are coming to an end, if not already. Over the next 10 years I would like to expand what we can do and have more physicians and comfortable to do procedures that make sense for patients and nationwide optometry.

What’s your guilty pleasure food? Three years ago, I went to Ireland and I tried Irish whisky. When I came home, I decided to explore the entire whiskey world. That morphed into bourbon, Irish whisky, Japanese whisky, etc. That’s my guilty pleasure.

What’s the craziest thing you’ve ever done? When I spent the summer in Pennsylvania with two optometrists and decided that I wanted to do this the rest of my life. At the time I was playing softball at a junior college in Kansas. I called my coach two weeks before school started and said I’m not coming back. I applied to go undergrad at Northeastern State University because I thought if I was already there I would have a better shot of getting into optometry school. I was accepted about a week before school started. I picked up my stuff at home, drove to Oklahoma, and started at NSU the next week completely sight unseen. —Vernon Trollinger

What is your role as an optometrist changing in the next 10 years? I think we are going to build on what we have done. I see stronger pillars on the medical side because of the way patient demographics are changing. The days of selling glasses and doing refractions are coming to an end, if not already. Over the next 10 years I would like to expand what we can do and have more physicians and comfortable to do procedures that make sense for patients and nationwide optometry.
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Treatment for ocular hypertension and glaucoma is usually initiated with medical therapy, and newer drugs with novel mechanisms of action are now available, including the nitric oxide (NO)-donating prostaglandin F2α analogue (PGA) latanoprostene bunod (LBN). In this activity, the role of NO in glaucoma and the effects of the NO-donating moiety and the PGA component of LBN on IOP lowering are discussed.

EDUCATIONAL HIGHLIGHTS:
• Descriptions of the NO pathway and the role of NO in relation to glaucoma
• Summaries of pivotal trial data for the newest medical therapies for glaucoma
• Case-based discussion utilizing the new medical treatment option in patients with ocular hypertension and open-angle glaucoma

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COPE approved for 1.5 credits for optometrists
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COPE Course Category: Glaucoma

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CE MONOGRAPH

Navigating New Approaches for Glaucoma Management
THE ROLE OF NITRIC OXIDE

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LEARNING METHOD AND MEDIUM
This educational activity consists of a supplement and fifteen (15) study questions. The participant should, in order, read the learning objectives contained at the beginning of this supplement, read the supplement, answer all questions in the post test, and complete the Activity Evaluation/Credit Request form. To receive credit for this activity, please follow the instructions provided on the post test and Activity Evaluation/Credit Request form. This educational activity should take a maximum of 1.5 hours to complete.

CONTENT SOURCE
This continuing education (CE) activity captures content from a regional dinner meeting series.

ACTIVITY DESCRIPTION
To address the educational needs of optometrists, this case-based program will focus on elucidating the role of nitric oxide in glaucomatous eyes, including treatment strategies that use nitric oxide's mechanism of action on the trabecular meshwork to increase aqueous humor outflow and to achieve target intraocular pressure levels via new therapeutic options. Case discussions will interpret clinically relevant data supporting the efficacy and safety of this nitric oxide–donating treatment option. The desired results of this activity are for optometrists to improve their management of patients with glaucoma early in the disease process when outflow treatments can be most effective in helping prevent glaucoma progression.

TARGET AUDIENCE
This educational activity is intended for optometrists.

LEARNING OBJECTIVES
Upon completion of this activity, participants will be better able to:
• Describe the downstream signaling effects of nitric oxide in relation to glaucoma
• Discuss the effects of nitric oxide on the trabecular meshwork
• Apply data from clinical trials on nitric oxide–donating agent(s) for lowering intraocular pressure

ACCREDITATION STATEMENT
COPE approved for 1.5 CE credits for optometrists.
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INTRODUCTION

Glaucoma is a progressive optic neuropathy that is estimated to affect more than 3 million Americans and to account for up to 12% of all cases of blindness. Intraocular pressure (IOP) is the only modifiable risk factor for glaucoma, and results from multiple large prospective randomized controlled clinical trials have proven the benefit of IOP lowering for both normal-tension and hypertensive disease.

Treatment for ocular hypertension and glaucoma is usually initiated with medical therapy, and newer drugs with novel mechanisms of action are now available. This educational activity focuses on the role of nitric oxide (NO) in glaucoma and of latanoprostene bunod (LBN), a novel NO-donating prostaglandin F2α analogue, for IOP lowering. The activity will review the science pertaining to NO as a therapeutic target for glaucoma; summarize results from clinical trials establishing the efficacy, safety, and tolerability of LBN; and present case-based discussions illustrating application of the data to implement evidence-based approaches for patient care with this new agent.

