Torics For Astigmatism: Soft Lenses, Hard Choices, p. 24

jmi

July 15, 2013

REVIEW® OF OPTOMETRY

Part 1 of 2

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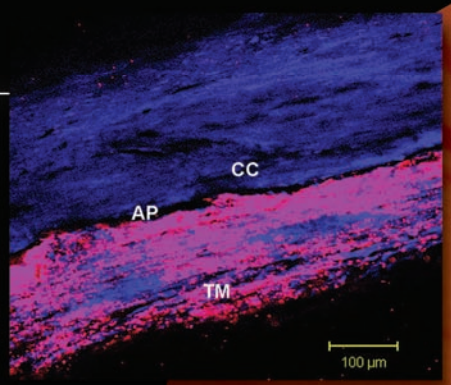

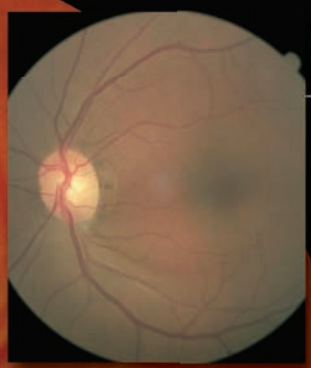

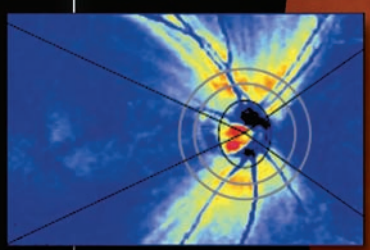

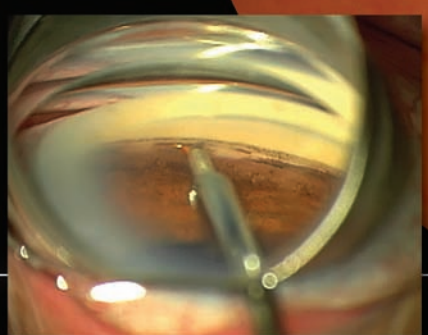

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VOL. 150 NO. 7 ■ JULY 15, 2013

IN THE NEWS

The brain's **pleasure response** to tasting **chocolate** can be measured through the eyes using standard **electroretinography**, according to a study in the journal *Obesity*. The researchers found that electrical signals in the retina spiked high when participants tasted a small piece of chocolate brownie. "What makes this so exciting is that the eye's **dopamine** system was considered separate from the rest of the brain's dopamine system," says Jennifer Nasser, RD, PhD, of Drexel University. If validated, this method could be useful for research and clinical applications in **food addiction and obesity prevention**.

Low birth weight may be a risk factor for **age-related vision loss**, according to a recent study in *PLOS One*. In a rat model, underweight subjects were more likely to experience decreased **night vision and reduced visual function** over time than their normal birth weight counterparts. If this same causal link exists in humans, the researchers say, then clinicians will need to closely monitor the vision-related concerns of patients who were born underweight.

"Predator" bacteria are effective against **antibiotic-resistant bacteria**, such as *Pseudomonas aeruginosa* and *Serratia marcescens*, according to another recent study in *PLOS One*. "Our work demonstrates that predatory bacteria have the ability to attack 'real-life' Gram-negative human pathogens associated with ocular infection," the researchers conclude. Also, "the presence of high concentrations of predatory bacteria [doesn't] appear to be harmful to human cells."

More Details on Dua's Layer of the Cornea

Perhaps discovered two decades ago, its meaning for primary eye care is unsure. **By John Murphy, Executive Editor**

When a "new layer" of the cornea was reported last month, it made headlines in the scientific and lay press. Some even went so far as to say that ophthalmic textbooks will need to be rewritten.

But, what is its significance—if any—for primary eye care?

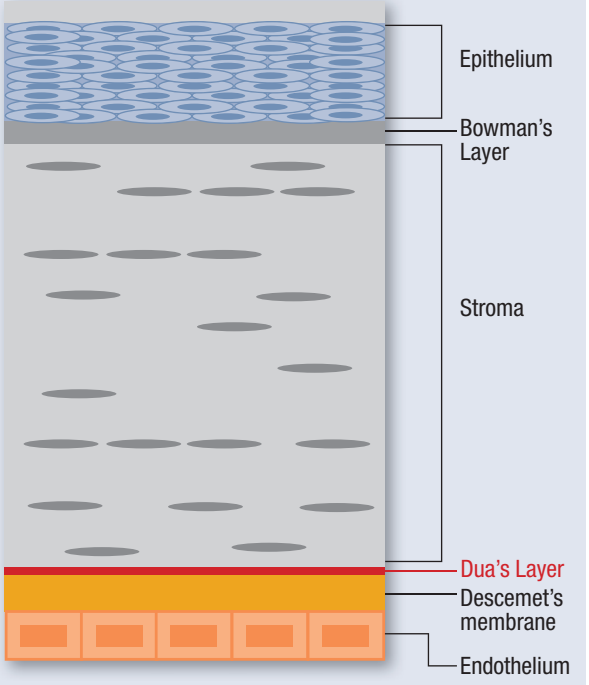
At issue: Researchers in the UK have described a newly discovered and very thin layer of the cornea.[1] It has been dubbed "Dua's layer" after its main discoverer, Harminder S. Dua, MD, PhD, professor of ophthalmology and visual sciences at the University of Nottingham. It's a tough, well-defined, acellular lining only about 10µm to 15µm thick, sandwiched between the corneal stroma and Descemet's membrane (DM).

"In the operation of deep anterior lamellar keratoplasty (DALK), surgeons were observing 'things' that they could not make sense of," Dr. Dua says. After performing various lamellar corneal surgeries—corneal transplants, in particular—Dr. Dua hypothesized that another layer of the cornea might exist to cause these phenomena. To confirm this, he and his colleagues simulated corneal transplants by injecting air into corneal grafts to carefully separate the distinct layers of the cornea. Then, they closely examined the

Continued on page 6

Six Layers of the Cornea?

A recent paper identifies a sixth corneal layer—Dua's layer—between the posterior stroma and Descemet's membrane.



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More Details on Dua's Corneal Layer

(continued from page 6)
layers using electron microscopy.

They found that the separation of layers that yielded the strongest tissue was not between the stroma and the DM, as believed. Rather, the ideal separation was between the deep stroma and this unrecognized layer.

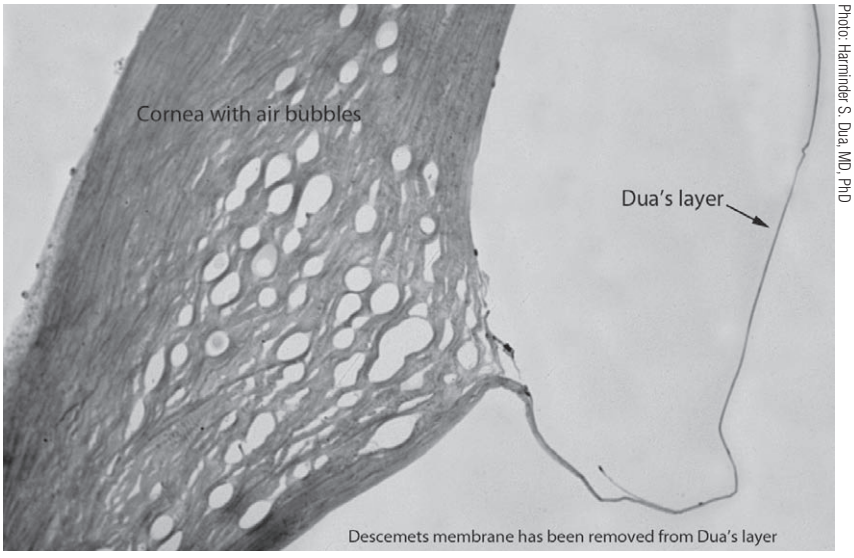

Photo: Harminder S. Dua, MD, PhD

To find Dua's layer, researchers injected air into corneal grafts to carefully separate the layers of the cornea, then inspected the layers under an electron microscope.

"Thus far, all surgeons thought that they were separating the DM from the stroma in the operation of DALK. We have proved that this is not so, but that this new layer offers the plane of cleavage in most cases," Dr. Dua says. "And, because this layer is so tough, it keeps the eye much stronger than it would have been if only DM was left behind. Knowledge of this layer will now enable surgeons to understand the operation better and make it safer with improved patient outcomes."

For instance, graft tissue composed specifically of endothelium, DM and Dua's layer could be used in endothelial keratoplasty. This may allow a better and more easily performed method of this procedure, with fewer grafts wasted due to tears in the DM, Dr. Dua says.

Also, the discovery of this layer may have implications in such conditions as descemetocele (protrusion of Descemet's membrane through the cornea) and acute corneal hydrops in keratoconus (edema due to spontaneous rupture in Descemet's membrane—and possibly Dua's layer).

Incidentally, Dr. Dua may not have been the first to report this layer. A paper published in 1991 by Perry Binder, MD, describes a network of fibers located at the interface of the posterior stroma and DM, although it was not identified as a distinct corneal layer.[2] When contacted for his perspective, Dr. Binder, who is currently a clinical professor of ophthalmology at Gavin Herbert Eye Institute, University of California–Irvine, declined to comment for this story.

For now, Dr. Dua and his team will be putting the layer to the test—literally. "The bursting pressure of this layer is around 700mm to 900mm Hg," he says. "We are currently building a [more] sensitive pressure gauge and should have more accurate figures in the not too distant future. When the layer bursts, it does so with a pretty loud popping sound … suggesting its strength."

Dr. Dua suggests that this is an important discovery, with wide-ranging implications. But he denies a quote in the lay press attributed to him: "This is a major discovery that will mean that ophthalmology textbooks will literally need to be re-written."

But will *optometry* textbooks need to be re-written? No need to stop the presses just yet, it seems.

"As Dr. Dua mentions, knowledge of the existence of this layer may help with our understanding of why certain keratoconus patients develop corneal hydrops and why certain patients with descemetoceles don't experience a rupture," says John Pole, OD, MS, professor at Michigan College of Optometry, Ferris State University. "In the fall, when I teach my students corneal anatomy and physiology, I will mention that there is a suggestion of a new corneal layer and that its importance seems to be related to the new corneal transplantation procedures. [But] its impact on primary care at this time will be small."

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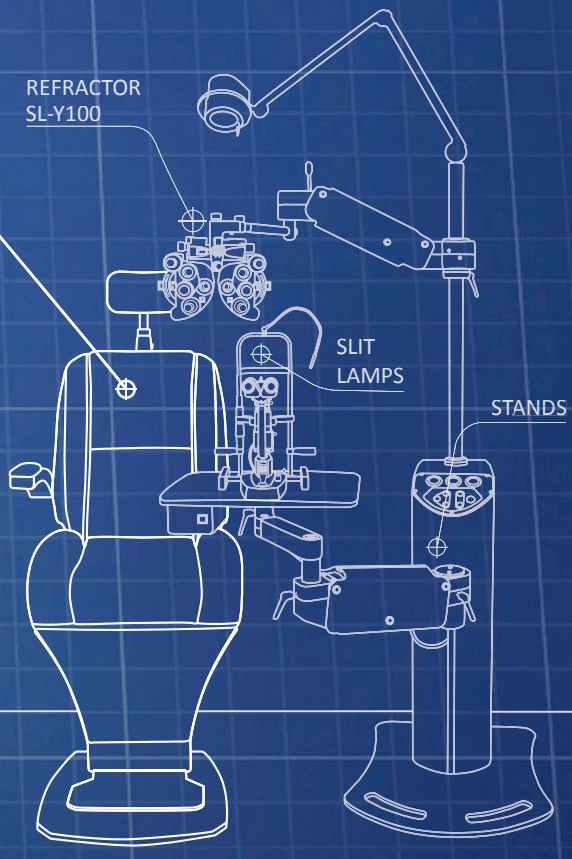

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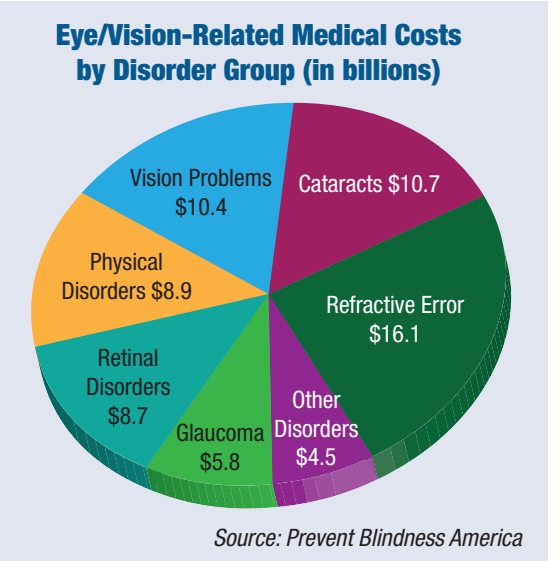
Vision Problems Cost US $139 Billion

America is spending a pretty penny on eye disorders and vision loss—much more than previous estimates have suggested, according to a new report commissioned by Prevent Blindness America.

At a cost of $139 billion per year, vision problems are among the most expensive health issues in the nation, according to PBA's report, "Cost of Vision Problems: The Economic Burden of Vision Loss and Eye Disorders in the United States."



Source: Prevent Blindness America

"We feel that we now have a true estimate of the current and growing costs of eye disease in this country," says Hugh R. Parry, president and chief executive officer of PBA. "Armed with that information, we can address the need for increased prevention, research and health care options."

Co-author John Wittenborn presented an overview of the data at the second annual Focus on Eye Health National Summit in Washington DC on June 18. He summarized a breakdown of estimated costs of eye disorders and vision loss to government ($47.4 billion), private insurance ($20.8 billion in direct medical costs and $1.3 billion for long-term care), and patients and their families ($71.6 billion).

This data serves as an update to a similar 2007 PBA report, and provides a much more comprehensive view of the economic challenges associated with vision problems.

"This study highlights the significant lack of funding we dedicate to the prevention of vision problems," says Jeff Todd, PBA's chief operating officer. "Currently, the federal government allocates just under $500,000 to support the work of the CDC's Vision Health Initiative. When compared to the $139 billion annual cost, that comes out to significantly less than one cent toward prevention of every dollar that vision problems cost our country."

In addition to a revised methodology, the new report includes cost data across the age spectrum—for the first time including children—and considers all disorders related to the eye.

"It gives us a baseline estimate of the total burden in cost," Mr. Wittenborn says. "So, the next question is, 'What do we do to start mitigating this burden?' It underscores the fact that prevention can possibly avert serious future costs."

To access the full report, visit http://costofvision.preventblindness.org.

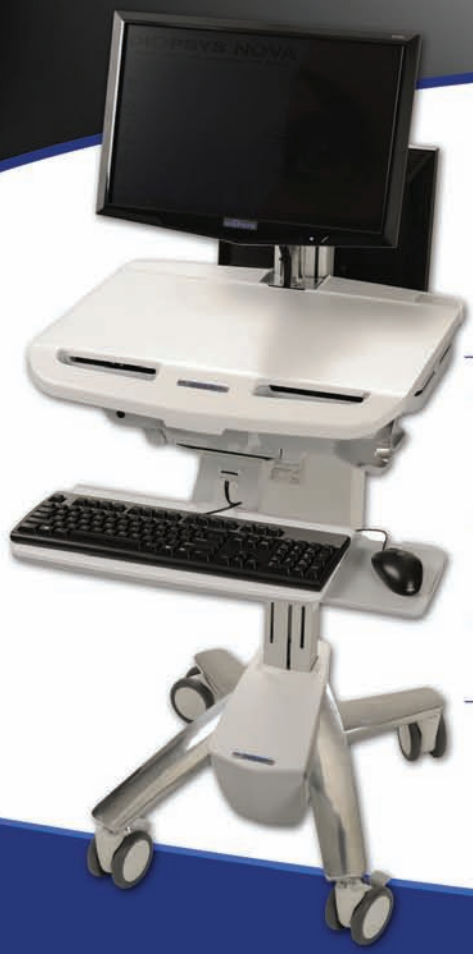
New Texas Law Limits Managed Care Plans' Ability to Set OD Fees

A new law in Texas prevents managed care plans—including medical and vision plans—from controlling fees on an optometrist's products and services *not covered* by the plan.

The bill, SB 632, was signed into law by Gov. Rick Perry in mid-June. Specifically, it says that an insurance contract cannot limit the fees that an optometrist charges for non-covered products or services. It also says a contract cannot require discounts on non-covered products or services.

"Over the past several years, our member doctors have complained that new benefit plan designs had the tendency to have steeper and steeper discounts required of the optometrist on non-covered services and products," says Thomas A. Lucas, Jr., OD, legislative chair of the Texas Optometric Association. "In many cases, the optometrist was required to accept the terms of the new benefit design in order to become credentialed or stay credentialed with the company for their traditional benefit plan designs."

Now, optometrists in Texas "will be able to set their prices on goods and services at rates that make sense for their business and reflect local market conditions," says Dr. Lucas, who advanced the legislation. Comparable laws are already in effect in Kentucky and Maryland. "I encourage each state association to consider working with their state legislatures to pass similar legislation," Dr. Lucas says. The Texas law goes into effect on September 1, but it applies only to contracts entered into or renewed after January 1, 2014.



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Novel Agent Offers Hope for Uveal Melanoma

The experimental oral drug selumetinib is the first systemic drug to show significant clinical benefit in patients with metastatic uveal melanoma, according to clinical trial results presented at the 2013 Annual Meeting of the American Society of Clinical Oncology in Chicago.

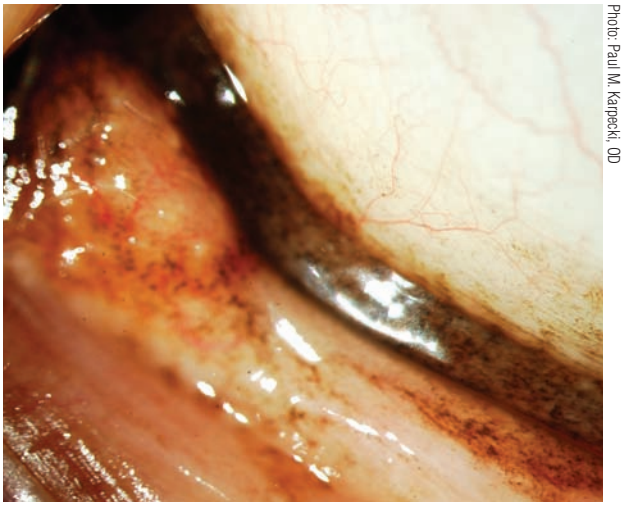

Photo: Paul M. Karpecki, OD

A novel drug called selumetinib, if approved, would be the first oral drug to effectively treat uveal melanoma (above).

In this Phase II study of 98 patients with metastatic uveal melanoma, researchers randomly assigned 47 patients to receive selumetinib and 49 patients to receive temozolomide, the current standard chemotherapy agent for skin melanoma. In the selumetinib group, 50% of patients experienced statistically significant tumor shrinkage, with 15% achieving major shrinkage. By comparison, no patients in the temozolomide group achieved significant tumor shrinkage.

In addition, selumetinib was shown to control tumor growth more than twice as long as temozolomide—for nearly 16 weeks vs. seven weeks.

Although uveal melanoma is rare—only 2,500 cases are diagnosed in the US each year—about half of patients diagnosed eventually develop metastatic disease. There is currently no drug approved specifically for treatment of this cancer.

"This is the first study to show that a systemic therapy provides significant clinical benefit in a randomized fashion to advanced uveal melanoma patients, who have very limited treatment options," says lead investigator Richard D. Carvajal, MD, a medical oncologist at Memorial Sloan-Kettering Cancer Center in New York. "This clinical benefit has never been demonstrated with other conventional or investigational agents, which is all we have been able to offer patients for decades."

Dr. Carvajal is now planning a multicenter, randomized trial to attempt to repeat the drug's effect. "If we can confirm selumetinib's effectiveness in treating advanced uveal melanoma in this follow-up trial, it will become the standard therapy for this disease." ■

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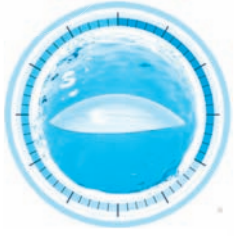

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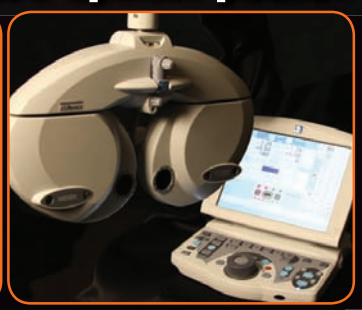

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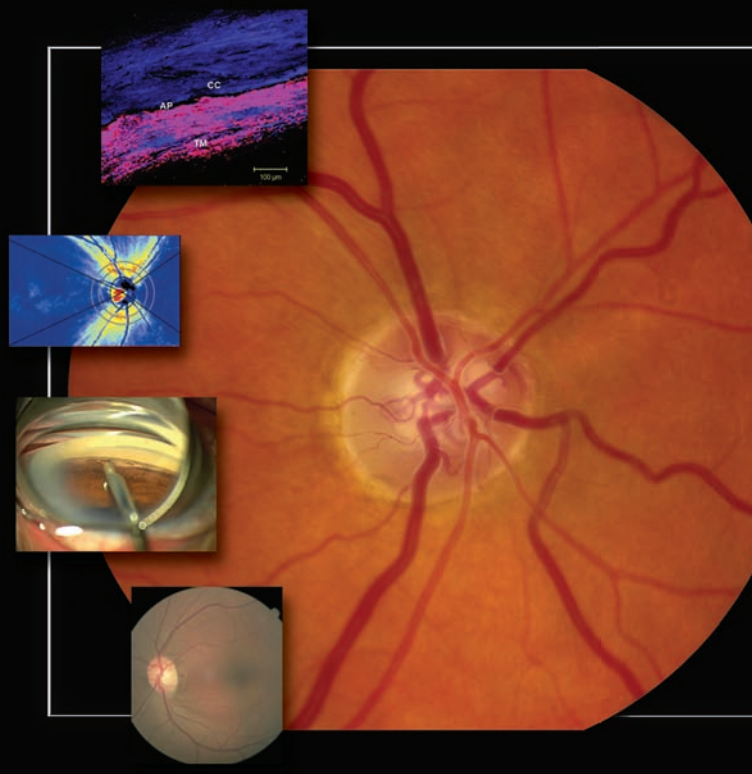

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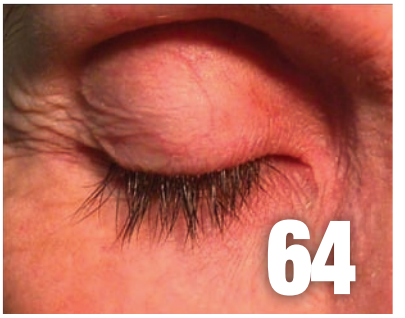

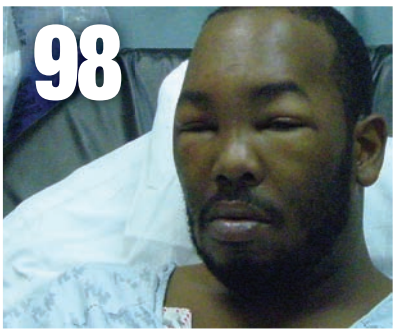

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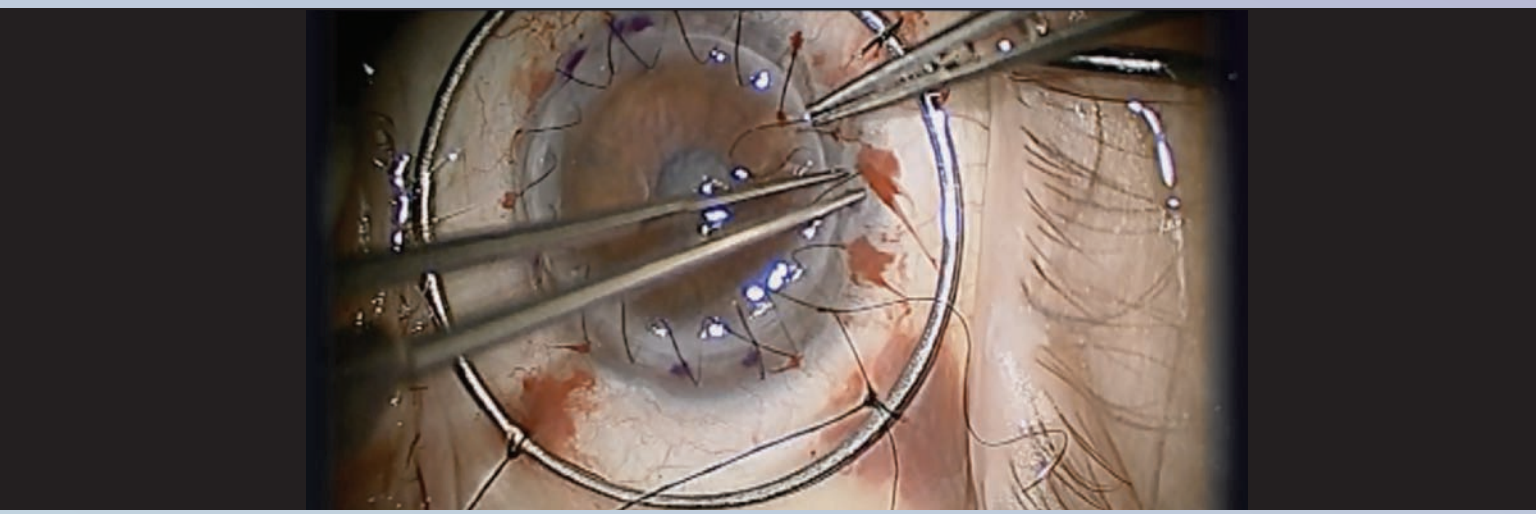
Surgical Minute

By Derek N. Cunningham, OD, and Walter O. Whitley, OD, MBA



See the view through the operating microscopes of some of the best eye surgeons in the US, with expert commentary from comanaging optometrists.

Surgical Minute

PK: Right on the Button

When all else fails, penetrating keratoplasty offers a chance for better acuity.

By Derek N. Cunningham, OD, and Walter O. Whitley, OD, MBA

On The Web >> View a narrated video of penetrating keratoplasty.

Penetrating keratoplasty (PK) is a full-thickness transplant in which the damaged central cornea (7mm to 9mm) is removed and replaced with donor tissue. Compared with other types of tissue transplants, it has a long and outstanding record of success; more than 46,000 corneal transplants were performed in 2011, according to Eye Bank Association of America.

The most common indications for penetrating keratoplasty are regrafting, keratoconus, Fuchs' endothelial dystrophy, pseudophakic bullous keratopathy, perforated corneas, traumatic scars and viral keratitis.

The advantages of penetrating keratoplasty include the full removal of damaged corneal tissue, improved optical clarity, restored corneal anatomy, ease of performance compared to other corneal transplant procedures, improved cosmetic appearance and the potential for good optical results.

Some disadvantages are a higher risk of graft rejection, post-op astigmatism, suture management, intraocular complications and traumatic corneal rupture.

Variations of the procedure include deep anterior lamellar keratoplasty (DALK), Descemet's stripping endothelial keratoplasty (DSEK) and Descemet's membrane endothelial keratoplasty (DMEK). The choice of procedure (PK or one of the above variations) depends on which corneal layers have been affected.

The procedure begins with the preparation of the donor tissue. A trephine (a circular cutting device) is used to cut the donor cornea, followed by trephination of a similar sized portion (7mm to 9mm) of the patient's cornea. Once the recipient's corneal button has been removed, the anterior chamber is filled with balanced salt solution or sodium hyaluronate and the donor button is placed into position.

Four cardinal sutures of 10-0 nylon are placed at 90° intervals in the donor graft, just above Descemet's membrane. The sutures are then passed into the recipient's cornea at the same level, at approximately 1.5mm into the host tissue. Once the needle is passed though, the suture is tied and buried. After the cardinal sutures are in place, suturing can be completed with a single running suture or interrupted sutures.

Postoperatively, patients are prescribed topical antibiotics for one to two weeks as well as topical steroids, which are tapered over several months. Many times, patients are kept on low-dose topical steroids to reduce the risk of graft rejection and failure. Sutures can be removed as soon as two to three months, if needed. Or, if a patient has little astigmatism and the sutures are not causing any problems, they can be left in place for many years.

As comanaging optometrists, our main concern is the long term management and visual function. Postoperatively, corneas may take anywhere from 18 to 24 months to fully stabilize, so be sure to continuously monitor patients for adequate visual acuity and functional vision. Communicate with your corneal specialist to decide when patients are sufficiently stable for contact lenses. A specialty contact lens (GP or hybrid) may be considered as soon as three months after surgery, but may need several changes and modifications once the sutures are removed. ■

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REVIEW® OF OPTOMETRY

Tracking Glaucoma's Progression

The field is evolving rapidly, but optometry's involvement remains inconsistent. Could OD-to-OD referrals help us move forward? **By Jack Persico, Editor-in-Chief**

Glaucoma—a condition strongly associated with gradual, incremental change—is suddenly moving fast. In recent years the subspecialty has gained a few new medications, several "minimally invasive" surgical procedures and nothing short of a radical overhaul in the capabilities of its diagnostic technology. OCT and other new imaging modalities can document changes to the optic nerve head, ganglion cell complex and retinal nerve fiber layer with previously unheard-of precision.

Have you observed these trends and decided glaucoma is just not for you? If your practice is primarily comprised of young, healthy patients seen for routine eye care and refraction, it may not seem worthwhile to place much emphasis on glaucoma beyond the obligation to screen and refer. Managing glaucoma requires a different mindset and workflow than the wellness visits typical of many optometry practices. These patients need chronic, lifelong care, and even your best efforts will only help to slow progression, not restore vision.

But the opportunity for greater OD involvement is compelling. "I consider glaucoma the consummate optometric disease because the majority of patients can be managed successfully and without too much complexity," says glaucoma specialist James Fanelli, OD.

We all know about the demographic inevitability that is giving rise to a greater need for care of age-related diseases like glaucoma. Ophthalmology's ranks are overloaded with glaucoma patients. That field, although never too friendly toward optometry, is in need of qualified assistance in providing long-term care. MDs prefer surgery, and will eventually cede most routine glaucoma care to optometry. But the wide disparity in capabilities among ODs makes it difficult for optometry to advance.

Some ODs find OCT invaluable in documenting glaucomatous changes, but many still rely on fundus photography. Some use an ocular response analyzer to correct IOP calculations for the influence of corneal biomechanics—but about one in four ODs don't even own a pachymeter, thus omitting the role of central corneal thickness entirely. A few ODs use ultrasound biomicroscopy to visualize the anterior chamber angle in ways that surpass even OCT; most others get by with a humble gonio lens. Oklahoma and Kentucky ODs can perform SLT; their colleagues in Massachusetts can't even prescribe Timoptic.

It's confusing, to say the least. "The future is already here, it's just not evenly distributed," sci-fi novelist William Gibson said. He was remarking on the rise of technology culture in Asia (when it eclipsed the west in the 1990s) but the point feels especially true of glaucoma care in optometry.

