5 Patients Who Need UV Protection—and Why, p. 28

March 15, 2014

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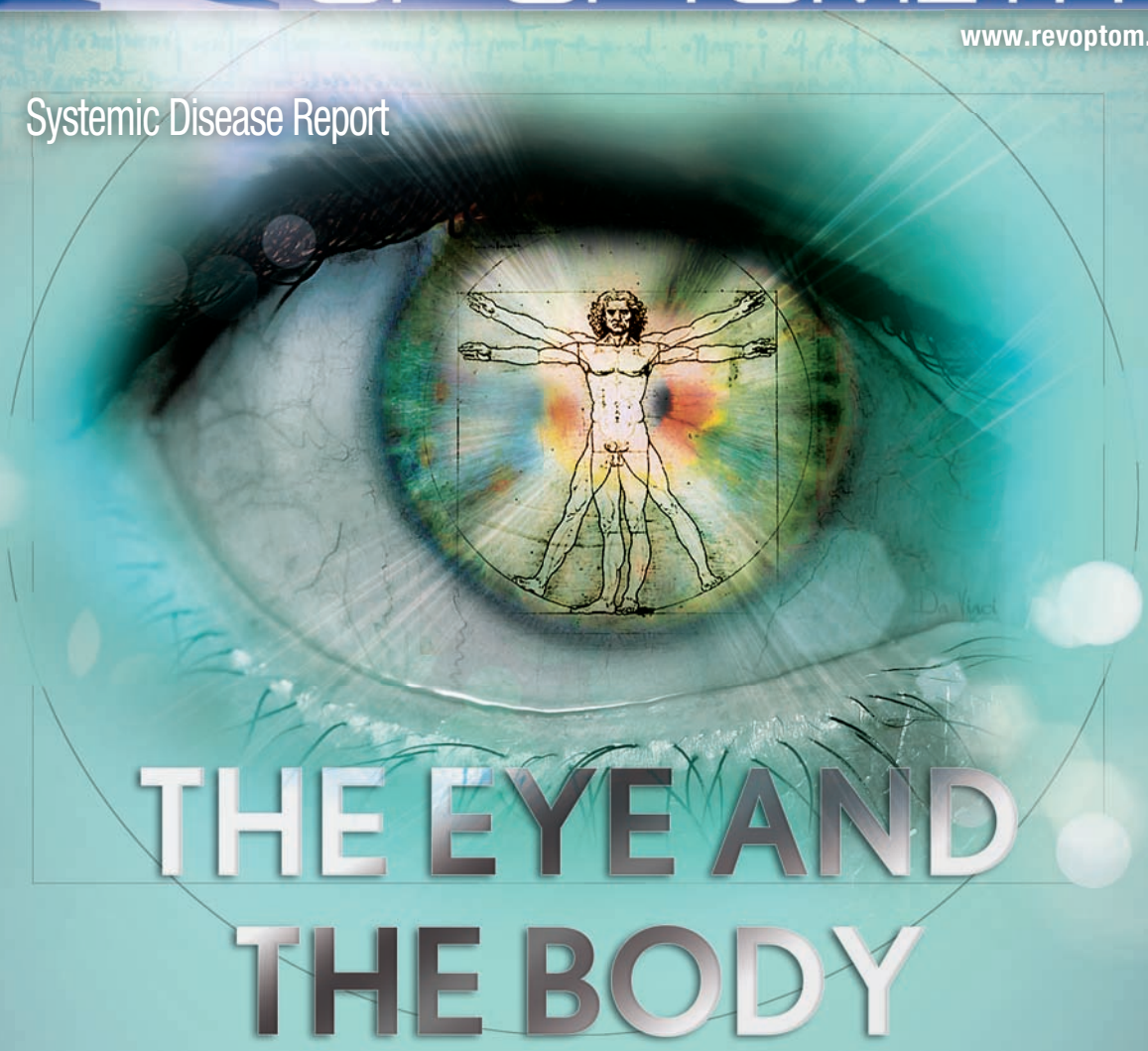
Systemic Disease Report



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†The sixth measure was conjunctival staining.

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Reference: 1. Morgan P, Chamberlain P, Moody K, et al. Ocular physiology and comfort in neophyte subjects fitted with daily disposable silicone hydrogel contact lenses. *Cont Lens Anterior Eye.* 2013;36(3):118-125.

VOL. 151 NO. 3 ■ MARCH 15, 2014

IN THE NEWS

The **University of Alabama at Birmingham** has named **Kelly K. Nichols, OD, MPH, PhD**, as **dean of its School of Optometry**, following the retirement of Dean Rod W. Nowakowski, OD, PhD. "It is an honor and a privilege to be selected as dean of the UAB School of Optometry," Dr. Nichols said. "I look forward to working together with Provost [Linda] Lucas and the talented and dedicated faculty to continue the tradition of clinical and research excellence." Dr. Nichols takes office on June 25.

Dua's layer, discovered last year, is a 15µm layer of the cornea located between the corneal stroma and Descemet's membrane. The researchers who found it now report online in *British Journal of Ophthalmology* that Dua's layer is also linked to the **trabecular meshwork**. They determined that the collagen fibers of Dua's layer branch out to form a meshwork such that the trabecular meshwork's collagen core is actually an extension of Dua's layer. "This finding … has the potential to impact future research into the TM and glaucoma," they concluded.

The world's largest manufacturer of prescription eyeglass lenses, **Essilor International**, has agreed to buy the world's second largest supplier of contact lenses, **Coastal Contacts Inc.**, for $387 million. The transaction is expected to close in the second quarter of 2014.

Vision Training a Grand Slam for Baseball Team

College baseball players improved vision and won games after vision training. **By Michael Hoster, Managing Editor**

Photo: University of California, Riverside

After vision training, the University of California, Riverside baseball team had 41 more runs in 2013.

The University of California, Riverside baseball team enjoyed a significant on-field performance boost following two months of vision training. Players had a 31% improvement in visual acuity, which led to 4.4% fewer strikeouts, an estimated 41 more runs and four or five more winning games in their 2013 season, according to a study in the February 17 issue of *Current Biology*.

"I didn't think we would see as much of an improvement as we did," says UCR head baseball coach Doug Smith. "Our guys stopped swinging at some pitches and started hitting at others."

The authors believe that this is the first study to show that perceptual learning can yield quantifiable vision improvements in normally sighted individuals.

During the study period, the players used custom software built into an electronic vision training program (Ultimeyes, Carrot Neurotechnology) for 25 minutes per day, four days a week. The program instructed players to find and select patterns (Gabor targets) that specifically stimulated neurons associated with the early visual cortex. These stimuli were made increasingly dimmer as the simulation progressed, which forced the players to focus and concentrate more intensely.

"The goal of the program is to train the brain to better respond to the inputs that it gets for the eye," said lead author Aaron Seitz, PhD, associate professor of psychology at UC, Riverside. "When we go to the gym and exercise, we are able to increase our physical fitness; it's the same thing with the brain. By exercising our mental processes, we can promote our mental fitness."

After two months of vision training, the players reported that they saw the ball more clearly, were able to see further on the field and could more easily distinguish between low-contrast objects.

"The demonstration that seven players reached 20/7.5 acuity—the ability to read text at three times the distance of a normal observer—is

Continued on page 10

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Exercise Preserves Vision in AMD

Moderate aerobic exercise helps protect the structure and function of nerve cells in the retina after damage, say researchers at the Emory Eye Center and the Atlanta VA Medical Center, who investigated this in a mouse model of macular degeneration.

The findings, published in the February 12 issue of the *Journal of Neuroscience*, are the first to suggest that aerobic exercise can have a direct neuroprotective effect on retinal health and vision.

"This research may lead to tailored exercise regimens or combination therapies in treatments of retinal degenerative diseases," says coauthor Machelle Pardue, PhD. "Possibly in the near future, ophthalmologists could be prescribing exercise as a low-cost intervention to delay vision loss."

The researchers trained mice to run on a treadmill for one hour per day, five days per week, for two weeks. After the animals were exposed to toxic bright light to induce retinal degeneration, they exercised for two more weeks.

The investigators found that the exercised mice had nearly twice the number of photoreceptor cells as those that spent the equivalent amount of time on a stationary treadmill, and their retinal cells were more responsive to light.

Photo: Salk Institute of Biological Studies

After retinal degeneration, mice that exercised had twice the number of photoreceptors as mice that didn't exercise.

The researchers were able to show that the effects of exercise come partly from a growth factor called BDNF, which has been linked in other studies to the beneficial effects of exercise. The exercised mice had higher levels of BDNF in the blood, brain and retina.

The researchers also demonstrated that chemically blocking BDNF receptors negated the protective effects of aerobic exercise.

"One point to emphasize is that the exercise the animals engaged in is really comparable to a brisk walk," Dr. Pardue says. "One previous study that examined the effects of exercise on vision in humans had examined a select group of long-distance runners. Our results suggest it's possible to attain these effects with more moderate exercise."

The investigators are now testing whether other exercise regimens are even more protective, and whether exercise is beneficial for other retinal diseases, such as glaucoma and diabetic retinopathy.