GLAUCOMA AND THE TRABECULAR MESHWORK

Intraocular pressure is the balance between aqueous humor production and its outflow. Aqueous humor is produced by the nonpigmented ciliary epithelial cells in the posterior chamber and then travels in the channel between the iris and the lens into the anterior chamber. Aqueous humor outflow from the anterior chamber occurs through 2 pathways: the trabecular outflow and the uveoscleral outflow. In the trabecular outflow pathway—also known as the “conventional” outflow pathway—aqueous humor percolates through the trabecular meshwork (TM) into Schlemm canal, where it enters collector channels, flows into aqueous veins, and then moves into episcleral veins.

In the uveoscleral, or “nonconventional”, outflow pathway, aqueous moves through and between the tissues of the ciliary body, into the supraciliary and suprachoroidal spaces, and eventually into the vortex veins and orbital vessels. Aqueous outflow through the uveoscleral pathway is independent of IOP and decreases with age.
The trabecular outflow pathway is the primary route of aqueous outflow, and resistance to aqueous outflow through the TM is thought to be the main cause of increased IOP in primary open-angle glaucoma (POAG). The TM is divided into 3 regions: the inner uveal meshwork, the middle corneoscleral meshwork, and the juxtacanalicular tissue that is the site of greatest resistance to outflow. The juxtacanalicular tissue is made up of a loosely arranged extracellular matrix and endothelial cells, elastic fibers, and an inner wall with vacuoles and finger-like projections into Schlemm canal.

Aqueous outflow through the trabecular pathway is dependent on IOP. In a healthy eye, the TM responds to an increase in IOP by decreasing resistance to outflow in order to maintain homeostasis. In eyes with ocular hypertension or glaucoma, increased cell contractility and extracellular matrix deposition in the juxtacanalicular tissue increase outflow resistance and the ability of the tissue to respond to elevated IOP, leading to increased IOP.

NITRIC OXIDE: ROLE IN INTRAOCULAR PRESSURE REGULATION AND GLAUCOMA

Nitric oxide is a ubiquitous endogenous signaling molecule that has a critical role in many physiologic processes, including IOP regulation. Nitric oxide initiates a pathway leading to inhibition of actin-myosin interaction that results in TM cell relaxation, widening of the intercellular spaces in the juxtacanalicular tissue and Schlemm canal, and increased aqueous outflow (Figure 2).11

Knowledge of the role of NO on the TM and trabecular aqueous outflow suggests NO augmentation as a therapeutic approach for glaucoma. Further evidence to support this idea derives from studies showing that IOP in animal models is affected by interventions that increase or decrease NO levels in the eye. In humans, data show that compared with controls, eyes with open-angle glaucoma have lower levels of NO metabolites in the aqueous humor and of NO in TM and Schlemm canal tissue (Figure 3). In addition, analyses of NO metabolites in the aqueous humor and of NO in TM and controls, eyes with open-angle glaucoma have lower levels of NO metabolites in the aqueous humor and of NO in TM and Schlemm canal tissue (Figure 3).14-16 In addition, analyses of NO metabolites in the aqueous humor and of NO in TM and controls, eyes with open-angle glaucoma have lower levels of NO metabolites in the aqueous humor and of NO in TM and Schlemm canal tissue (Figure 3).

This new class of IOP-lowering drugs includes nipradilol, an NO-donating beta blocker that is commercially available in Japan and approved in that country for the reduction of IOP in patients with glaucoma.18 Studies evaluating nipradilol reported that it reduces IOP in patients with normal-tension glaucoma (NTG) and that it increases ocular blood flow in eyes with NTG as well as in normal eyes.19 In addition, compounds that link bimatoprost, brinzolamide, and other carbonic anhydrase inhibitors with an NO-donating moiety are being developed as IOP-lowering medications.21,22

LATANOPROSTENE BUNOD: EFFICACY AND SAFETY DATA REVIEW

LBN is an NO-donating drug that is commercially available in the United States, with a US Food and Drug Administration–approved indication for the reduction of IOP in patients with open-angle glaucoma or ocular hypertension.23 LBN is composed of the prostaglandin analogue latanoprost acid linked to the NO-donating moiety bunod. It received US Food and Drug Administration approval for marketing in November 2017, and is recommended to be instilled as 1 drop in the affected eye(s) once daily in the evening.24

LATANOPROSTENE BUNOD: EFFICACY AND SAFETY DATA REVIEW

LBN, 0.024%, was compared with timolol maleate, 0.5%, in 2 phase 3 trials, APOLLO and LUNAR. Each study included approximately 400 patients who were randomized 2:1 to use LBN once daily in the evening or timolol twice daily for 3 months. Mean untreated IOP at baseline in all study groups was approximately 26.5 mm Hg.