A Team Approach

This issue's focus on glaucoma hopes to level the playing field a bit. The CE course on page 52 reveals the breadth of the latest imaging capabilities. But be mindful that adding a new piece of technology alone won't be sufficient for advancing your practice. "One doesn't—or at least shouldn't—buy the equipment and *then* see if you develop the interest and acumen to use it," Dr. Fanelli says. "The decision to buy is a conscious one and should be a part of the goals of the practitioner and the practice."

Not everyone needs to gear up, of course. "I think of ODs as the general practitioners of eye care," says Dr. Fanelli. "GPs manage a wide variety of ailments, and each one practices to his/her comfort level. Some may treat GI abnormalities, while others may hand off those folks to gastroenterology." The same is true in glaucoma, he says.

Instead of turning to ophthalmology as usual, explore the idea of OD-to-OD referral. Dr. Fanelli says he's getting more and more of those, where a fellow optometrist sends the patient to him for either a second opinion or for testing that they don't have—and they dictate the terms of the encounter.

"Letting the other OD tell me what they want me to do sets the stage for how much involvement I have in the patient's care," he says. "That's easier for non-chronic conditions, as it's usually a treat-and-stabilize situation. For glaucoma, I want to know from them exactly what they want me to do." It keeps you in control, and the patient in your practice, while improving care. Everybody wins. ■

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What're You Complainin' About?

'What is your chief complaint?' It's a question that we've asked ever since we were wee little optometry students. The answers are still surprising. **By Montgomery Vickers, OD**

When I was in optometry school, they drummed it into our heads to ask the patient the reason for coming to see us. This item—the "chief complaint" or "CC"—has been found on countless records in every doctor's office since the first doctor eviscerated a patient to make sure she wasn't a witch.

So, in that grand tradition of demon hunting, I've always tried to get to the root of the chief complaint. You might find signs of diabetes and save a patient's life, but if you forget to address their "itchy eyes," you're a lousy eye doctor.

My Favorite Complaints

After 34 years in practice, here's a collection of my favorite answers from patients to that age-old question: "What is your chief complaint about your vision and eyes?"

- "I can't see well enough to text when I'm driving."
- "My wife's glasses don't work any more."
- "My left eye really bothers me all day." (Note that this patient was pointing to her right eye the whole time and, to the end of the exam, still called it her left eye.)
- "My glasses won't stay in my pocket."
- "Your contact lens is stuck in my eye."
- "My reading went bad as soon as I met you."
- "Feels like I have a bug in my eye." (He did.)
- "I need a new TV."
- "My dog licked my glasses."
- "My left eye went blind six months ago."
- "I see the moon on your face."
- "There a dip in my back."
- "I have a new invention to keep glasses from sliding and want you to invest in it." (It involved a surgeon implanting a magnet under the skin between the eyes.)
- "I can't hear anything."
- "I got fingernail polish remover in my eye and, when I went to wash it out with eyedrops, I put fingernail polish remover in it again."
- "My blind eye is my good eye now."
- "You tell me. You're supposed to be the doctor."
- "All eye doctors are idiots."
- "Good comas run in my family."
- "I need you to remove my eye."
- "I saw my shadow behind my house."
- "I cannot afford a new phone."
- "My regular eye doctor is too old, so he died."
- "My bank is closing."
- "I lost three teeth after I got my last glasses."
- "I wanted to ask you if you have life insurance."
- "When I get turned on, my ¶#^!$ bends." (I swear this actually happened. I was an intern at Dr. Walter Ramsey's office at the time.)
- "When I stare at my husband, I get sick."
- "I only wear my glasses when I want to see something."
- "I drove over so you could fill out these papers that say I'm legally blind."
- "I haven't had a check-up since prison."
- "I dreamed about this."
- "When I open my eyes, I see better."
- "My chief complaint? He's in the car."

Oh, yes, there are more. How do your favorite chief complaints stack up? ■

New DAILIES TOTAL1® Water Gradient Contact Lenses: Comfort Redefined

A new era in contact lenses for a new era in comfort. — **Mile Brujic, OD**

When I graduated from optometry school in 2002, silicone hydrogel lenses had been available for several years, but most of the lenses we fit were still hydrogels. Over the last decade we have seen a major transition in soft contact lens prescribing, motivated by the hope that increasing oxygen flow to the cornea would enhance ocular health and comfort.

Oxygen Permeability

Unique among tissues, the avascular cornea gets much of its oxygen directly from the air, and, to varying degrees, contact lenses can impede that process. Over time, diminished corneal oxygen flow can result in physiological changes, including edema, epithelial microcysts, limbal hyperemia, and neovascularization.[1]

The demand for greater oxygen transmissibility led to the addition of silicone, an extremely oxygen permeable material, to the hydrogel lens matrix. Silicone hydrogel solved the oxygen transmissibility problem, and the incidence of serious hypoxia-related complications was reduced to almost zero.[1,2]

Silicone and Comfort

Unfortunately, while silicone is highly oxygen permeable, it is also extremely hydrophobic. Even embedded in a hydrogel matrix, hydrophobic silicone moieties can migrate to the lens–air interface. At the lens surface, tiny hydrophobic areas can form and coalesce, reducing surface lubrication and potentially creating discomfort during blink.

To address this challenge, material scientists tried surface treatments to encapsulate the silicone and added wetting agents to the lens matrix to improve surface moisture. These strategies have worked well, but a subset of patients continues to remain uncomfortable.

A New Approach: The Water Gradient

The novel material (delefilcon A), from which DAILIES TOTAL1® contact lenses are made, has brought a new era in contact lens comfort. The first and only water gradient contact lenses, DAILIES TOTAL1® contact lenses are 33% water at their core, but over 80% water in the 6 microns between the core and the surface.[4]* The result is that DAILIES TOTAL1® contact lenses combine outstanding surface lubricity for comfort throughout the day with high oxygen transmissibility (Dk/t of 156 at –3.00 D), and essentially no silicone at the surface.

Thanks to the water gradient, the remarkable surface of DAILIES TOTAL1® contact lenses is exceptionally lubricious, offering a smooth, wet surface for the lids to slide over during blink. Indeed, DAILIES TOTAL1® contact lenses have the lowest coefficient of friction of any daily disposable contact lenses tested.[5] The result is outstanding comfort from beginning to end of day.

In an ongoing multicenter European clinical study (n = 280), patients preferred DAILIES TOTAL1® contact lenses to their habitual lenses by a ratio of 13 to 1.[6]** That startlingly high level of preference was replicated in my own patients' enthusiastic reactions to these lenses.

A High-performance Product

When I introduce DAILIES TOTAL1® water gradient contact lenses, patients are naturally curious about what makes them different from the ones they currently wear. I describe the revolutionary water gradient concept, emphasizing that the low water content core makes the lenses highly breathable, while the highly lubricious surface makes them exceptionally comfortable.

COMFORT COUNTS

Comfort issues are surprisingly common among contact lens wearers—even ones who never complain about discomfort. Industry studies show us that the overwhelming majority of patients with discomfort symptoms simply don't tell us about them—even when we ask. I have found that when I ask patients about their lens-wearing experience, they typically answer "good" or "fine." But when I ask them to rank it on a scale of zero to 10, they will rate it as a 6 or 7.

To me, 6 or 7 out of 10 is an opportunity to improve a patient's wearing experience. We know that lack of comfort is the number one reason patients give up on contact lens wear.[3] I want my patients to truly enjoy contact lens wear and to be happy with the lenses I prescribe. Their health, and that of my practice, depends on it.

* In vitro measurement of unworn lenses.
** Percentage of wearers agreeing with statement "I prefer these lenses to my previous contact lenses."

Mile Brujic, OD, is a partner of Premier Vision Group, a four location optometric practice in Northwest Ohio.

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Do You Feel the Pressure?

Optometrists are taking on greater responsibility in glaucoma management. But this requires closer stringency in coding. **By John Rumpakis, OD, MBA, Clinical Coding Editor**

One of the biggest no-no's is coding in a pattern and by diagnosis. That is, every patient who has the same diagnosis gets coded in exactly the same way.

Rather, each patient needs to be approached as an individual, with a unique personal and family history, unique clinical findings and the need for unique medical decision-making for the individual's specific case. Therefore, each patient will also have a unique and individual medical necessity established in the record for any special ophthalmic testing to be done. Likewise, the frequency of the office visits and the special ophthalmic testing are decisions you make on an individual basis for each patient.

Understanding your state- or region-specific payer guidelines associated with the appropriate CPT procedure codes is the only way to understand the complexities of managing your glaucoma patient properly. Let's start by looking at the diagnostic tests and the accompanying codes typically associated with glaucoma.

Office Visits

Your office visits can be coded using the 920XX codes and the 992XX codes. But remember that the office visit code that you use *must* be based upon the individual patient and the actual medically-necessary testing that you performed and recorded in the medical record. Don't assume that because your diagnosis is related to glaucoma that your office visit is automatically elevated to a higher code.

Codes for typical special ophthalmic procedures include:

- 92020 – Gonioscopy
- 92083 – Visual field, threshold
- 92132 – Scanning computerized ophthalmic imaging, anterior segment
- 92133 – Scanning computerized ophthalmic imaging, posterior segment, optic nerve
- 92250 – Fundus photography
- 76514 – Pachymetry

The frequency of these procedures is determined by both the medical necessity and the local coverage determinations established within your specific contracted carrier policies and your evaluation of the patients' specific presentation. It is becoming more common that carriers are classifying glaucoma into mild, moderate and advanced stages, each with their own specific clinical protocol for frequency of tests (primarily in regard to OCT and visual fields).

(Special note: In last month's column regarding performing OCT and fundus photography on the same date of service, please keep in mind that a diagnosis of glaucoma was *not* included in the eligible disease states to allow the use of modifier -59.)

Diagnosis Coding

In January 2012, changes were made in the ICD-9 coding system that now allow us to also specify the severity of the disease. This is consistent with the migration to the ICD-10 system coming in October 2014. So if there is a confirmed diagnosis of glaucoma, a second diagnosis should also be included to indicate the stage of glaucoma. Enter one of the following as a secondary diagnosis to indicate the stage of the disease:

- 365.70 – New; Glaucoma stage unspecified
- 365.71 – New; Mild stage glaucoma
- 365.72 – New; Moderate stage glaucoma
- 365.73 – New; Severe stage glaucoma
- 365.74 – New; Indeterminate stage glaucoma

For example, here's how moderate stage primary open-angle glaucoma is coded in the ICD-9 system:

- Primary diagnosis – 365.11 (primary open angle glaucoma)
- Secondary diagnosis – 365.72 (moderate stage glaucoma)

In the ICD-10 system, this diagnosis will be indicated in a single code:

- H40.11X2 – Primary open angle glaucoma, moderate stage

Providing glaucoma care is a growing segment in optometry. Be mindful of always diagnosing, treating and coding for the individual patient, and not simply by the diagnosis. By doing so, you will have the upper hand in determining the medical necessity for performing both office visits and ordering any special ophthalmic tests. Ultimately, every patient decision must be based on your determination of medical necessity, not on how you get paid. ■

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Torics for Astigmatism:

Soft Lenses, Hard Choices

With contact lens dropout an ever-present concern, too much is at stake to ask astigmats to compromise their vision.

By Jane Cole, Contributing Editor, and Colleen Mullarkey, Senior Editor

Many patients—and practitioners, for that matter—still hold onto the belief that astigmats and soft contact lenses don't mix. But with the advent of new lens designs and materials, experts say that's just not the case any more. Recent studies have suggested that astigmats who are new wearers or previous contact lens dropouts achieve visual acuity comparable to spectacles when fitted with toric soft lenses.[1]

Today's soft toric designs and materials offer better optics, improved stability, a wider range of stock parameters and the option of daily disposability. "Additionally, there are a number of smaller niche laboratories making more custom-parameter lenses now than in the past, so we have a lot of choices for people who might not fit into one of the disposable types of lenses," says Douglas Benoit, OD, of Concord, NH. Thus, the challenge in fitting astigmatic patients is no longer a dearth of options, but rather *which* option to choose from the wide variety now available.

Increased chair time and patients' financial reservations are noteworthy obstacles as well—but the one justifies the other, successful practitioners say. If you're adept at giving astigmatic patients crisp vision, they'll be more willing to pay for the additional cost of toric lenses and your professional expertise in fitting them.

Let's take a look at some of the new advances and how they can improve care for your astigmatic patients.

Changes in Soft Torics

Silicone hydrogels and daily disposables—the newest players in the soft toric lens market—now provide a fairly substantial parameter range, offer greater ease in fitting and have better predictability, stability and reproducibility than previously, says Glenda Secor, OD, a private practitioner in Huntington Beach, Calif.

• ***Silicone hydrogels.*** These lenses now account for more than 80% of new toric soft lens fits in the United States.[2] They are a popular option because silicone materials have been shown to decrease the likelihood of complications, such as hyperemia, dryness and discomfort.[3] Silicone hydrogels also enhance oxygen transmissibility, which can prevent corneal neovascularization due to low oxygen tension beneath the thick prism ballast of a toric hydrogel lens design, says Steven Grant, OD, of Costa Mesa, Calif. In the past few years, manufacturers have ushered in a number of new silicone hydrogel lenses for astigmatic patients with improved stabilization designs.

• ***Daily disposables.*** "The advent of daily soft torics has dramatically improved convenience for patients who want a more frequent replacement option, especially when they go swimming or play sports," says

optometrist Robert Grohe of Chicago. Daily disposable toric lenses first arrived on the market more than a decade ago and the options have continued to increase since, providing astigmats more convenience without sacrificing efficacy. Studies have shown that disposable toric lenses provide the same visual acuity, centered fit and comfort as daily-wear lenses, but with fewer deposits and less ocular reactions.[4]

• ***Expanded parameters.*** Despite the proven clinical efficacy of soft torics in astigmats, optometrists often had a difficult time finding the right fit in the past due to limited parameters. However, recent advances in soft torics have added more cylinder power and axis options, enabling ODs to help a wider range of astigmatic patients.

"Cylinder power in the past used to go up to about -1.75 to -2.25, but lately, the cylinder powers have been expanding up to the four- to five-diopter range," Dr. Grohe says. "While high cylinder prescriptions are more complicated, these are very motivated patients who benefit from the expanded parameter options and more precise vision."

• ***Multifocal soft torics.*** In the past, astigmatic patients with presbyopia had little option but to wear reading glasses over their contact lenses. But today, patients now have more freedom with lenses that combine correction for both astigmatism and presbyopia. Researchers have found that multifocal soft torics provide optimal distance and near vision quality without compromising stereopsis.[5]

In addition to a few options from large manufacturers, several custom laboratories also manufacture conventional soft toric multifocal contact lenses. "As optics continue to improve, I think multifocal soft torics are going to be a growth

opportunity for the future," Dr. Grohe says.

• ***Niche labs.*** For difficult-to-fit patients, a number of laboratories can produce custom-lathed soft toric contact lens options with hydrogel materials. Dr. Benoit says his go-to specialty labs produce custom toric soft lenses with expanded parameters that the larger manufacturers are not currently offering. "These smaller labs have increased what we can do, so more patients are able to wear toric soft contact lenses than in the past," he says.

A more recent addition to the market, Definitive (efrofilcon A, Contamac) is a latheable made-to-order, daily-wear silicone hydrogel material, which works well for high astigmatic patients wishing to wear soft lenses. It is now available through a number of specially authorized labs.

• ***More stable lens designs.*** "In the past five or six years, we have seen much more stability and predictability with soft toric lenses," says optometrist Jeffrey Krohn of Fresno, Calif. In fact, research has confirmed it. Clinicians at Indiana University studied the rotational fitting characteristics of five toric lenses and found 10° or less rotation with 95% of the lenses and less than 5° of rotation with 80% of the lenses.[6]

"Before, we were making a lot of calculations because we were observing 15°, 20° or even 30° of rotation on a fairly routine basis," Dr. Krohn says. Newer advances in design, he says, give doctors more confidence in ordering diagnostic lenses. "We put the lenses on and know we are going to be pretty close."

Spherical or Soft Toric?

ODs have often turned to spherical lenses in the past because they have few, if any, rotational issues; however, they are not designed to provide astigmatism correction and toric lenses have since improved considerably. Some patients with low levels of astigmatism can tolerate spherical lenses, but at which point is it best to fit a soft toric instead of a spherical lens? "I think once you get above 0.75D of astigmatism, if the patient's spherical component is below plus or minus four, you should really be thinking about a soft toric as opposed to a sphere," Dr. Benoit says. "And if a patient's distance component is greater than a plus or minus four, when they get to about 1.25 cylinder, you really need to consider (a toric)."

Dr. Secor agrees about the -0.75 cylinder threshold as a general principle, but says it should be even less in patients with vertical or oblique astigmatism. Because with-the-rule astigmatism is more forgiving with uncorrected cylinder, 0.70D of cylindrical correction must be present before she will fit a toric lens. Dr. Grohe agrees that more patients will probably find a greater tolerance in a soft toric if they have with-the-rule astigmatism, while those with against-the-rule and oblique astigmatism may have narrower success.

Another question that often arises with soft torics vs. spherical designs: Can an OD use the spherical equivalent as opposed to using the actual prescription? In the past, when cylinder powers were limited, this was a necessary evil. "Today we can

give the patient a more precise trial soft toric lens and see how he or she does," Dr. Grohe says. Usually, the outcomes are quite positive. Recent research has shown that astigmats achieve better visual acuity when refitted with toric soft lenses compared to spherical contact lenses.[1]

Dr. Grohe has recently seen more patients buying into this level of quality—even if it means a few extra dollars out of their pockets. Some patients on vision care plans want to get the most out of their benefit allowance by minimizing the cost of the design they choose, so that they get more lenses for their money. Although spherical lenses are generally less expensive than soft torics, Dr. Grohe has noticed that his patients—even those who may be on a limited budget—often choose the toric lens once they have trialed it. Another selling point he emphasizes: Spherical lenses, in general, exhibit a greater tear rate, but toric lenses, which are thicker and more durable, tend to last longer and require less frequent replacement.

When GP is the Way to Go

If a patient has astigmatism and needs a bifocal or multifocal contact lens, Dr. Benoit finds gas permeable designs are generally superior. "With that said, there are a number of laboratories making soft lenses that correct astigmatism and include a bifocal as well," he says.

Dr. Secor typically prescribes a GP design if the corneal cylinder is equal to the refractive cylinder, especially on with-the-rule corneas. She also finds gas permeable lenses to be a good option for highly allergic patients because they tend to stay cleaner and proteins don't adhere to them as easily as they do to soft lenses.

If a patient has irregular astigmatism or is currently happy in their gas permeable lens, Dr. Grohe will go with the GP instead. He also recommends GPs for patients with corneal disease or keratoconus, as well as those who have undergone penetrating keratoplasty. "In the face of new soft toric products, the GP industry will need to counter with a continued commitment to developing new materials and solutions," he says.

Wish List for the Future

While the toric soft lens market has greatly expanded, doctors still have a few wish-list items for the future. Dr. Grohe would like to see more companies use lens polymers that contain UV absorbent technology, while Dr. Benoit hopes to see the use of silicone hydrogel materials increase.

"With silicone products, you don't have to worry about oxygen flow to the cornea. The big concern 30 years down the road—after a person has worn lenses all that time—is whether or not there will there be problems because they aren't getting enough oxygen," Dr. Benoit says. "Having a lens that is able to deliver more oxygen is really beneficial."

Other items include expanded options in high cylinders, oblique axis and multifocal torics. And high on many doctors' lists is the development of a silicone hydrogel daily disposable toric. If the rapid advances in toric material and design over the past few years are any indication, these dreams could very well become reality in the near future.

Improved Patient Care

Of course, one of the biggest improvements in the newer soft toric designs is better vision. "We have the term 'masking astigmatism,' which I'm not a fan of," Dr. Grant says. "If I have a patient with 20/25 vision or 20/30 vision and I can now give them 20/20 vision, I think it's incumbent on me to provide the best vision possible, and it reduces the dropouts." He's also found that the expanded parameters and low cylinders of the new soft torics have satisfied the previously unmet needs of certain patients and, in turn, allowed for much better visual comfort.

Some doctors have found that the increased options in daily soft torics have helped eliminate problems such as solution sensitivity and irritation to the cornea or lids. "Daily disposables fortunately increase compliance quite a bit because there is nothing simpler than just throwing the lens away after one use," Dr. Benoit says.

All of these new developments in toric soft lenses have helped streamline the fitting process. "Patients these days are interested in getting the best care, but they are not interested in spending hours in the office," Dr. Grohe says. "New improvements in lenses minimize the amount of chair time that was once traditionally needed."

In the past, Dr. Grohe often found soft toric fitting laborious—insert lens, wait 30 minutes for it to settle, take measurements, then make adjustments based on rotation or mislocation. "With the new lens designs and improved manufacturing, lens performance has become more dependable," he says. "You can put a lens on a patient, know it is more predictable and get more stable visual acuity in a shorter period of time." ■

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Future Glaucoma Drugs Target Trabecular Outflow

Rho-kinase inhibitors offer a new path to lower IOP by significantly decreasing trabecular outflow resistance. **By Patrick A. Scott, OD, PhD**

A new, emerging class of hypotensive drugs—Rho-kinase inhibitors—is being developed as a possible treatment for patients with ocular hypertension (OHT) and primary open-angle glaucoma (POAG).

Many of these drugs are in different stages of development, and those being studied in clinical trials have largely been shown to be safe and efficacious. Here is a short and digestible overview of this new, exciting class of glaucoma drugs.

Are New Drugs Needed?

Currently, the only way we can treat OHT and POAG is to lower intraocular pressure medically or surgically. Oculohypotensive drugs lower IOP in one of three ways:

- Decreasing production of aqueous humor (beta-blockers, carbonic anhydrase inhibitors and alpha-2 agonists).
- Increasing drainage of aqueous humor through the uveoscleral outflow pathway (prostaglandin analogs).
- Indirectly increasing outflow facility through the trabecular meshwork (pilocarpine).

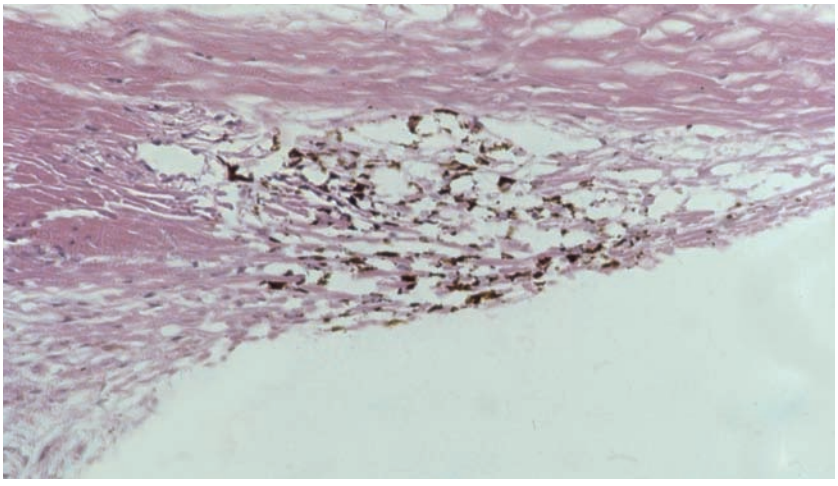

Image: Thomas Freddo, OD, PhD

Unlike prostaglandins, which lower intraocular pressure by increasing drainage of aqueous humor through the uveoscleral pathway, Rho-kinase inhibitors improve drainage through the trabecular meshwork (above).

Bear in mind that the trabecular meshwork (TM) accounts for the bulk (70% to 90%) of total aqueous humor outflow.[1,2]

Although current ocular hypotensive medications are effective, they also have some clear disadvantages. Aqueous suppression agents may decrease oxygen and nutrient supplies to non-vascularized tissue, like the cornea, lens and TM. Prostaglandins do not significantly improve trabecular outflow, and cholinergic drugs typically have unwanted, local tissue side effects, refractive side effects and the potential for systemic issues.[3]

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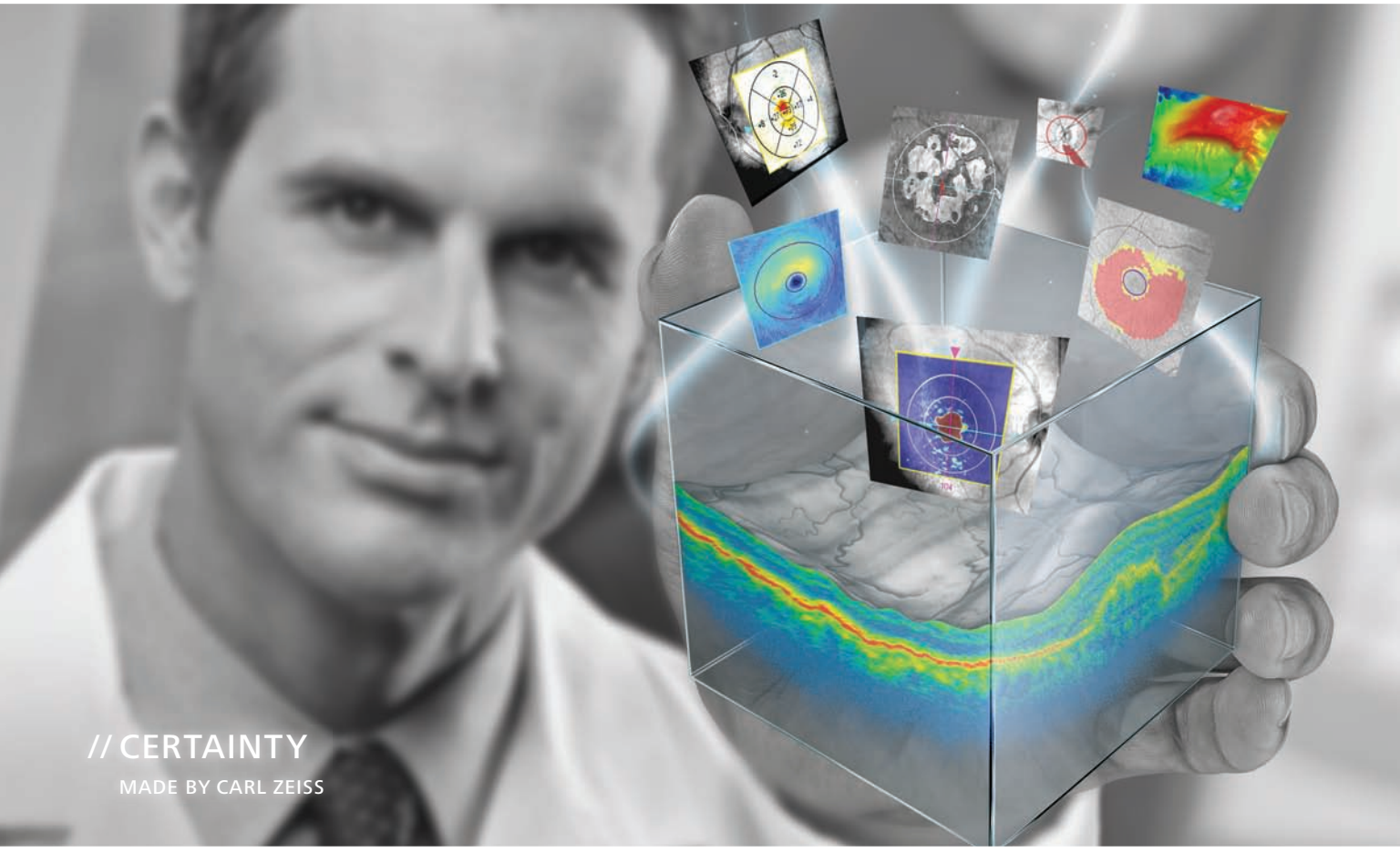

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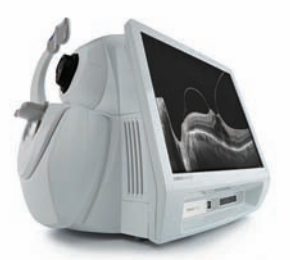

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Given these disadvantages, you may wonder: Why haven't other drugs been developed that target the trabecular pathway? The problem with targeting the TM is that we don't know the exact mechanism that resists aqueous humor as it traverses the TM and subsequent structures. (These structures include—in order of the outflow of aqueous humor—the juxtacanalicular connective tissue [JCT], the inner wall of Schlemm's canal and, lastly, the lumen of Schlemm's canal. However, most of the resistance to aqueous humor is believed to be generated in the JCT of TM, the inner wall lining of Schlemm's canal, or both.[4-7])

Thus, without having a specific target and clear understanding of the underlying mechanism that regulates resistance to aqueous humor in normal eyes—let alone eyes with glaucoma—investigators have had difficulty developing drugs that increase outflow through the trabecular pathway.

However, recent ocular perfusion studies with drugs that inhibit the Rho-associated kinase (ROCK) pathway in animal models have shown enhanced drainage of aqueous humor through the trabecular pathway, which has led to exploration and development of a promising new class of drugs for treatment of OHT and POAG: Rho-kinase inhibitors.[8-11]

Rho-kinase Inhibition

Rho-kinase inhibitors (RKIs) work at the cellular level by inhibiting the ROCK signaling pathway. The ROCK signaling pathway promotes cell contractility and adhesion of fibroblast cells (e.g., JCT cells).[12-14] Simply put, RKIs induce structural changes to the cytoskeletal framework of fibroblasts that make them more flexible.

Inhibition of the ROCK pathway not only has great promise for treating glaucoma, but also has therapeutic potential for cardiovascular and pulmonary diseases, prostate cancer, neurological disorders and corneal endothelial wound healing.[15-21]

In the eye, inhibiting the ROCK pathway with RKIs is thought to lower IOP by inducing cellular relaxation and disrupting focal adhesions in the TM and the inner wall endothelial lining of Schlemm's canal.[8]

Although the exact mechanism for this increase in outflow facility is unknown, ocular perfusion studies in enucleated cows and monkeys with RKI Y-27632 (a selective inhibitor of specific isoforms for ROCK-I and ROCK-II) have shown significant increases in outflow facility that coincide with an increase in the effective filtration length and separation between the inner wall endothelial cells and underlying JCT (in cows), and between JCT cells and their matrix (in monkeys).[9,10] It may be that RKI Y-27632 increases outflow facility by relaxing the cytoskeleton and disrupting the connectivity between inner wall endothelial cells and between JCT cells, which in turn may decrease resistance to aqueous by redistributing outflow patterns through looser regions in the JCT and the inner wall. This hypothesis is supported in similar findings of enucleated pig eyes treated with RKI Y-27632 and monkey eyes with RKI AR-12286.[8,22]

In human studies, though, the morphological changes in the JCT/inner wall region differed from the animal studies, and therefore warrant further investigation. Specifically, ocular perfusion of RKI Y-27632 in enucleated normal human eyes showed a 134% increase in outflow facility, which correlated with the available area for aqueous humor outflow.[23]

Topical RKIs Lower IOP

The IOP-lowering effects of topical RKIs have been documented in a number of human studies.

For example, investigators in Japan administered RKI SNJ-1656 to healthy patients at dosages of 0.003%, 0.01%, 0.03%, 0.05% and 0.1% QD or BID, and revealed a dose-dependent drop in IOP at two and four hours post-instillation, with a noted side effect of mild conjunctival hyperemia.[24]

A study examining the hypotensive effect of topical administration of RKI AR-12286 at dosages of 0.05%, 0.1% and 0.25% in patients with elevated IOP showed clinically significant reductions in mean IOP that were dose-dependent.[25] The largest reductions in IOP (28%) were produced with a BID dosage of 0.25% AR-12286, with the only adverse side effect of note being trace to moderate conjunctival hyperemia that lasted four hours or less.