"This is a very intriguing study, and probably worth following up in humans," says D. Joshua Cameron, PhD, assistant professor at Western University of Health Sciences College of Optometry, whose research also centers on the neurobiological development of eye disease. "I would expect that humans might require more than just a few weeks of moderate exercise, and any changes in humans will probably be much less pronounced [because] … the human disease generally progresses over a much longer time-frame."

While exercise likely would contribute to overall health, and consequently prevent/delay disease onset—including a progressive eye disease such as AMD—"advising any patient who can safely do moderate, frequent exercise is likely to be beneficial to them for many health reasons, not just eye health," Dr. Cameron says.

Lawson EC, Han MK, Sellers JT, et al. Aerobic exercise protects retinal function and structure from light-induced retinal degeneration. J Neurosci. 2014 Feb 12;34(7):2406-12.

High-Tech Glasses Help Surgeons 'See' Cancer Cells

The distinction between normal tissue and cancerous tissue is not always clear to the naked eye. But new high-tech glasses developed at the Washington University School of Medicine in St. Louis will bring cancer cells to new light.

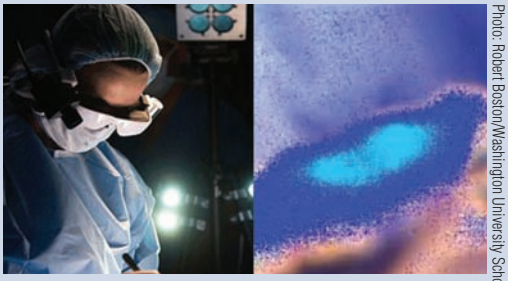

Photo: Robert Boston/Washington University School of Medicine

When viewed through the newly developed eyewear, cancer cells glow blue, helping to ensure that no stray tumor cells are left behind in surgery. These glasses could reduce the need for follow-up surgeries intended to remove previously unseen cancer cells, investigators say.

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Two New Optometry Schools Planned

The University of Pikeville, located in the Appalachian Mountains of eastern Kentucky, announced it will create the state's first college of optometry.

University president James Hurley, EdD, said that the Kentucky College of Optometry will open in the fall of 2016 with an inaugural class of 60 students, and be housed in a newly built facility. It would be the 22nd college of optometry in the United States.

The university has completed a feasibility study, and an advisory committee (including Kentucky optometrists Joe E. Ellis and Jerald F. Combs) will help move the college of optometry forward. The university has also started a search for the college's dean.

The University of Pikeville College of Optometry, to open in 2016, would be Kentucky's first optometry school.

Dr. Hurley said that the new college is necessary to meet the demand for eye care. "More than 25% of our counties in the commonwealth [of Kentucky] don't have a practicing optometrist." Also, there are no other schools of optometry in the South within hundreds of miles.

However, less than 50 miles away, the Appalachian College of Optometry (which was first announced three years ago) is moving forward in Grundy, Va.

Officials from Appalachian College of Optometry recently signed an agreement with Emory & Henry College, in Emory, Va., to work together toward the development of the school of optometry in Grundy. The agreement formalizes an effort to achieve accreditation for the school.

The school will likely be renamed Emory & Henry College, School of Optometry, although the final decision has not been made, said current president Brian Looney, OD.

Nevertheless, the optometry school expects to open in the fall of 2016 with a class of 48 students, Dr. Looney said.

Single Injection Restores Light Perception in Blind Mice

Intraocular injection of a novel compound enables healthy retinal ganglion cells to perceive light in the absence of functioning rod and cone receptors in mice, according to a study in the February 19 issue of *Neuron*.

The findings suggest that the experimental chemical, DENAQ, could temporarily restore visual function in patients with retinitis pigmentosa or age-related macular degeneration who've experienced severe photoreceptor degeneration.

In this study, a single injection of DENAQ was administered to mice with functional, nonfunctional or degenerated photoreceptors. The retinal ganglion cells in the diseased-retina mice showed strong light sensitivity after DENAQ treatment. But mice with intact photoreceptors had no response to DENAQ treatment.

The researchers determined that the compound only photosensitized ganglion cells if the subjects' rods and cones were degenerated. Thus, they predict that DENAQ could be the most effective in patients with end-stage degenerative retinal disease.

"Further testing on larger mammals is needed to assess the short- and long-term safety of DENAQ and related chemicals," says lead author Richard H. Kramer, PhD, professor of molecular and cell biology at the University of California, Berkeley. "It will take several more years, but if safety can be established, these compounds might ultimately be useful for restoring light sensitivity to blind humans. How close they can come to re-establishing normal vision remains to be seen."

Tochitsky I, Polosukhina A, Degtyar VE, et al. Restoring visual function to blind mice with a photoswitch that exploits electrophysiological remodeling of retinal ganglion cells. Neuron. 2014 Feb 19;81(4):800-13.

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Multivitamins Decrease Cataract Risk in Men

Long-term use of daily multivitamin supplements may lower cataract risk in men by about 9%, according to researchers with Brigham and Women's Hospital and Harvard Medical School.

The randomized, double-blind study, published in the February issue of *Ophthalmology*, was conducted from 1997 to 2011 on more than 14,600 male doctors age 50 and older (part of the Physicians' Health Study II). Half took a common multivitamin, as well as vitamin C, E and beta carotene supplements. The others took a placebo. Of the multivitamin group, 945 cases of cataract were reported, compared with 872 for those on placebo—a decreased risk of 9%, researchers say. That number was four percentage points higher for nuclear cataract.

"If multivitamins really do reduce the risk of cataract, even by a modest 10%, this rather small reduction would nonetheless have a large public health impact," says William Christen, ScD, lead author of the study and a researcher at Harvard Medical School.

Interestingly, there were 152 new cases of visually significant AMD in the multivitamin group compared to 129 in the placebo group—a finding that seems to contradict results of studies such as AREDS. However, researchers clarified that the studies had different nutrient supplements, dosing and objectives.

"This finding of more cases of AMD in the multivitamin group than in the placebo group, though not statistically significant, does raise some concerns," Dr. Christen said. "Clearly, this finding needs to be examined further in other trials of multivitamin supplements in both men and women."

Christen WG, Glynn RJ, Manson JE, et al. Effects of multivitamin supplement on cataract and age-related macular degeneration in a randomized trial of male physicians. Ophthalmology. 2014 Feb;121(2):525-34.

Baseball Vision Training

Continued from page 4

dramatic and required players to stand 40 feet back from the eye chart in order to get a measurement of their vision," Dr. Seitz added.

Even more impressive, the players began to perform better on the diamond. They had fewer strikeouts and generated more runs following the training period, which the researchers believe may have translated into an additional four to five team victories during the season.

"As with most other aspects of our function, our potential is greater than our normative level of performance," said Dr. Seitz. "Understanding the rules of brain plasticity unlocks great potential for improvement of health and wellbeing."

Going forward, the researchers hope to use their training program to improve poor visual acuity in cataract, macular degeneration and amblyopia patients. ■

Deveau J, Ozer DJ, Seitz AR. Improved vision and on-field performance in baseball through perceptual learning. Curr Biol. 2014 Feb 17;24(4):R146-7.

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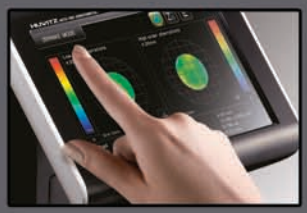

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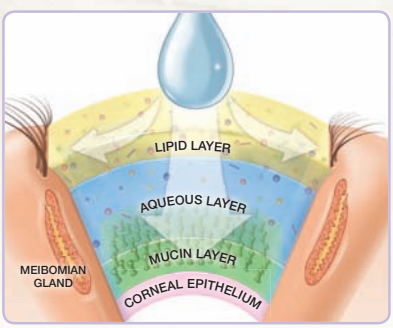

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References: 1. Akpek EK, Smith RA. Overview of age-related ocular conditions. *Am J Manag Care.* 2013;19 (5 suppl):S67-S75. **2.** Korb DR, Blackie CA, Meadows DL, Christensen M, Tudor M. Evaluation of extended tear stability by two emulsion based artificial tears. Poster presented at: 6th International Conference on the Tear Film and Ocular Surface: Basic Science and Clinical Relevance; September 22-25, 2010; Florence, Italy.