Follow-up visits in APOLLO and LUNAR were scheduled at week 2, week 6, and month 3, and IOP was measured at 8 AM, 12 PM, and 4 PM at each visit. Both APOLLO and LUNAR met their primary efficacy end point, demonstrating noninferiority of LBN to timolol in its IOP-lowering efficacy at each of the specified time points at each follow-up visit.

In APOLLO, mean reductions from baseline IOP across all time points at all visits ranged from 7.7 to 9.1 mm Hg for the LBN group and from 6.6 to 8.0 mm Hg for the timolol group (P ≤ .002), and mean IOP was significantly lower in the LBN group than in the timolol group at every time point at all visits (P < .001) (Figure 4). Adverse events occurred at similar rates in the 283 patients receiving LBN and the 135 patients receiving timolol. The most common adverse events were eye irritation (3.9% for LBN, 2.2% for timolol) and conjunctival hyperemia (2.8% for LBN, 1.5% for timolol).

Figure 2. Pathway of nitric oxide leading to smooth muscle relaxation.11 Abbreviations: cGMP, cyclic guanosine monophosphate; IOP, intraocular pressure; PKG, protein kinase G; TM, trabecular meshwork.


Figure 4. Mean IOP across all visits at each time point in APOLLO and LUNAR.25,26
In LUNAR, mean IOP reductions across all assessments ranged from 7.5 to 8.8 mm Hg for LBN and from 6.6 to 7.9 mm Hg for timolol. At all time points at all visits, except at 8 am at the week 2 visit, mean IOP was significantly lower in eyes treated with LBN than in eyes treated with timolol (P ≤ .025) (Figure 5). As in APOLLO, the most common adverse events in the 277 patients receiving LBN and the 135 patients receiving timolol in LUNAR were eye irritation (7.2% for LBN, 4.4% for timolol) and conjunctival hyperemia (9.0% for LBN, 0.7% for timolol).

Data on long-term efficacy and safety of LBN were gathered in an open-label extension study that included 737 patients from APOLLO and LUNAR who continued on LBN or were crossed over from timolol beginning at month 3. Open-label treatment with LBN continued for 9 months in APOLLO and for 3 months in LUNAR. In this extension study, patients who crossed over from timolol had an additional 6.3% to 8.3% reduction in mean diurnal IOP, which provides further evidence that LBN has a more potent IOP-lowering effect than does timolol. Adverse events in patients using LBN over a longer term were primarily mild to moderate in severity, with the most common being conjunctival hyperemia (5.9%), eye irritation (4.6%), and eye pain on instillation (3.5%).

Of interest, considering that a prostaglandin analogue is currently considered first-line treatment for IOP lowering, LBN was compared with latanoprost, 0.005%, in the phase 2, randomized, double-masked VOYAGER study. VOYAGER randomized 413 patients to once-daily treatment with latanoprost or 1 of 4 different concentrations of LBN. Mean diurnal IOP decreased by an average of 1.23 mm Hg more in patients treated with LBN, 0.024%, than in those treated with latanoprost (P = .005). Although LBN, 0.024%, contains a higher concentration of latanoprost than does latanoprost, 0.005%, the higher amount is not likely to explain the greater IOP-lowering effect of LBN, considering evidence that increasing the dosage of latanoprost 2.5-fold does not increase its treatment benefit. Because of this, it might stand to reason that the NO-moiety in LBN contributes to this greater efficacy, but this has yet to be fully supported. The adverse event profile of LBN in VOYAGER was consistent with the experience in the phase 3 trials, with pain upon instillation and conjunctival and ocular hyperemia being the most common adverse events associated with LBN.