Researchers have shown that combining 0.25% AR-12286 and 0.5% travoprost produces an ocular hypotensive effect that was clinically and statistically greater than travoprost alone, which suggests that a combination therapy of RKI/prostaglandin analog may be a highly effective ocular hypotensive treatment.[26]

However, this may not be the case with other combinations of RKIs and ocular hypotensive drugs. For example, RKI Y-27632 reduced intraocular penetration of timolol maleate that presumably was due to increased systemic elimination through the conjunctival vasculature.[27] Therefore, a multi-drug regimen of RKIs and other ocular

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  - The only events seen significantly more often with RESCULA than with timolol were burning and stinging and burning/stinging upon instillation; these events were generally mild and transient[2,4]
- No labeled drug-drug interactions[1,4]

Indication

RESCULA (unoprostone isopropyl ophthalmic solution) 0.15% is indicated for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Important Safety Information

RESCULA is contraindicated in patients with hypersensitivity to unoprostone isopropyl or any other ingredient in this product.

RESCULA has been reported to increase pigmentation of the iris, periorbital tissues, and eyelashes. Patients should be advised about the potential for increased brown iris pigmentation which is likely to be permanent.

RESCULA should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Macular edema, including cystoid macular edema, has been reported. RESCULA should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

*In pooled safety analyses of pivotal trials comparing RESCULA with timolol maleate 0.5%.[4]

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Brief Summary of Prescribing Information for RESCULA.

INDICATIONS AND USAGE
Rescula (unoprostone isopropyl ophthalmic solution) 0.15% is indicated for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

DOSAGE AND ADMINISTRATION
The recommended dosage is one drop in the affected eye(s) twice daily.

Rescula may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If two drugs are used, they should be administered at least five (5) minutes apart.

CONTRAINDICATIONS
Rescula is contraindicated in patients with hypersensitivity to unoprostone isopropyl or any other ingredient in this product.

WARNINGS AND PRECAUTIONS
Iris Pigmentation
Unoprostone isopropyl ophthalmic solution may gradually increase the pigmentation of the iris. The pigmentation change is believed to be due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. The long term effects of increased pigmentation are not known. Iris color changes seen with administration of unoprostone isopropyl ophthalmic solution may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. Treatment with Rescula solution can be continued in patients who develop noticeably increased iris pigmentation. Patients who receive treatment with Rescula should be informed of the possibility of increased pigmentation.

Lid Pigmentation
Unoprostone isopropyl has been reported to cause pigment changes (darkening) to periorbital pigmented tissues and eyelashes. The pigmentation is expected to increase as long as unoprostone isopropyl is administered, but has been reported to be reversible upon discontinuation of unoprostone isopropyl ophthalmic solution in most patients.

Intraocular Inflammation
Rescula should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Macular Edema
Macular edema, including cystoid macular edema, has been reported. Rescula should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Contamination of Tip and Solution
To minimize contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use. There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products.

Use with Contact Lenses
Rescula contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to application of solution and may be reinserted 15 minutes following its administration.

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

In clinical studies, the most common ocular adverse reactions with use of Rescula were burning/stinging, burning/stinging upon drug instillation, dry eyes, itching, increased length of eyelashes, and injection. These were reported in approximately 10–25% of patients. Approximately 10–14% of patients were observed to have an increase in the length of eyelashes (≥ 1 mm) at 12 months, while 7% of patients were observed to have a decrease in the length of eyelashes.

Ocular adverse reactions occurring in approximately 5–10% of patients were abnormal vision, eyelid disorder, foreign body sensation, and lacrimation disorder.

Ocular adverse reactions occurring in approximately 1–5% of patients were blepharitis, cataract, conjunctivitis, corneal lesion, discharge from the eye, eye hemorrhage, eye pain, keratitis, irritation, photophobia, and vitreous disorder.

The most frequently reported nonocular adverse reaction associated with the use of Rescula in the clinical trials was flu-like syndrome that was observed in approximately 6% of patients. Nonocular adverse reactions reported in the 1–5% of patients were accidental injury, allergic reaction, back pain, bronchitis, increased cough, diabetes mellitus, dizziness, headache, hypertension, insomnia, pharyngitis, pain, rhinitis, and sinusitis.

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

Voluntary reports of adverse reactions occurring with the use of Rescula include corneal erosion.

There have been rare spontaneous reports with a different formulation of unoprostone isopropyl (0.12%) of chemosis, dry mouth, nausea, vomiting and palpitations.

USE IN SPECIFIC POPULATIONS
Pregnancy Category C - There are no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, RESCULA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Pediatric Use - the safety and efficacy of RESCULA in pediatric patients have not been established.

It is not known whether RESCULA is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when RESCULA is administered to a nursing woman.

No overall differences in safety or effectiveness of RESCULA have been observed between elderly and other adult populations.

CLINICAL PHARMACOLOGY
Mechanism of Action
Rescula is believed to reduce elevated intraocular pressure (IOP) by increasing the outflow of aqueous humor through the trabecular meshwork. Unoprostone isopropyl (UI) may have a local effect on BK (Big Potassium) channels and CIC-2 chloride channels, but the exact mechanism is unknown at this time.

STORAGE AND HANDLING
Store between 2°–25°C (36°–77°F).

For more detailed information please read the Prescribing Information.

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Revised 01/2013

References: **1.** RESCULA [package insert]. Bethesda, MD: Sucampo Pharmaceuticals, Inc; 2012. **2.** Data on file. CSR C97-UIOS-004. Sucampo Pharmaceuticals, Inc. **3.** Data on file. CSR C97-UIOS-005. Sucampo Pharmaceuticals, Inc. **4.** Data on file. Integrated summary of clinical safety. Sucampo Pharmaceuticals, Inc. **5.** McCarey BE, Kapik BM, Kane FE; Unoprostone Monotherapy Study Group. Low incidence of iris pigmentation and eyelash changes in 2 randomized clinical trials with unoprostone isopropyl 0.15%. *Ophthalmology.* 2004;111(8):1480-1488.

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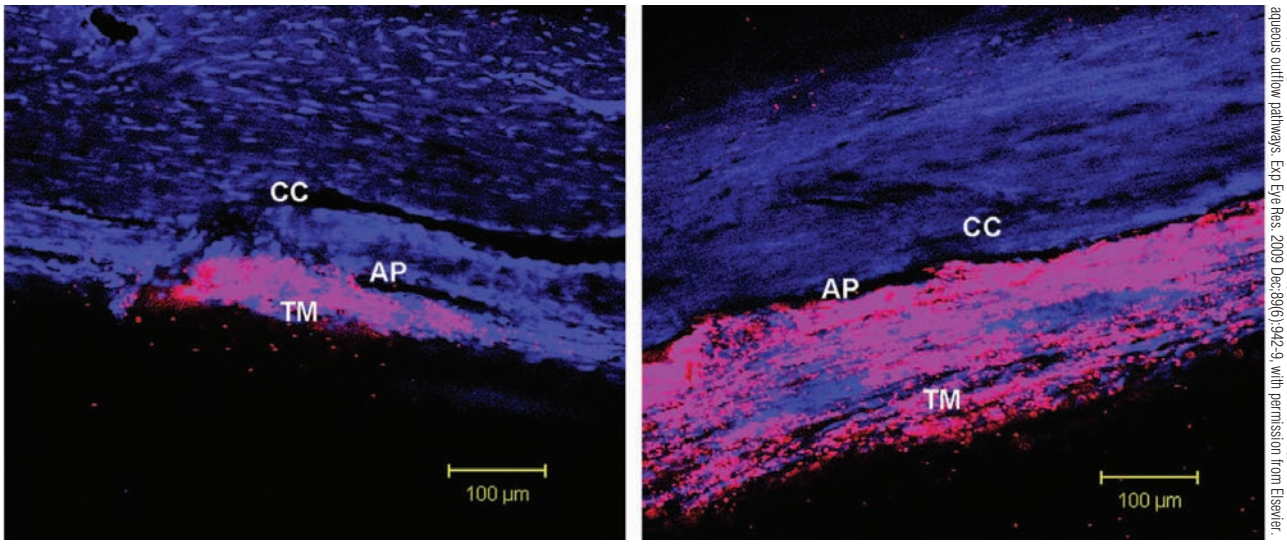

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Rho-kinase inhibitors (RKIs) appear to lower IOP by inducing cellular relaxation and disrupting focal adhesions in the trabecular meshwork (TM) and the inner wall endothelial lining of Schlemm's canal. Confocal microscopic analysis demonstrates the penetration of an RKI in an animal study. In a control eye (left), the tracer dye concentrated in only a small segment of the TM. In an eye treated with RKI (right), the drug was distributed more uniformly throughout the TM.

hypotensive drugs may require the clinician and patient to be mindful of the order and timing of RKI administration.

Additional Benefits to Ocular Tissue

Investigators are finding that, in addition to lowering IOP, RKIs have other benefits for the eye:

• ***Protect human trabecular meshwork cells.*** Oxidative stress is known to occur in glaucoma and causes upregulation of pro-inflammatory cytokines interleukin (IL)-6 and IL-8, which have been linked to cellular senescence in human trabecular meshwork cells. Cell culture studies have shown that human TM cells treated with RKI Y-27632 exhibit reduced expression of IL-6 and IL-8 mRNA after oxidative stress, which suggests that RKIs may have a protective effect on human TM cells.[28]

• ***Improve blood flow to optic nerve.*** Vasospasm and altered hemodynamics are believed to play a role in certain types of glaucoma, especially normal-tension glaucoma.[29-30] Studies in rabbits have provided evidence that systemic or topical application of the RKI fasudil (used to induce vasodilation and improve cerebral blood flow after cerebral vasospasm and stroke) may also suppress impaired blood flow to the optic nerve head.[34]

• ***Facilitate corneal endothelium wound healing.*** Topical RKI Y-27632 has been shown to promote wound healing in primates with partially injured corneal endothelia.[21] RKI Y-27632 increased corneal endothelial cell density and restored function in these animals, which suggests RKIs may be a potential therapeutic treatment for certain forms of corneal endothelial cell dysfunction in humans.

• ***Protect retinal ganglion cells.*** Glutamate and N-methyl-d-aspartate (NMDA) neurotoxicity have been implicated in retinal ischemia and optic neuropathy, and have been shown to cause degeneration of retinal neuronal cells. In rats with NMDA-induced neurotoxicity, retinal RhoA and ROCK-II protein levels increased and the number of retina ganglion cells decreased; however, intravitreal injection of the RKI fasudil significantly prevented these effects.[35]

• ***Decrease fibrosis.*** One of the main obstacles preventing successful glaucoma surgery is subconjunctival fibrosis. Topical RKI Y-27632 has been shown to decrease subconjunctival scarring after filtration surgery in rabbits.[36]

Potential Drawbacks

RKIs are potent vasodilators and, when administered topically to the eye, have been shown to induce conjunctival hyperemia and subconjunctival hemorrhages.[37] Also, extensive dilation of the conjunctival microvasculature may decrease the effect of concomitantly administered topical drugs by rapidly increasing extraocular clearance from the ocular cavity to the systemic circulation.[27]

RKIs in the Pipeline

Pharmaceutical companies, such as Senju Pharmaceuticals, Novartis, Kowa, Santen, Aerie, Inspire and others, are exploring ROCK signaling and the effects of RKIs. RKIs are not yet commercially available and many are still in early phases of development. RKIs to be on the lookout for are Y-27632, AR-12286, ATS907, ATS8535, AR-13324 and AMA0076.[38-41]

With current ocular therapeutics and laser/surgical modalities, the only means by which clinicians and surgeons have the ability to slow or stop the progression of glaucoma is to reduce intraocular pressure. Recent evidence suggests that other factors (e.g., local autoimmune disorders, oxidative stress, excitotoxicity and mitochondrial dysfunction) may be involved that cause continued disease progression, and IOP reduction alone may be an insufficient treatment in many patients with POAG. New therapies like Rho-kinase inhibitors could revolutionize the way in which we treat glaucoma. RKIs in early clinical trials appear to be safe and highly effective in lowering IOP, and may even provide neuroprotection to retinal ganglion cells at increased risk in patients with OHT and POAG.

Future investigations may focus on enhanced delivery systems for the drug or prodrug formulations to maximize and localize drug delivery and reduce the risks of unwanted side effects or potential toxicity. Furthermore, proper drug concentration for optimal efficacy, dosing schedule, as well as evaluating potential positive and negative interactions with other therapeutic hypotensive drugs in combination, need to be further evaluated to determine if these agents will be more useful as an adjunct to current treatment strategies or as stand-alone monotherapy. ■

Dr. Scott is an assistant professor of ophthalmology and visual sciences at the University of Louisville School of Medicine, in Kentucky. He has no financial interest in any of the products or companies mentioned.

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19th Annual Glaucoma Report

A Close-Up Look at Microinvasive Glaucoma Surgery

MIGS procedures can safely and effectively reduce intraocular pressure in patients with mild to moderate glaucoma. **By Leonid Skorin, Jr., OD, DO, MS**

Glaucoma surgery has entered a renaissance period. In recent years, emerging technologies for microinvasive glaucoma surgery (MIGS) have set the stage for revolutionary approaches that target patients with mild to moderate glaucoma. This modern era of glaucoma surgery has clearly placed improved patient safety at the center of innovation.

MIGS is a term that encompasses a wide variety of new instruments and techniques that are rapidly being adapted by ophthalmic surgeons. Examples of FDA-approved MIGS devices include Trabectome (NeoMedix Corporation) and the iStent Trabecular Micro-Bypass Stent (Glaukos Corporation). Other MIGS technologies include the Ex-Press Glaucoma Filtration Device (Alcon Laboratories), the AquaSys Implant (AquaSys) and the CyPass MicroStent (Transcend Medical). The Trabectome instrument has been available the longest, receiving FDA approval back in 2004. Additionally, the iStent just received FDA clearance in 2012.

Glaucoma Surgery 101

The lowering and stabilization of intraocular pressure (IOP) is the only proven treatment for glaucoma.[1,2] Contemporary glaucoma surgery decreases IOP in the eye either by inhibiting aqueous production or by enhancing its outflow. An example of the former is endoscopic cyclophotocoagulation (ECP), where energy from a diode laser is directly applied to the ciliary processes that produce the aqueous in the eye (*see "Consider ECP for Glaucoma," November 2008*).

Most of the other glaucoma surgeries enhance aqueous outflow. The procedures that do this can be divided into those that form a bleb (extra-scleral drainage) and those that enhance physiologic outflow ("ab interno").

• ***Bleb surgery.*** The bleb-forming incisional glaucoma surgeries lower IOP by creating a direct communication between the anterior chamber and subconjunctival space. This procedure completely bypasses the conventional route of aqueous drainage through the trabecular meshwork, Schlemm's canal and the collecting channels.

The subconjunctival fluid collects focally within the bleb and the aqueous resorbs into the episcleral venous system.[3] The two classic bleb-forming surgeries are trabeculectomy and glaucoma drainage implantation (tube shunts).

• ***Ab interno surgery.*** This surgical approach, on the other hand, eliminates the need for conjunctival dissection—thus, there is no bleb formation. The procedure either

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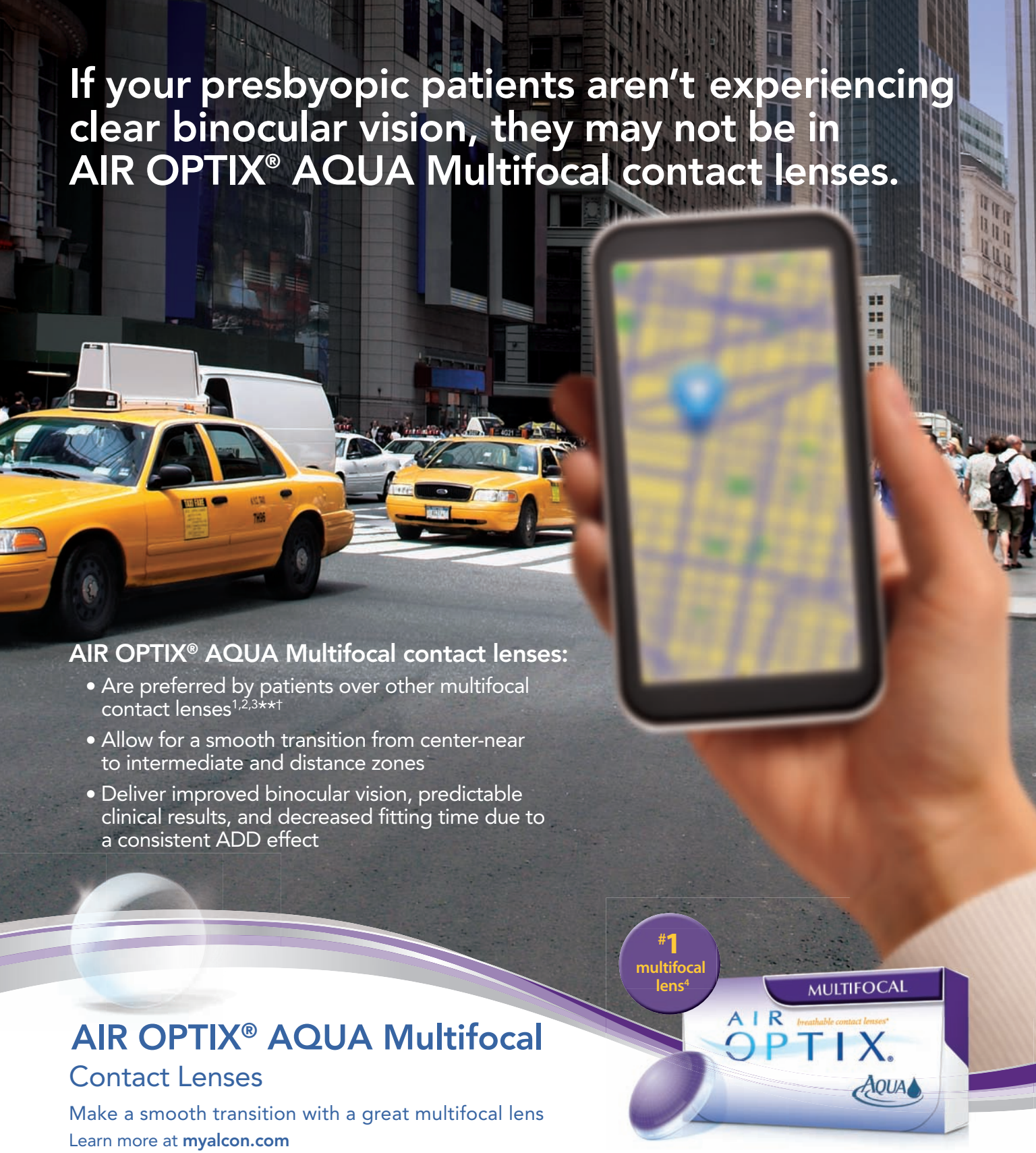

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References: 1. In a randomized, subject-masked clinical study at 20 sites with 252 patients; significance demonstrated at the 0.05 level; Alcon data on file, 2009. **2.** Rappon J. Center-near multifocal innovation: optical and material enhancements lead to more satisfied presbyopic patients. *Optom Vis Sci.* 2009;86:E-abstract 095557. **3.** In a randomized, subject-masked clinical trial at 6 sites with 47 patients; significance demonstrated at the 0.05 level; Alcon data on file, 2008. **4.** Based on a third-party industry report, 12 months ending October 2012; Alcon data on file.

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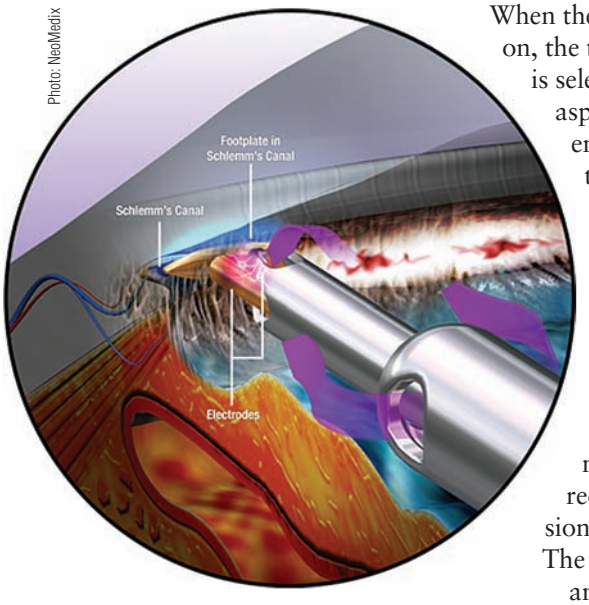


1. Triangular configuration of the handpiece tip, which is inserted through the trabecular meshwork into Schlemm's canal.

removes the trabecular meshwork and inner wall of Schlemm's canal or bypasses these two structures—effectively re-establishing aqueous outflow directly into the collecting channels.

This direct access to the collecting channels is significant because the trabecular meshwork is the anatomic location that poses the greatest resistance to aqueous outflow.[4] Examples of ab interno glaucoma surgeries include Trabectome and iStent, both of which are MIGS procedures.

Trabectome Instrumentation

The Trabectome consists of a 19.5-gauge insulated handpiece that fits through a 1.7mm corneal incision. The handpiece is connected to a console with irrigation and aspiration, and a high-frequency electro-surgical generator. The handpiece's triangular, sharp point assists in its insertion through the trabecular meshwork and into Schlemm's canal (*figure 1*).

When the instrument is turned on, the trabecular meshwork is selectively vaporized and aspirated by a series of energy pulses. Rather than cause thermal ablation, the bursts disrupt and disintegrate the tissue (*figure 2*).[5,6] A 90° to 120° strip of trabecular meshwork tissue is removed via one surgical incision (*figure 3*). (Removal of more than 120° of tissue requires two surgical incisions into the cornea.)

The irrigation, aspiration and electro-surgical functions are controlled by the surgeon's foot pedal. The initial power setting, which also is controlled by the surgeon, ranges from 0.7 watts to 0.9 watts.[7,8]

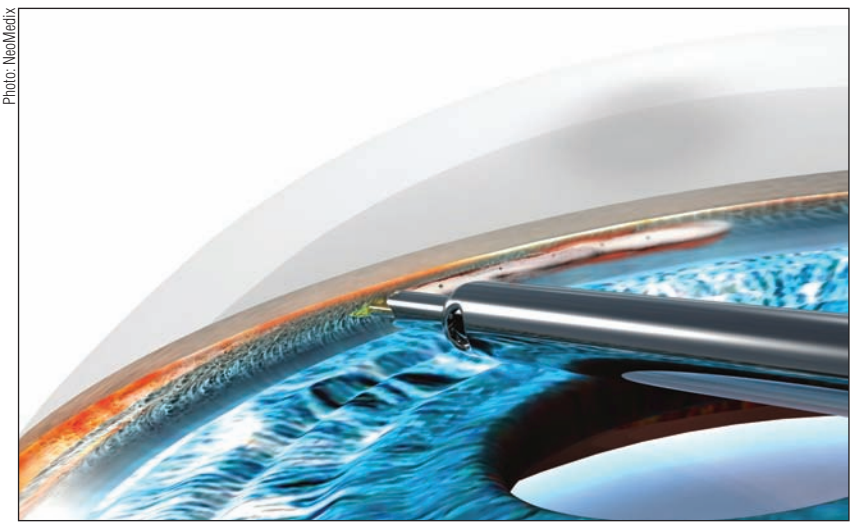
The tip of the handpiece is very sharp and must not touch the iris during its advancement in the anterior chamber, because consequential bleeding would obscure the image and potentially force the surgeon to abort the procedure.

Trabectome Surgery

If the trabectome surgery is being performed in combination with cataract extraction, the typical preoperative dilating, non-steroidal anti-inflammatory drug and antibiotic regimen is indicated.[8] In the standalone trabectome surgery, however, 1% or 2% pilocarpine is administered to yield pupillary miosis for easier instrument access into the chamber angle.[3] Viscoelastic is injected into the anterior chamber and the handpiece is advanced towards the opposite chamber angle. This almost always is the nasal angle because the clear corneal incision will be placed temporally, which makes the trabecular meshwork accessible to the surgeon. Visualization of the chamber angle is achieved with a goniosurgical lens (a modified Swan-Jacobs lens) that is placed on the cornea (*figure 4*).

An interesting aspect of this surgery is the positioning of both the patient and the surgeon. The patient's head is rotated away from the surgeon. This helps expose the temporal approach to the cornea. By rotating the surgical microscope

Photo: NeoMedix



2. The trabecular meshwork and inner wall of Schlemm's canal are selectively vaporized and aspirated using high-frequency bursts of electrocautery heat energy.

The Benefits and Dangers of BLUE LIGHT

By Christian Sotty

The blue light region in the visible light spectrum has captured the interest of scientists due to its role in non-visual biological mechanisms such as regulation of the circadian cycle. This part of blue light can have a positive impact on health, and it ranges from 465 to 495 nanometers (nm) (Blue-Turquoise light).[1] However, in the range of 415 to 455 nm (Blue-Violet light), it has been established that light induces a high level of mortality in the retinal pigment epithelium (RPE) cells.[2] Blue light (also known as high energy visible light) ranges from 380 nm to 500 nm. It is emitted by both natural (sun) and artificial light sources, such as LED lighting.

Synchronizing our biological clock

Light, and in particular "good" blue light, also known as "chronobiological light," regulates our individual circadian rhythm. We need to reset our biological clocks daily in order to synchronize our biological rhythm. Our clock transmits to a number of parts of the body, such as the liver, muscles, heart, kidneys and other organs. All biological functions need to work at the right moment, and because our biological clock drives this particular rhythm, it ensures particular functions are active at the right time.

"Light acts on the retina through the action of specific cells—melanopsin-containing ganglion cells—which are different from the cones and rods that are the photoreceptors used in vision," said Claude Gronfier, INSERM (French Institute of Health and Medical Research) chronobiology researcher. "When these ganglion cells are activated by blue light, they transmit a nerve signal that runs along the optic nerve and, rather than activating the visual structures in the brain, activates non-visual structures such as our internal circadian clock. So it's exposure to light that resets the time on the biological clock."

Blue light and AMD

Recently, it has been shown that exposure to light contributes to the early occurrence of age-related macular degeneration (AMD).[3] *In-vitro* experiments on porcine cell cultures point specifically to blue light, which is more energy intensive. Macular pigments are natural filters for these wavelengths. Unfortunately, pigments don't accumulate well in the retina as we age or when disease starts.

"It's essential to combine several approaches to help explain the pathophysiological impact of light on the retina and the part played by these effects on retinal conditions," said Serge Picaud, INSERM director of research at the Paris Vision Institute.

"This multidisciplinary aspect was one of the challenges of a recent project in which we tried to determine toxic wavelengths in the visible spectrum. Our main aim was to calculate the relative quantity of light reaching the retina in each wavelength. We measured the toxicity of these relative irradiances using an AMD porcine cell model.

"The work enabled us to define the most phototoxic spectral bands against this cellular model," he said. "Optics specialists from Essilor took part in the project to help us design optical devices to calculate retinal light irradiances and to manipulate concepts involving light, while researchers from the Paris Vision Institute brought their knowledge of vision and their know-how in experimental biology as applied to the retina. It was important to be able to draw on the results to establish preventive strategies designed to limit the initial development or further progress of visual pathologies."

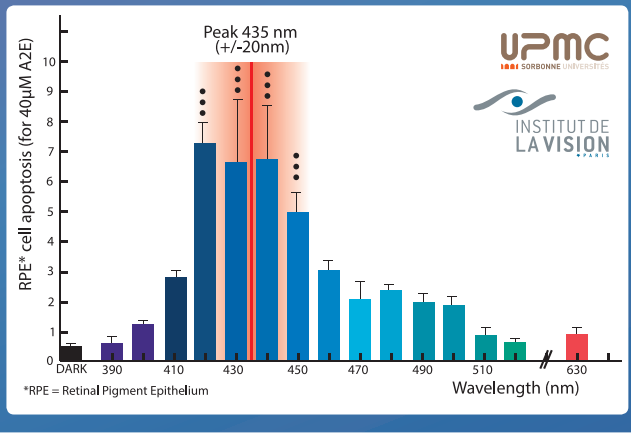
10-nm illumination bands

The blue light spectrum is very wide, ranging in broad terms from 380 to 500 nm. It was important to target the blue wavelengths that were most harmful and control the illumination values used to expose the cells to light.

"We produced an illumination device that allowed us to convey light on very restricted, narrow wavelengths—and we split the visible light spectrum into 10-nanometer bands," said Emilie Arnault, photobiology project manager in the Translational Systemic and Therapeutic Biology of Vision department at the Paris Vision Institute. "Each band was guided by an optic fiber toward a cell incubator. This allowed us to split the visible light spectrum and precisely control the degree of illumination for each wavelength. We were able to produce intensities of illumination in proportion to those of the solar spectrum for each 10 nm band."

All of these elements confirm the importance of the research currently conducted to accurately describe the wavelengths of blue light: we need to be able to distinguish good from bad clearly so that we can then develop a sophisticated filtering system to address the harmful effects of one while retaining the positive effects of the other.

RPE Cell Death per Wavelength[2]



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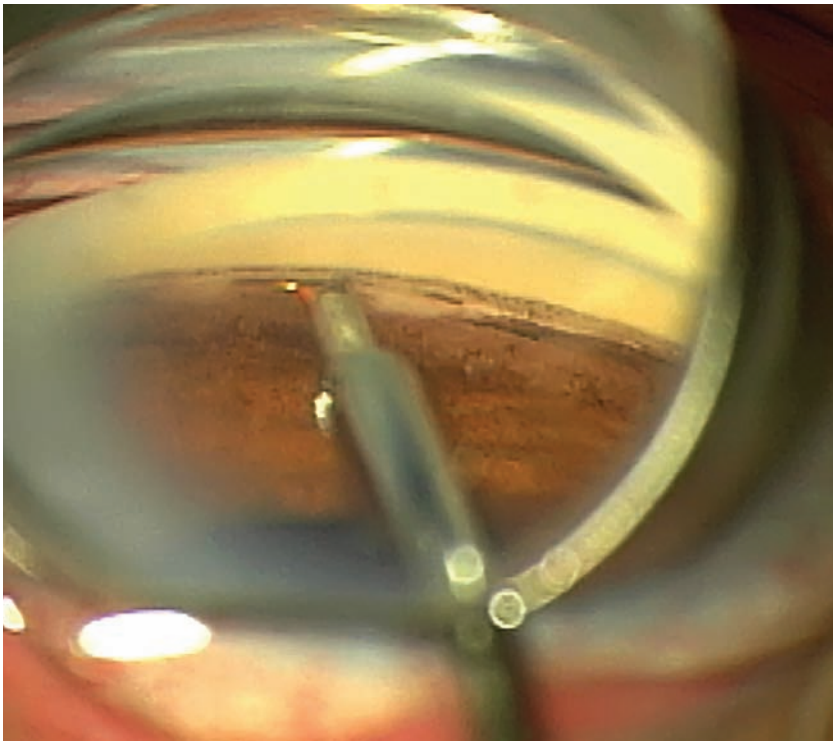

3. A strip of 90° to 120° of tissue usually is removed via one surgical incision.

45°, the nasal chamber angle will be revealed with gonioscopic viewing. The overall combined angle from the patient's eye in primary gaze is approximately 70° to 80°. (This positioning reminds me of how a rider would sit on a chopper motorcycle.)