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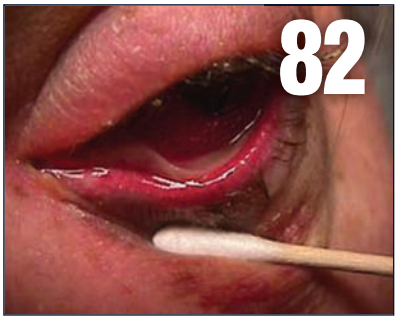

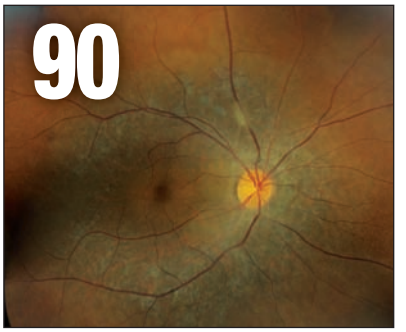

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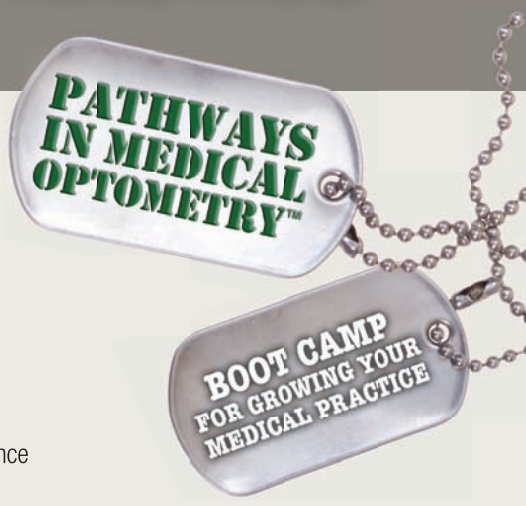

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Beyond the Eye

We are more than just "eye doctors" —so, let's make sure that our patients and our medical colleagues know that. **By Paul M. Karpecki, OD, Chief Clinical Editor**

In considering this month's focus on systemic disease and the eye, I see three areas of significance for our profession: the now-mainstream role of systemic medications in optometry, the value of routine eye exams in allowing us to diagnose numerous systemic diseases, and the importance of interprofessional communications with physicians who manage systemic health. All point to better care and convenience for our patients.

Oral Meds and Optometry

We in optometry often have the opportunity to marvel at just how well the body is connected. Many patients with ocular manifestations of systemic disease won't improve until their systemic health does.

I recall a patient sent to me with a diagnosis of a chemical burn while working in an Eastern Kentucky coal mine. We tried to get his very large corneal abrasion to close, using bandage lenses, pressure patching and ample lubrication (no amniotic membrane options at that time). After seven days battling a persistent epithelial defect, we asked if he had any symptoms of fatigue, increased urination or frequent thirst. He affirmed all three, so we ordered fasting blood levels. A normal reading is below 100; his measured 496!

After a few days of treatment with metformin by a specialist, he not only felt better—his persistent epithelial defect had closed. It was a clear example of how an ocular condition related to a systemic disease will not resolve fully unless the systemic disease is controlled.

Such connections often influence our therapeutic choices, as when we treat MGD and rosacea with oral tetracyclines, preseptal cellulitis with oral antibiotics, or Sjögren's with oral secretagogues. We must also be vigilant for ocular side effects of oral drugs patients may be taking, such as Plaquenil (which requires monitoring for bull's eye retinopathy), or ocular dryness due to drugs such as antihistamines, contraceptives and antidepressants.

Healthy Bodies, Healthy Eyes

I'm fascinated that it's considered "the norm" to visit a dentist every six months, even in the absence of scientific evidence of a need for semi-annual dental visits. Dentists reinforce this behavior by performing teeth cleaning, so that people get a tangible benefit from the experience. They also emphasize oral and systemic wellness, looking for diseases ranging from lingual cancers to Sjögren's syndrome.

Surely, an eye examination goes much further than a dental visit in ensuring systemic health and ocular wellness—nearly every patient would consider the loss of vision far worse than losing teeth. We have an incredible opportunity to educate patients of the need for wellness exams, perhaps not every six months but at least yearly. Statistics show that most patients only see an eye doctor once every 26 months!

Perhaps we need to educate the patient that, via a thorough eye exam, we can determine cholesterol levels (arcus of the cornea, retinal Hollenhorst plaques), diabetes (retinal exam, lens autofluorescence), hypertension, brain tumors, rheumatoid arthritis, sarcoid, rosacea, lupus, Sjögren's and many more.

I think patients would be thrilled to know these conditions are on our radar during an ocular health examination. It would help us reinforce the need for a wellness visit at least yearly. I can tell you that patients who have been diagnosed with serious systemic diseases at my office were truly grateful for that "routine" eye exam.

OD-MD Collaboration

Years ago, I made a preliminary diagnosis of Sjögren's in a 48-year-old lady with severe dry mouth, nose bleeds, significant tooth decay and severe dry eye. In a letter to a local rheumatologist, I stated, "As you know, there is a very high correlation between non-Hodgkin's lymphoma and Sjögren's. Yearly monitoring would be appreciated."

Three days later, he called to thank me for the letter. He said he'd check all his Sjögren's patients for NHL going forward. Two years later, he approached me at a meeting and said he had diagnosed NHL in at least a half dozen patients since our collaboration. And since then, he has referred over 100 Sjögren's patients to the practice!

We can debate whether the eyes are the window to the soul, but they truly are to the body. And we are the gatekeepers. ■

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No Cure for the Common Code

ICD-9? Annoying. ICD-10? Weird yet complicated. But those are nothing compared to ICD-11—I didn't crack the code. The code cracked me. **By Montgomery Vickers, OD**

I just "virtually" attended the AOA's latest ICD-10 webinar. I liked that I could be there without actually being there—I even attended the webinar in my underwear, which created quite a stir at the Starbucks where I logged on.

So began the most absurd 55 minutes of my life. If you know me, it should disturb you greatly that *this* was my life's most absurd 55 minutes.

It took the speaker—who was amazing and intelligent about the whole thing—about 15 minutes to describe the best way to code for *one* diagnosis on *one* patient with *one* specific problem. And this is an expert in ICD-10, not some numbskull old-timer like me! To do this right, I'll have to schedule only *one* patient a day!

Get Ready for ICD-11

I decided to see if I could find out what's to come in the next ICD evolution. The good news? The next ICD incarnation addresses the craziness of the ICD-10 system. The bad news? It does so by being so stupid that it makes ICD-10 look like the Good Ol' Days.

Here's a quick example:

The patient presented with acute onset eye pain and redness plus blurry vision, which began at the same moment his face collided with a Fulvous Whistling duck while he was hang-gliding in Venezuela.

ICD-9? Easy. It's *379.91–Eye Pain* and *918.1–Corneal Abrasion*.

ICD-10? There's a specific code for it: *W61.62XA–Struck by Duck, Initial Encounter*. (Really!)

How about ICD-11 on an even easier patient?

Not so easy. Follow along…

A patient presented with light sensitivity OD that started one evening around 7:00 PM and has persisted for one week.

First, open your "British Reference Manual, Volume 1," and try to find:

- Right eye—not in Latin, you idiot; in Olde English—RYGHT! Use the code "R."
- When did this start? One enchanted EVENING! Code is "E."
- What time did this start? 7:00? No, too specific! Use "AROUND" or "ABOUT" 7:00. Code is "A."
- Light sensitive? Is it spelled "Lyght," "Plight"(p is silent), "Leight," "Lahyett"? OK, it's just "light." This is easy—just refer to the second reference manual under "Ouchy Things" and you'll soon find "LIGHT," which is coded "L."
- How long has this hung around? Since LAST WEEK? Stick an "L" in there again—not to be confused with the previous "L" which, of course, requires a request for a different font (in this case, Comic Sans) so as to not make the auditors think you mean there are *two* "Last Weeks" or *two* "Lights" involved.
- How bad was the pain? Was it bad enough to: Blink, Rub, Wince, Yell, Scream, Wet Pants, Get Drunk or Kill Self? This code must be very specific, so if the patient simultaneously Winced and Wet Himself, then the claim will be denied. So, we'll just say "YELL," which is code "Y."
- Did you answer all the patient's questions? You have to code that with a "?" modifier.

So, in this case, the ICD-11 code is: "REALLY?"

Yes, really.

On a brighter note, ICD-12 will be much easier because its concept depends on the demise of all health care in the United States by then.

ICD-12 is actually just a bus ticket to see a faith healer in Cabo. One way. ■

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An Ounce of Prevention

Optometrists are doing a good job catching eye disease. But are we doing enough to prevent it and promote ocular wellness? **By John Rumpakis, OD, MBA, Clinical Coding Editor**

This column spends a great deal of time on certain basic medical coding and compliance concepts—like medical necessity and properly recording the chief complaint—so that your office encounters can be legitimately submitted to a medical carrier for appropriate reimbursement of your professional services and expertise.

I try to provide advice to help you prevent and avoid any potential reimbursement problems. And it got me to thinking: Are we, as optometrists, providing adequate preventive advice to our patients?

I realize that most ODs provide preventive advice every single day:

- "Don't sleep in your contacts."
- "Use your glaucoma medication every night."
- "Take these nutriceuticals to help prevent AMD."
- "Wear your plus lenses when you read."

…And so on. It is inherent in what we do for patients.

Yet, our health care system is heading quickly toward outcomes-based care, which aims to prevent sequelae by providing the best treatment and advice before something goes wrong.

So, what do we as optometrists do in the area of both preventive care and ocular wellness? (*See "Wellness and Prevention, Defined," above.*)

What Do Dentists Do?

I recently was invited to a meeting that focused on the subject of "ocular surface wellness." It was a very interesting meeting with some of the top experts in our field, discussing not only what we're doing for ocular surface issues like meibomian gland disease or contact lens dropout, but whether we can do anything to prevent these conditions from even happening.

Wellness and Prevention, Defined

Wellness: the quality or state of being in good health, especially as an actively sought goal.

Prevention: the act or practice of stopping something bad from happening.

Source: www.merriam-webster.com

A dentist and a dermatologist also presented to the group and discussed how their professions became proactive on wellness. The dermatologist indicated that much of her work is increasingly related to wellness and prevention. The dentist made a point that prevention and wellness has been a widely accepted mandate within his profession since the 1940s.