LBN, 0.024%, was also investigated in the JUPITER study conducted in Japan, which enrolled 130 patients with ocular hypertension or open-angle glaucoma, including NTG, pigmentary, or pseudoexfoliative disease. At baseline, untreated IOP in study eyes averaged 19.6 mm Hg and was between 15 and 21 mm Hg in 75% of eyes. The results of JUPITER indicate that LBN is effective in eyes with a lower starting IOP. After 52 weeks of treatment, mean IOP in study eyes decreased by an average of 5.2 mm Hg (-26.3%). Mean IOP in LBN-treated fellow eyes (n = 126) decreased from 18.7 mm Hg at baseline to 14.4 mm Hg (-23%) after 52 weeks. The most common ocular adverse events associated with LBN in the study eyes were conjunctival hyperemia (17.7%), growth of eyelashes (16.2%), eye irritation (11.5%), and eye pain (10.0%); all ocular adverse events were mild to moderate in severity.

CASE DISCUSSIONS

Case 1
From the Files of Danica Marrelli, OD

A 58-year-old white male presented in February 2017 for a glaucoma evaluation. He was referred because of his optic disc appearance and family history of glaucoma. The patient’s mother had glaucoma. He did not know the stage, but reported that she had vision loss and her only treatment had been topical medications.

The patient was a high myope (-8.0 D OU) who wore glasses for correction. His only medical issue was dyslipidemia, for which he used no medication, and he was allergic to penicillin.

The patient’s examination findings just prior to his referral were best-corrected visual acuity (BCVA) of 20/20 OU; normal pupils and slit-lamp examination results; IOP of 18 mm Hg OU; cup-to-disc ratio of 0.55V OU in a relatively small optic nerve; and paviorstone degeneration OU. On presentation for glaucoma evaluation in February 2017, BCVA was 20/20 OU; IOP was 19 mm Hg OD and 21 mm Hg OS; and central corneal thickness was 607 μm OD and 615 μm OS. On gonioscopy, the angles were open to the ciliary body. There were no secondary signs of glaucoma.
Figure 6 shows findings from imaging and visual fields. The retinal nerve fiber layer (RNFL) shows thinning OU, but with more thinning OD than OS.

Dr Marrelli: Would you diagnose glaucoma in this patient?

Dr Madonna: I think that more information is needed. His family history, small discs with a larger cup, and RNFL thickness asymmetry are concerning. Although he appears to have some RNFL thinning, RNFL might be approximately 20 µm thinner on average in high myopes than in emmetropes. 31

Dr Marrelli: Do you routinely perform macular ganglion cell analysis in high myopes?

Dr Madonna: I get a macular scan and optic nerve scan in all patients. I do not use the information for diagnosis, but it is something I like to follow as part of my evaluation for glaucoma because high myopes have a thinner RNFL, owing to the myopia and not to glaucoma. One needs to be very careful about using optical coherence tomography (OCT) RNFL measurements in diagnosing glaucoma in high myopes.

Dr Marrelli: I agree. Although we might expect to see that the ganglion cell layer and RNFL are thinner in high myopes, change over time in these layers should not be any greater than that in other patients.

Dr Chaglasian: I also get macular OCT in patients with glaucoma because these images can be helpful in both diagnosis and in following patients over time. For patients with other conditions, eg, diabetes, these images can help identify pathology not related to glaucoma. I agree that the findings need to be interpreted cautiously in high myopes because of the potential for artifactual and false-positive readings of the ganglion cell layer in the macular region.

I believe the macular OCT is also helpful to look for structure-function correlation between the OCT and visual field. Although changes on OCT and visual field do not always
correlate, we can be more confident about our diagnosis when they do. If the findings do not match up and a diagnosis of glaucoma is uncertain, then I start looking at what risk factors for glaucoma progression are present to help me decide if I can monitor the patient or should initiate therapy.

Dr Marrelli: In looking at the structure and function in this patient, there is some correlation between RNFL thinning and a visual field defect, but it is not a perfect correlation. I was not convinced that this patient had glaucoma. When I am uncertain, I am never afraid to wait and watch for changes. Although the patient’s family history, optic disc appearance, and visual field raised suspicion, it was the first time he had done visual field testing, so I wanted to see if the findings were repeatable. In the Ocular Hypertension Treatment Study, 86% of initial abnormal reliable visual fields were not confirmed on retest.

Dr Madonna: We should not forget that patients can have preperimetric glaucoma, in which there is structural change without function loss. Conversely, this patient has visual field loss without obvious structural loss in the OS. Without obvious structural change, I would likely follow him rather than start treatment.