After the trabecular material is removed, the surgical incision is closed with a suture to ensure a leak-proof wound.[9] The patient is placed on routine postoperative medications as well as 1% pilocarpine TID to QID for at least one month. The pilocarpine helps keep the iris tissue out of the angle, minimizes contraction of the surgical opening and limits scar tissue formation.

• ***Postoperative complications.*** Trabeculectomy surgery and glaucoma drainage implants carry a higher risk of postoperative complications than most MIGS procedures, including Trabectome. Trabeculectomy has a 1% per year risk of endophthalmitis and other frequent vision-threatening outcomes, such as persistent hypotony, choroidal detachments, aqueous misdirection (malignant glaucoma), blebitis and bleb leak.[10,11] Drainage implants can cause complications, such as motility disturbances, hypotony, corneal decompensation and tube erosions.[12]

The most frequent complications seen with Trabectome are transient hyphema and elevated IOP at one-day post-op.[3] Bleeding at the surgical site occurs routinely during the removal of trabecular meshwork tissue with this procedure. Additionally, postoperative cataract development is less likely following Trabectome than after other bleb-forming surgeries (unless there is inadvertent perioperative lens damage). Hypotony also is rare because the corneal incision is closed with a suture. Over time, the chamber angle trabecular meshwork may undergo scarring and close the cleft, causing an IOP increase (*figure 5*).[3]

• ***Success rate.*** The anticipated postoperative IOP range associated with Trabectome surgery is in the mid teens.[3] Results from a retrospective review of 1,127 Trabectome procedures (738 Trabectome-only and 366 Trabectome-phacoemulsification surgeries) show an IOP reduction in Trabectome-phacoemulsification of 18% at 12 months, and a 40% reduction for Trabectome-only at 24 months.[13] Additionally, other studies have indicated that patients use 33% to 40% less topical glaucoma medication for up to two years postoperatively.[3,6]

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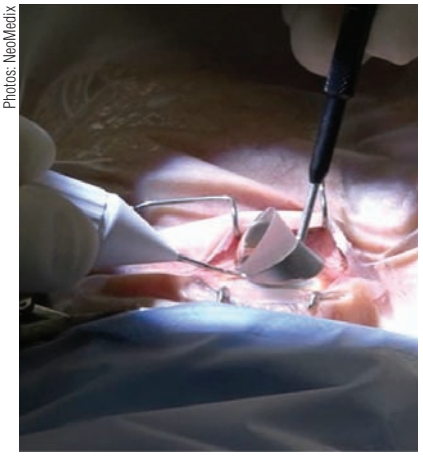

4, 5. Surgical positioning of the Trabectome handpiece within the eye and the goniosurgical lens on the cornea (left). Gonioscopy shows a wide-open surgical cleft one month after Trabectome surgery.

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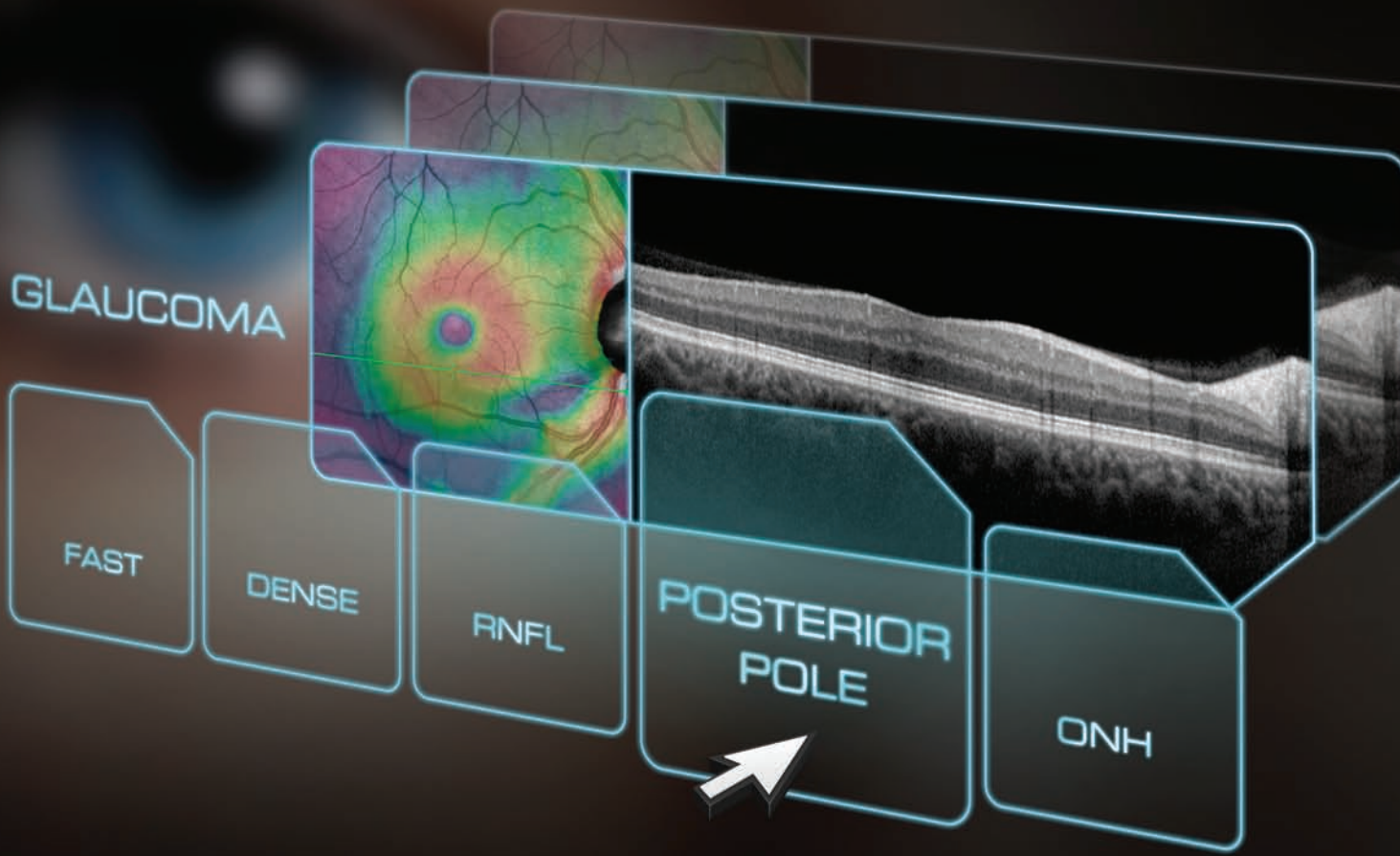

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iStent Technology

Similar to the Trabectome, implantation of the iStent is an ab interno procedure that fundamentally eliminates the need for conjunctival dissection.

Glaucoma surgeons have learned that implanting larger drainage devices does not always yield a better result. Based on this lesson, the iStent is the smallest medical device ever implanted into humans—less than 1mm in length and 0.5mm in width (*figure 6*).[14]

6. The iStent is the smallest medical device ever implanted into humans.

The titanium stent is self-trephining and is implanted using an injector. After the device is implanted into Schlemm's canal via the trabecular meshwork, the greatest resistance to aqueous outflow is bypassed.

Just like with Trabectome surgery, direct visualization of the chamber angle and its structures is achieved via a goniosurgical lens and an operating microscope. A stable anterior chamber is important in the early postoperative period. Therefore, as with Trabectome surgery, a suture may need to be placed through the corneal surgical incision.

• ***Success rate.*** Schlemm's canal is not a continuous chamber that encircles the eye 360° degrees. Instead, the canal has 20 to 35 collector channels, and an iStent typically accesses only one or two of these.[14] So, more than one stent may need to be implanted to achieve additional IOP lowering.

Combined cataract surgery and iStent implantation also can be performed. Usually, the cataract surgery is done before the iStent placement. In a one-year prospective trial, 240 eyes with mild to moderate glaucoma were randomly assigned to cataract surgery and iStent implantation (stent group) or cataract surgery alone (control group).[15] The researchers found that a significantly higher proportion of patients in the stent group (72% vs. 50%) achieved a postoperative IOP measurement of less than 21mm Hg without medication.[15]

A two-year safety and efficacy follow-up study showed similarly favorable results.[16] Sixty-one percent of patients who underwent stent implantation achieved an IOP measurement of 21mm Hg or lower without the use of ocular hypotensive medications, compared to 50% of patients who underwent cataract surgery alone.

With the advent of the new MIGS procedures, all eye care clinicians should experience a welcome shift in the treatment of glaucoma patients. Gone will be the days of patients needing to use three or even four different pressure-lowering medications. Also gone will be waiting until the disease has advanced far enough to warrant a more aggressive and complicated extra-scleral drainage surgery.

Because of the increased safety associated with MIGS procedures, as well as their efficacy in mild to moderate glaucoma and ease of surgical application, more and more anterior segment surgeons will be incorporating these techniques during the next few years. ■

Dr. Skorin is the senior staff ophthalmologist at Mayo Clinic Health System in Albert Lea, Minn., and is an assistant professor of ophthalmology at the Mayo Clinic College of Medicine. He is certified in Trabectome, but has no direct financial interest in any of the products mentioned.

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PAMELA LOWE, OD, FAAO

Dr. Lowe is the owner and director of Professional Eye Care Center Inc. in the greater Chicago area.

Streamline the Multifocal Fitting Process

Tips for achieving success with multifocals for the everyday practitioner.

Contact lens practitioners and their patients may encounter complications during the fitting process of any lens, but multifocals may lead to additional complications if the practitioner and the patient don't clearly communicate. Therefore, streamlining the multifocal fitting process will benefit you, your practice, and your patients.

Any of the following factors can result in an unsatisfactory fitting experience for patient and practitioner.

- ***Poor communication about the fitting process.*** Patients need to be aware that the fitting process is just that—a process—and that finding success may require more than one visit.
- ***Failure to set realistic expectations.*** Patients need to go into multifocal contact lens wear knowing that their vision won't be as good as it was when they were younger. It's important for you, the expert, to be confident in the fit process. Your confidence and attitude will have a positive impact on the patient.

Being aware of these pitfalls and proactively avoiding them will increase your multifocal fitting success.

5 Steps to Ensure Success

These pitfalls can easily be avoided by following the steps. Doing so will set yourself—and your patients—up for a successful multifocal fitting experience.

1. ***Set expectations early.*** Let each patient know at the onset of lens fitting that they can achieve good multifocal contact lens vision by working and communicating with you.
2. ***Confirm multifocal suitability.*** Patients need to have no or a low amount of cylinder in their habitual correction and be motivated and excited to try the lenses.
3. ***Listen to your patients' needs before and during the fitting process.*** Always be in tune to each patient's distance and near visual demands as well as any special viewing situations that are unique to them.
4. ***Know when to make adjustments.*** Recognize the need to adjust the contact lens type or consider other options. Don't chase your tail by casually adjusting powers and adds without considering the design and science behind the lens optics. If you're using the AIR OPTIX® AQUA Multifocal contact lens, you can always turn to the fitting guidelines to help ensure fit success.
5. ***Use the ace up your sleeve.*** Having a go-to lens, such as the AIR OPTIX® AQUA Multifocal contact lens, helps to reduce fitting complications, which should increase patient satisfaction. AIR OPTIX® AQUA Multifocal contact lenses are the #1 selling multifocal lens.[1]

> "This lens makes soft multifocal lens fitting a pleasure, rather than a chore."

An Answer to Presbyopic Prayers

Due to the AIR OPTIX® AQUA Multifocal contact lens's Precision Profile Design and binocular optics, it is imperative to rely on the fitting guidelines. This lens makes soft multifocal lens fitting a pleasure, rather than a chore. And, with baby boomers firmly in the presbyopic zone and Generation X-ers following right behind them, it has been a great source of satisfaction (and referrals) that keeps my practice vital and growing!

Reference: 1. Based on third-party industry report, 12 months ending March 2013; Alcon data on file.

19th Annual Glaucoma Report

Is Normal Tension Glaucoma a Clinically Distinct Entity?

Perspectives on the unique challenges and unanswered questions raised by this apparent anomaly. **By Leo Semes, OD, and Jamie C. Reid, OD**

Normal tension glaucoma (NTG) is among the greatest enigmas in eye care. In fact, some believe that as a separate diagnosis, it is a distinction without a difference. Those who prefer to characterize NTG as a separate entity point to evidence of alterations of blood flow to the eye among NTG patients, for example. This may help to explain why patients with intraocular pressure (IOP) in the normal range suffer glaucomatous damage.

As we learn more about the pathogenesis of glaucoma in general, some new ideas emerge. Maybe the statistically normal range of pressure is an erroneous construct. Perhaps the answer is perfusion pressure to the optic nerve head (ONH). Maybe the mechanism is related to an imbalance of intracranial pressure (ICP), which is indexed to cerebrospinal fluid pressure (CSFP). Could it be that the IOP climbs above the normal range at other times than when sampled in the office setting? Could NTG be related to peripheral vascular dysregulation, anatomical variations or even genetics? Is normal tension glaucoma a unique diagnosis or an overlap? All of these processes have been proposed over the years.

The distinction between the subset of open-angle glaucoma patients who have consistently "normal" intraocular pressure (IOP) and those whose IOP is measured above that upper limit is completely arbitrary. That population may represent between 20% and nearly 40% of cases of diagnosed glaucoma in the United States.[1] The notion of pressure-independent damage consistent with a diagnosis of glaucoma suffered at IOP within the statistically normal range has been a difficult diagnosis for many years.[2] Early and ongoing studies on IOP-lowering strategies for stalling progression have offered management guidance.

The Collaborative Normal Tension Study Group (CNTGSG) evaluated whether IOP should be reduced in patients with NTG. After the five-year trial, CNTGSG results found that 12% (7/61) of medically or surgically treated patients vs. 35% (31/79 controls) of untreated patients exhibited visual field or optic disc progression.[3] Their results showed a positive benefit from a 30% reduction of IOP with disease progression. Even though the treated group benefited from the lower IOP, there was still progression among those patients.

Should we lower IOP further than 30%? This study was performed before prostaglandins and prostamides were approved for treatment of glaucoma. Therefore, further IOP reduction was difficult to obtain at the time of the study.

Later, CNTGSG published a study looking at the medical history of the untreated patient to investigate a common factor among the NTG patients. History of hypertension, undergoing

Potential Contributors to NTG

- Low optic nerve perfusion pressure (either situational or continuous)
- Low blood pressure
- Low cerebrospinal fluid pressure
- Situationally elevated IOP
- Systemic vascular dysregulation signs (e.g., cold extremities, migraine sufferer)

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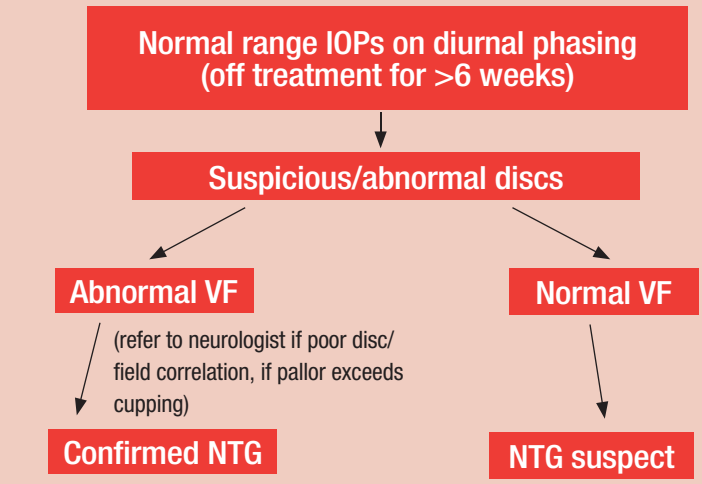
major surgery, migraine and non-migraine headaches, and family history of stroke, glaucoma and diabetes were all reported as common factors. However, females with a history of migraines were identified to have a great risk of developing rapid visual field deterioration.[4] Perhaps we should be looking more carefully at vascular regulation of blood flow to the optic nerve.

A more recent work—the Low-Pressure Glaucoma Study (LoTGS)—looked at visual field progression with monotherapy of brimonidine tartrate 0.2% vs. timolol maleate 0.5% (both dosed BID).[5] Despite similar average IOP-lowering effects from both drugs, the brimonidine treatment group had a much lower rate (9.1%) of visual field progression vs. the timolol group (39.2%).

The mystery remained: If IOP is lowered by the same amount, why the difference in progression? A review of the evidence has shown that alpha-2 adrenergic agonists may confer neuroprotective properties in experimental optic nerve injuries.[6] Evidence for such efficacy in human glaucoma damage is lacking.

Before enumerating potential connections with NTG, let's look at the differential diagnoses. A comprehensive approach includes complete ocular and systemic histories. For example, has there ever been a history of blunt trauma or an episode of acute blood loss? Our clinic serves a patient who, as a teenager, severed his right radial artery. This required hospitalization, but his optic nerve on that side is markedly more damaged than the fellow eye. Despite consistently very low IOP, he has shown slow progression over two decades of follow-up.

Algorithm for the Practical Management of a Patient With Confirmed or Suspected Normal Tension Glaucoma



Establish baseline data
- Baseline reproducible VF by threshold perimetry
- Baseline "damage causing" IOP
- 3D optic disc imaging

Look for progression
- Serial IOPs (for progressive increase)
- Serial optic disc examination/analysis (+ look for disc hemorrhages)
- Serial visual fields (3x per year)
- Subjective deterioration

Establish baseline data
- Check optic disc size and C/D ratio against normative HRT database

Look for change
- Serial optic disc exam/analysis
- Serial visual fields

Progression detected (objective or subjective)
- Exclude treatable risk factors (e.g., nocturnal hypotension, vasospasm, abnormal rheology)
- Reduction of baseline IOP by 25-30%

Systemically, episodes of acute (e.g, accident or surgery requiring blood transfusion) or chronic blood loss (e.g, bleeding ulcer) may be important contributors to observed disc damage that may be stable or result in a vulnerable ONH. In these situations with statistically normal IOP, appropriate ancillary testing may prove a better clinical course than potentially invasive testing. Ischemic optic neuropathies (e.g., NAION, GCA) are other masqueraders of NTG with distinct clinical characteristics that would require a separate description beyond this discussion.

Definitive guidance for neuroimaging considerations in questionable cases of NTG has been reported.[7] Those of younger age at initial observation (<50 years), with decreased visual acuity (VA poorer than 20/40), specific visual-field defects respecting the vertical midline or pallor greater than cupping are the ideal candidates for such investigations.

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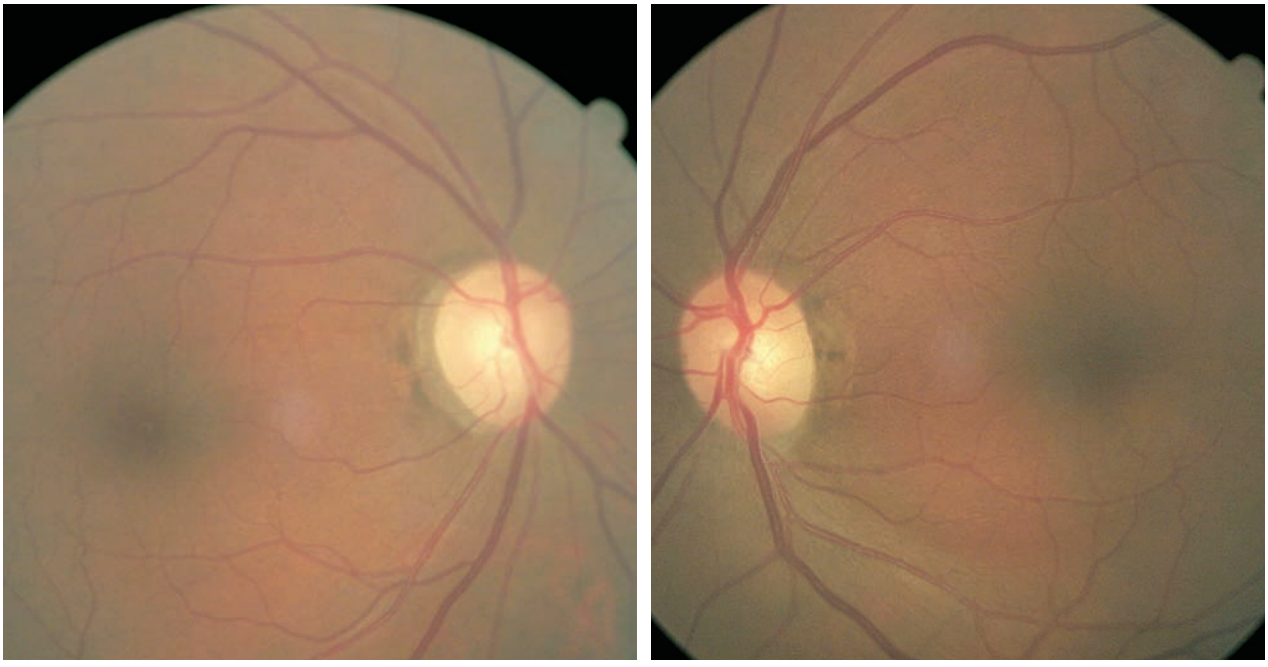

Optic nerve head images of a 72-year-old black female who has been followed at UAB Eye Care for over 30 years. Since her previous visit a year earlier, she developed an inferior rim notch in the right eye. There is corroborating evidence from imaging and visual field data. She was initiated on IOP-lowering treatment. The fellow eye did not show change. Note the disc asymmetry.

Blood Flow Regulation and Dysregulation

Much of the evidence favoring a distinct category for NTG comes from blood flow studies. These include the notion of peripheral vascular dysregulation, as evidenced by cold extremities, specific measures of nail fold capillary blood flow, the cold pressor test and careful blood flow measurements of the retinal and choroidal blood flow.[8-10] The cellular and molecular considerations in these scenarios are beyond the scope of this article and involve oxidative mechanisms and nitric oxide regulation, for example. The interested reader is referred to a review on the topic published earlier this year.[10]

Perhaps related to glaucoma in general is the idea of the balance between IOP opposing perfusion pressure to the optic nerve head. Mean perfusion pressure has been linked to progressive glaucomatous damage in the Barbados eye study, an association reviewed recently.[11] Mean perfusion pressure links the parameters of systolic and diastolic blood pressure with measured IOP.

One surrogate that may be applied to clinical situations is the diastolic ocular perfusion pressure (DOPP). Simply subtracting the IOP from the diastolic BP gives this result. The range of normal or threshold for safety remains elusive, however. In a practical sense, the lower the value, the more likely the risk for hypoperfusion. The evidence presented here suggests that low perfusion pressure is associated with greater and more progressive glaucomatous damage, making the case for hypoperfusion as the most likely candidate, but perhaps not the only one, to explain observed glaucomatous damage in the absence of elevated IOP.[11] So, as clinicians we should pay attention to the IOP and BP among our NTG patients and those suspected of glaucoma in general.

Other recent evidence implicates low nocturnal ocular perfusion pressure as a risk factor for NTG.[12] This study incorporated 24-hour IOP and blood pressure monitoring to provide a profile of the interaction. The results support the evidence favoring a defective autoregulatory mechanism among NTG patients. Interestingly, this report is from a non-ophthalmic publication. The idea of relative ischemia as a contributor to optic nerve deterioration, however, is not new in the ophthalmic literature. The idea had been suggested more than two decades earlier.[13]

Going forward, if we can merge the data from these two measurements, perhaps a clearer picture of glaucomatous damage at "normal"

intraocular pressure will emerge.

Most recently a distinction between ocular and systemic blood flow parameters of normal subjects and those with either early NTG or POAG has been reported.[14] Interestingly, the authors reported that among a broad panel of ocular and systemic findings there is considerable overlap between both glaucoma groups in the early stages of these diseases but distinct from normal subjects serving as controls. While the vascular alterations described are not those routinely measured, they included peripheral arterial stiffness, carotid intima-media thickness and ocular perfusion pressure. The authors conclude that NTG and POAG are points on a continuum rather than distinct entities.

CSF pressure

It is well known that increased intracranial pressure results in the clinical observation of a swollen optic disc, or papilledema. What could be the implication of *reduced* intracranial pressure? The notion of a connection to glaucoma has been crystalized recently.[15] In summary, it looks something like this: The combined influences of IOP, systemic blood pressure and cerebrospinal fluid pressure (CSFP) interact at the level of the lamina cribrosa. Measuring only the transcorneal pressure (IOP) as is done clinically may be inadequate to explain glaucomatous damage and NTG in particular.

Mentioned earlier was the influence of reduced ocular perfusion, an emerging measure and influence in glaucoma (both high- and low-pressure). The model includes the presence of low systemic blood pressure, either in general or situationally at night, being associated with low CSFP, which produces an abnormally high trans-laminar pressure diffential. This scenario is similar to the condition of CSFP in the normal range with the IOP being elevated as a component of the mechanism of glaucomatous damage. This model is proposed to explain why patients with NTG have low systemic blood pressure, and why eyes with normal- and high-pressure glaucoma may develop similar optic disc damage patterns.

Management of NTG

Whether one believes that NTG is a separate entity, emerging evidence points to potential new management strategies beyond lowering IOP. Traditional (in-office, snapshot) measurement of IOP is inadequate to characterize its day-long, 24-hour behavior. Similarly, a single blood pressure measurement does not characterize a patient's blood pressure during the night or when performing other activities. Introducing CSFP into the mix may help to explain damage at (or to) the level of the lamina cribrosa.

The interaction among all three of these parameters may give clinicians an improved picture of progression in glaucomatous damage (especially NTG). How will this be done? Documenting a 24-hour blood pressure profile is possible; these data may be available from the patient's cardiologist, for example. Technology for 24-hour IOP measurement is currently in clinical trials in the US, although no device is currently FDA approved. Look to the future for clinical applications. Patterns in this paradigm may not be consistent, leading to confusion or explanation of variability.[16] Finally, incorporating the influence of CSFP, while perhaps the most tedious to measure clinically, may allow more information on glaucomatous damage and especially that in NTG.

Concretely, it has been known for many years that the topical beta-blockers are relatively ineffective when administered at night. Systemic absorption may reduce systemic blood pressure and, by extension, perfusion to the optic nerve. Therefore, especially in susceptible individuals, topical beta-blockers should not be administered at night.[17,18] In fact, in those glaucoma patients treated for systemic hypertension with documentation of progression in the face of "controlled" IOP, the prescriber should be consulted with the evidence.[11-13]

The future is bright for our ability to better characterize glaucomatous damage, regardless of whether the IOP is outside or within the statistically normal range. Given a better knowledge of the factors surrounding and producing glaucomatous damage will also give us more effective tools for preventing or minimizing it. Apart from the traditional management of glaucoma (lowering IOP), however, no consistent evidence for any alternative strategy to preserve structure and function in NTG has emerged victorious.

Connecting the Dots Clinically

The normal IOP range is a statistically defined as ranging from roughly 10mm to 21mm Hg. We know that some patients will tolerate a higher IOP without damage while others will show progressive damage when the IOP is within the normal range. Clearly, pressure-independent factors are involved. As mentioned above, these may

include situational elevations of IOP, systemic vascular regulation factors, the influence of systemic medications and most recently reported, CSFP. Given our current inability to continuously measure IOP, looking at other clinical measures such as 24-hour blood-pressure monitoring and CSFP may be useful but tedious in the normal clinical setting.

One suggestion has been to observe spontaneous venous pulse at the optic nerve head. The results of a recent study using color Doppler imaging to measure retinal vessel blood velocities showed that, on average, glaucoma patients had lower retinal vein velocities.[19] Combined with the lower prevalence of spontaneous venous pulsation among glaucoma patients, especially NTG, the implication is that this may represent altered hemodynamics within the eye and orbit. If one accepts this premise, then the influence of reduced CSFP rises in significance as a probable metric for glaucomatous damage and perhaps an index of the likelihood of progression. ■

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The Optic Nerve in NTG

Any discussion of NTG must include optic disc hemorrhages. The observation of an optic disc hemorrhage has been associated with glaucoma, and NTG specifically, to the extent that these are referred to eponymously as Drance Hemorrhages in tribute to Stephen Drance who established this connection.[20] The flame- or splinter-shaped hemorrhage crosses the disc margin and has been associated by some with a greater likelihood of progression. Other studies, however, show little difference in visual field deterioration, but greater structural change (i.e., RNFL loss).[21]

Recently, a report of sophisticated measures between NTG and HTG patients has suggested that NTG patients may show more central visual field damage.[22] The authors suggest considering a 10-2 visual field testing protocol to measure progression. Stereometric parameters measured with the Heidelberg Retinal Tomograph-III, however, did not distinguish between the HTG and NTG groups.[22] Another recent report has suggested that systemic hypertension in a setting of optic disc hemorrhage is associated with NTG.[23] The confusion surrounding risk of progression (vs. a sign consistent with a diagnosis) has a number of explanations, including the particular population studied, the stage of disease at initial intervention, means of measurement, and so on.

These pressure-independent considerations support the notion that systemic factors are involved as pressure-independent influences in NTG. Does that suggest alternative means of managing NTG other than lowering IOP? No strategy has emerged to give consistent guidance for such an approach. Clinicians should be aware of potential red flags among systemic connections with NTG and consult the patient's primary care provider. What has been suggested is that the natural history of this enigmatic disease labeled NTG may be one of slow progression.[24,25]

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Advertorial

Your Peroxide Patients Are Not Telling You the Whole Truth

By Chris Snyder, OD, MS, FAAO
Director, Professional Relations, Bausch + Lomb Incorporated

While there have been several innovations within the multi-purpose segment in the last 3 years, the same cannot be said for the hydrogen peroxide product category. There has been a lack of innovation in peroxides for almost a decade. This leads us to ask: is there a similar opportunity for improvement in peroxide-based lens care?

Hydrogen peroxide-based lens care products are a significant part of the US soft lens care market, used by approximately 12% of contact lens wearers (13 years of age or older).[1] Current peroxide products are often prescribed to help solve lens wear-related issues of discomfort (particularly dryness symptoms) or to avoid suspected sensitivities to some multi-purpose solution (MPS) formulations. Today's peroxide lens care solutions are justifiably regarded highly for their cleaning, disinfection and comfort characteristics. Therefore, when a struggling patient is prescribed a peroxide lens care system, their lens wearing experience often improves. But, is it possible that current peroxide users still suffer from unstated issues?

A recent study, administered outside of Eye Care Professionals' (ECPs') offices, was designed to evaluate whether peroxide users still face challenges in their lens wearing experience.[2] One hundred fifty soft contact lens wearers who regularly use peroxide solution completed an online survey to identify any issues and symptoms they experience. Those patients also described how they deal with their lens wearing challenges.