The problem lies, of course, in a single simple question: How do we get paid for prevention? (More on that important question in an upcoming column.)

Prevent, Don't Lament

Realize that we impact our patients' quality of life by maintaining a healthy ocular surface. Everything from quality of vision to contact lens intolerance, to cataract and refractive surgery, depends on having a healthy ocular surface.

But even though we know that dry eye and meibomian gland disease occur in the majority of Americans, optometrists still tend to be remedial in our approach to ocular surface disease rather than preventive.

A parallel to consider: Does the dermatologist wait for someone to get skin cancer before recommending a daily application of sunscreen containing an appropriate SPF? Of course not. Each and every patient gets a proactive, preventive statement about skin wellness and a recommendation for it.

Can't we do that in our practices? Couldn't we remind our patients to use artificial tears in each eye every time they brush their teeth? "Two drops a day keeps your contacts in play."

You get the idea.

Wellness and prevention are both new and old concepts for us. We practice them daily—but not in the most modern sense or in a consistent manner.

If your goal is to create and maintain the very best vision and quality of life for your patients, perhaps the answer is very simple: Be your patients' advocate for the problems that they encounter today and for those that you can prevent from happening tomorrow. ■

Please send your questions and comments to CodingAbstract@gmail.com.

Tear Film Lipids and Successful Contact Lens Wear

Careful lens selection and clear patient counseling can reduce lipid deposition in contact lens wear.

Christine W. Sindt, OD, FAAO

The lipid layer is crucial to normal tear film function: it limits aqueous evaporation, creates a smooth, stable refracting surface, and provides a barrier to foreign materials. Itself a complex structure, the lipid layer is composed of a thin layer of polar lipids that stabilizes the thicker layer of nonpolar lipids that rides above it (and which acts as a barrier to the environment). This polar lipid interface adheres the nonpolar lipids to the aqueous compartment and allows the lipid layer to spread evenly across the polar aqueous portion of the tear film.[1]

LENS-TEAR FILM DYNAMICS

When a contact lens is placed on the eye, it changes the physical chemistry of the ocular environment, altering mucin production, decreasing tear film stability and increasing tear osmolarity.[2] The contact lens divides the tear volume, creating a pre-lens tear film on the surface of the lens and a post-lens tear film between the lens and the cornea. The average, non-disrupted tear film is around 4 microns thick, but the pre-lens tear film is only about 2.5 microns.[2]

A thinner tear film is less stable, and a thinner lipid layer is associated with reduced tear-film breakup time (TFBUT): Over a contact lens, the TFBUT is typically about 5 to 10 seconds, compared to 20 to 30 seconds without a lens in place.[3]

Tear lipids can adhere to microscopic hydrophobic domains on a silicone hydrogel lens surface. When exposed to light and oxygen for prolonged periods, these adhered lipids can degrade, further reducing lens wettability. Tear film instability, lens deposition, and reduced lens wettability can all contribute to symptoms of dryness and irritation in wearers.

IMPACT OF LENS MATERIAL

Patient-to-patient differences in tear film chemistry account for some of the variation in patients' ability to tolerate a soft contact lens material; the other important factor is the hydrophobicity of the lens surface.

- Contact lens wear alters and thins the tear film
- Hydrophobic areas on the contact lens surface attract tear film lipids
- Adhered lipid deposits break down, further diminishing lens wettability
- Plasma coating can produce a hydrophilic surface on silicone hydrogel lenses, keeping them relatively deposit-resistant

Both "conventional" hydroxyethyl methacrylate (HEMA)-based lenses and silicone hydrogel lenses contain both hydrophilic and hydrophobic polymer chains. These polymer chains tend to orient themselves according to their environment. Dryness in the environment of the lens—eg, from a TFBUT shorter than the inter-blink interval—will draw the hydrophobic (lipophilic) chains of the lens polymer toward the lens surface, which can further disrupt tear spreading and lead to lipid deposition.

The chemistry of silicone insures that silicone hydrogel lenses have far more hydrophobic polymer chains than HEMA-based lenses; and, as a result, silicone hydrogel lenses must rely on surface modifications to "sequester" these hydrophobic chains. Such modifications include plasma treatment, changing the composition and length of the polymer chains, and adding wetting agents (either to the lens itself or to the soaking solution). Each of these techniques produces a different surface environment, and, consequently a different degree of resistance to lipid deposition.[1]

IN THE CLINIC

On the surface of the lens, the effects of lipid deposits can range from decreased wettability and TFBUT to frank, visible fouling and a decrease in optical clarity. When I see a patient with heavily lipid-deposited lenses, I take a comprehensive look at their lens material, lens solution, care regimen, and eyelid hygiene. I identify and address blepharitis and any associated meibomian gland dysfunction in order to ensure a baseline tear film quality.

If a patient can't (or doesn't want to) wear a daily disposable lens, I select a reusable contact lens material with a highly wettable surface, and pair it with a solution that will effectively reduce lipid deposits and help maintain surface wettability. I also counsel patients carefully about their lens care routines, emphasizing the importance of digital rubbing to help dislodge deposits.

Ultimately, my goal is to keep patients' eyes healthy, seeing well, and feeling comfortable. Contact lens wear affects the ocular surface in many ways, and certainly impacts tear film stability. But choosing a lens and care system that can keep the lens surface wettable—while reducing lipid deposition—should help maintain patients' tear film stability and lens wearing satisfaction.

Christine W. Sindt, OD, FAAO, is director of the contact lens service and a clinical associate professor of ophthalmology and visual sciences at the University of Iowa, Iowa City, IA.

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Guarding Your Patients' Eyes from Harmful Light

Part One: the Importance of Education

By Kirk Smick, OD

This three-part series will discuss preventative actions for preserving eye health and providing complete protection from the negative effects of ultraviolet (UV) and blue light. Part one will focus on education and offer a basic rundown on UV and blue light, including their sources, as well as risks and benefits associated with them. Next month's column will tackle the topic of protection and prevention; and for the final part of this series, an engaging point-counterpoint awaits you.

As clinicians, we have always suspected that high-energy visible (HEV) light, otherwise known as blue light, may cause damage to the eye. Thanks to dedicated researchers, we now know that blue light, part of the visible light spectrum that reaches the back side of the eye, can damage the retina and more specifically, has been implicated in the development of age-related macular degeneration (AMD).[1–3]

Most patients are familiar with the potential dangers of ultraviolet (UV) light, which can penetrate the cornea at the front of the eye and cause cataracts; however, very few patients are aware that certain wavelengths of *visible light* are also damaging to their eyes. Both UV and blue light are present everywhere: indoors and outdoors.

Sources of UV and Blue Light

Sunlight emits both UV and blue light all year long, and the amount of exposure can vary depending on time of day, location, and even the season. Although the level of exposure can vary, eyes are exposed to UV light 365 days a year. And 40% of this UV exposure occurs when we are not in full sunlight, which reinforces the need for UV protection on both clear and sun lenses.

Sunlight is also a well-established source of blue light, but this energetic light can also transmit to the eye from numerous *indoor* sources, such as smart phones, computer monitors and many modern LED and compact fluorescent light sources.[4] In fact, many of these devices emit an extremely high level of blue light, a fact that many patients may not realize.

Predictably, our patients will be exposed to even greater levels of indoor blue light in the coming years. In fact, forecasts for LED uptake in the residential segment are at 50% for 2016 and 70% for 2020.[5] This is especially concerning, considering the fact that LED sources contain 35% harmful blue light levels.[6]

Cumulative and constant exposure to blue light from LED lighting and electronic devices will continue to damage the retinal cells and can eventually lead to retinal cell death. Today, we are being exposed to blue light in our homes and in our everyday lives at higher levels than ever before, and these levels will continue to rise in the coming years. Let's take a closer look at the negative effects of blue light.

The Dangers of Blue Light

The most harmful band of blue light is Blue-Violet light, as discovered by a joint study conducted by the Paris Vision Institute and Essilor International.[3] Blue-Violet light ranges from 415 nm to 455 nm, and has been identified as the band of visible light most harmful to retinal cells. Additionally, blue light has measurable effects on retinal pigment epithelial cell apoptosis.[7] Blue light in this range causes maximum retinal cell death, and in turn, is one of the risk factors for the development of AMD. The connection between blue light and AMD makes it imperative for us to educate patients and help them protect their eyes from these potentially damaging elements. We'll delve further into AMD, but before we do, let's lighten the mood and examine the positive physiological effects of blue light.

The Positive Side of HEV Light

Some sun exposure is vital, as it delivers vitamin D to the body. Light is essential for us to see and recognize colors, and also plays a key factor in contrast sensitivity. Light also helps in visual acuity, and without enough of it, vision is affected and is not clear. In addition to visual functions, light is necessary for various *non-visual* functions of the body. Research has identified that Blue-Turquoise light, ranging from 465 nm to 495 nm, is essential to our vision, as it adjusts the size of the pupil to allow enough light through.[3] Blue-Turquoise light aids in the regulation of our sleep/wake cycle, and also helps the body distinguish day from night.[3] This in turn,

enables us to maintain and regulate memory, mood and hormonal balance.