Dr Marelly: Even when I am certain that a patient has glaucoma, I always get at least 3 IOP readings before I start therapy. In this patient, I wanted to be sure that I was not missing a higher IOP. On return visits, his IOP ranged from 16 to 20 mm Hg OD and from 16 to 21 mm Hg OS.

He also had a second visual field test done fairly soon after the first and a third after 6 months. On repeat testing, the visual field defect in his right eye became a little bit inferior but was primarily superior, which correlated better with the structural evaluations of the ganglion cell layer and RNFL, and he began to show a consistent but mild superior defect in the left eye that correlated with some inferior thinning (Figure 7).

Dr Madonna: The serial OCT testing also shows evidence of more structural damage and of a greater intereye difference. The asymmetry in RNFL thickness has increased from 6 to 14 µm, and the superior and inferior peaks in the RNFL TSNIT (temporal, superior, nasal, inferior, temporal) curve are blunted in the right eye.

Dr Marrelli: Would you diagnose NTG in this patient?

Dr Chaglasian: I would just call it open-angle glaucoma. Identifying glaucoma as normal tension has a potential implication for setting an IOP reduction target of 30%, similar to reduction targets in patients with OAG, and for evaluating the patient for other conditions that have been associated with NTG, such as migraine or Raynaud phenomenon. NTG might also be more difficult to treat, but it also tends to be less progressive than high-tension glaucoma.

Dr Marrelli: The classic patient with NTG is an older woman who has migraines and disc hemorrhages, someone I would want to avoid treating with a beta blocker, but there is no other real implication for management. Many feel that beta blockers should be avoided in patients with NTG because they might adversely affect optic nerve perfusion.

On the basis of the repeat testing, I was more confident diagnosing glaucoma in this patient and initiating treatment. What would be your target IOP considering he has mild glaucoma, his peak IOP is 20 or 21 mm Hg, and he is also relatively young?

Dr Madonna: I think there is a tendency to aim for a 30% lowering because that is within the range attainable with a prostaglandin analogue. Achieving a 30% lowering, however, is more likely when the untreated IOP is at least in the mid-20s, so it might be more difficult in this patient. Nevertheless, I would still set my target at 13 to 15 mm Hg, which corresponds to approximately a 30% lowering.

Dr Marrelli: I tell students that I do not set the target IOP according to what I think I can achieve, but rather according to what I think is appropriate for controlling the patient’s glaucoma. I think the IOP in this patient should be 14 to 15 mm Hg, so the next question is, How can I reach that?

Figure 7. Repeated visual fields and retinal nerve fiber layer images of the patient in Case 1.
Dr Madonna: The results of the JUPITER study come to mind. In this study, treatment with LBN, 0.024%, reduced mean IOP from 19.6 mm Hg at baseline to 14.4 mm Hg.30

Dr Marrelli: LBN was not available when I was initiating treatment for this patient. I wanted to start him on a prostaglandin analogue, but his wife was concerned that the medication might change the color of his blue eyes. A colleague of mine started the patient on a beta blocker. At return visits after 1 and 2 months, his IOP was 17 to 18 mm Hg OD and 16 to 18 mm Hg OS.

I counseled the patient that I did not expect a prostaglandin analogue would change his eye color because that effect typically occurs in patients with hazel eyes.39 He consented to switch treatment and was started on latanoprost, but after 1 month, his IOP was still 18 mm Hg OD and 17 mm Hg OS.

I considered if poor adherence or poor instillation technique explained the lack of benefit. The patient claimed he was using the medication as prescribed, and I believed him because his eyelashes were growing. I evaluate appropriate instillation technique by asking patients during a visit to show me how they put in a drop of artificial tears; this patient had no problem with administration. Then, I considered if I had missed the true peak IOP.

Although I had measured IOP several times before initiating treatment, I told the patient to stop using his medication and had him return after 1 month for diurnal IOP measurements. None of the values were above 21 mm Hg. Samples of LBN arrived that day, and I started the patient on LBN. At multiple follow-up visits, his IOP ranged from 13 to 16 mm Hg OD and 12 to 15 mm Hg OS. The patient reported mild stinging with drop instillation, but he tolerated the LBN well, and he is continuing to do well after 18 months of treatment.

Dr Madonna: I think the medication washout was a good idea and that it is something we do not do often enough. I believe that there are hyper-responders to some medications, and the only way we will identify them is to reestablish a baseline before starting a new medication.