The results show that more than half of patients using hydrogen peroxide solutions with their soft contact lenses still experience issues or symptoms. Fifty two percent (52%) of respondents reported difficulty while wearing contact lenses during activities such as long hours at a computer screen, in air conditioned or smoky environments, or while watching TV or a movie *(Figure 1)*. The main issue reported was discomfort. In fact, 43% of peroxide patients reported still experiencing discomfort, with 31% feeling the need to use eye drops regularly to address this discomfort.[3]

These findings may surprise many ECPs. However, peroxide patients may not be telling their ECPs about continuing issues they may have. The reason why these patients do not share their lens wearing challenges is not really known. One hypothesis is that since so many peroxide patients have previously been experiencing problems and found some relief when trying peroxide, their expectation for further improvement is limited. Another possibility is that since ECPs often switch patients to peroxides as a last ditch effort to keep them in frequent replacement lenses, a patient would rather suffer in silence than risk being taken out of contact lenses.

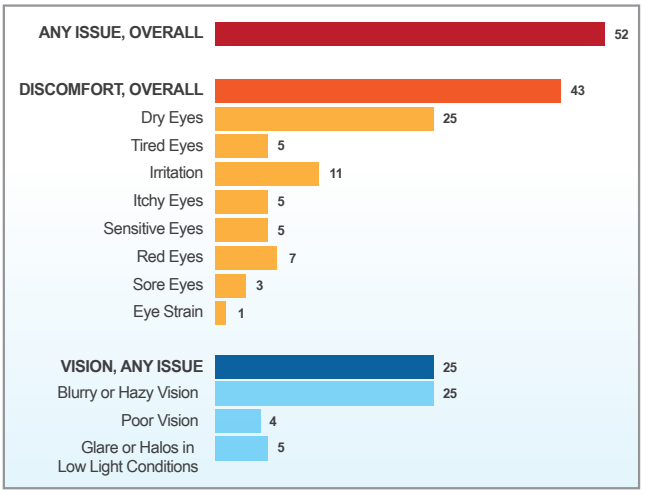

Figure 1: Percentage of patients reporting issues as a result of contact lens wear (modified from Reference 4)

So how can ECPs know if patients are truly having issues with their contact lenses? Is it worth discussing with patients, if patients will not raise their issues proactively? If a patient seems happy, why switch their lens care solution? The answer is simple: even though a patient seems happy, an innovative lens care solution may make their lens wearing experience even better. Biotrue® multi-purpose solution provides a great recent example. While many patients seemed quite happy with their previous MPS solutions before trying Biotrue® MPS, 9 out of 10 patients reported that Biotrue makes wearing contact lenses easier on their eyes than their usual solution.[4] This suggests that there is room for improving the lens wearing experience of even seemingly satisfied and happy patients.

Since eye care professionals tend to recommend peroxide solutions to patients who are experiencing issues of discomfort, dryness or irritation while wearing lenses, it is important to recognize that over 50% of those patients who use peroxide continue to experience such problems.[3] ECPs should expect manufacturers to continue to introduce new solutions that make lenses even more comfortable for today's, and even tomorrow's, peroxide patients.

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HL-6258-1

19th Annual Glaucoma Report

The Impact of Imaging Devices on Glaucoma Management

HRT, GDx and OCT can help you diagnose and monitor glaucomatous damage with outstanding accuracy and repeatability. **By Pinakin Gunvant Davey, OD, PhD**

The classic triad of visual field compromise, nerve head damage and elevated intraocular pressure no longer fully constitutes a glaucoma diagnosis.[1] Although intraocular pressure arguably remains the most important risk factor, its absolute value may be elevated or remain within the statistical limits of normality—largely depending upon the type of glaucoma—and the patient may still develop disease.

While visual field assessment remains the most popular functional vision test for glaucoma, it is influenced by subjective considerations—particularly a patient learning curve. Further, a non-computerized evaluation of the optic nerve, while objective, may be influenced by inter-observer variability. Nonetheless, obtaining objective measurements of the optic nerve and nerve fiber layer structure is highly advantageous to any eye care practitioner—particularly if the data is repeatable and reproducible.

Fortunately, computerized imaging technologies can obtain an automated evaluation of structural damage in eyes at risk for glaucoma that's relatively independent of disease severity and long-term variability.[2]

The most useful technologies for the detection and evaluation of glaucoma include scanning laser ophthalmoscopy, scanning laser polarimetry and optical coherence tomography. These devices may yield similar information, but they have fundamental differences that make their measurements non-interchangeable.

This article explores the technology associated with these imaging devices, and helps clarify their diagnostic and/or prognostic value. Further, it addresses common imaging artifacts that can complicate or distort diagnostic results.

Scanning Laser Ophthalmoscopy

The Heidelberg Retina Tomograph-III (HRT-III, Heidelberg Engineering) scanning laser ophthalmoscope provides topographical data of the optic nerve and peripapillary retina. Using a high-speed raster scanning technique and diode laser for illumination, the HRT-III obtains multiple 2D images of the retina and optic nerve. Beginning at the vitreoretinal interface and terminating beyond the bottom of the cup, the HRT-III acquires 16 to 64 images to a maximum depth of 4mm.

The number of optic sections varies per patient. For example, eyes with deep cupping have more sections (and hence, more 2D images) than those with less cupping. The optic sections are combined to produce a 3D topography of the optic disc surface. This capture process is repeated up to six times, and the best

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Goal Statement: Computerized imaging technologies can obtain an automated evaluation of structural damage in eyes at risk for glaucoma that's relatively independent of disease severity and long-term variability. This article explores the technology associated with these imaging devices, and helps clarify their diagnostic and/or prognostic value. Further, it addresses common imaging artifacts that can complicate or distort diagnostic results.
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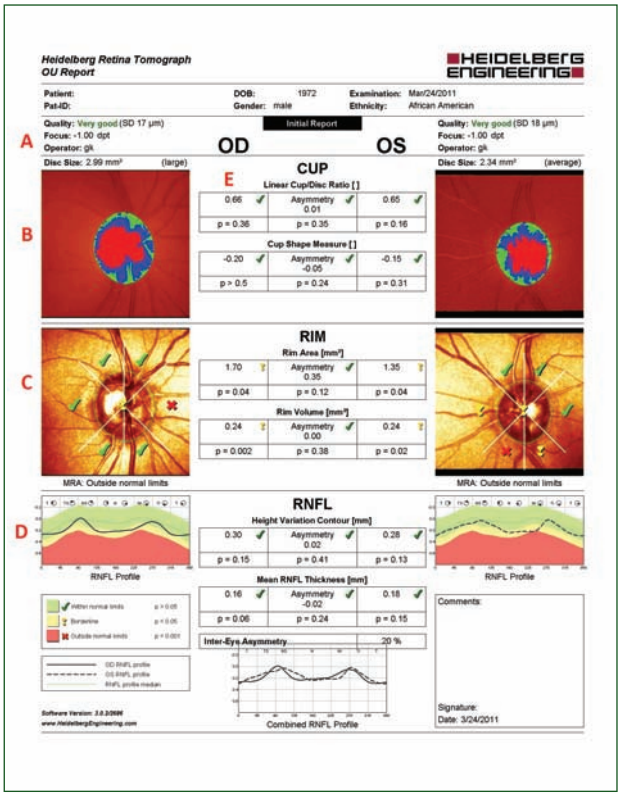


1. A report generated by Heidelberg Engineering's Retina Tomograph-III (HRT-III). Section A reveals scan reliability as well as disc size, which is obtained once the operator outlines its margin. Section B is a pseudo-isochromatic fundus image that shows the rim and cupping. Red color represents the cupping, whereas blue and green illustrate rim tissue. Section C shows the MRA analysis of various optic disc sectors. Section D shows the retinal nerve fiber layer (RNFL) in the temporal, superior, nasal, inferior, temporal (TSNIT) regions. Section E provides information garnered via the measurement of several parameters, as well as the asymmetry analysis and its statistical significance.

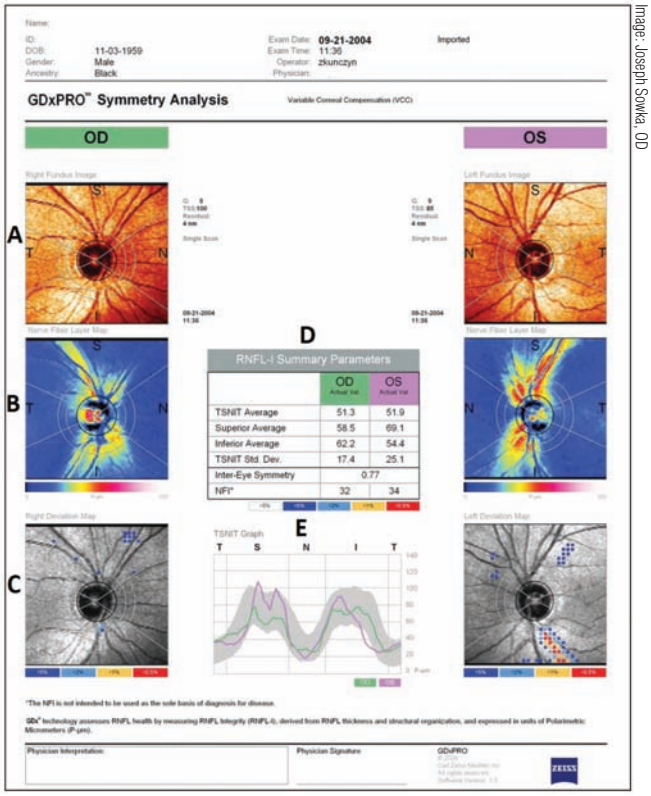


Image: Joseph Sowka, OD

2. An output obtained using Carl Zeiss Meditec's GDx-Pro scanning laser polarimeter. Sections A, B and C represent the pseudo-isochromatic fundus image, RNFL thickness plot and the deviation plot, respectively. Section C of the left eye shows a cluster of superpixels located in the inferior temporal region that potentially indicate early damage. Sections D and E provide various parameters as well as the TSNIT RNFL plot.

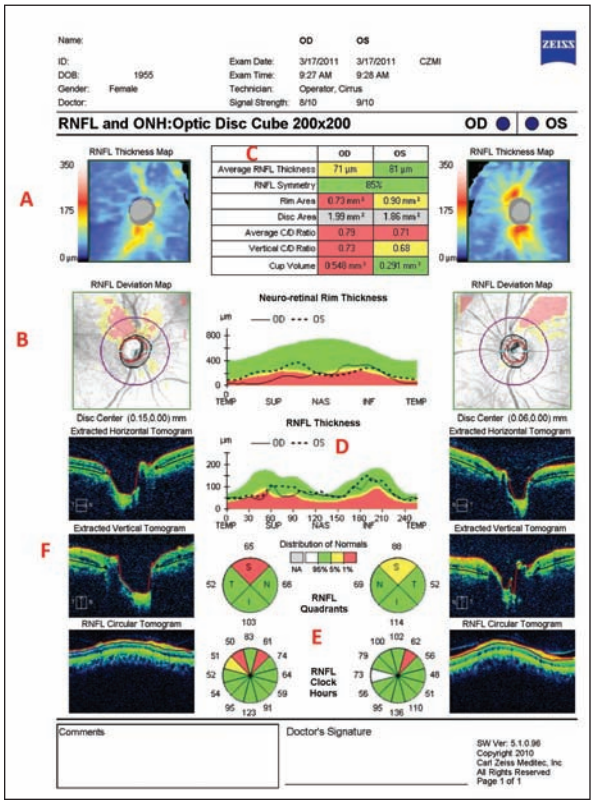
three scans are selected and averaged to obtain the final output.

• ***Interpretation of an HRT-III output.*** There are various report formats, which display different data sets captured by the device. The scan quality is judged on standard deviation—the lower the value, the better the scan quality (*figure 1*).

HRT-III provides useful information on optic disc size, classifying it as small, average or large once the user has outlined the optic disc margin. The device's optic disc analysis provides information regarding the optic cup, neuroretinal rim and retinal nerve fiber layer (RNFL). The patient's right and left eyes are compared for asymmetry. All parameters provided also are compared to the normative database to determine if the measurements are normal, borderline or outside the statistical limits of normality.

A color-coded figure provides the cupping information. The cupping is illustrated in red, whereas the neuroretinal rim is represented by blue and green (blue highlights the sloping rim and green shows the stable rim). The cup volume is provided as one of the parameters, which appear elevated in eyes suspicious for glaucoma or progressive neuroretinal rim loss. The cup shape values are negative in a healthy eye, but positive in glaucoma suspects. Additionally, measurements of rim area and rim volume decrease upon progression of glaucomatous optic neuropathy.

Once the optic disc outline is established, the device automatically generates the Moorfields Regression Analysis (MRA), an application that analyzes areas of the neuroretinal rim to predict a patient's risk of glaucoma. Arguably, MRA is the single most clinically useful parameter generated by the HRT-III (*see, "MRA in*



3. An output of the RNFL analysis on Carl Zeiss Meditec's Cirrus HD-OCT. Section A shows the thickness map, and section B shows the fundus image and highlights regions that are not within statistical limits of normality. Section C provides a table of various parameters. Section D shows the TSNIT RNFL thickness profile. Section E illustrates thickness in various sectors and clock hours, respectively. Sections B, C, D and E are color-coded to indicate whether the thickness measurement region or specified parameters are either within or outside the statistical limits of normality. Section F reveals the vertical and horizontal tomogram of the disc and peripapillary retina, which provide a layer-by-layer thickness profile. The circular tomogram in Section F is the cross-sectional thickness profile from the purple ring region displayed in section B.

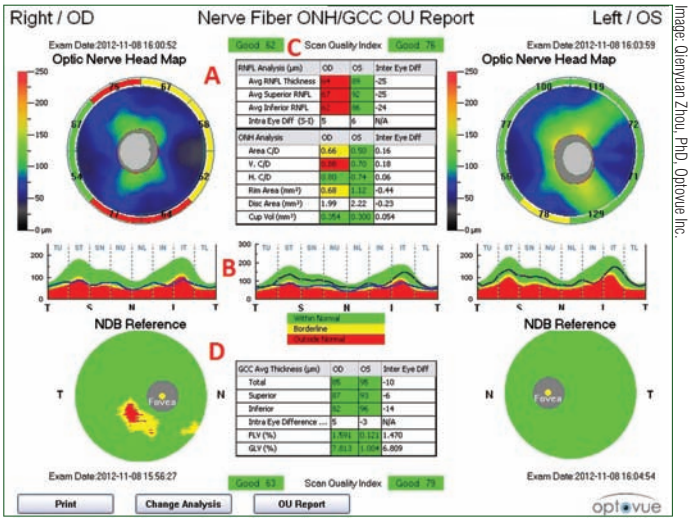


Image: Qienyuan Zhou, PhD, Optovue Inc.

4. A combined output of the RNFL and ganglion cell complex obtained with Optovue's iVue OCT. Section A provides thickness information around the disc; section B illustrates RNFL thickness in TSNIT region; and section C shows the various parameters. Section D reveals the ganglion cell complex parameters and the map. Data from the right eye shows that the inferotemporal macular region exhibits statistically significant damage. All sections are color coded to emphasize statistical significance.

Detail," page 59).

The device also measures the RNFL 360° degrees, just outside the disc margin. This is a distinctly different diameter than what is provided by either scanning laser polarimetry or optical coherence tomography. So, keep in mind that an RNFL measurement obtained by one technology will not match values documented by other devices.

Finally, it is important to note that all HRT parameters within normal limits are assigned a green check mark; those that are borderline are assigned a yellow exclamation point; and those that are outside normal limits are assigned a red X.

• *Previous-generation devices.* The underlying mathematical principles employed in scanning laser ophthalmoscopy are universal, and have remained widely unchanged over time. So, the fundamental diagnostic accuracy of HRT-III is comparable to that exhibited by previous-generation units, HRT-I and HRT-II. For example, stereometric parameters obtained by the HRT-I correspond to those captured by the HRT-II.[3]

Scanning Laser Polarimetry

Carl Zeiss Meditec manufactures the GDx-Pro, the only commercially available, current-generation scanning laser polarimeter. GDx-Pro uses a near-infrared laser (780nm) in a raster pattern to image both the macula and peripapillary region.[4]

A basic understanding of "birefringence" and "retardation" is necessary to better understand how this technology images the optic nerve. Birefringence is an optical property of highly organized and parallel structures that split a light wave by a polar material (polarized light) into two components. These components travel at different velocities, which creates a relative phase shift. The phase shift is termed retardation. The GDx-Pro is a confocal scanning laser ophthalmoscope that is capable of measuring retardation.

Following a measurement of the anterior segment, the device can accurately derive the RNFL's birefringence/retardation. Research

shows that a measurement of RNFL retardation via scanning laser polarimetry correlates well with a histologic measurement.[5,6]

• ***Interpretation of GDx-Pro output.*** To generate a baseline measurement, scanning laser polarimetry requires a calculation of anterior segment birefringence. This measurement is only necessary when examining the patient for the first time. (If the patient undergoes refractive or cataract surgery, however, he or she should undergo a second anterior segment birefringence evaluation.[7-9])

Next, the device obtains the peripapillary retina birefringence. Clinicians have the option to scan the eye either once or three times. Multiple scans take longer to complete, but the resulting mean measurement likely is more reliable.

The output of optic nerve head and peripapillary images are divided into three parts: the fundus image, the RNFL map and the deviation map (*figure 2*). The fundus image in a GDx-Pro printout is captured via monochromatic light and should not be used as a substitute for traditional funduscopy. This image is only used to evaluate the focus, centration and/or illumination of the optic nerve.

The retinal nerve fiber layer map provides information about its thickness in a 20° image, with the optic nerve in the center. In healthy eyes, the inferior and superior RNFL should be thick and are represented with bright red and yellow—whereas the nasal and temporal regions are thinner and are depicted by cooler colors. The deviation map provides further information if the RNFL thickness points on the 20° degree image are within 5%, 2%, 1% or 0.5% of the statistical limits of normality.

The two white rings shown on the three image maps signify the region where the RNFL was measured, as well as provide a thickness profile of the RNFL in the temporal, superior, nasal, inferior and temporal (TSNIT) region of the peripapillary retina in both eyes. There are various thickness parameters, such as TSNIT average, inferior average and superior average, which are provided with color-coding to indicate if they are within the statistical limits of normality.

The GDx-Pro also generates a machine learning classifier known as the Nerve Fiber Indicator (NFI), which ranges between zero and 100. Higher NFI values suggest damage. Numerous studies have shown that the NFI is the best GDx parameter at differentiating between healthy and glaucomatous eyes.[10-13]

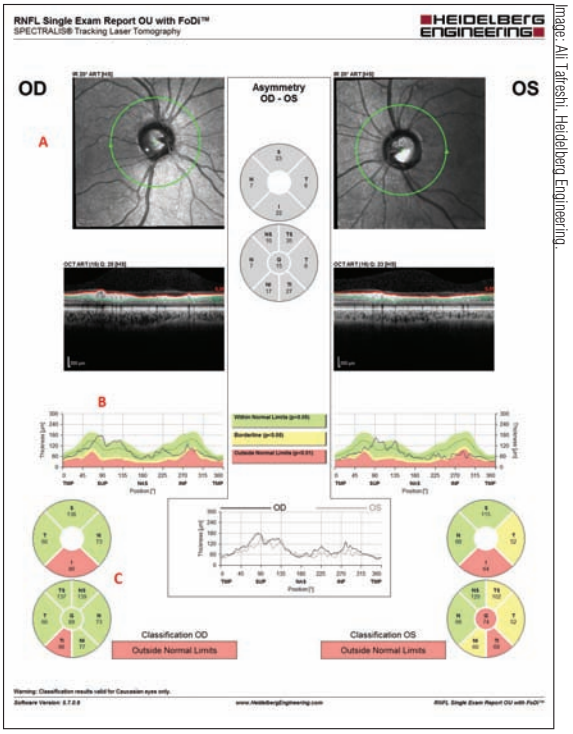


Image: Ali Tafreshi, Heidelberg Engineering.

5. An evaluation of the RNFL on Heidelberg Engineering's Spectralis. Sections A, B and C show the fundus image, RNFL thickness profile in the TSNIT region and RNFL thickness in various quadrants, respectively. Both sections B and C are color coded to emphasize statistical significance.

• ***Previous-generation devices.*** Each successive GDx technology has been designed to correct imaging errors regularly encountered with prior units. For example, the first such device—the GDx-FCC—used a standard correction factor that compensated for anterior segment birefringence. Then, because anterior segment birefringence differs across patient populations, the next-generation device—the GDx-VCC—was designed to account for birefringence variations.[14,15]

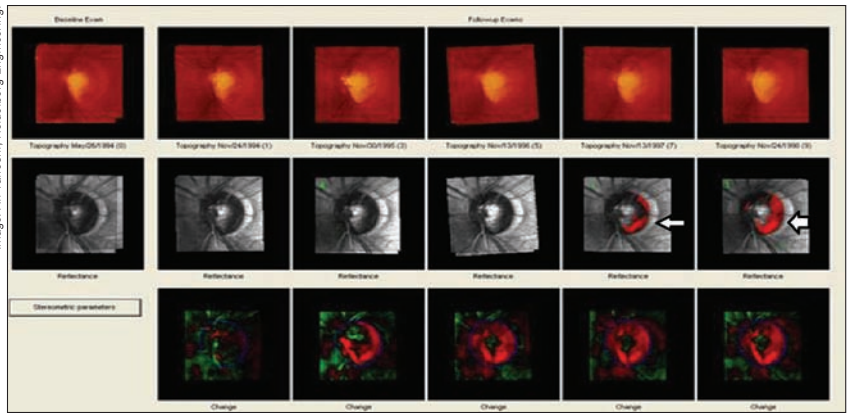
The current-generation device—the GDx-Pro—was designed to more accurately characterize the RNFL, effectively decreasing the number of atypical retardation patterns often captured by GDx-VCC.[16] Multiple studies have indicated that the GDx-Pro has better repeatability and diagnostic ability than the GDx-VCC.[17-19] So, it is safe to say that newer-generation polarimetry devices are indeed more accurate than older-generation GDx units.

Optical Coherence Tomography

It is almost an understatement to suggest that OCT has revolutionized ophthalmic imaging. OCT is one of the most rapidly adopted technologies in eye care, and is capable of obtaining cross-sectional or tomographic scans of biological tissue in vivo.

The principles of OCT are similar to those of ultrasound devices; however, it uses light instead of sound. The axial scans are compiled to obtain the B-scan of the specific location being evaluated. The time-domain (TD) OCT is capable of

Image: Ali Tafreshi, Heidelberg Engineering.



6. A topographical change analysis output obtained using HRT-III. The arrows indicate thickness changes. Note the thinning documented in the rim area.

capturing approximately 400 axial scans per second and providing a resolution of 10µm axial and 15µm transverse, whereas the spectral-domain (SD) OCT obtains between 26,000 and 40,000 axial scans per second and provides a resolution of 5µm axial and 15µm transverse. Further, SD-OCT uses a broader bandwidth light source than TD-OCT—capturing much larger volumes of data in a shorter duration.

• ***Interpretation of an OCT output.*** On the OCT printout, the RNFL thickness map (*figure 3*) appears similar to the color-coded map generated by the GDx-Pro. The deviation map indicates whether the scanned region is within the statistical limits of normality. Also like the GDx-Pro, the associated fundus image helps you evaluate centration and focus as well as identify any imaging errors. Again, this information should not used as a substitute for fundus photography.

The purple ring located on the RNFL thickness map signifies the TSNIT region. This is used to calculate average RNFL thickness and symmetry. The RNFL thickness profile obtained from the purple ring around the optic nerve is plotted graphically to obtain symmetry information. The graph has three color-coded regions:

- Green suggests 95% normal distribution.

- Yellow suggests less than 5% but greater than 1% normal distribution (e.g., borderline).

- Red suggests less than 1% normal distribution (e.g., outside of normal limits).

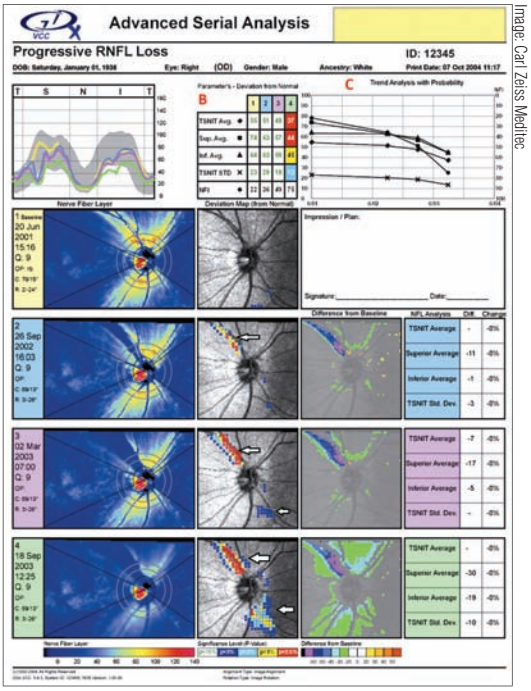
The OCT readout also provides several diagnostic parameters, including cup-to-disc ratio, cup volume, disc area and rim area, as well as RNFL values in each quadrant and each clock hour.

Several OCT systems can perform a separate macula region scanning to obtain ganglion cell analysis (*figure 4*). Different manufacturers approach the analysis with slight variations. Optovue's RTVue SD-OCT and iVue perform a ganglion cell complex analysis, which includes the nerve fiber layer, ganglion cell layer and the inner plexiform layer. Carl Zeiss Meditec's Cirrus HD-OCT evaluates the ganglion cell layer and inner plexiform layer. Keep in mind, there is no consensus on whether one analysis yields more accurate results than the other.[20]

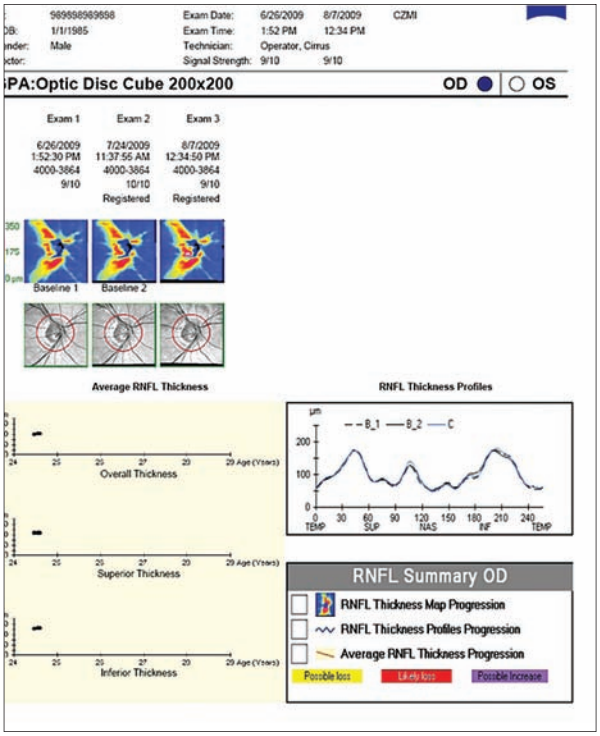
• ***Previous-generation devices.*** As is the case with scanning laser polarimeters, the newer-generation spectral-domain OCT units are a marked improvement over their older time-domain counterparts. Compared to TD-OCT, spectral-domain devices offer improved image resolution and faster scanning speed. The diagnostic accuracy of TD-OCT is similar to SD-OCT, and the population mean RNFL values may not vary significantly.[21-23] (Note: RNFL measurements on TD-OCT tend to be thicker than those obtained via SD-OCT—except in cases of advanced glaucoma.[23])

Several companies manufacture SD-OCT devices, such as Bioptigen, Carl Zeiss Meditec, Heidelberg Engineering, Optos, Optovue and Topcon. When identifying glaucomatous optic neuropathy, these

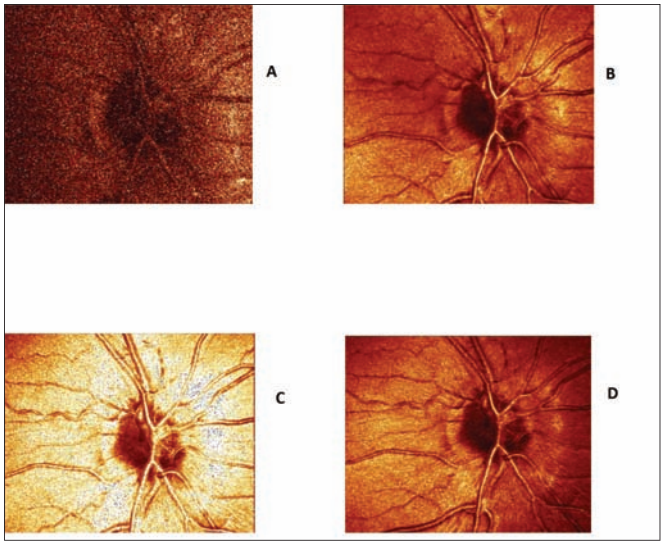
Image: Carl Zeiss Meditec



7. An advanced serial analysis on GDx-VCC. The deviation map shows an increase in superpixels (see arrow), which highlights progressive RNFL thinning. The parameters shown in section B, as well as the trend over time shown in section C, exhibit progressive decline.



8. A Guided Progression Analysis of an ocular hypertensive patient taken with Cirrus HD-OCT. The scans show no short-term progressive damage on both the RNFL thickness profile and RNFL summary, which provides evidence that the patient has not converted to glaucoma.



9. Poor ocular surface health can decrease signal strength and image quality, which in turn decreases diagnostic accuracy. Section A shows an image of severe dry eye. Section B reveals improvement upon artificial tear instillation. Section C shows the same patient with 2.00D myopic defocus. This image is overexposed, with visible artifacts. Section D shows the same patient with an appropriate focus.

devices yield very similar results, despite individual differences in resolution and scanning speed.[24]

Progression Detection

Detecting progression over time in eyes at risk for glaucoma (or with confirmed glaucoma) is one of the more challenging tasks eye care clinicians face. Progressive change in an optic nerve and peripapillary retina is both subtle and slow, and can be easily overlooked during casual observation. That is why imaging devices' objectivity and reproducibility are of great benefit.

All imaging devices include parameters that can be followed over time to monitor progression. Such algorithms are based on simple regression analysis that evaluates changes between follow-up visits.

Following a subsequent scan, the device's imaging software identifies whether parameter values demonstrated a statistically significant increase or decrease since the previous exam.

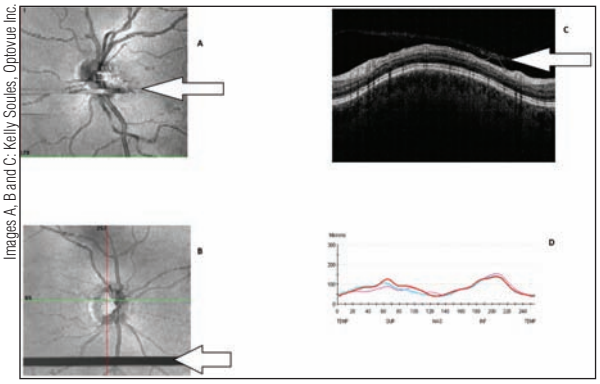
HRT-III, for example, includes a topographical change analysis. This tracking module statistically compares topographic values in small, discrete regions called superpixels. This method is distinctly different than a basic trend analysis that compares raw topography values between follow-up scans. (*Figure 6* shows an optic nerve head with progressive damage compared to the baseline scans.) Studies have shown that this may be useful in identifying progressive damage in glaucoma.[25,26]

Additionally, the GDx-VCC and GDx-Pro have an advanced serial analysis that measures trend over time. This feature helps the clinician detect and monitor progressive, glaucomatous change (*figure 7*). More recently, researchers have developed a Guided Progression Analysis (GPA) database for the GDx-Pro. This module evaluates changes in a 20º area of the image map, TSNIT curves and thickness parameters. Initial reports indicate that this may further help to identify progressive damage.[27-29] The GDx-Pro GPA software is not yet FDA approved.