Now that we've seen that not all light is bad, it's time to turn back to the detrimental effects of blue light; in particular, the risk for developing AMD.

AMD: Risk Factors and Prevalence

AMD ranks third among the global causes of visual impairment, with a blindness prevalence of 8.7%.[8] The number of AMD cases is expected to more than double, from two million in 2010 to five million by 2050,[9] and is the leading cause of legal blindness in people ages 65 and older.[10] Risk factors for AMD include a genetic background (having a first-generation family member with the disease) and environmental and lifestyle factors (i.e., smoking, diet, BMI and light exposure).

In my practice, I target specific patients with whom I want to discuss AMD risk factors and preventative measures. Typically, these are patients who have early signs of AMD or have a parent who has the condition. I also talk to children who are constantly in front of a computer screen or video game, as well as patients with active lifestyles who are concerned about wellness in all aspects of their healthcare.

Optometry is getting more and more involved in the diagnosis and management of AMD as the U.S. population continues to age, and while the next part in this series will primarily focus on prevention and protection, I'll provide a bit of a teaser on the topic.

Identifying the Lines of Defense

With AMD on the rise, there is an obvious and immediate need for our profession to step up to the plate. The results of the Age-Related Eye Disease Study 2 (AREDS2) have shown that combinations of neutraceuticals can help prevent the onset of AMD.[11] Selective light filters also offer protection from the damaging effects of harmful Blue-Violet light.

Another new layer of protection—Crizal® Prevencia™ No-Glare lenses (Essilor)—is available for at-risk AMD patients. Crizal Prevencia offers both front- and back-of-lens protection from harmful light—including UV and Blue-Violet light—and is designed to selectively filter out this harmful light while letting beneficial light pass through. Furthermore, it's proven to deflect harmful Blue-Violet light by 20%, which in recent lab tests led to a **25% reduction in retinal cell death**.[12,13] The lenses selectively deflect just the range of HEV light that has been shown to be responsible for increased cellular death. With Crizal Prevencia No-Glare lenses, other beneficial light still comes into the eye and penetrates the lens, in turn giving us perfectly clear vision.

No matter what method(s) of prevention or protection you employ, it all comes back to education—both ours and our patients.

Did you know?

Fifty percent of UV exposure received by the eye has been reflected by a surface (e.g., clouds, the floor, a building).[14]

Education is Key

Clearly we need light in order to function, but we need to manage what type of light we expose ourselves to, when we expose ourselves to it and for how long. It is critical that we educate our patients about the dangers of UV and blue light. Key questions to ask a patient might include:

- How do you protect your eyes on a daily basis?
- Do you have a family history of macular degeneration/AMD?
- How much time do you spend in front of digital devices?
- How much time do you spend outdoors?
- How are you currently protecting your eyes against UV damage?

As the prevalence of AMD grows, and the use of LED lighting and digital devices continues to rise, it is essential for optometrists to remain at the forefront of ensuring that our at-risk patients are properly educated on the dangers of UV and blue light exposure and are prescribed the appropriate lenses to protect their precious vision.

Dr. Smick is chief of Optometry Services at Clayton Eye Center and an owner of the facility. He also serves as a technical advisor to many companies in the ophthalmic industry and has helped pioneer several visual advances, including bifocal contact lenses.

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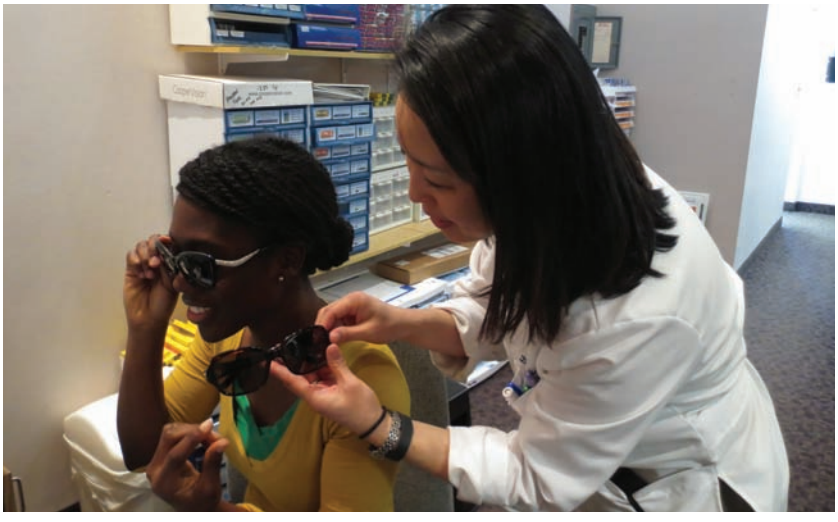
5 Patients Who Need UV Protection and Why

Taking a thorough patient history is the first step in formulating personalized recommendations for UV protection. **By Cheryl G. Murphy, OD, Contributing Editor**

Optometrists and eye care professionals are well versed in relaying the importance of daily sun protection to their patients—but do patients really follow through with these recommendations? Profiling patients and providing them with reasons why they specifically are at risk for damage from UV radiation may help to improve their compliance in using UV protection.

UV radiation is harmful to eyes. Overexposure to UV can have short-term effects such as UV keratitis and long-term effects like pinguecula and pterygia, acceleration of cataracts, and an increased risk of retinal damage. In addition, the skin of the lids—particularly the lower lids and the skin surrounding the orbits—need to be shielded from the sun's harmful rays in order to decrease the chance of cancerous growths in these areas.

Because UV light is a part of the natural world, we need to find out how much time our patients spend outdoors and in what types of environments. Not only does an individual's genetic makeup, physical characteristics, age and family history matter when assessing their risk of potential damage from UV, their everyday surroundings and habits matter as well. Taking a thorough patient history is the first step in formulating personalized recommendations for UV protection.



Julia Garr, OD, of Washington, DC, always educates patients that, while UV-blocking contact lenses help to protect parts of the eye from UV radiation, sunglasses should also be used to shield the entire eye and the surrounding skin.

Let's look at five profiles of patients who need UV protection—and some information that you can give them about why they specifically should guard against UV radiation.

AS YOUR PATIENT'S DAY CHANGES, SO WILL THEIR IOP.

For your patients in need of a PGA,

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INDICATIONS AND USAGE
TRAVATAN Z® (travoprost ophthalmic solution) 0.004% is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

Dosage and Administration
The recommended dosage is 1 drop in the affected eye(s) once daily in the evening. TRAVATAN Z® Solution should not be administered more than once daily since it has been shown that more frequent administration of prostaglandin analogs may decrease the IOP-lowering effect. TRAVATAN Z® Solution may be used concomitantly with other topical ophthalmic drug products to lower IOP. If more than 1 topical ophthalmic drug is being used, the drugs should be administered at least 5 minutes apart.

IMPORTANT SAFETY INFORMATION
Warnings and Precautions

Pigmentation—Travoprost ophthalmic solution has been reported to increase the pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as travoprost is administered. After discontinuation of travoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. The long-term effects of increased pigmentation are not known. While treatment with TRAVATAN Z® Solution can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes—TRAVATAN Z® Solution may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of lashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation—TRAVATAN Z® Solution 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 during treatment with travoprost ophthalmic solution. TRAVATAN Z® Solution 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.

Angle-closure, Inflammatory, or Neovascular Glaucoma — TRAVATAN Z® Solution has not been evaluated for the treatment of angle-closure, inflammatory, or neovascular glaucoma.

Bacterial Keratitis—There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial.

Use With Contact Lenses—Contact lenses should be removed prior to instillation of TRAVATAN Z® Solution and may be reinserted 15 minutes following its administration.

Adverse Reactions
The most common adverse reaction observed in controlled clinical studies with TRAVATAN Z® Solution was ocular hyperemia, which was reported in 30 to 50% of patients. Up to 3% of patients discontinued therapy due to conjunctival hyperemia. Ocular adverse reactions reported at an incidence of 5 to 10% in these clinical studies included decreased visual acuity, eye discomfort, foreign body sensation, pain, and pruritus. In postmarketing use with prostaglandin analogs, periorbital and lid changes including deepening of the eyelid sulcus have been observed.

Use in Specific Populations
Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use.

For additional information about TRAVATAN Z® Solution, please see Brief Summary of full Prescribing Information on adjacent page.

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(travoprost ophthalmic solution) 0.004%

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

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DOSAGE AND ADMINISTRATION
The recommended dosage is one drop in the affected eye(s) once daily in the evening.
TRAVATAN Z® (travoprost ophthalmic solution) should not be administered more than once daily since it has been shown that more frequent administration of prostaglandin analogs may decrease the intraocular pressure lowering effect.

Reduction of the intraocular pressure starts approximately 2 hours after the first administration with maximum effect reached after 12 hours.

TRAVATAN Z® Solution 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.

CONTRAINDICATIONS
None

WARNINGS AND PRECAUTIONS
Pigmentation
Travoprost ophthalmic solution has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes. Pigmentation is expected to increase as long as travoprost is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of travoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long term effects of increased pigmentation are not known.

Iris color change 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. While treatment with TRAVATAN Z® (travoprost ophthalmic solution) 0.004% can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes
TRAVATAN Z® Solution may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of lashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation
TRAVATAN Z® Solution 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 during treatment with travoprost ophthalmic solution. TRAVATAN Z® Solution 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.