Dr Marrelli: My favorite phrase in the glaucoma clinic is to say, "Step down from the ledge." And what I mean by that is that there is no need to make a rash decision when choosing therapy, which in this case would have been to add a second medication. I aim to keep treatment as simple as possible.

Case 2
From the Files of Michael Chaglasian, OD

A 67-year-old female presented wanting new reading glasses and reporting that she noticed an occasional shadow in her right eye. She was last seen for an examination 7 years ago, and her last medical examination occurred 18 months ago.

The patient was in good health and had no remarkable personal ocular history, but her mother and uncle had glaucoma. She believed that her relatives were using multiple medications for their glaucoma and had other treatments, but she did not know if they had significant vision loss.

The patient’s BCVA was 20/20 OU. Slit-lamp examination results were unremarkable. Intraocular pressure was 36 mm Hg OD and 24 mm Hg OS. Pachymetry test results were 540 μm OD and 550 μm OS. Gonioscopy showed the angle was open to the ciliary body band and light pigmentation. Dilated examination revealed an old small posterior vitreous detachment, which accounted for the shadow the patient described.

Figure 8 shows her optic nerve photographs, visual fields, and OCT images. The visual field shows a superior defect OD. The OCT of her right eye shows inferior RNFL and ganglion cell layer thinning. The left eye also shows inferior RNFL and ganglion cell layer loss, but it is less than that in the right eye.

Dr Chaglasian: Given all the clinical findings, it is clear that this patient has glaucoma and needs treatment. The question is when to start treatment, and would you be comfortable having her come back on another day to measure IOP again before starting therapy?

Dr Madonna: Considering her IOP, I expect that some practitioners would want to start treatment immediately. I like to measure IOP at 3 visits before starting treatment, so I would want her to return for additional measurements.

Dr Marrelli: As a general rule, I do not start treatment to lower IOP the first time I see a patient, but I make exceptions according to the extent of structural damage and the level of IOP. In this particular case, I would be comfortable having the patient come back a few times to measure IOP.

If the IOP was unchanged, and considering the patient’s relatively young age along with the significant visual field defect in the right eye, I would try to achieve 45% to 50% IOP lowering in the right eye. If, however, the IOP in the right eye was only 24 mm Hg when remeasured on the next day and 26 mm Hg a week later, I might be comfortable targeting an IOP of 20 mm Hg, but would also choose a medication that would reduce IOP fluctuation because this is also a risk factor for glaucoma progression.40 Prostaglandin analogues have been shown to reduce IOP fluctuation.41

Dr Chaglasian: I agree that it would be helpful to have the patient return for repeat IOP measurements before starting treatment. The information will provide a better understanding of IOP peak, range, and diurnal fluctuation, which is important information for choosing treatment and assessing the response. The patient needs to be informed, however, that she has glaucoma. It is important that she returns for follow-up because the glaucoma needs to be treated, and further evaluation will determine the best approach for treatment.

Do new medications for glaucoma have a role in treating patients like this who present with moderate-stage disease at a young age?

Dr Madonna: A goal when treating any patient is to achieve the desired benefit with the lowest treatment burden. Considering the results of the phase 2 and 3 clinical trials comparing LBN with latanoprost and timolol, respectively, LBN could be considered a good choice for this patient because of its potential to provide maximum IOP lowering with the convenience of a single drop.25,26 Although it remains to be proven, I also think about the potential for treatment with an NO-donating compound to structurally modify the TM in a way that could reduce the risk of progression long term.

Dr Marrelli: If it turns out that I am aiming for a 45% to 50% reduction in IOP in this patient, I expect she might need to be treated with > 1 medication. Still, I prefer to start with monotherapy, and I would recommend starting this patient on LBN. Then, if further IOP lowering is needed, I would add another agent.

Treatment options and goals were discussed with the patient, and she was started on LBN once every evening OU. After 2 weeks, IOP was 20 mm Hg OD and 18 mm Hg OS. The patient denied any significant side effects and continued on...
LBN. She was instructed to return in 4 to 6 weeks and told that if she was continuing to tolerate LBN and if her IOP was controlled, the next follow-up visit would be after 2 or 3 months. Visit frequency thereafter would be every 3 to 4 months.