The Cirrus HD-OCT includes a GPA database, which is very similar to that used by the GDx-Pro (*figure 8*) and is FDA approved. All follow-up scans are compared to baseline data. After two consecutive examinations show statistically significant optic nerve loss, the results are flagged and labeled as "possible progression" or "likely progression" if the third consecutive scan shows progressive damage compared to baseline.

Imaging Artifacts

Although invaluable in clinical practice, all ophthalmic imaging devices are susceptible to artifacts.



Images A, B and C: Kelly Soules, Optovue Inc.

10. Additional imaging errors. Section A reveals an eye movement artifact that is seen as non-continuous blood vessels and optic disc. Section B shows blink artifact illustrated as a band of missing data. Section C shows a segmentation error of the RNFL, which the algorithm has outlined as an incorrect upper and lower layer, erroneously including the RNFL. Section D shows three consecutive scans obtained using TD-OCT, which were obtained one minute apart in a patient who moved his eye.

As is the case with other clinical diagnostic techniques, some artifacts can be controlled to a certain degree. Generally, imaging artifacts reduce signal strength and cause measurement errors, limiting the device's diagnostic abilities. Here are some of the most common artifact causes:

• ***Poor ocular surface.*** Multiple studies have analyzed the effect of ocular surface dryness and tear film instability on imaging outcomes.[30-32] To minimize the deleterious impact of dry eye, instruct your patients to blink regularly between scans or use artificial tears/lubricants to help establish a uniform surface (*figure 9*). Also, be sure to avoid initiating procedures that require ocular contact until after imaging is complete.

• ***Insufficient light.*** Similarly, reduced pupil size and optic media can affect imaging, because the amount of light reaching retina will be decreased.[26] This causes an erroneous estimation of parameters, and could yield a false positive diagnosis. In cases with miotic pupil or cataract, it is ideal to dilate the pupil to obtain optimal image quality.

• ***Eye movement.*** Involuntary eye movement often leads to measurements of an unintended region.[29] This could produce major diagnostic errors (*figure 10*). The device also may fail to identify appropriate retinal layers, which could result in segmentation errors.

Today, these errors are becoming less common with advanced instrumentation—and algorithms currently are in development to provide image registration. If you observe such errors, be sure to perform imaging again.

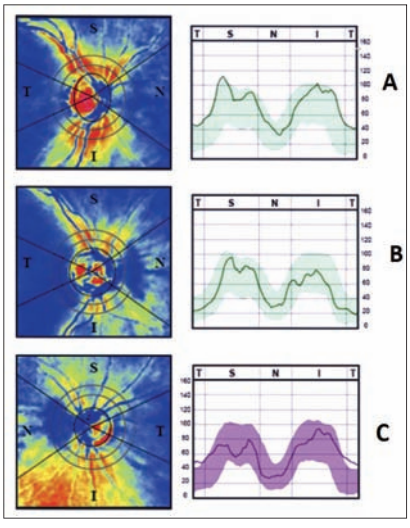
• ***Limited choroidal pigmentation.*** Atypical birefringence patterns may be seen when imaging eyes with poor choroidal pigmentation (also know as "blond fundus"). This anatomic anomaly typically influenced results obtained via previous-generation polarimetry devices (e.g., GDx-VCC).

These patterns have been observed in 10% to 15% of patients.[11,33] Affected images do not follow the normal physiological pattern of the nerve fiber layer. Instead, the RNFL map usually shows "bicycle spoke" pattern or "tie-dye" appearance (*figure 11*). In such instances, patients often were deemed inappropriate candidates for GDx-VCC imaging. Fortunately, the GDx-Pro has dramatically decreased the prevalence of these atypical patterns caused by poor pigmentation.[34]

Glaucoma imaging devices have made a long journey—from implements of research interest to clinically useful technology. Newer and more advanced systems have allowed clinicians to better understand and appreciate the correlation of structural and functional loss within the context of glaucoma.[35-40] Such information can help improve your diagnostic and prognostic ability when managing glaucoma patients.

Future advances in adaptive optics and transverse resolution will enable us to image cones, astrocytes, ganglion cells and dendrites in greater detail.[41] Such information will further enhance patient care and improve our understanding of glaucoma pathogenesis. ■

Dr. Davey is an associate professor at Western University of Health Sciences College of Optometry in Pomona, Calif. His research centers upon retinal physiology, with the primary intent to improve the clinical management of glaucoma. He served as the principal investigator in the GDx-Pro Normative Database Study and the Optovue iVue Normative Database Study, and has



11. Three eyes with an atypical retardation pattern—also known as "tie-dye" appearance in RNFL thickness profile map. These are a result of poor signal-to-noise ratio due to choroidal pigmentation. These scans are an outcome of an artifact, and should not be used in patient management.

received equipment support from Carl Zeiss Meditec, Heidelberg Engineering and Optovue.

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MRA in Detail

Developed by David Garway-Heath, MD, and colleagues in London, United Kingdom, the Moorfields Regression Analysis allows the clinician to perform a cross-sectional analysis and determine if an eye is at risk for glaucomatous damage or is within normal limits.[42,43]

The analysis exploits prior knowledge that the neuroretinal rim area is positively correlated with disc size (e.g., the larger the disc size, the greater is the rim area) and that the rim area narrows in eyes with glaucomatous optic neuropathy.[44-47] The MRA indicates whether the rim area of an eye is within 95%, 99% or 99.9% of that in the normal population.

The optic nerve is divided into six sectors. The superior 90º is divided into superior nasal and superior temporal. Similarly, the inferior 90º are divided into inferior nasal and inferior temporal. The nasal and temporal 90º comprise the remaining two sectors. If a rim area ranges between 95% and 99% or greater than 99% of the predicted population, the interval is labeled as borderline or outside normal limits.

The importance of optic disc measurements were investigated in an ancillary subgroup to the Ocular Hypertension Treatment Study, and were found to be a significant predictor of glaucomatous optic neuropathy in patients with elevated intraocular pressure.[48] Additionally, a more recent report from the same study population indicated that these parameters are as effective as stereo photographs at estimating the risk of primary open-angle glaucoma in a group of ocular hypertensives.[49]

OSC QUIZ

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1. What likely is the single most important risk factor associated with glaucoma?
a. Elevated intraocular pressure.
b. Optic disc size.
c. Genetics.
d. Visual field appearance.

2. Which statement about glaucoma imaging devices is true?
a. Scanning laser ophthalmoscopy, scanning laser polarimetry and optical coherence tomography (OCT) provide similar data that is interchangeable.
b. Scanning laser ophthalmoscopy, scanning laser polarimetry and OCT provide similar data that is not interchangeable.
c. Scanning laser ophthalmoscopy, scanning laser polarimetry and OCT provide dissimilar data.
d. None of the above.

3. Which imaging device uses a high-speed raster scanning technique and diode laser for illumination to obtain multiple 2D images of the retina and optic nerve?
a. Heidelberg Retina Tomograph-III (HRT-III, Heidelberg Engineering).
b. GDx-Pro (Carl Zeiss Meditec).
c. RTVue SD-OCT (Optovue)
d. None of the above.

4. How is the scan quality of HRT-III images evaluated?
a. With green check marks located around the optic nerve.
b. Standard deviation (e.g., the lower the values, the better the image quality).
c. Color-coded parameters.
d. None of the above.

5. Which HRT-III parameter arguably is the most important to consider regarding glaucoma risk prediction?
a. Moorfields Regression Analysis (MRA).
b. Cup Shape Detection.
c. Cup Depth Analysis.
d. Retinal Nerve Fiber Layer Detector.

6. Which device uses the fundamental principles of birefringence and retardation to evaluate the retinal nerve fiber layer (RNFL)?
a. Scanning laser ophthalmoscopy.
b. Scanning laser polarimetry.
c. OCT.
d. None of the above.

7. To accurately assess the birefringence/retardation of the RNFL using scanning laser polarimetry, you must first:
a. Obtain an accurate refraction using retinoscopy.
b. Establish a baseline via measurement of anterior segment birefringence.
c. Measure pars plana birefregence.
d. All of the above.

8. Which statement related to the 20° fundus image provided by scanning laser polarimetry is true?
a. It is an excellent substitute to fundus photography, because the image is acquired using pinhole scanning raster imaging.
b. It is a poor substitute to fundus photography, because it only provides a 20° field of view.
c. It is not a substitute to fundus photography, because it is acquired using only a monochromatic light source.
d. None of the above.

9. Which GDx-Pro parameter is best for differentiating between glaucomatous and healthy eyes?
a. Superior Average RNFL thickness.
b. Inferior Average RNFL thickness.
c. Average RNFL thickness.
d. Nerve Fiber Indicator.

10. Which error commonly associated with GDx-VCC is experienced less frequently on GDx-Pro?
a. Anterior segment birefringence miscalculations.
b. Atypical retardation patterns.
c. Diagnostic artifacts secondary to macular edema.
d. None of the above.

11. The principles of optical coherence tomography are similar to that of which other diagnostic technology?
a. Ultrasound.
b. X-rays.
c. CT scan.
d. None of the above.

12. Time-domain OCT can provide an axial resolution of:
a. 1µm.
b. 5µm.
c. 10µm.
d. 15µm.

13. Spectral-domain OCT can provide an axial resolution of:
a. 1µm.
b. 5µm.
c. 10µm.
d. 15µm.

14. Approximately how many axial scans per second can be obtained using spectral-domain OCT?
a. Up to 5,000.
b. Up to 10,000.
c. Up to 40,000.
d. More than 60,000.

15. Which statement regarding time-domain (TD) and spectral-domain (SD) OCT is true?
a. The overall diagnostic accuracy of TD-OCT is similar to that of SD-OCT.
b. The mean RNFL measurement obtained via TD-OCT is markedly lower than that obtained via SD-OCT.
c. The mean RNFL measurement obtained via TD-OCT is markedly higher than that obtained via SD-OCT.
d. None of the above.

16. What precaution can help you obtain a clear optimal image in a patient with poor ocular surface health?
a. Instill a drop of artificial tears.
b. Ask the individual to blink regularly.

OSC QUIZ

c. Avoid contact procedures that cause irritation.
d. All of the above.

17. Why do reduced pupil size and optic media typically cause imaging errors?
a. Reduced light/illumination reaches the retina.
b. Frank inability to obtain image.
c. Increased patient discomfort during the imaging process.
d. All of the above.

18. What is a common explanation for imaging an unintended region?
a. Poor ocular surface health.
b. Insufficient light.
c. Involuntary eye movement.
d. None of the above.

19. Which device often yields atypical imaging results in patients who present with poor choroidal pigmentation?
a. GDx-VCC.
b. GDx-Pro.
c. RTVue SD-OCT.
d. HRT-III.

20. What is the fundamental basis of MRA?
a. The neuroretinal rim area positively correlates with optic disc size.
b. The neuroretinal rim area negatively correlates with optic disc size.
c. The neuroretinal rim area has no correlation with optic disc size.
d. None of the above.

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22. Related to your practice needs: ① ② ③ ④ ⑤
23. Will help you improve patient care: ① ② ③ ④ ⑤
24. Avoided commercial bias/influence: ① ② ③ ④ ⑤
25. How would you rate the overall quality of the material presented? ① ② ③ ④ ⑤
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27. The difficulty of the course was:
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PGAs and the Sinking Sulcus

Have you noticed certain side effects—sulcus deepening, eyelid ptosis, loss of periorbital fat—among patients on prostaglandin analogs? **Edited by Paul C. Ajamian, OD**

Q A number of my glaucoma patients have become concerned with dark circles and a "sunken look" to their eyes after using a prostaglandin for a period of time. This is particularly noticeable among patients on unilateral therapy. What's going on?

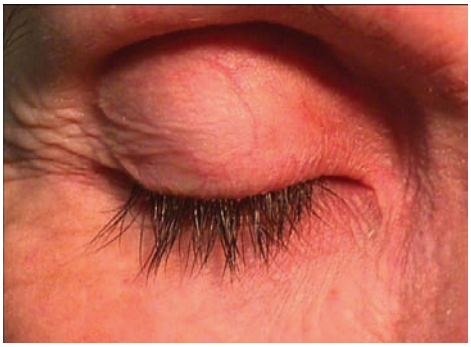
A A recent study by Louis R. Pasquale, MD, and colleagues at the Glaucoma Service at Massachusetts Eye and Ear confirmed that some glaucoma patients who take a prostaglandin analog (PGA) can develop a constellation of symptoms referred to as prostaglandin-associated periorbitopathy (PAP). This includes deepening of the upper eyelid sulcus, upper lid ptosis, enophthalmos and loss of the inferior orbital fat pads.[1]

These symptoms "can be easily dismissed as age-related adnexal findings in bilateral users, [but have] been recognized in several small case series involving both unilateral and bilateral PGA users," the authors write.[1] These findings were associated with the three original PGAs.

How PGAs cause or contribute to PAP is unknown, but the deepening of the upper eyelid sulcus and the loss of inferior orbital fat seems to involve the PGAs' effects on periorbital fat cells.

"The exact mechanism of action is still being investigated on why PGAs are causing this sunken appearance," says Brett King, OD, who is part of a large glaucoma practice near Kansas City.

Dr. King points to an earlier study (also by researchers at Mass. Eye and Ear) that suggested that "FP-prostanoid receptor activation by the PGA inhibits differentiation in several cell lines, preventing fat cell specific gene expression. This results in denser tissue with less fat," he says.[2]



Prostaglandins may cause periorbital problems, such as sulcus deepening (above) or upper lid ptosis, that might even affect vision.

This may not just be a cosmetic problem, either. In the recent study, Dr. Pasquale and colleagues concluded that PGA-associated levator muscle dysfunction and upper lid ptosis "represent significant side effects that could impact visual function in glaucoma patients."

Q If patients complain, what should I do about it?

A "While this side effect appears to be relatively common, I do not have a lot of patients complaining of the sunken appearance," Dr. King says. Patients have more complaints about hyperpigmentation of the lids than the loss of periorbital fat, he says.

He says that when starting patients on treatment, discuss the possible side effects of medications—including cosmetic side effects. "In my experience, most patients prefer medications with less systemic side effects. But some are very concerned with cosmetic issues," Dr. King says. "Obviously, unilateral dosing highlights the differences and will elicit more patient concern."

So, when treating only one eye, take this into consideration to choose the most appropriate drop. Be sure to lay out the potential side effects and options for the patient, and clearly document in the chart that you did so.

"As with hyperpigmentation, some recovery of the inferior fat pads can occur upon discontinuing the medication," he says.[3] "But the superior sulcus hollowing is possibly more permanent."[1] If this becomes problematic, try switching the patient to a different class of medication.

"Also, advise patients to wipe away the residue from the medication a couple minutes after application, as this may help reduce the hyperpigmentation of periocular tissue," Dr. King says. ■

1. Shah M, Lee G, Lefebvre DR, et al. A cross-sectional survey of the association between bilateral topical prostaglandin analogue use and ocular adnexal features. PLoS One. 2013 May 1;8(5):e61638.
2. Filippopoulos T, Paula JS, Torun N, et al. Periorbital changes associated with topical bimatoprost. Ophthal Plast Reconstr Surg. 2008 Jul-Aug;24(4):302-7.
3. Aydin S, Isikligil I, Teksen YA, Kir E. Recovery of orbital fat pad prolapsus and deepening of the lid sulcus from topical bimatoprost therapy: 2 case reports and review of the literature. Cutan Ocul Toxicol. 2010 Sep;29(3):212-6.

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Just a Little Off Center

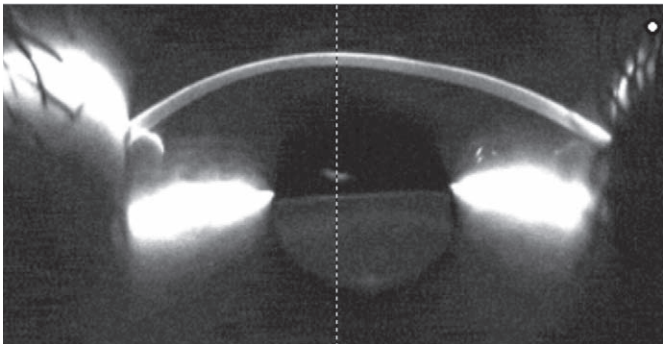
A challenging case, this keratoconus patient has a markedly displaced corneal apex inferiorly that makes fitting difficult. **Edited by Joseph P. Shovlin, OD**

Q I have a patient with keratoconus who has a very steep inferiorly displaced apex—every corneal lens rides low, as expected. Which approach would you recommend as an alternative? Would a hybrid work, or would a scleral be a better option?

A "An inferiorly displaced apex in keratoconus is a challenge to fit—corneal lenses often will not center, as they position over the steepest part of the cornea," says Dennis Burger, OD, clinical professor of optometry at the University of California at Berkeley. Fortunately, just a small percentage of keratoconic patients have a markedly inferior-decentered corneal apex, and there are now new options for fitting lenses to corneas of this type. These include specialized soft, hybrid and scleral lenses.

• *Large diameter lens.* Optometrist Edward S. Bennett prefers to start with an intralimbal diameter design, such as Rose K2IC (Blanchard) or Dyna Intra-Limbal (Lens Dynamics). Designed to fit within the limbus, these large-diameter lenses (11.2mm) share many fitting characteristics with standard rigid gas permeable lenses, while providing the comfort and irregular corneal masking that is characteristic of sclerals. If that design decenters, which may have been the case with this patient, a scleral or hybrid design would be indicated.

• *Hybrid lens.* "A hybrid design is sometimes a viable alternative; although it's important to ensure that the lens is not fitting too tightly, resulting in patient awareness and possibly peripheral corneal complications," says Dr. Bennett, associate professor and co-chief of the Contact Lens Service at the University of Missouri-St. Louis College of Optometry. "My preference would be for some type of mini-scleral design (i.e., 14mm to 16mm), as good centration, comfort and vision is often achieved."



This image shows a patient with a displaced apical center and cone diameter greater than 5mm to 6mm.

• *Scleral lens.* When dealing with a very steep inferiorly displaced apex, Dr. Burger finds that a scleral lens is the best option. "The rigid surface of the scleral provides good vision; the lenses are durable and they can also be custom designed," he says. "By using the scleral lens, I am able to vault the cornea and rest the lens on the sclera—this prevents lens decentration."

Although the fitting goal is to vault the entire cornea, bearing still may occur on a displaced apex. If this happens, Dr. Burger uses a reverse geometry design. Reverse geometry scleral lenses are indicated in patients with displaced corneal apices, pellucid marginal degeneration, corneal transplants, post-radial keratotomy and any condition where the peripheral cornea is steep. "These lenses have a steeper secondary curve, allowing for the lens to fit steeper in the peripheral cornea," he says. "They allow for clearance of the cone."

Scleral edges must be designed to prevent blood vessel blanching, as tight lenses will lead to discomfort. "Diagnostic lens fitting is mandatory, as empirical fitting does not work," Dr. Burger warns. "When fit properly, the scleral lens is very comfortable for the patient to wear—the combination of large lens stability, excellent optics, customizable parameters and good comfort make the scleral option the lens of choice for this patient."

With the recent introduction of many new scleral lens designs, most laboratories have consultants who can help guide you through the fitting process. In addition, many major contact lens meetings offer hands-on fitting workshops. Finally, organizations such as the Scleral Lens Education Society (www.sclerallens.org) and GP Lens Institute (www.gpli.info) have helpful resources available on their websites. ■

A COMPROMISED CONTACT LENS SURFACE CAN COMPROMISE PATIENT COMFORT

BY DR. JOHN PRUITT, PHD

John Pruitt currently serves as Project Head, Biocompatibility Projects in Alcon Vision Care's Research and Development department.

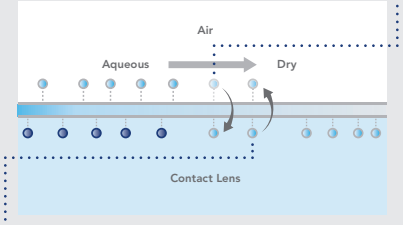
Patients don't want to think about their contact lenses. But with some silicone hydrogel materials, dehydration and deposit buildup can interrupt comfortable lens wear. A compromised lens surface can be at the root of the problem.

There's more to the surface than meets the eye

While the surface of a silicone hydrogel contact lens may seem static, it's actually quite an active component. Silicone hydrogel contact lenses contain both hydrophobic (water-repelling) and hydrophilic (water-loving) polymers that move and reorient at the surface during wear[1]—particularly when exposed to air and tear film changes between blinks.

Exposure to air sets the SiHy surface in motion

Hydrophilic (water-loving) molecules on the contact lens surface rotate inward seeking more moisture.



Hydrophobic (water-repelling) silicone sites rotate outward at the same time.

This results in **hydrophobic spots** on the surface of the contact lens that attract lipids and protein, resist rewetting and may cause discomfort.

A lot depends on the surface dynamics of a silicone hydrogel contact lens. It has been shown that some silicone hydrogel contact lens materials can attract up to 31X more deposits than other available silicone hydrogel contact lens options[2,3] (Fig.1)

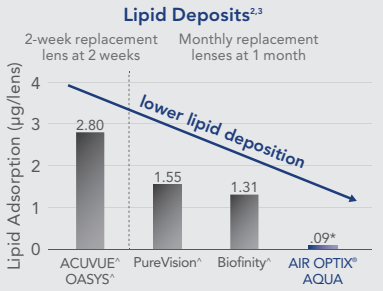
Fig. 1 – Surface defends against daily deposits

ACUVUE^ OASYS^ contact lenses
No permanent plasma treatment and an uneven surface[4]

Biofinity^ contact lenses
No permanent plasma treatment[5]

PureVision^ contact lenses
Surface made up of silicate islands that do not completely cover the surface[4]

AIR OPTIX® AQUA contact lenses
A permanent, chemically-bonded plasma treatment for a smooth, continuous surface[4]



*All differences between AIR OPTIX AQUA® contact lenses and competitive brands statistically significant (p<0.0001).

Manufacturers attempt to defend their contact lenses in different ways

Taking a closer look at silicone hydrogel contact lens technology sheds light on different manufacturers' attempts to protect lenses from dryness and deposits by masking silicone molecules on the lens surface.

ACUVUE^ OASYS^ contact lenses are made of a material containing polyvinyl pyrrolidone (PVP). This binds to water, but does not completely mask the silicone which leads to increased lipid deposits. With substantial silicone mobility, silicon levels reach approximately 10% at the surface of a dry contact lens.[6,7]

Biofinity^ contact lenses are made of a material composed of modified silicone macromers, making the lenses more wettable. However, the lens still allows silicone to be exposed at the surface—attracting lipids that decrease wettability. Silicone remains mobile with large levels of silicon present at the surface (>10%) when the contact lens is exposed to air.[6,8]

PureVision^ contact lenses undergo plasma oxidation, which converts surface silicone to silicate "glass." The surface cracks produce "glass-like" silicate islands. Exposed silicone in the cracks results in high lipid uptake.[6,9,10]

Lotrafilcon B contact lenses, such as **AIR OPTIX® brand contact lenses,** feature a unique, permanent plasma surface created by a fusion process. This permanent surface minimizes the mobility of the hydrophilic and hydrophobic sites during blinks by preventing the silicone in the lens material from being exposed to the air.[10] This smooth, protective surface allows tears to spread evenly over it, promoting moisture retention and minimal deposit buildup. With surface integrity that lasts throughout the wearing period, less than 1% silicon is measured at the surface of a dry contact lens.[8]

Conclusion

The silicone in silicone hydrogel contact lenses is highly desirable for improved oxygen transmission, but silicone can lead to poor wetting and lipid deposits. Look closer at the contact lens surface to achieve superior deposit resistance, clear vision and consistent comfort.

^Trademarks are the property of their respective owners.

Important information for AIR OPTIX® AQUA (lotrafilcon B), AIR OPTIX® AQUA Multifocal (lotrafilcon B) and AIR OPTIX® for Astigmatism (lotrafilcon B) contact lenses: For daily wear or extended wear up to 6 nights for near/far-sightedness, presbyopia and/or astigmatism. Risk of serious eye problems (i.e., corneal ulcer) is greater for extended wear. In rare cases, loss of vision may result. Side effects like discomfort, mild burning or stinging may occur.

Important information for AIR OPTIX® NIGHT & DAY® AQUA (lotrafilcon A) contact lenses: Indicated for vision correction for daily wear (worn only while awake) or extended wear (worn while awake and asleep) for up to 30 nights. **Relevant Warnings:** A corneal ulcer may develop rapidly and cause eye pain, redness or blurry vision as it progresses. If left untreated, a scar, and in rare cases loss of vision, may result. The risk of serious problems is greater for extended wear vs. daily wear and smoking increases this risk. A one-year post-market study found 0.18% (18 out of 10,000) of wearers developed a severe corneal infection, with 0.04% (4 out of 10,000) of wearers experiencing a permanent reduction in vision by two or more rows of letters on an eye chart. **Relevant Precautions:** Not everyone can wear for 30 nights. Approximately 80% of wearers can wear the lenses for extended wear. About two-thirds of wearers achieve the full 30 nights continuous wear. **Side Effects:** In clinical trials, approximately 3-5% of wearers experience at least one episode of infiltrative keratitis, a localized inflammation of the cornea which may be accompanied by mild to severe pain and may require the use of antibiotic eye drops for up to one week. Other less serious side effects were conjunctivitis, lid irritation or lens discomfort including dryness, mild burning or stinging. **Contraindications:** Contact lenses should not be worn if you have: eye infection or inflammation (redness and/or swelling); eye disease, injury or dryness that interferes with contact lens wear; systemic disease that may be affected by or impact lens wear; certain allergic conditions or using certain medications (ex. some eye medications). **Additional Information:** Lenses should be replaced every month. If removed before then, lenses should be cleaned and disinfected before wearing again. Always follow the eye care professional's recommended lens wear, care and replacement schedule. Consult package insert for complete information, available without charge by calling **(800) 241-5999** or go to **myalcon.com**.

References: 1. Epstein A, Stone R. Surface and Polymer Chemistry: The Quest for Comfort. *Review of Cornea and Contact Lenses.* 2010;147(1):15-19. **2.** Ex vivo measurement of lipid deposits on lenses worn daily wear through manufacturer-recommended replacement period; CLEAR CARE® Cleaning and Disinfecting Solution used for cleaning and disinfection; significance demonstrated at the 0.05 level; Alcon data on file, 2008. **3.** Nash W, Gabriel M, Mowrey-McKee M. A comparison of various silicone hydrogel lenses; lipid and protein deposition as a result of daily wear. *Optom Vis Sci.* 2010;87:E-abstract 105110. **4.** AFM 2.5 x 2.5 micron image; Alcon data on file, 2006. **5.** AFM 2.5 x 2.5 micron image; Alcon data on file, 2009. **6.** Huo Y, Rudy A, Wang A. Impact of ethylene oxide butylene oxide copolymers on the composition and friction of silicone hydrogel surfaces. Tribol Lett. 2012;(45):505-513. **7.** Alcon data on file, 2010, 2011. **8.** Alcon data on file, 2011. **9.** Zhao Z, Carnt N, Aliwarga Y, Wei X, Naduvilath T, Garrett Q, Korth J, Willcox M. Care regimen and lens material influence on silicone hydrogel contact lens deposition. *Optom Vis Sci.* 2009;86(3):251-259. **10.** Jones L, Senchyna M, Glasier M-A, Schickler J, Forbes I, Louie D, May C. Lysozyme and lipid deposition on silicone hydrogel contact lens materials. *Eye & Contact Lens.* 2003;29(IS):575-579.

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When Clotting is a Factor

When patients suffer an ocular or cerebral vascular event at a relatively young age, a clotting disorder could be the culprit.

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

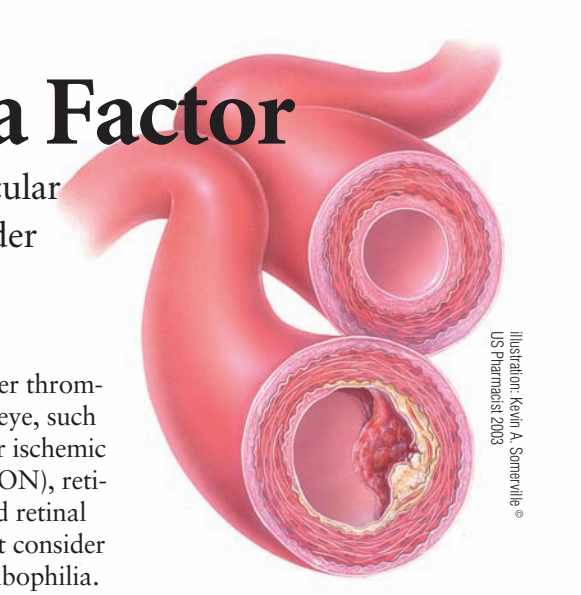


Illustration: Kevin A. Somerville © US Pharmacist 2003

Blood clotting is a natural and necessary process in the body—we rely on it to stop us from bleeding too much when an injury occurs. The wound triggers the clotting process, drawing certain chemicals in the blood to the site, where they solidify into a clot and plug the injured part of the blood vessel. Another set of natural chemicals in the blood counterbalance these clotting factors to stop the blood from clotting too much.

When too much clotting factor upsets this natural balance, it's known as thrombophilia (or a hypercoagulable state).[1] Many patients who have this condition never experience any medical issues as a result—thrombophilia simply increases the likelihood that they could develop an unwanted blood clot. When we encounter thrombotic conditions in the eye, such as non-arteritic anterior ischemic optic neuropathy (NAION), retinal artery occlusion and retinal vein occlusion, we must consider the possibility of thrombophilia.

Hereditary Hypercoagulable Conditions[1-4]

- Factor V Leiden gene mutation
- Prothrombin gene mutation
- Elevated homocysteine
- Abnormal fibrinolytic system, including hypoplasminogenemia, dysplasminogenemia and elevated plasminogen activator inhibitor (PAI-1)
- Deficiencies of proteins that prevent clotting (antithrombin, protein C and protein S)
- Elevated fibrinogen or dysfunctional fibrinogen (dysfibrinogenemia)
- Elevated factor VIII and other factors, including IX and XI

What Causes Thrombophilia?

Hypercoagulable states may be inherited or acquired. Acquired hypercoagulable states may occur as a result of surgery, trauma, medications, pregnancy or medical conditions, such as cancer, diabetes and obesity.[1,2]

As optometrists, we need to be particularly aware of antiphospholipid antibody syndrome, an acquired, hypercoagulable autoimmune disorder that can not only lead to retinal vascular occlusion, but also life-threatening complications, such as heart attack and stroke.[2]

With inherited forms of thrombophilia (*see "Hereditary Hypercoagulable Conditions," left*), patients are genetically predisposed with a tendency to form unwanted clots. The most common hereditary blood clotting disorder in the United States, Factor V Leiden gene mutation, affects 4% to 10% of whites.[3,4] Genetically at-risk patients who develop blood clots usually do so when additional risk factors are present, such as obesity, smoking, oral contraceptives and hormone replacement therapy.[1,3,4]

Diagnostic Work-up

As always in cases of suspected systemic disease, perform a careful evaluation of the patient's personal and family medical histories. A targeted review of systems for hypercoagulable states should include:[1,3,4]

- Family history of abnormal blood clotting.
- Abnormal blood clotting in patients younger than age 50.
- Thrombosis in unusual sites, such as veins in arms, liver, intestines, kidney and brain.
- History of "idiopathic" blood clots.
- Recurrent blood clots.
- Multiple miscarriages.
- Stroke at a young age.
- Myocardial infarction.