Angle-closure, Inflammatory or Neovascular Glaucoma
TRAVATAN Z® Solution has not been evaluated for the treatment of angle-closure, inflammatory or neovascular glaucoma.

Bacterial Keratitis
There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Use with Contact Lenses
Contact lenses should be removed prior to instillation of TRAVATAN Z® 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. The most common adverse reaction observed in controlled clinical studies with TRAVATAN® (travoprost ophthalmic solution) 0.004% and TRAVATAN Z® (travoprost ophthalmic solution) 0.004% was ocular hyperemia which was reported in 30 to 50% of patients. Up to 3% of patients discontinued therapy due to conjunctival hyperemia. Ocular adverse reactions reported at an incidence of 5 to 10% in these clinical studies included decreased visual acuity, eye discomfort, foreign body sensation, pain and pruritus. Ocular adverse reactions reported at an incidence of 1 to 4% in clinical studies with TRAVATAN® or TRAVATAN Z® Solutions included abnormal vision, blepharitis, blurred vision, cataract, conjunctivitis, corneal staining, dry eye, iris discoloration, keratitis, lid margin crusting, ocular inflammation, photophobia, subconjunctival hemorrhage and tearing.

Nonocular adverse reactions reported at an incidence of 1 to 5% in these clinical studies were allergy, angina pectoris, anxiety, arthritis, back pain, bradycardia, bronchitis, chest pain, cold/flu syndrome, depression, dyspepsia, gastrointestinal disorder, headache, hypercholesterolemia, hypertension, hypotension, infection, pain, prostate disorder, sinusitis, urinary incontinence and urinary tract infections.

In postmarketing use with prostaglandin analogs, periorbital and lid changes including deepening of the eyelid sulcus have been observed.

USE IN SPECIFIC POPULATIONS
Pregnancy
Pregnancy Category C
Teratogenic effects: Travoprost was teratogenic in rats, at an intravenous (IV) dose up to 10 mcg/kg/day (250 times the maximal recommended human ocular dose (MRHOD), evidenced by an increase in the incidence of skeletal malformations as well as external and visceral malformations, such as fused sternebrae, domed head and hydrocephaly. Travoprost was not teratogenic in rats at IV doses up to 3 mcg/kg/day (75 times the MRHOD), or in mice at subcutaneous doses up to 1 mcg/kg/day (25 times the MRHOD). Travoprost produced an increase in post-implantation losses and a decrease in fetal viability in rats at IV doses > 3 mcg/kg/day (75 times the MRHOD) and in mice at subcutaneous doses > 0.3 mcg/kg/day (7.5 times the MRHOD).

In the offspring of female rats that received travoprost subcutaneously from Day 7 of pregnancy to lactation Day 21 at doses of ≥ 0.12 mcg/kg/day (3 times the MRHOD), the incidence of postnatal mortality was increased, and neonatal body weight gain was decreased. Neonatal development was also affected, evidenced by delayed eye opening, pinna detachment and preputial separation, and by decreased motor activity.

There are no adequate and well-controlled studies of TRAVATAN Z® (travoprost ophthalmic solution) 0.004% administration in pregnant women. Because animal reproductive studies are not always predictive of human response, TRAVATAN Z® Solution should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers
A study in lactating rats demonstrated that radiolabeled travoprost and/or its metabolites were excreted in milk. It is not known whether this drug or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when TRAVATAN Z® Solution is administered to a nursing woman.

Pediatric Use
Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use.

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

Hepatic and Renal Impairment
Travoprost ophthalmic solution 0.004% has been studied in patients with hepatic impairment and also in patients with renal impairment. No clinically relevant changes in hematology, blood chemistry, or urinalysis laboratory data were observed in these patients.

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Two-year carcinogenicity studies in mice and rats at subcutaneous doses of 10, 30, or 100 mcg/kg/day did not show any evidence of carcinogenic potential. However, at 100 mcg/kg/day, male rats were only treated for 82 weeks, and the maximum tolerated dose (MTD) was not reached in the mouse study. The high dose (100 mcg/kg) corresponds to exposure levels over 400 times the human exposure at the maximum recommended human ocular dose (MRHOD) of 0.04 mcg/kg, based on plasma active drug levels. Travoprost was not mutagenic in the Ames test, mouse micronucleus test or rat chromosome aberration assay. A slight increase in the mutant frequency was observed in one of two mouse lymphoma assays in the presence of rat S-9 activation enzymes.

Travoprost did not affect mating or fertility indices in male or female rats at subcutaneous doses up to 10 mcg/kg/day [250 times the maximum recommended human ocular dose of 0.04 mcg/kg/day on a mcg/kg basis (MRHOD)]. At 10 mcg/kg/day, the mean number of corpora lutea was reduced, and the post-implantation losses were increased. These effects were not observed at 3 mcg/kg/day (75 times the MRHOD).

PATIENT COUNSELING INFORMATION
Potential for Pigmentation
Patients should be advised about the potential for increased brown pigmentation of the iris, which may be permanent. Patients should also be informed about the possibility of eyelid skin darkening, which may be reversible after discontinuation of TRAVATAN Z® (travoprost ophthalmic solution) 0.004%.

Potential for Eyelash Changes
Patients should also be informed of the possibility of eyelash and vellus hair changes in the treated eye during treatment with TRAVATAN Z® Solution. These changes may result in a disparity between eyes in length, thickness, pigmentation, number of eyelashes or vellus hairs, and/or direction of eyelash growth. Eyelash changes are usually reversible upon discontinuation of treatment.

Handling the Container
Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

When to Seek Physician Advice
Patients should also be advised that if they develop an intercurrent ocular condition (e.g., trauma or infection), have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice concerning the continued use of TRAVATAN Z® Solution.

Use with Contact Lenses
Contact lenses should be removed prior to instillation of TRAVATAN Z® Solution and may be reinserted 15 minutes following its administration.

Use with Other Ophthalmic Drugs
If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes between applications.

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5/13 TRV13049JAD

Construction/Outdoor Workers

People who work outdoors are exposed to 10% to 20% more UV light than the average indoor worker.[1] Pair that with the fact that UV radiation is usually most intense between the hours of 10 a.m. and 4 p.m.—which coincides with the typical hours of a dayshift or workday—and one can see why outdoor workers must make sun protection a priority.

Even if an outdoor worker wears a hat, the brim only blocks his or her eyes from UV light coming from directly overhead. Hats do not protect from indirect UV radiation that is reflected off the ground and low-level, angled surfaces.

Most patients realize that direct UV radiation is dangerous, but are not aware that indirect or reflected UV radiation can also be hazardous. When it comes to the amount of UV light that is reflected off of an object, the surface of the object matters. Some surfaces are more reflective than others. A surface painted bright white, for example, reflects about 22% of the sun's UV radiation.[2] (*See "How Surfaces Reflect UV Radiation," right.*)

Even surfaces that don't seem to be inherently reflective can be a source of indirect UV radiation. For example, dry grass in winter bounces about 3% to 5% of the sun's radiation back up toward our eyes.

Another little-known precaution for outdoor workers: Sunglasses are essential for partly cloudy days. The worst exposure conditions can be with a high sun and light overcast because the light clouds further scatter the UVR to lower elevation angles.[3] So, ocular exposure on a partly cloudy day is actually greater than on a clear, sunny day.

Be sure to prescribe high quality UVA/UVB protection to outdoor workers in order to shield them from direct and indirect UV radiation.

Jeffrey Roth, OD, of Syracuse, NY, always educates patients on the importance of protection from reflected UV radiation during snowy, wintery months.

How Surfaces Reflect UV Radiation

Ground reflectance is the most critical determinant of ocular exposure to UVB radiation. Here are UVB reflectance percentages for horizontal surfaces at "high noon" on a sunny day.[2]

• Fresh snow	88%
• Dirty snow	59%
• Sea foam (surf)	25% to 30%
• House paint (white, metal oxide)	22%
• Dry sand	15% to 18%
• Concrete pavement	8% to 12%
• Wet sand	7%
• Black asphalt	4% to 9%
• Soil	4% to 6%
• Lawn grass, winter	3% to 5%
• Lawn grass, summer	2% to 4%

Outdoor Enthusiasts

Even if patients don't work outdoors, they may play outdoors. Outdoor enthusiasts who spend a lot of time outside after work or on the weekends also require appropriate UV protection. Boaters, swimmers and beachgoers need to take note and protect themselves properly while spending a day by the waves because sea foam reflects up to 30% of UV light, while dry sand can reflect more than 15%.[2]

Fresh snow and ice can reflect 80% to 90% of ultraviolet radiation, so everyone should use UV protection during the winter months. However, those who spend a considerable amount of time outdoors in the snow, like skiers and snowboarders, are at an even higher, more imminent risk for damage from UV radiation. Intense, indirect UV radiation for

even as few as two hours can cause UV keratitis or "snow blindness."[4] UV-blocking goggles are a must while out on the slopes to ensure protection against the dangerous amounts of UV reflected off the snow, which can cause this temporary but debilitating and painful corneal condition.