Case 3
From the Files of Richard J. Madonna, MA, OD

A 75-year-old black female presented with a history of severe, ischemic branch retinal vein occlusion (BRVO) OD that occurred 8 years earlier. The patient had refused treatment for 2 years after the BRVO and then had multiple laser treatments and anti-vascular endothelial growth factor injections, but she continued to have recurrent macular edema. BCVA was now 20/400 OD and 20/20 OS.

The patient was on amlodipine for hypertension and mesalamine for ulcerative colitis. She was a thin, very active woman, and enjoyed reading.

The patient was diagnosed with POAG at the time she had the BRVO. Her IOP was 23 mm Hg OU at that time. She has been using latanoprost OU and dorzolamide/timolol OU, and had selective laser trabeculoplasty (SLT) performed OS.
4 years ago. At visits over the last 12 months, IOP in the left eye was 13, 16, 14, and 13 mm Hg (~39% reduction).

The patient’s most recent visual field showed a dense superior arcuate scotoma. The 7-year progression analysis showed a loss of 1.1% per year.

The 7-year progression trend analysis of her OCT showed the inferior RNFL thickness OS was decreasing fairly rapidly at a rate of 3.64 µm/year. She also had macular thinning superior and inferior OS (Figure 9). The 10-2 visual field showed progressive loss in the inferior hemifield, and the macular OCT showed progressive loss in both hemifields.

**Dr Madonna:** This is a monocular woman who is active and an avid reader. She is losing vision in her left eye that will affect her vision-related quality of life by interfering with her ability to read and navigate independently.

I think we would agree that IOP control has not been adequate in this patient. One option would be to switch her latanoprost to LBN because LBN might lower IOP by an additional 1 to 2 mm Hg and might have an additional structural benefit on the TM. Before LBN was available, I might have considered adding another medication from another class. Now that we have new medications, however, there are very few patients whom I treat with more than 3 medications.

I would be hesitant to recommend tube surgery in this patient because she is monocular, but I would consider a minimally invasive glaucoma surgical procedure if she needed cataract surgery. Because I have confidence that she will return for follow-up, I might even consider carefully washing out all her medications and starting LBN as monotherapy with the expectation that she will probably need monotherapy.

**Dr Chaglasian:** I would also want to know the untreated IOP in this patient, and I think that she likely would not experience any real harm from undergoing a washout and having a higher IOP for 1 to 2 weeks. With the availability of new IOP-lowering medications, I find myself doing a washout more often, with the idea that I might ultimately be able to simplify and optimize the treatment regimen.

I recognize, however, that asking patients to return for additional visits can have financial consequences for them and carry other burdens. Therefore, I explain that I truly believe there is benefit from doing a washout or repeat IOP measurements because the information I get could improve the treatment plan.

**Dr Marrelli:** I am not sure I would be comfortable washing out all medications in this patient who has significant vision loss. I think that switching latanoprost to LBN or to the netarsudil/latanoprost fixed combination are reasonable choices. Netarsudil is a Rho kinase and norepinephrine transporter inhibitor that reduces IOP by increasing aqueous outflow through the TM, decreasing pressure within the episcleral venous system, and suppressing aqueous humor production. The phase 3 MERCURY-1 trial investigating netarsudil/latanoprost met its primary efficacy end point, showing statistical superiority of the fixed combination to each of its active components for providing a lower mean IOP at 8:00 am, 10:00 am, and 4:00 pm at week 2, week 6, and month 3. Netarsudil/latanoprost lowered IOP by an additional 1.8 to 3.0 mm Hg vs netarsudil and by an additional 1.3 to 2.5 mm Hg vs latanoprost. Conjunctival hyperemia was the most frequent ocular adverse event.
41.0% of 244 patients in the netarsudil group, and in 14.0% of 236 patients treated with latanoprost. In the netarsudil/latanoprost group, 7.1% of patients discontinued treatment because of conjunctival hyperemia.

Performing SLT also could be reasonable. The potential for benefit with SLT might be low in this patient, considering that her IOP is fairly low and that the response to IOP is greater in eyes with a higher baseline IOP.46 It is likely that SLT will do no harm. Realistically, it might be necessary to initiate > 1 single intervention for this patient.

**TAKE-HOME POINTS**

Intraocular pressure is a balance between aqueous humor production and outflow.

Aqueous outflow occurs through the TM and uveoscleral pathways.

- Most outflow occurs through the TM pathway

Elevated IOP in POAG is primarily caused by increased aqueous outflow resistance at the TM.