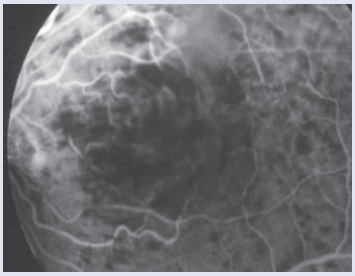
Although no single test can diagnose thrombophilia, we can perform a battery of lab tests to rule out or gather more information about the condition. (*See "Ruling Out Thrombophilia," page 70.*)

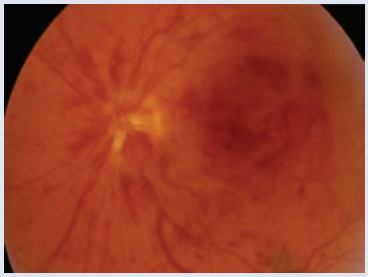
To help diagnose inherited hypercoagulable states, we can order genetic tests for Factor V Leiden (activated protein C resistance) and prothrombin gene mutation (G20210A), as well as testing

Case Report: Sudden Vision Loss Suggests Hypercoagulable State

• **History.** A healthy 36-year-old white female presented with a chief complaint of sudden vision loss in her left eye, which occurred earlier that morning. Her medications included an oral contraceptive, and she reported a family history of "blood clots" and heart disease. Her personal health history was negative for hypertension, diabetes, dyslipidemia and heart disease.

• **Diagnostic data.** Best-corrected visual acuity was 20/20 OD and 20/50 OS. Dilated funduscopy revealed a non-ischemic central retinal vein occlusion with mild foveal edema OS (*figures 1 and 2*).



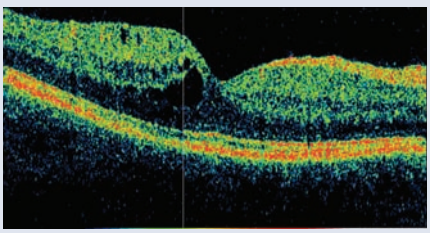


1,2. Dilated funduscopy revealed that our patient had a non-ischemic central retinal vein occlusion with mild foveal edema OS.

• **Management.** We scheduled the patient to return in two weeks for follow-up of the CRVO. In the meantime, she discontinued the birth control med after consultation with her primary care physician and gynecologist. Because the patient recently had a complete physical examination showing no diabetes, hypertension or hyperlipidemia, we ordered a targeted blood work-up to rule out hypercoaguable states.

Results of these tests were positive for the Factor V Leiden gene mutation. We referred her to a hematologist, who prescribed aspirin therapy as the initial medical management. The patient's immediate family members were evaluated (and possibly treated) for any genetic blood clotting mutations.

At her two-month follow-up visit, the macular edema had reduced (*figure 3*) and visual acuity improved to 20/30. She will return for follow-up in a month.



3. OCT images showed the macular edema had reduced at her two-month follow-up.

Ruling Out Thrombophilia

The most appropriate lab tests to exclude a diagnosis of thrombophilia include:[2,4]

- PT-INR: Prothrombin time (PT) is used to calculate the International Normalized Ratio (INR)—which is also used to monitor the condition in those taking warfarin (Coumadin, Bristol-Myers Squibb).
- Activated partial thromboplastin time (aPTT) measures the time it takes blood to clot. (This test is also used to monitor the condition in those taking heparin.)
- Fibrinogen levels
- Complete blood count (CBC)
- HbA1C
- Lipid panels

antithrombin activity, protein C activity, protein S activity and fasting plasma homocysteine levels.[5-8]

To help diagnose acquired hypercoagulable states, we can order anticardiolipin antibodies (ACA) or beta-2 glycoproteins and lupus anticoagulants (LA). Heparin antibody testing should be performed in patients who develop low platelet counts while exposed to heparin.[2,5,6]

The Eye in Thrombophilia

The prevalence of inherited hypercoaguable states is much higher in patients with venous thromboembolism (which includes CRVO) as compared to the general population.[9] For instance, the 5% incidence of Factor V Leiden in the general population jumps to 20% to 50% in patients with venous thromboembolism, while prothrombin G20210A jumps from 2% to 3% up to 6% to 8%.[9] The prevalence of hyperhomocysteinemia is 5% to 10% in the general population, but doubles to 10% to 20% in those with venous thrombotic disease.[9] Coupled with acquired hypercoagulation, the prevalence numbers become even more significant.

Hypercoagulable states may give rise to local thrombotic lesions in discrete segments of veins or arteries; therefore, focal thrombosis may involve the vessels that supply the retina, optic nerve, or both. It is important for the optometrist to be aware of the major inherited genetic mutations that lead to thrombophilia, especially in cases of young patients with diagnosed central retinal vein occlusion lacking any positive systemic history.

Retinal vein occlusion has been reported in association with Factor V Leiden, hyperhomocysteinemia, protein C deficiency, antithrombin deficiency, protein S deficiency and antiphospholipid antibody syndrome.[9] Retinal arterial occlusion has been linked with hyperhomocysteinemia and elevated lipoprotein(s), while NAION has been reported in patients with Factor V Leiden and elevated lipoprotein(s).[9]

Standard treatment and management protocols for RVO/RAO/NAION apply. In addition, appropriate medical treatment for the systemic cause is necessary and may help prevent recurrences of thromboembolic disease in the eye and elsewhere.

Treatment Approaches

Medical treatment is indicated when a blood clot develops in a vein or artery (including retinal vein and retinal arterial occlusion).[5-7] Anticoagulant medications are used to prevent systemic problems, such as heart attack or stroke, that might occur at a later time.

The most commonly used drugs include:

- *Aspirin*, which has an antiplatelet effect by inhibiting the enzyme cyclooxygenase, which in turn impedes thromboxane A2, an important intermediary involved in the clotting process.
- *Coumadin* (warfarin, Bristol-Myers Squibb), which comes in tablet form.
- *Heparin*, a liquid medication delivered by either intravenous or subcutaneous injections.[10] (Low-molecular weight heparin is injected subcutaneously once or twice a day and can be taken at home.)
- *Arixtra* (fondaparinux, GlaxoSmithKline), which is injected subcutaneously.

In taking the proper steps toward screening and detection, we can help the patient and potentially affected family members get appropriate treatment and decrease their chances of life-threatening vascular disease, such as pulmonary embolism, myocardial infarction and deep vein thrombosis. ■

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A 'Lesion of Doom?'

This patient presented with a black spot near her left optic nerve. Could it be a cancerous growth? **By Mark T. Dunbar, OD**

A 63-year-old Hispanic female was referred for evaluation of a "black spot" located in the fundus of her left eye. Recently, a neurologist examined the patient following a stroke that involved the right side of her brain one month earlier. The neurologist noted a dark lesion in her left eye upon direct ophthalmoscopy.

The patient reported a near full recovery from the stroke, with some residual weakness in her left shoulder. Her only visual complaint was poor near vision, which was corrected with over-the-counter reading glasses. This was her first eye exam.

Her systemic history was significant for hypertension. Current medications included lisinopril and low-dose aspirin.

On examination, her visual acuity was correctable to 20/20 OD and 20/25 OS. Extraocular motility was full, and the adnexal examination was unremarkable OU. Confrontation visual fields were full to careful finger counting OU. Her pupils were equally round and reactive to light, with no evidence of afferent defect. The anterior segment examination showed early nuclear sclerotic cataracts OU. Intraocular pressure measured 14mm Hg OD and 15mm Hg OS.

Dilated fundus examination of the right eye was unremarkable. Examination of the left fundus revealed the presence of a dark lesion; however, the macula and periphery were unremarkable.

Take the Retina Quiz

1. Which test is necessary to help establish the diagnosis?
   a. Fluorescein angiography.
   b. Echography.
   c. Excisional biopsy.
   d. No tests are necessary.

2. What is the correct diagnosis in this case?
   a. Choroidal melanoma with optic nerve involvement.
   b. Optic nerve melanoma.
   c. Combined hamartoma of the retinal pigment epithelium (RPE) and retina.
   d. Melanocytoma.

3. What is the most appropriate treatment?
   a. Iodine 125 plaque brachytherapy.
   b. Enucleation.
   c. External beam radiation, followed by enucleation.
   d. Observation.

4. What is the likely five-year mortality rate for this patient?
   a. 0%.
   b. 15%.
   c. 40%.
   d. 70%.

For answers, go to page 98.

Discussion

Ophthalmoscopic examination of our patient's left eye revealed the typical clinical picture of an optic nerve melanocytoma, which is nothing more than a benign pigmented tumor involving the optic nerve. Melanocytomas are often dark brown to black in color, and may appear slightly elevated with feathery edges. These lesions typically extend from the optic nerve, over the disc margin, to involve the nearby choroid or sensory retina.[1]

Melanocytomas commonly present unilaterally and often are diagnosed near age 50. Researchers have suggested that these lesions are not recognized early because they are not large enough or sufficiently pigmented to be recognized on examination until later in life.[2]

The primary differential diagnosis for melanocytoma is juxtapapillary choroidal melanoma. Melanomas typically are not as black as melanocytomas. Instead, they exhibit a more mottled gray or yellow-white appearance, and do not insinuate into the nerve fiber layer. Further, choroidal melanomas are more frequently seen in lighter pigmented individuals, and are exceedingly rare in both blacks and Asians. By contrast, melanocytomas are seen with greater frequency in dark-complected individuals. In fact, the presence of a pigmented lesion involving the optic nerve in a black patient is highly suggestive of a melanocytoma.

Melanocytoma is reported to occur more frequently in females;

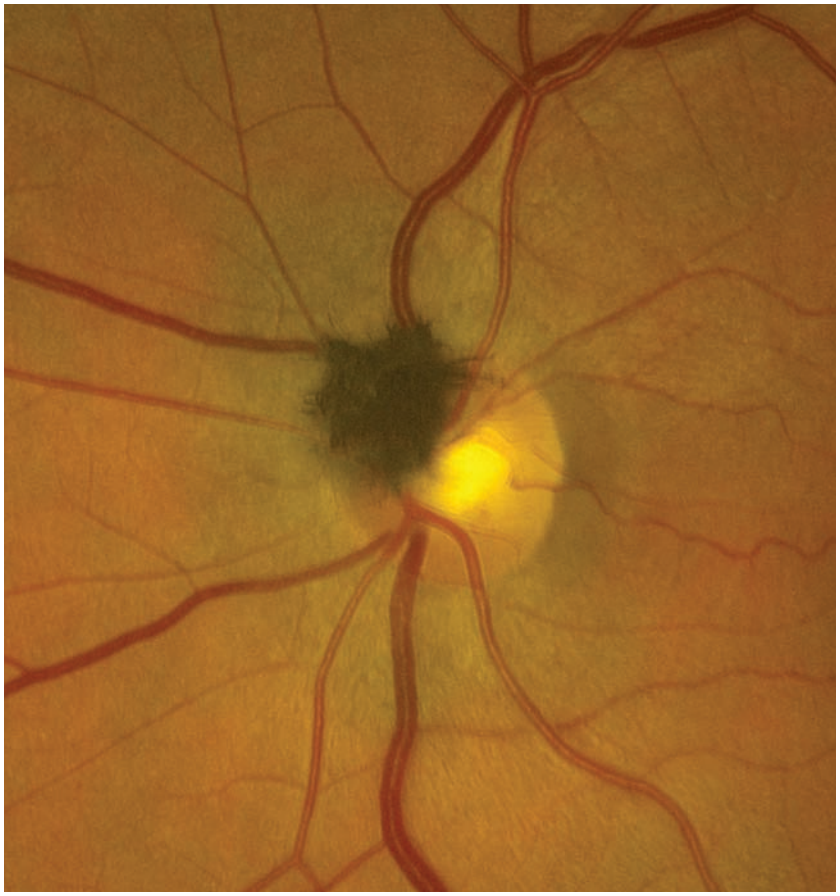
however, there is no known reason for this predilection.[1] Additionally, no strong systemic associations for melanocytoma have been found.[1]

Ocular complications from melanocyoma include optic disc edema, subretinal fluid, intraretinal edema, yellow exudates, focal hemorrhage, vitreous seeding and retinal vein obstruction. Complications leading to visual symptoms occur in approximately 26% of patients with melanocytoma.[1,2] Intraretinal tumor extension, as well as the presence of subretinal fluid, have been known to cause vision loss. Afferent pupillary defect occurs in 9% to 30% of cases.[2]

Traditionally, melanocytoma was considered an indolent lesion that does not grow; however, researchers have noted that 15% of these lesions show some slow enlargement over a number of years.[1] Interestingly, there is a small risk of malignant transformation in an estimated 1% to 2% of cases.[1] Risk factors for malignant transformation include progressive growth and visual field loss, as well as no juxtapapillary choroidal involvement.

Keep in mind that the aforementioned features also can occur in ischemic tumor necrosis, and therefore cannot be used as the only criteria for determining malignant transformation.[1]

Diagnosis of melanocytoma often is confirmed by ophthalmoscopic examination. Additional testing may include fundus photography, fluorescein angiography, visual field examination and optical coherence tomography (not to make the diagnosis, but rather to evaluate the impact on the patient's vision as well as establish a baseline for follow-up testing). OCT imaging isn't useful in evaluating the specific features of melanocytoma; but, it can help determine the presence and extent of subretinal fluid or intraretinal edema, which may be difficult to see otherwise.[1]



Fundus photograph of our patient's left eye shows a peculiar lesion involving the optic nerve. What is the correct diagnosis?

Some level of visual field loss occurs in up to 90% of patients with melanocytoma. Enlarged blind spot is the most common visual field defect; however, arcuate and nerve fiber bundle defects may also occur.

The prognosis for patients with melanocytoma typically is excellent. At the time of diagnosis, patients should be photodocumented as well as undergo visual field testing to establish a baseline.[1] Follow-up should be performed yearly, with a dilated examination and fundus photography to monitor for subtle growth.

We discussed the findings with our patient and asked her to return for a visual field examination in four to six months. Future follow-up visits also will provide us with the opportunity to monitor for lesion enlargement. ■

Thanks to Jacob Woldt, OD, resident at Bascom Palmer Eye Institute in Miami, for contributing this case.

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My, What Big Eyes You Have

Thorough histories are critical when patients present with unexplained pupil dilation.

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

It was a strange scenario. A 32-year-old woman believed that her vision was getting blurry the evening before, but ignored it and went to bed. When she woke up the next day, her vision was "terrible." After it failed to improve over several hours, she saw her internist emergently. He immediately referred her for a consultation.

Systemically, the patient was healthy and had no significant medical history. She used no current medications and denied any drug allergies. She had never worn glasses and rarely had her eyes examined, because her vision always had been "excellent."

She was a healthy, well-nourished woman in no apparent physical distress. Her uncorrected visual acuity was 20/200 in each eye. Extraocular muscle testing showed no restrictions, and confrontation visual fields were normal in both eyes. Her eyelids were symmetrical, with no evidence of ptosis or eyelid retraction. However, of particular interest, we noted that she had bilaterally round, fixed and dilated pupils.

Neither pupil reacted to light or near accommodative stimuli. Her pupils measured 8.5mm OD and 9.0mm OS. Testing of the relative afferent visual system was impossible because of impaired pupillary reactivity.

Her fundus evaluation revealed normal optic discs and retinae OU. Interestingly (and tellingly), binocular indirect ophthalmoscopy was performed without the use of any mydriatic agents, because of the size of her dilated and unreactive pupils. Upon questioning, the patient denied trauma as well as use of any topical or systemic medications.

This presented quite the clinical conundrum. In this month's column, we will describe how to evaluate patients who present with one or both pupils dilated.

Pupillary Evaluation

Evaluating pupils in both bright and dim light is vitally important. Further, pupils must be tested for response to both light stimulus (direct and consensual responses) and a near target (near synkinetic response). A history of pharmacologic use must be ascertained. A mydriatic agent will cause pupils to be round and unreactive to both light and near testing. A sympathetic agent will yield round, dilated pupils that likely will react—albeit sluggishly—to light and near stimulation.

A history of trauma should be sought as well. Should the patient have experienced ocular trauma, carefully examine the iris via biomicroscopy for contributory signs, such as iridodialysis or pupil sector paralysis, because trauma can result in a fixed and dilated pupil. A famous example is singer David Bowie, who received a permanently fixed, dilated pupil at age 13 during a fight over a girl.

Typically, when encountering a dilated pupil, there will be some associated degree of anisocoria. When encountering this situation, the first step is to establish whether the anisocoria changes with ambient lighting. This will help you determine where the issue may lie in the pupillary pathway.

Anisocoria, which is greater in bright illumination, is indicative of parasympathetic dysfunction. This finding suggests the pupil fibers that travel in concert with cranial nerve (CN) 3 have sustained damage—especially if there's also evidence of localized ptosis and extraocular muscle paralysis.

A cause of CN3 paralysis with pupil dilation may be an expanding intracranial aneurysm. In this instance, the aneurysm may rupture and cause a potentially fatal subarachnoid hemorrhage.[1,2] This scenario should be suspected when encountering a dilated, poorly reactive pupil in an eye with associated ptosis and adduction, elevation and depression deficits. Aneursymal compression is marked by head or retro-orbital pain and anisocoria with ipsilateral pupil dilation, because the expanding aneurysm compresses the pupillomotor fibers as well as the pain-sensitive dura and other such structures.[3] However, an isolated dilated pupil in an ambulatory patient with no eyelid or ocular motility deficits is not indicative of an aneurysm.

Anisocoria that changes between

Contact lens dryness:

Patients aren't the only ones who are suffering.

How this unspoken issue is affecting your patients—and your practice.

MORE THAN **50%** of current contact lens wearers report experiencing feelings of dryness, even though they may not tell their optometrists about it. So, how can optometrists get patients to recognize and discuss contact lens dryness? And, how will that impact their practices?

If patients say their lenses are "fine," chances are they're not fully satisfied with their lenses—or their optometrists. Optometrists who can turn that "fine" into "great" become the heroes—setting themselves apart from the rest of their peers.

Uncovering Lens Dryness

In order to fully understand a patient's experience, optometrists should consider a direct approach. Ask probing questions, such as, "How do your monthly lenses feel after wearing them for 3 to 4 weeks?" Or, "How would you rate your lenses on a scale of 1 to 10?" Any answer other than "10" allows optometrists to dig deeper and uncover the hidden symptoms of contact lens dryness—giving the opportunity to introduce a superior option and create true happiness, the kind that leads to referrals.

Get Patients Talking

The experience optometrists provide their patients is a direct reflection of their practice. If they're not happy with their lenses, they're not happy with their optometrists—and they're not referring their friends and family to them.

"If you only meet their expectations, they won't leave your office and post on Facebook®, send a Tweet™, or tell a co-worker, neighbor, or their spouse about what a great experience they had."
– Dr Turner

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Featured Clinician **Charles Turner, OD**

With 7 years of experience building his own practice in the Charleston, South Carolina area, Dr Turner has seen first-hand how addressing contact lens dryness with a special focus on the patient experience and contact lens education can impact practice growth. Interestingly, half of Dr Turner's patients are from neighboring towns, and don't mind driving further for his comphrehensive approach to eye care. Dr Turner is a consultant for Johnson & Johnson Vision Care, Inc. and has been compensated for his contributions.

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*Young G, Sulley A, Hunt C. Prevalence of astigmatism in relation to soft contact lens fitting. *Eye Contact Lens.* 2011;37(1):20-25.

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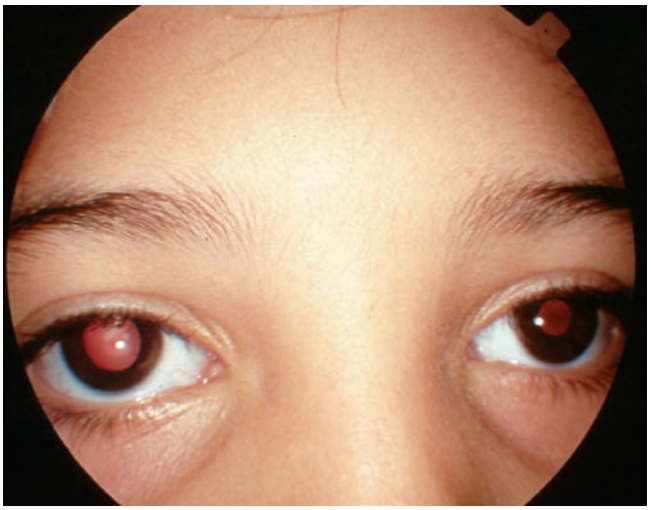
light and dim illumination suggests a tonic pupil. That is, the suspect pupil is dilated and larger in bright illumination, but may be smaller in dim illumination. The iris margin may be irregular and the pupil misshapen due to a sector paralysis. Tonic pupils (sometimes referred to as internal ophthalmoplegia) result from damage to the parasympathetic innervation to the eye, specifically at the ciliary ganglion or short ciliary nerves. This results in decreased iris sphincter and ciliary body function.[4-6]

A tonic pupil responds minimally to light and marginally better to near stimuli, with extremely slow constriction and re-dilation—a term known as light-near dissociation. In addition to the tonicity of both the pupillary light reaction and accommodation, other clinical signs that may be seen include segmental palsy of the iris sphincter and denervation hypersensitivity to dilute cholinergic agents.

Pharmacological testing aids in the diagnosis of tonic pupil. In the vast majority of cases, dilute pilocarpine (0.125%) will induce pupillary constriction after 30 to 45 minutes—while normal pupils will not respond at all.

If the pupil fails to constrict following instillation of 0.125% pilocarpine, try 1% pilocarpine solution. If the pupil also fails to constrict with 1% pilocarpine, the dilation is likely due to pharmacological mydriasis, traumatic iridoplegia, sphincter ischemia or iatrogenic damage from prior intraocular surgery.

In our patient, the absolute unreactivity of each pupil—with no ocular motility deficits or ptosis—led us to suspect that she did not harbor an intracranial aneurysm, but rather had some pharmacologic misadventure. This was confirmed when retinoscopy revealed +2.00D latent hyperopia in each eye that was correctable to 20/20, indicating cycloplegia.



A dilated tonic pupil OD.

Disturbingly, she still denied any medication use—specifically topical decongestant agents as well as scopolamine patches for seasickness. She also denied any incidents that could be related to the onset of blurred vision. A detailed probing of her entire itinerary from the day before finally revealed that she had attended a flower and plant show at the local civic center. When asked about what had transpired at the show, the patient remembered that she had handled many plants. This caused her allergies to flare, and she rubbed her eyes repeatedly.

To her, this action seemed inconsequential—but it led to our answer. Atropine is a naturally occurring tropane alkaloid extracted from plants of the *Solanaceae* family, which includes the deadly nightshade (*Atropa belladonna*), Jimson weed (*Datura stramonium*) and mandrake (*Mandragora officinarum*).

Likely, while handling one of these plants, some of the alkaloid extract was transferred to her hand and subsequently introduced into her eyes through rubbing. She was educated about the occurrence and monitored.

Over the course of the next two weeks, the cycloplegia and mydriasis dissipated and the patient returned to normal.

Finding the cause of a dilated pupil can be a challenging exercise. Trauma, pharmacologic agents and numerous other conditions can cause pupillary dilation. An intracranial aneurysm, with its attendant morbidity and mortality, can also cause a dilated pupil.

However, in lieu of any other abnormalities, rest assured that an aneurysm will not likely be the cause of an isolated dilated pupil in an ambulatory patient. Knowing this, should David Bowie ever wander into your practice, don't refer him for neuroimaging based solely upon his dilated pupil. ■

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The Pupil Becomes the Teacher

Pupil testing is a critical neurological screening technique that is frequently overlooked, but often helps guide us to the correct diagnosis.

By Paul M. Karpecki, OD, and Diana L. Shechtman, OD

Pupil testing typically is a quick diagnostic procedure conducted by either an eye care provider or, more commonly, a technician. It usually involves swinging a pen light from eye to eye to assess both the direct and consensual pupillary response. For some clinicians, this can be both difficult and frustrating. However, if performed diligently, pupil testing can save a patient's sight—or life.

Pupil Testing 101

Under normal circumstances, light entering either eye elicits the exact same pupillary response. But if, for example, there is a lesion in the patient's right optic nerve or retina, light directed to that eye will not yield a normal response in either pupil.

Interestingly, however, when light is shined in the patient's healthy contralateral eye, both the left and right pupils will react normally and consistently.[1] Such an obvious difference in pupillary response points to a right eye abnormality, such as optic neuropathy.

Screening for Neuro-Ophthalmic Disorders

• ***Horner's syndrome.*** During pupil testing, anisocoria (a difference in pupil size) is important to measure because it can reveal an underlying problem with the afferent pupillary pathway. Such a finding can help uncover the existence of a lesion located along the pathway of either the supply from the Edinger-Westphal nucleus to the sphincter muscle of the iris (Adie's pupil), or the ocular sympathetic supply to the dilator pupil muscle of the iris (Horner's syndrome).

Keep in mind that a physiological anisocoria is a harmless condition, whereas Horner's syndrome can be indicative of several potentially fatal conditions, including stroke, a cancerous tumor of the lung apex (pancoast tumor), a tear in the carotid artery's endothelium or a spinal cord injury.[2-6]

Because Horner's syndrome affects the sympathetic nerves, patients typically present with a smaller pupil, a ptosis and a lack of sweating on the affected side of the face (also known as the classic triad of meiosis, ptosis and anhydrosis).[7]

• ***Third nerve palsy.*** This is another significant condition that may be detected via pupillary testing. In this instance, patients typically exhibit a dilated or "blown" pupil as well as ptosis. Take note, however, that a third nerve palsy can occur with little to no pupillary involvement.[8] Nevertheless, such a presentation typically restricts extraocular motor functioning.

Third nerve palsy is a medical emergency that warrants immediate imaging to rule out associated conditions, such as a cerebral aneurysm, compressive mass or even multiple sclerosis. In fact, if a third nerve palsy is noted—either with or without a history of trauma—immediate referral to an emergency room is required.[9,10]

• ***Neurosyphilis.*** One additional condition to screen for via pupillary testing is neurosyphilis, which can cause severe vision and hearing loss, psychiatric complications and even death.[11-13] One particular ophthalmic finding often can help you confirm the final diagnosis of neurosyphilis—an Argyll Robertson pupil.

The best way to remember this testing approach is to create an acronym using the first letters of each word in "Argyll-Robertson pupil:"

- ARP: Accommodative Response Present.

Then, simply invert the acronym:

- PRA: Pupillary Response Absent (to light stimulus).

A patient with a positive Argyll-Robertson finding will exhibit a small pupil that constricts poorly to direct light, but briskly when a near target is presented.[14] The moment you confirm this diagnosis, refer the patient to an infectious disease specialist for appropriate laboratory testing and treatment before further morbidity occurs.

Pupil Testing for Glaucoma?

Because the condition typically presents as an asymmetric neuropathy, pupillary testing potentially could be used to detect glaucoma. In fact, one study showed that pupil testing could help reveal photosensitive ganglion cell damage associated with glaucoma.[15]

So, why is pupil testing not

routinely included in a glaucoma work-up? One primary reason is that pupillary response frequently would be too subtle during the earliest stages of disease. Also, the swinging flashlight test is difficult to perform accurately on patients with dark irides.

However, advanced pupillary testing devices such as RAPDx (Konan Medical) could help eye care practitioners more accurately diagnose conditions that yield a relative afferent pupillary defect (RAPD), including glaucoma.[15,16]

RAPDx measures pupillary responses to direct and consensual light and accommodation while the patient looks at a series of color illuminations. The direct and consensual response is plotted on a graph, so you can easily determine the extent of RAPD present.

Pupil screening is one of the most infrequently applied diagnostic tests, because it is difficult to perform and challenging to interpret. Still, you simply cannot afford to discount its diagnostic and prognostic value when evaluating patients for sight- and life-threatening neuro-ophthalmic disorders. ■

Dr. Karpecki is a paid consultant to Konan Medical. Neither he nor Dr. Shechtman has direct financial interest in any of the products mentioned.

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The Avellino Gene Detection System (AGDS) Test enables patients and their physicians to make a more informed decision when considering vision correction surgery. With purported 100% accuracy, the test positively identifies the Avellino corneal dystrophy genetic mutation that puts carriers at high risk of experiencing eventual blindness as a result of refractive procedures such as LASIK, LASEK or PRK, the company says.

The AGDS Test involves a simple mouth swab from a patient's cheek. The sample is then sent to Avellino's certified molecular diagnostic testing facility. Within 24 to 48 hours, the results are provided to the physician to share with the patient.

Based on a negative result, patients are able to undergo the planned procedure with confidence. Individuals identified as positive for the genetic mutation will be advised against surgery and encouraged to take protective measures, such as minimizing exposure to UV light by wearing appropriate protective lenses, to help postpone the progression of ACD symptoms.

Contact Lenses

Dailies Total1

After more than a decade of product development, Alcon recently introduced its Dailies Total1 (delefilcon A) water gradient contact lenses to the US market. These daily disposables have a gradient design in both their material composition and water content, which enhances performance at the core and lens surface.

Dailies Total1 lenses are comprised of a highly breathable silicone hydrogel core, with a low water content of 33% that transitions to a hydrophilic surface gel comprised of more than 80% water content, approaching 100% water content at the outer surface, the company says.

Available in trial packs of five and retail packs of 30 and 90, the lenses have a diameter of 14.1mm, an 8.5mm base curve and a center thickness of 0.09mm at -3.00D. They are currently available with a power range of -0.50D to -6.00D (in 0.25D steps); and -6.50D to -10.00D (in 0.50D steps).

Visit www.alcon.com.

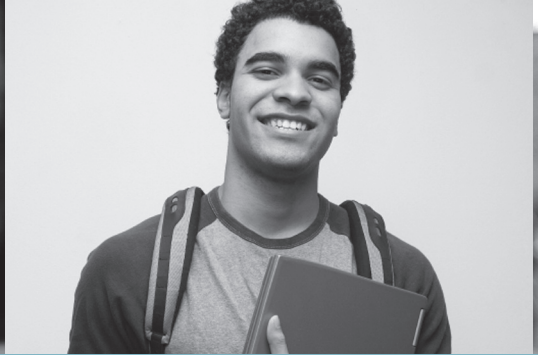
Children's Sunglasses

Junior BanZ

With summer in full swing, it's a good time to talk with your patients about the importance of sunglasses for children—who are more susceptible to absorbing UV radiation, because their eyes have less protective pigment than adults. A new addition to the Baby BanZ sunglasses collection, the Junior BanZ line is made for boys and girls ages four to 10.

JBanZ come with their own color-coordinated neoprene carrying case with a zipper clasp, as well as a removable neoprene strap for active kids. Their flexible temples resist breakage, and the wraparound design adds extra protection from wind and debris for kids on the run, the company says. Designed for the wear and tear of playground and after-school activities, JBanz also shield children's eyes from harmful rays with 100% UVA/UVB protection.