Boaters and beachgoers should also wear polarized UVA/UVB-blocking sunglasses because they too are at risk for UV keratitis due to the potential for the high reflectance of UV radiation off of the water.

Climbers and trailseekers, beware: Altitude also influences the intensity of UV radiation. When traveling to higher elevations, UV radiation is more dangerous whether or not there are snow-capped mountains. For every 1,000 feet that we ascend in altitude, our eyes are subjected to 5% to 7% more UV radiation.[5] This is due not only to snow, but because the atmosphere is thinner at higher altitudes and filters out less UV.

Again, eye care professionals need to nudge their outdoorsy patients to proactively protect themselves from UV so that they can enjoy the sunshine and the great outdoors guilt-free and without detriment to their short-term or long-term ocular health.

Kids

Every parent knows the importance of protecting their children's skin from the sun, but what about their eyes? Kids, who tend to spend more time outdoors than adults, make up another patient population that needs UV-blocking sun protection. Up to 50% of the total UV we're exposed to by age 60 occurs before we reach age 20.[6]

Because the long-term effects of sun damage are cumulative, the longer that people are left unprotected from the sun's harmful rays over the course of their lifetime, the more likely they will suffer damage to their eyes.

What makes the eyes of kids especially vulnerable to UV radiation, besides the amount of time they spend outside during childhood? Children's crystalline lenses are usually clear as glass at birth, so UV light is able to pass right through. Adults experience a natural discoloration or slight yellowing of the lenses as the crystalline lenses mature, which actually helps to filter out some short wavelength light.[7] Because of this, adults with nuclear sclerotic lens changes are slightly better protected against potential cumulative retinal damage from UV radiation compared to children who have immature, clear crystalline lenses.

Of course, as adults' lenses mature, they'll eventually need cataract surgery; and, unless they receive UVA-blocking and blue-violet light-filtering IOLs, they'll again be at an increased risk for retinal damage.

Every time a parent remembers to smear sunscreen on their child's face before heading out the door, the parent should also remember to grab their child's UVA/UVB-blocking sunglasses. Parents will be doing their children a great favor by getting their kids into the healthy habit of proactively protecting their eyes from the sun early on in life.

Contact Lens Wearers

Some patients may think they don't need to bother wearing sunglasses because their contact lenses block UVA/UVB. This is simply not true. Yes, UVA/UVB-blocking contact lenses prevent UV radiation from reaching the cornea and structures behind it, like the lens and the retina, but contacts don't cover everything. The conjunctiva is left vulnerable to UV radiation, as well as the skin of the lids and brow bone. In addition, the lids and brow bone are typically areas of the face where most people avoid applying sunblock because they fear they will get sunblock in their eyes.

But these spots need protection, too. Approximately 5% to 10% of all skin cancers occur in the eyelids.[8,9] Basal cell carcinoma is the most frequently encountered (90% to 95%) type of eyelid tumor, followed by squamous cell carcinoma, sebaceous cell carcinoma and, lastly, malignant melanoma. Although basal cell carcinoma tends to grow slowly and does not frequently metastasize, it can be very destructive if left untreated, extending into deeper layers of

Blue Light in the Spotlight

Near-UV or blue-violet light is a hot topic in research journals lately. Blue-violet light is visible light from natural sources (like sunlight) and artificial light sources (like CFLs and LED screens). It is very close to ultraviolet light in its wavelength and its link to retinal damage is currently being investigated.

As studies unfold and the knowledge of this newfound hazard is passed on to the public, there will be a growing demand for patient protection from blue-violet as well as UV radiation. There are already ophthalmic products on the market that provide both UV-blocking and selective blue-violet filtering protection.

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the skin and invading periorbital tissues and bone.[10]

Tumors need to be removed early before they cause damage to vital ocular structures, but detection can be difficult due to their inward growth pattern.[8,9,11] Eyelid tumors can grow under the skin for years before any clue appears on the surface.[8,9,11]

Displaying a few pairs of sunglasses in your contact lens dispensary may remind both you and your contact lens patient that the conjunctiva, lids and unprotected areas of periocular skin also require proper UVA/UVB protection. The good news is that because contact lenses have taken care of the patient's prescription, a pair of non-Rx, high quality sunglasses will take care of the rest, and then the patient can walk out of the eye doctor's office fully protected.

In sunny Los Angeles, Maylin Gonzalez, OD, (left) tells her patients that sunglasses are not just fashionable, they are part of a healthy lifestyle that includes eating right, exercising and avoiding environmental hazards like UV.

Health-Conscious Individuals

Today's health-conscious individuals are concerned with their genetic predispositions for certain diseases and illnesses. They also have a desire to take charge and minimize their interaction with common toxins and environmental hazards. Living a healthy lifestyle helps patients feel empowered, knowing they are doing what they can to directly protect and improve their health. Eating right, exercising and avoiding environmental hazards are all parts of living a healthy lifestyle.

UV protection can help safeguard our patients' eyes from environmental hazards posed by UV light. Patients who suffer from or are at risk for retinal damage need to make sun protection a priority. Epidemiological studies have found a relationship between chronic sunlight exposure and AMD.[12] Add to this the increasing magnitude of macular degeneration among the rapidly growing elderly population. Specifically, researchers predict that the number of Americans with early AMD is expected to nearly double by 2050—from 9.1 million to 17.8 million.[13]

If patients have a family history of AMD and other risk factors that make them vulnerable to UV damage—such as fair skin, light eyes and a fair retina—urge them to take action against UV radiation by wearing sun protection for their eyes when outdoors.

As with much of optometry and medicine, patient education is crucial when attempting to cultivate successful compliance with recommended precautions and treatments. Most patients take what their doctors say seriously, but what matters most is what they do after they leave the office. Individualized care and prescribed recommendations tend to hold more weight than a blanket statement that UV is bad.

By providing each patient with personalized suggestions, as well the scientific explanations and evidence behind those suggestions, eye care professionals stand a better chance of the patient taking their doctor's directions to heart and protecting themselves from UV radiation. ■

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The Legacy of AREDS

AREDS-2 raised eyebrows, but could also open doors to 'pharmacogenomics' and more meaningful use of personalized genetic testing. **By Dennis Ruskin, OD**

Modern scientific methodology—specifically, the randomized clinical trial (RCT)—is considered a critical component of evidence-based medicine to separate fact from fiction regarding interventions, drugs, nutrition and other strategies we use to treat our patients safely and effectively. A well-designed, large-scale clinical trial that is considered valid, reliable and unchallenged is critical to the emergence of a standard of care; however, the results achieved are only as good as the design of the clinical trial.

New research concerning AMD has raised a few eyebrows among enthusiasts of ocular nutrition. The dialogue centers on two particular studies—the AREDS-2, authored by National Eye Institute Deputy Clinical Director Emily Chew, MD, and a polymorphism genomic paper, authored by Carl Awh, MD, a private practice ophthalmologist in Nashville. Dr. Chew's research is a classic RCT that investigated the addition of new nutrients to the current AREDS formula, while Dr. Awh's study predicted subject response to AMD with antioxidants and zinc.

Although both studies used the same clinical information, the genomic paper reanalyzed a statistically significant sample of subjects' data and genetic samples from AREDS-1. The methodologies differed significantly, which led to contrasting conclusions in treatment. The resulting controversy places us in a precarious position as we determine appropriate nutrient recommendations for patients with moderate or advanced AMD and those at risk for AMD.

At times, clinical trials are challenged due to confounding errors, such as investigator bias, inaccurate assumptions about the drug or nutrient interaction, or an insufficient number of subjects enrolled in subsets, causing statistically insignificant findings in the analysis of primary or secondary randomization.[1]

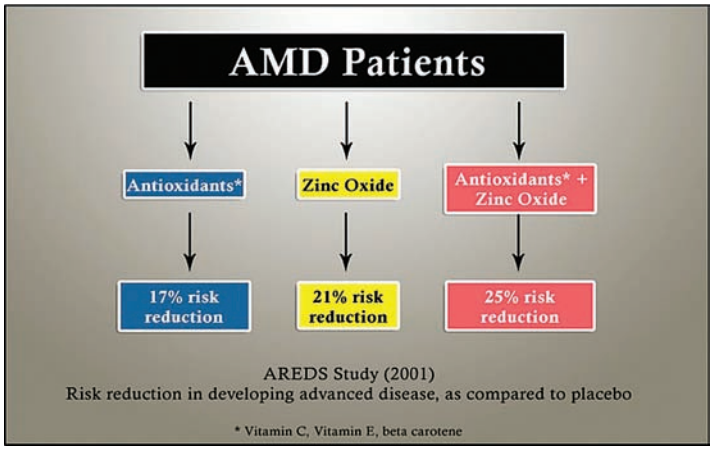
AREDS-1

Widespread public use of commercial vitamins and minerals to treat AMD—with few definitive answers on their safety and efficacy—initiated the AREDS-1 RCT in 2005. The National Eye Institute (NEI) sponsored this randomized, placebo-controlled, double-masked clinical trial primarily concerned with studying the effects of a nutrient combination on the progression of AMD.

According to the AREDS-1 findings, the risk to advanced AMD decreased by 25% in stage III. Though the formulation slowed the progression from stage III to stage IV, it did not halt the progression of AMD (*figure 1*).[1] The zinc subset had a 21% risk reduction and antioxidants had a 17% risk reduction related to the progression of AMD in stages III and IV (*figure 2*).[2] The evidence did not support the use

of these supplements for prevention in the early stages I and II.