Nitric oxide is a signaling molecule that increases trabecular outflow facility.

LBN links the prostaglandin analogue latanoprost acid with the NO-donating miyost-ebun group.

- Latanoprost increases uveoscleral aqueous outflow
- Nitric oxide increases trabecular meshwork aqueous outflow

LBN effectively lowers IOP in eyes with low/normal IOP (NTG) to high IOP (POAG).

- In comparative clinical trials, LBN had a greater IOP-lowering effect than did timolol maleate, 0.5%, and propranolol hydrochloride.
- LBN was safe and well tolerated; the most common adverse events associated with its use in the pivotal clinical trials were conjunctival hyperemia (< 10%) and eye irritation (< 6%)
1. Elevated IOP in eyes with POAG is primarily related to:
   a. Overproduction of aqueous humor
   b. Decreased aqueous humor outflow through the uveoscleral pathway
   c. Increased episcleral venous pressure
   d. Aqueous humor outflow resistance at the TM

2. Nitric oxide lowers IOP by:
   a. Exerting its effect in episcleral endothelial cell smooth muscle
   b. Activating the cyclic adenosine triphosphate signaling pathway
   c. Relaxing cells in the TM
   d. Decreasing aqueous humor production

3. Analyses of data from the Nurses’ Health Study and Health Professionals Follow-Up Study showed an association between:
   a. Higher dietary nitrate intake and decreased risk for POAG
   b. Higher dietary nitrite intake and decreased risk for POAG
   c. Use of nitroglycerin and increased risk for POAG
   d. Use of nitroglycerin and increased risk for POAG

4. Which of the following is NOT an NO-donating compound?
   a. Bunod
   b. Netarsudil
   c. Nipradilol
   d. LBN

5. LBN is thought to lower IOP by increasing uveoscleral outflow and:
   a. Reducing aqueous humor production
   b. Increasing trabecular outflow
   c. Decreasing episcleral venous pressure
   d. All the above

6. In a phase 2 clinical trial, LBN, 0.024%, lowered IOP from baseline by ___ mm Hg more than did latanoprost, 0.005%.
   a. 0.78
   b. 1.00
   c. 1.23
   d. 1.78

7. Phase 3 clinical trials compared LBN with
   a. Netarsudil
   b. Timolol maleate
   c. Latanoprost
   d. Vehicle

8. In the phase 3 clinical trials, LBN lowered IOP from baseline by ________ mm Hg.
   a. 3.3 to 5.1
   b. 4.7 to 6.8
   c. 6.5 to 8.0
   d. 7.5 to 9.1

9. Which were the most common (< 10%) ocular treatment-emergent adverse events associated with LBN in phase 3 clinical trials?
   a. Conjunctival hyperemia and dry eye
   b. Conjunctival hyperemia and eye irritation
   c. Ocular hyperemia and increased iris pigmentation
   d. Eye pain and foreign body sensation

10. The phase 3 MERCURY-1 trial demonstrated significantly greater IOP-lowering with fixed combination netarsudil/latanoprost than with ________________.
    a. LBN
    b. Netarsudil alone and latanoprost alone
    c. Timolol
    d. Vehicle

11. Through which 2 pathways does aqueous humor outflow from the anterior chamber occur?
    a. Trabecular and uveoscleral
    b. Trabecular and nonconventional
    c. Uveoscleral and conventional
    d. None of the above

12. What is the level of NO and its metabolites within the aqueous, TM, and Schlemm canal tissue in eyes with open-angle glaucoma compared with that in healthy eyes?
    a. Greater
    b. Lower
    c. Equal
    d. Unknown

13. LBN is composed of the prostaglandin analogue latanoprost acid linked to ________________.
    a. Rho kinase inhibitor
    b. Beta blocker
    c. NO-donating moiety
    d. Additional prostaglandin analogue

14. In the JUPITER study, treatment with LBN, 0.024%, reduced mean IOP by an average of ___ mm Hg from the average baseline measure.
    a. 1.2
    b. 3.6
    c. 4.1
    d. 5.2

15. A patient with OHT has had normal visual fields for 3 years. The most recent visual field shows a new defect. How should this patient be managed?
    a. Patient should be treated immediately or have current treatment reassessed
    b. Neuroimaging should be performed to rule out central nervous system lesions
    c. The visual field finding should be ignored and the patient should be diagnosed on the basis of nerve images instead
    d. Visual fields should first be retested to determine if the defects reappear