Visit www.banzworld.com. ■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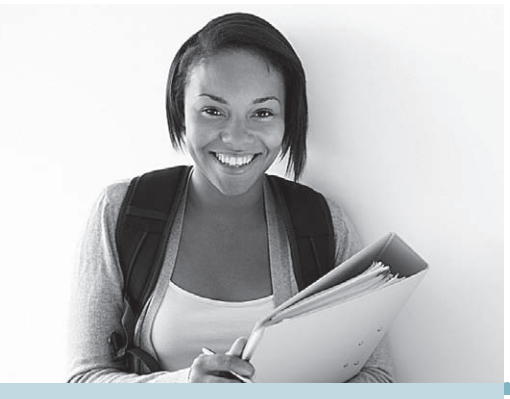

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■ **25-28.** *Bermuda 2013.* Fairmont Hamilton Princess, Bermuda. Hosted by: *Review of Optometry.* Meeting chair: Paul Karpecki, OD. CE hours: 14. Contact Lois DiDomenico at ReviewMeetings@Jobson.com or (866) 658-1772. Visit www.revoptom.com/conferences.

■ **26-27.** *2013 Gold Coast Summer Conference.* Hilton Sandestin Resort, Destin, Fla. Sponsored by: Alabama Optometric Association and UAB School of Optometry Alumni Association. Visit www.alaopt.org.

■ **26-28.** *Nova See St. Simons.* The King and Prince Beach & Golf Resort, St. Simons, Ga. Sponsored by: Nova Southeastern University College of Optometry and Luxottica. CE hours: 17. Contact Vanessa McDonald, manager of continuing education, at oceaa@nova.edu. Visit http://optometry.nova.edu/ce.

August 2013

■ **1-4.** *2013 Annual Continuing Education Conference.* Wedgewood Resort, Fairbanks, Alaska. Hosted by: Alaska Optometric Association. Email akoa@alaska.com or call (907) 770-3777. Visit www.akoa.org.

■ **2-3.** *Summer Education Event.* Blue Harbor Resort, Sheboygan, Wis. Hosted by: Wisconsin Optometric Association. Email joleen@woa-eyes.org or call (608) 824-2200. Visit www.woa-eyes.org.

■ **3-4.** *Colorado Vision Summit.* Crowne Plaza Hotel Denver International Airport, Denver, Colo. Hosted by: Colorado Optometric Association. Visit www.coloradovisionsummit.org or call (303) 863-9778.

■ **3-5.** *Annual Educational Retreat 2013.* South Seas Island Resort, Sanibel, Fla. Hosted by: Southwest Florida Optometric Association Inc. CE hours: 14. Contact Brad Middaugh, OD, at swfoa@att.net or (239) 481-7799. Visit www.swfoa.com.

■ **7.** *New Jersey Academy Chapter 1-Day Seminar.* Jumping Brook Country Club, Neptune, Contact Dennis H Lyons, OD at dhl2020@aol.com or (732) 920-0110.

■ **18.** *Super Sunday 2013.* NSU Orlando Campus. Hosted by: Nova Southeastern University College of Optometry. Faculty: Paul Chous, OD, MA, and Kimberly Reed, OD. CE hours: 8. Contact Vanessa McDonald at oceaa@nova.edu or (954) 262-4224. Visit http://optometry.nova.edu/ce.

■ **22-25.** *106th SCOPA Annual Meeting.* Myrtle Beach Marriott Resort & Spa at Grand Dunnes, Myrtle Beach, SC. Hosted by: South Carolina Optometric Physicians Association. CE hours: 21. Visit http://southcarolina.aoa.org.

■ **23-25.** *UAB Continuing Education & Alumni Weekend.* Volker Hall, UAB Campus. Hosted by: UAB School of Optometry, Birmingham, Ala. CE Hours: 18. Contact Candie Bratton at (205) 934-5701 or uabsoce@uab.edu. Visit www.uab.edu/optometry.

■ **24.** *San Antonio Ophthalmic Symposium.* Westin Riverwalk Hotel, San Antonio, Texas. Hosted by: *Review of Optometry.* Contact Lois DiDomenico at ReviewMeetings@Jobson.com or (866) 658-1772. Visit www.revophth.com/saos2013.

September 2013

■ **6-8.** *FCO Annual Educational Conference.* Holiday Inn Resort, Pensacola Beach, Fla. Hosted by: Fellowship of Christian Optometrists. Contact Mike Goen at foreknown@aol.com or (850) 530-9626. Visit www.fcoint.org/services/annualConference.html.

■ **8-9.** *Northeast Optometric Congress.* Westford Regency Inn and Conference Center, Westford, Mass. Email Kathleen Prucnal, OD, at drkaprucnal@msn.com or visit www.oepf.org.

■ **13-15.** *Vermont Optometric Association Annual Meeting.* Hilton Hotel and Conference Center, Burlington, Vt. Hosted by: Vermont Optometric Association. Contact David J. DiMarco, OD, at djd@nveyecare.net or (802) 524-9561.

■ **19-21.** *Envision Conference.* Hyatt Regency Minneapolis, Minneapolis, Minn. Email info@envisionconference.org or call (316) 440-1530. Visit www.envisionconference.org.

■ **19-22.** *GWCO Congress 2013: Focused on the Future.* Oregon Convention Center, Portland. Hosted by: Great Western Council of Optometry. Featured speaker: Jim Trunick, OD. Contact Wayne Oman, deputy director, at gwco@gwco.org or (503) 654-1062. Visit www.gwco.org.

■ **20-22.** *New Technology & Treatments West Coast 2013.* Marriott Del Mar, San Diego. Hosted by: *Review of Optometry.* Contact Lois DiDomenico at ReviewMeetings@Jobson.com or (866) 658-1772. Visit www.revoptom.com/conferences.

■ **20-22.** *44th Annual Colorado Vision Training Conference.* YMCA of the Rockies, Estes Park, Colo. Contact Jamie Anderson, OD, FCOVD, (303) 325-2019 or jamie@highlinevisioncenter.com. Visit www.visioncare.org.

■ **21-22.** *Fall Conference 2013.* Steele Auditorium, NSU Campus, Orlando, Fla. Hosted by: Nova Southeastern University College of Optometry. Program Director: Joseph Sowka, OD. Contact Vanessa McDonald at oceaa@nova.edu. Visit http://optometry.nova.edu/ce.

■ **21-22.** *4th Annual Everything Retina Symposium.* Westin Riverwalk Hotel, San Antonio, Texas. Hosted by: University of Houston College of Optometry. CE hours: 16. Call (713) 743-1900 or visit http://ce.opt.uh.edu/live-events/ers2013.

■ **22.** *CE Forum XVII.* The Hotel Hershey, Hershey, Pa. Hosted by: Central Pennsylvania Optometric Society. CE hours: 6. Email Mary Good, OD, at cposrsvp@gmail.com.

October 2013

■ **2.** *6th Annual Prevent Blindness America Swing Fore Sight*

Golf Tournament. Bali Hai Golf Club in Las Vegas. Contact Danielle Disch at ddisch@preventblindness.org or (312) 363-6022. Visit preventblindness.org/swingforesight.

■ **2-5.** *International Vision Expo & Conference West 2013*. Sands Expo & Convention Center, Las Vegas. Call (800) 811-7151 or visit www.visionexpowest.com.

■ **4.** *Hudson Valley Optometric Society Fall Seminar*. The Grandview, Poughkeepsie, NY. Hosted by: Hudson Valley Optometric Society. Featured Speaker: Eric Schmidt, OD. CE hours: 5. For more information, contact Brian Powell, OD, at drbrianpowell@gmail.com. Visit www.hvos.org.

■ **6-7.** *SECO London 2013*. Hosted by: SECO International and the Association of Optometrists. CE hours: 12. Visit www.secointernational.com/london-2013.html.

■ **8-12.** *COVD 43rd Annual Meeting*. Rosen Shingle Creek, Orlando, Fla. Hosted by: College of Optometrists in Vision Development. Visit www.covd.org or call (330) 995-0718.

■ **10-11, 11-13.** *VOSH International Meeting/COPR Annual Conference*. Ritz Carlton Hotel, San Juan, Puerto Rico. Hosted by: VOSH International and Colegio De Optómetras de Puerto Rico (COPR). Visit www.covd.org or call (330) 995-0718.

■ **12-13.** *3rd Annual Forum on Ocular Disease*. WDW Swan and Dolphin Resort in Orlando, Fla. Hosted by: PSS EyeCare. CE hours: 18. Contact Sonia at education@psseyecare.com or go to www.PSSeyecare.com and click on "Orlando."

■ **19-21, 23-25.** *CE in Italy: Florence and/or Castiglion Fiorentino, Tuscany*. To register for one or both of these programs, contact James Fanelli, OD, at jamesfanelli@ceinitaly.com or call (910) 452-7225. Visit www.ceinitaly.com.

■ **23-26.** *Academy 2013 Seattle*. Washington State Convention Center, Seattle. Hosted by: American Academy of Optometry. Visit www.aaopt.org/meetings/academy2013.

November 2013

■ **2-3.** *Essentials in Eyecare: Board Certification Preparatory & Optometric CE Program*. Marriott Pittsburgh North, Pittsburgh, Pa. Hosted by: Pennsylvania College of Optometry. CE hours: 16 hours. Email ilene@poaeyes.org for more information or visit http://pennsylvania.aoa.org.

■ **10.** *Virginia Academy of Optometry Annual Educational Conference*. The Inn at Fredricksburg Square, Fredricksburg, Va. Hosted by: Virginia Academy of Optometry. CE hours: 4. Featured speaker: Bruce Onofrey, OD, RPh. For more information, email vaacadoptom@yahoo.com. ■

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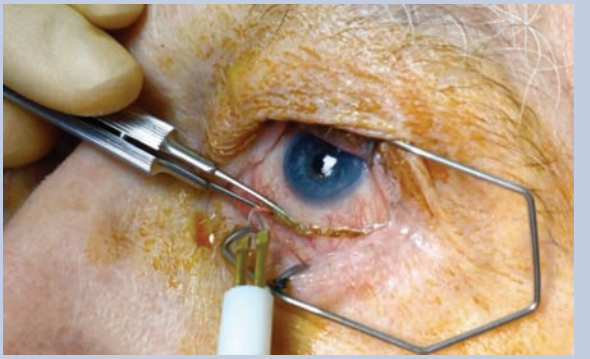
• *Clinical Perspectives in the Medical Management of Glaucoma*

The Challenge of Chalasis

It's more common than you may realize, and responds well to surgical intervention.

By Derek N. Cunningham, OD, and Walter O. Whitley, OD, MBA



Photo/video courtesy of Elizabeth Yeu, MD, and Thomas Joly, MD, Virginia Eye Consultants.

Go to www.revoptom.com or scan the QR code at left to see video footage of the procedure.

On The Web ›› View a narrated video of cautery and resection procedures.

One would expect a clinical entity as common as conjunctivochalasis to receive more attention than it does; surprisingly, it is often overlooked or disregarded. Although not sight threatening, conjunctivochalasis can lead to chronic ocular discomfort. Patients may be highly symptomatic, even early in the disease course, which is why we need to identify and treat the condition as soon as possible. As the disease progresses, symptoms may include ocular pain localized to the area of redundant conjunctiva, chronic foreign body sensation, epiphora and tearing. The excess conjunctiva can lead to a poor distribution of the tear film and excess movement of the conjunctiva, exacerbating the symptoms.

It is important to consider conjunctivochalasis in any patient who presents with ocular discomfort. Risk factors are increased age (50 and higher), history of dry eye disease, prior eye surgery or a history of conjunctival chemosis. The condition also may be associated with blepharitis and contact lens wear.

In symptomatic patients, redundant conjunctival folds between the lower lid margin and the globe are often seen temporally; however, it may present with 360° conjunctival involvement. Fluorescein and lissamine green staining can help identify areas of compromise.

The differential diagnosis can be difficult, as common signs and symptoms may be misleading. One tool that may help is tear film osmolarity. In symptomatic patients with a low osmolarity reading, conditions other than dry eye may be present. Pain is another differentiator—patients with ocular surface disease often complain of chronic irritation; however, those with conjunctivochalasis complain of pain specifically in the affected area. Lastly, conjunctivochalasis may look similar to conjunctival chemosis, which often responds to antihistamines and anti-inflammatories. If you get a limited response from such therapies, consider conjunctivochalasis as the diagnosis.

Conventional treatments include artificial tears and concurrent treatment of ocular surface inflammation (e.g., topical steroids, non-steroidals, cyclosporine). If unsuccessful, the next step would be surgical intervention via conjunctival cautery or resection, performed 1mm to 2mm away from the limbal area to preserve its stem cells. With either procedure, the goal is to tighten up the excess/loose conjunctiva, reducing friction and chronic irritation on the ocular surface.

Superficial conjunctival cautery is an effective treatment for mild to moderate disease; conjunctival resection is reserved for more advanced cases. Cautery essentially shortens the conjunctiva, while the clamped forceps help to create a seal at the base. For moderate to severe cases, resection is indicated, with or without an amniotic membrane graft, which some surgeons use to promote wound healing (others believe the cost of the membrane does not justify its use). The amniotic graft can be secured onto the conjunctiva with dissolvable sutures or fibrin tissue glue. Postoperative medications include topical antibiotics for one week, topical steroids for two weeks and topical NSAIDs for two weeks.

As comanaging doctors, optometrists play an integral role in identifying and treating this condition. A surgical referral is indicated to successfully treat this frequently overlooked diagnosis. ■

BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE

SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is a fixed combination of a carbonic anhydrase inhibitor and an alpha 2 adrenergic receptor agonist indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop of SIMBRINZA™ Suspension in the affected eye(s) three times daily. Shake well before use. SIMBRINZA™ Suspension may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

DOSAGE FORMS AND STRENGTHS

Suspension containing 10 mg/mL brinzolamide and 2 mg/mL brimonidine tartrate.

CONTRAINDICATIONS

Hypersensitivity - SIMBRINZA™ Suspension is contraindicated in patients who are hypersensitive to any component of this product.

Neonates and Infants (under the age of 2 years) - SIMBRINZA™ Suspension is contraindicated in neonates and infants (under the age of 2 years*) see Use in Specific Populations*

WARNINGS AND PRECAUTIONS

Sulfonamide Hypersensitivity Reactions - SIMBRINZA™ Suspension contains brinzolamide, a sulfonamide, and although administered topically is absorbed systemically. Therefore, the same types of adverse reactions that are attributable to sulfonamides may occur with topical administration of SIMBRINZA™ Suspension. Fatalities have occurred due to severe reactions to sulfonamides including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias. Sensitization may recur when a sulfonamide is re-administered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation *[see Patient Counseling Information]*

Corneal Endothelium - Carbonic anhydrase activity has been observed in both the cytoplasm and around the plasma membranes of the corneal endothelium. There is an increased potential for developing corneal edema in patients with low endothelial cell counts. Caution should be used when prescribing SIMBRINZA™ Suspension to this group of patients.

Severe Renal Impairment - SIMBRINZA™ Suspension has not been specifically studied in patients with severe renal impairment (CrCl < 30 mL/min). Since brinzolamide and its metabolite are excreted predominantly by the kidney, SIMBRINZA™ Suspension is not recommended in such patients.

Acute Angle-Closure Glaucoma - The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. SIMBRINZA™ Suspension has not been studied in patients with acute angle-closure glaucoma.

Contact Lens Wear - The preservative in SIMBRINZA™, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of SIMBRINZA™ Suspension but may be reinserted 15 minutes after instillation *[see Patient Counseling Information]*.

Severe Cardiovascular Disease - Brimonidine tartrate, a component of SIMBRINZA™ Suspension, has a less than 5% mean decrease in blood pressure 2 hours after dosing in clinical studies; caution should be exercised in treating patients with severe cardiovascular disease.

Severe Hepatic Impairment - Because brimonidine tartrate, a component of SIMBRINZA™ Suspension, has not been studied in patients with hepatic impairment, caution should be exercised in such patients.

Potentiation of Vascular Insufficiency - Brimonidine tartrate, a component of SIMBRINZA™ Suspension, may potentiate syndromes associated with vascular insufficiency. SIMBRINZA™ Suspension should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangitis obliterans.

Contamination of Topical Ophthalmic Products After Use - There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers have been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface *[see Patient Counseling Information]*.

ADVERSE REACTIONS

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

SIMBRINZA™ Suspension - In two clinical trials of 3 months duration 435 patients were treated with SIMBRINZA™ Suspension, and 915 were treated with the two individual components. The most frequently reported adverse reactions in patients treated with SIMBRINZA™ Suspension occurring in approximately 3 to 5% of patients in descending order of incidence were blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, and eye allergy. Rates of adverse reactions reported with the individual components were comparable. Treatment discontinuation, mainly due to adverse reactions, was reported in 11% of SIMBRINZA™ Suspension patients.

Other adverse reactions that have been reported with the individual components during clinical trials are listed below.

Brinzolamide 1% - In clinical studies of brinzolamide ophthalmic suspension 1%, the most frequently reported adverse reactions reported in 5 to 10% of patients were blurred vision and bitter, sour or unusual taste. Adverse reactions occurring in 1 to 5% of patients were blepharitis, dermatitis, dry eye, foreign body sensation, headache, hyperemia, ocular discharge, ocular discomfort, ocular keratitis, ocular pain, ocular pruritus and rhinitis.

The following adverse reactions were reported at an incidence below 1%: allergic reactions, alopecia, chest pain, conjunctivitis, diarrhea, diplopia, dizziness, dry mouth, dyspnea, dyspepsia, eye fatigue, hypertonia, keratoconjunctivitis, keratopathy, kidney pain, lid margin crusting or sticky sensation, nausea, pharyngitis, tearing and urticaria.

Brimonidine Tartrate 0.2% - In clinical studies of brimonidine tartrate 0.2%, adverse reactions occurring in approximately 10 to 30% of the subjects, in descending order of incidence, included oral dryness, ocular hyperemia, burning and stinging, headache, blurring, foreign body sensation, fatigue/drowsiness, conjunctival follicles, ocular allergic reactions, and ocular pruritus.

Reactions occurring in approximately 3 to 9% of the subjects, in descending order included corneal staining/erosion, photophobia, eyelid erythema, ocular ache/pain, ocular dryness, tearing, upper respiratory symptoms, eyelid edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival blanching, abnormal vision and muscular pain.

The following adverse reactions were reported in less than 3% of the patients: lid crusting, conjunctival hemorrhage, abnormal taste, insomnia, conjunctival discharge, depression, hypertension, anxiety, palpitations/arrhythmias, nasal dryness and syncope.

Postmarketing Experience - The following reactions have been identified during postmarketing use of brimonidine tartrate ophthalmic solutions in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to brimonidine tartrate ophthalmic solutions, or a combination of these factors, include: bradycardia, hypersensitivity, iritis, keratoconjunctivitis sicca, miosis, nausea, skin reactions (including erythema, eyelid pruritus, rash, and vasodilation), and tachycardia.

Apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in infants receiving brimonidine tartrate ophthalmic solutions *[see Contraindications]*.

DRUG INTERACTIONS

Oral Carbonic Anhydrase Inhibitors - There is a potential for an additive effect on the known systemic effects of carbonic anhydrase inhibition in patients receiving an oral carbonic anhydrase inhibitor and brinzolamide ophthalmic suspension 1%, a component of SIMBRINZA™ Suspension. The concomitant administration of SIMBRINZA™ Suspension and oral carbonic anhydrase inhibitors is not recommended.

High-Dose Salicylate Therapy - Carbonic anhydrase inhibitors may produce acid-base and electrolyte alterations. These alterations were not reported in the clinical trials with brinzolamide ophthalmic suspension 1%. However, in patients treated with oral carbonic anhydrase inhibitors, rare instances of acid-base alterations have occurred with high-dose salicylate therapy. Therefore, the potential for such drug interactions should be considered in patients receiving SIMBRINZA™ Suspension.

CNS Depressants - Although specific drug interaction studies have not been conducted with SIMBRINZA™, the possibility of an additive or potentiating effect with CNS depressants (alcohol, opiates, barbiturates, sedatives, or anesthetics) should be considered.

Antihypertensives/Cardiac Glycosides - Because brimonidine tartrate, a component of SIMBRINZA™ Suspension, may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with SIMBRINZA™ Suspension is advised.

Tricyclic Antidepressants - Tricyclic antidepressants have been reported to blunt the hypotensive effect of systemic clonidine. It is not known whether the concurrent use of these agents with SIMBRINZA™ Suspension in humans can lead to resulting interference with the IOP lowering effect. Caution is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines.

Monoamine Oxidase Inhibitors - Monoamine oxidase (MAO) inhibitors may theoretically interfere with the metabolism of brimonidine tartrate and potentially result in an increased systemic side-effect such as hypotension. Caution is advised in patients taking MAO inhibitors which can affect the metabolism and uptake of circulating amines.

USE IN SPECIFIC POPULATIONS

Pregnancy - *Pregnancy Category C:* Developmental toxicity studies with brinzolamide in rabbits at oral doses of 1, 3, and 6 mg/kg/day (20, 60, and 120 times the recommended human ophthalmic dose) produced maternal toxicity at 6 mg/kg/day and a significant increase in the number of fetal variations, such as accessory skull bones, which was only slightly higher than the historic value at 1 and 6 mg/kg. In rats, statistically decreased body weights of fetuses from dams receiving oral doses of 18 mg/kg/day (180 times the recommended human ophthalmic dose) during gestation were proportional to the reduced maternal weight gain, with no statistically significant effects on organ or tissue development. Increases in unossified sternebrae, reduced ossification of the skull, and unossified hyoid that occurred at 6 and 18 mg/kg were not statistically significant. No treatment-related malformations were seen. Following oral administration of ^{14}C-brinzolamide to pregnant rats, radioactivity was found to cross the placenta and was present in the fetal tissues and blood.

Developmental toxicity studies performed in rats with oral doses of 0.66 mg brimonidine base/kg revealed no evidence of harm to the fetus. Dosing at this level resulted in a plasma drug concentration approximately 100 times higher than that seen in humans at the recommended human ophthalmic dose. In animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent.

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

Nursing Mothers - In a study of brinzolamide in lactating rats, decreases in body weight gain in offspring at an oral dose of 15 mg/kg/day (150 times the recommended human ophthalmic dose) were observed during lactation. No other effects were observed. However, following oral administration of ^{14}C-brinzolamide to lactating rats, radioactivity was found in milk at concentrations below those in the blood and plasma. In animal studies, brimonidine was excreted in breast milk.

It is not known whether brinzolamide and brimonidine tartrate are excreted in human milk following topical ocular administration. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2%, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use - The individual component, brinzolamide, has been studied in pediatric glaucoma patients 4 weeks to 5 years of age. The individual component, brimonidine tartrate, has been studied in pediatric patients 2 to 7 years old. Somnolence (50-83%) and decreased alertness was seen in patients 2 to 6 years old. SIMBRINZA™ Suspension is contraindicated in children under the age of 2 years *[see Contraindications]*.

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

OVERDOSAGE

Although no human data are available, electrolyte imbalance, development of an acidotic state, and possible nervous system effects may occur following an oral overdose of brinzolamide. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored.

Very limited information exists on accidental ingestion of brimonidine in adults; the only adverse event reported to date has been hypotension. Symptoms of brimonidine overdose have been reported in neonates, infants, and children receiving brimonidine as part of medical treatment of congenital glaucoma or by accidental oral ingestion. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained.

PATIENT COUNSELING INFORMATION

Sulfonamide Reactions - Advise patients that if serious or unusual ocular or systemic reactions or signs of hypersensitivity occur, they should discontinue the use of the product and consult their physician.

Temporary Blurred Vision - Vision may be temporarily blurred following dosing with SIMBRINZA™ Suspension. Care should be exercised in operating machinery or driving a motor vehicle.

Effect on Ability to Drive and Use Machinery - As with other drugs in this class, SIMBRINZA™ Suspension may cause fatigue and/or drowsiness in some patients. Caution patients who engage in hazardous activities of the potential for a decrease in mental alertness.

Avoiding Contamination of the Product - Instruct patients that ocular solutions, if handled improperly or if the tip of the dispensing container contacts the eye or surrounding structures, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions *[see Warnings and Precautions]*. Always replace the cap after using. If solution changes color or becomes cloudy, do not use. Do not use the product after the expiration date marked on the bottle.

Intercurrent Ocular Conditions - Advise patients that if they have ocular surgery or develop an intercurrent ocular condition (e.g., trauma or infection), they should immediately seek their physician's advice concerning the continued use of the present multidose container.

Concomitant Topical Ocular Therapy - If more than one topical ophthalmic drug is being used, the drugs should be administered at least five minutes apart.

Contact Lens Wear - The preservative in SIMBRINZA™, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of SIMBRINZA™ Suspension, but may be reinserted 15 minutes after instillation.

U.S. Patent No:
6,316,441

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Patient Looks Just Swell…

By Andrew S. Gurwood, OD

History

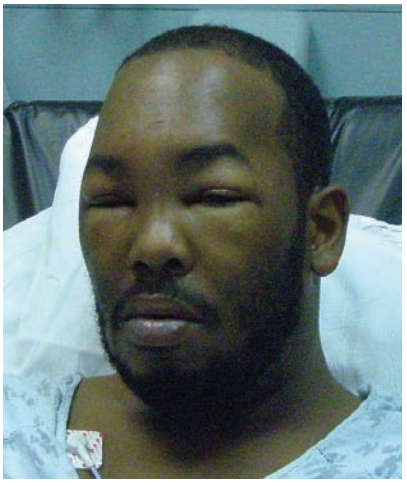
A 42-year-old black male presented to the hospital with facial swelling. The intensive care unit requested an ocular consult, because the patient reported "swollen eyes" that had persisted for three days.

While the patient explained that he had difficulty seeing because he was unable to open his eyes, he did not complain of pain or vision loss. When the lids were held open, his vision was intact. His ocular history was noncontributory.

His systemic history was significant for medically controlled hypertension and previous bouts of facial swelling. (However, in the past, the swelling didn't affect his eyes this dramatically.) He reported no known allergies of any kind.

Diagnostic Data

His best-corrected entering visual acuity was 20/20 OU at distance and near. This measurement was achieved when his lids were held open with the assistance of a Desmarres retraction blade.



Gross inspection of our 42-year-old patient reveals marked swelling around both eyes. What is your diagnosis?

External examination uncovered palpable, soft edema of the face and orbital adnexa without warmth, pain or tenderness. There was no evidence of afferent pupillary defect, and confrontational visual fields were normal.

Aside from the adnexal edema, the anterior segment findings were normal. Intraocular pressure measured 14mm Hg OU. Dilated funduscopy was within normal limits in both eyes.

Your Diagnosis

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

To find out, please visit www.revoptom.com. Click on the cover icon for this month's issue, and then click "Diagnostic Quiz" under the table of contents. ■

Thanks to Todd Dimmick, OD, of Philadelphia, for contributing to this case.

Retina Quiz Answers *(from page 72):* 1) d; 2) d; 3) d; 4) a.

Next Month in the Mag

Our August issue features the 36th Annual Diagnostic Technology Report. Topics include:

- *New Uses for OCT in Anterior Segment Care*
- *Diagnostic Technology Survey*

Also in August:

- *Optometric Study Center: Learn to Manage Ocular Emergencies* (earn 2 CE credits)
- *Clinical Skills: Use em' or Lose em'*
- *What's the Deal with Google Glass?*

Feedback

Review of Optometry welcomes questions and comments. E-mail Jack Persico, editor-in-chief, jpersico@jobson.com, with "Letter to the Editor" as the subject line. Or, write to *Review of Optometry*, 11 Campus Blvd., Suite 100, Newtown Square, PA 19073.

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NEW

For the treatment of elevated IOP

UNLOCK NEW TREATMENT POSSIBILITIES

SIMBRINZA™ Suspension provided additional 1-3 mm Hg IOP lowering compared to the individual components[1]

- IOP measured at 8 AM, 10 AM, 3 PM, and 5 PM was reduced by **21-35%** at Month 3[2-4]
- Efficacy proven in two pivotal Phase 3 randomized, multicenter, double-masked, parallel-group, 3-month, 3-arm, contribution-of-elements studies[2,3]
- The most frequently reported adverse reactions (3-5%) were blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, and eye allergy[1]
- Only available beta-blocker-free fixed combination[2,3]

INDICATIONS AND USAGE

SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is a fixed combination indicated in the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

Dosage and Administration

The recommended dose is one drop of SIMBRINZA™ Suspension in the affected eye(s) three times daily. Shake well before use. SIMBRINZA™ Suspension may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

IMPORTANT SAFETY INFORMATION

Contraindications

SIMBRINZA™ Suspension is contraindicated in patients who are hypersensitive to any component of this product and neonates and infants under the age of 2 years.

Warnings and Precautions

Sulfonamide Hypersensitivity Reactions—Brinzolamide is a sulfonamide, and although administered topically, is absorbed systemically. Sulfonamide attributable adverse reactions may occur. Fatalities have occurred due to severe reactions to sulfonamides. Sensitization may recur when a sulfonamide is readministered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

Corneal Endothelium—There is an increased potential for developing corneal edema in patients with low endothelial cell counts.

Severe Hepatic or Renal Impairment (CrCl <30 mL/min)—SIMBRINZA™ Suspension has not been specifically studied in these patients and is not recommended.

Adverse Reactions

In two clinical trials of 3 months' duration with SIMBRINZA™ Suspension, the most frequent reactions associated with its use occurring in approximately 3-5% of patients in descending order of incidence included: blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, and eye allergy. Adverse reaction rates with SIMBRINZA™ Suspension were comparable to those of the individual components. Treatment discontinuation, mainly due to adverse reactions, was reported in 11% of SIMBRINZA™ Suspension patients.

Drug Interactions—Consider the following when prescribing SIMBRINZA™ Suspension:

Concomitant administration with oral carbonic anhydrase inhibitors is not recommended due to the potential additive effect. Use with high-dose salicylate may result in acid-base and electrolyte alterations. Use with CNS depressants may result in an additive or potentiating effect. Use with antihypertensives/cardiac glycosides may result in additive or potentiating effect on lowering blood pressure. Use with tricyclic antidepressants may blunt the hypotensive effect of systemic clonidine and it is unknown if use with this class of drugs interferes with IOP lowering. Use with monoamine oxidase inhibitors may result in increased hypotension.

For additional information about SIMBRINZA™ Suspension, please see Brief Summary of full Prescribing Information on adjacent page.

References: 1. SIMBRINZA™ Suspension Package Insert. **2.** Katz G, DuBiner H, Samples J, et al. Three-month randomized trial of fixed-combination brinzolamide, 1%, and brimonidine, 0.2% [published online ahead of print April 11, 2013]. *JAMA Ophthalmol.* doi:10.1001/jamaophthalmol.2013.188. **3.** Nguyen QH, McMenemy MG, Realini T, et al. Phase 3 randomized 3-month trial with an ongoing 3-month safety extension of fixed-combination brinzolamide 1%/brimonidine 0.2%. *J Ocul Pharmacol Ther.* 2013;29(3):290-297. **4.** Data on file, 2013.

NEW

SIMBRINZA™

(brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2%

ONE BOTTLE. NEW POSSIBILITIES.

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