Overall, the results were statistically significant but modest. The Cochrane Reviews, an RCT repository that provides systematic reviews of primary research in human health care and health policy, found that the generalizability of these findings to other populations with different nutritional status was unknown; therefore, long-term harm from supplementation could not be ruled out.[3] Beta-carotene, for example, has been found to increase the risk of lung cancer in smokers and vitamin E has been associated with increased heart-failure risk.[3, 4]



1. Though the AREDS-1 forumation slowed progression from stage III to stage IV, it did not halt the progression of AMD.

There were also some concerns related to zinc and genitourinary complications. Many clinical investigators questioned the benefits of zinc and the antioxidant supplements used; they also wanted more time to study the effects of higher dose supplements.

Based on the AREDS-1 conclusions, should patients with moderate to severe AMD take antioxidant supplements? Some investigators voiced concerns about how the study was funded, and pointed out that there had been no replication of the data. Others noted the lack of long-term safety information, coupled with only a modest effect in reducing progression of AMD.

Encouraged by the preliminary data from AREDS-1, clinical investigators sought to discover if manipulation of the original formula could achieve double the AREDS-1 effect (a 50% decrease in progression of AMD). Many clinicians wanted to change dosing and include some nutrients not used in AREDS-1, such as the carotenoids lutein and zeaxanthin, which are found in high concentrations in the macula, but were not commercially available at the time of the original study. Further, previous studies associated high levels of lutein and zeaxanthin intake with lower risk of AMD.[5-8] These nutrients are believed to augment macular pigment optic density (MPOD), which protects the photoreceptors and the retinal pigment epithelium from the oxidative damage associated with exposure to blue light.

A follow-up analysis of AREDS-1 concerned the dietary habits of subjects who answered a food frequency questionnaire at baseline. The study indicated that subjects who consumed fish with long chain omega-3 fatty acids experienced a 25% decrease in AMD progression.[9] In addition, several investigators of independent peer-reviewed studies have reported findings that support omega-3 fatty acids in the management of AMD.[9-11]

Other effects of omega-3 in the literature suggest the following benefits: decreased triglyceride levels, which may affect atherosclerotic plaque formation; lowered blood pressure; reduction in heart attack risk, stroke and dangerous abnormal heart rhythm in patients with known heart disease; anti-inflammatory effect in patients with rheumatoid arthritis; and reduction in risk of breast and prostate cancers.[12-17]

Researchers also wanted to know whether reduced levels of zinc would affect the formulation's performance in decreasing progression of AMD, and if reduced zinc levels would decrease genitourinary complications.

There were concerns that current or prior smokers had a higher risk of lung cancer with beta-carotene in the formulation, so investigators also wanted to test whether eliminating beta-carotene altogether and substituting lutein/zeaxanthin would affect the results.

AREDS-2

Researchers started enrollment for AREDS-2 in 2006 with the intention of studying additional nutrient combinations against the benefits of the existing formula (Table 3). The primary randomization in AREDS included the original formula plus one of the following:

- 10mg of lutein/2mg of zeaxanthin
- Omega-3 fatty acids: 350mg docosahexaenoic acid (DHA)/650mg of eicosapentaenoic acid (EPA)
- Lutein/zeaxanthin plus DHA-EPA above

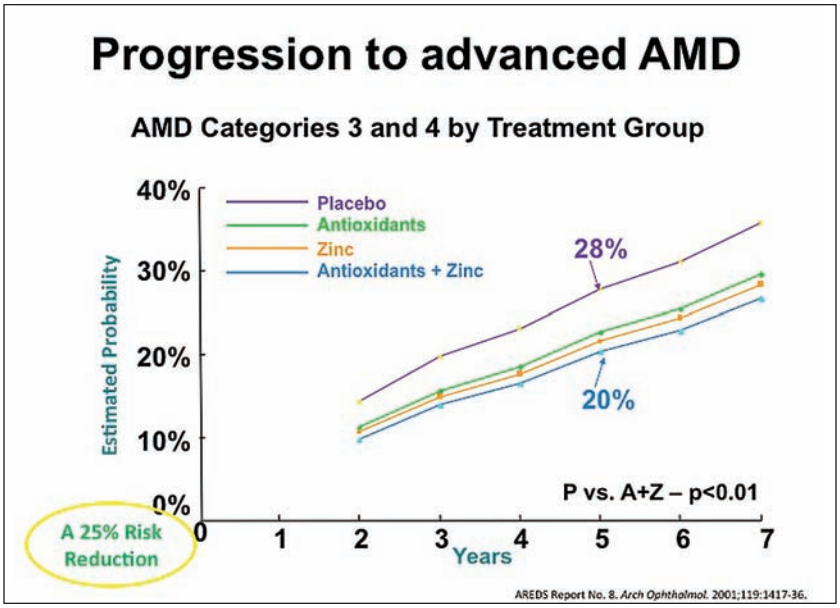
The secondary randomization

evaluated three subsets using the original formula plus one of the following:

- No beta-carotene
- Low zinc
- No beta-carotene and low zinc

Interestingly, the addition of lutein and zeaxanthin, and DHA/EPA, or both in the primary analysis, did not further reduce the risk of progression to advanced AMD.[17]

The authors of AREDS-2 sought to determine if a statistically significant sample of the general population would benefit from a specific nutrient formula. The study provided useful evidence to justify a redesign of the original AREDS-1 formula, since reducing the level of zinc and eliminating the beta-carotene did not reduce the efficacy of the supplements. However, there were confounding factors that could have adversely influenced the results.



2. The zinc subset had a 21% risk reduction and antioxidants had a 17% risk reduction related to the progression of AMD in stages III and IV.

AREDS-2 Uncertainties

• ***Study design issues.*** There were admitted limitations to the study results due to "a complicated design involving a secondary randomization which may have affected our ability to evaluate the role of lutein and zeaxanthin and DHA+EPA to the AREDS formula."[17]

• ***No control group.*** Due to the modest success of AREDS-1 results, it was ethically necessary to offer prior subjects of AREDS-1 the choice of taking the original AREDS-1 formula or not. In fact, most subjects opted to continue the original formula. Only 19 of about 4,000 (less than 0.05%) of the total enrolled subjects in AREDS-2 did not take the original AREDS-1 formula. Therefore, there was no true control group to compare findings in the AREDS-2 primary analysis.

• ***Omega-3 confounding factors.*** The study showed that taking 1000mg of omega-3 did not affect the progression in AMD patients. Some possible reasons include use of the ethyl ester form of omega-3, which is not as bioavailable as the triglyceride form, and the lipid-lowering effect of 1,000mg of omega-3, which may not be sufficient to obtain a desirable result.

Further, many subjects did not follow the study guidelines regarding their recommended nutrient intake. Approximately 84% of subjects took slightly more than 75% of the supplement pills, which could have skewed the results. Fourteen percent of subjects admitted to taking unauthorized additional supplements, either alone or in combination with their supplement pills, during the trial.

• ***Non-representative sample.*** AREDS-2 inducted mainly female, well-nourished whites; thus, the study sample was not representative of the biological diversity of the general population. The study group reported that they already consumed supplements, multivitamins or foods rich in lutein, zeaxanthin and omega fatty acids, in addition to the original AREDS supplement. AREDS-2 clinical investigator Paul Bernstein, MD, PhD, a leading carotenoid researcher, confirmed this.

Dr. Bernstein's work showed a linear relationship between diet or carotenoid-rich supplements and a more robust MPOD. He performed an ancillary study on his AREDS-2 subjects in which he measured MPOD and found their "usage of lutein and zeaxanthin supplements was exceedingly high, suggesting that we enrolled a very nutritionally aware cohort."[20] The inclusion of a larger group of subjects who have statistically significant nutrient deficiencies would likely offer more practical clinical information than studies on well-nourished subjects.

• ***Nutrient interactions.*** The primary study conclusion—that lutein and zeaxanthin with or without omega-3 fatty acids did not further reduce the risk of progression—may have been influenced by carotenoid competition.

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Interestingly, when compared with the subgroup that used the original AREDS formula plus lutein and zeaxanthin (without beta-carotene) to the subgroup in the primary randomization of original AREDS formula containing beta-carotene, lutein and zeaxanthin, there is an 18% lower risk of AMD progression. This result may occur because lutein, zeaxanthin and beta-carotene are carotenoids that do compete for absorption the human body.[20] Carotenoid competition may explain, in part, why lutein and zeaxanthin had no overall effect in the primary randomization, but a statistically significant effect when beta-carotene was removed in the secondary randomization. Therefore, this confounding error may be viewed by some observers as a significant study flaw affecting the results of the primary study.

Pharmacogenomics and AMD

In the past, large-scale RCT studies allowed industry to develop "blockbuster" drugs to treat an average population. Many now contend that the future of medical studies may focus on a more personalized approach to medicine—that is, developing interventions, drugs or nutrients to treat subsets of patients, each of whom may respond differently based on individual genetic factors.[21]

While the RCT is invaluable in understanding whether one treatment is better than another on a general platform, the findings may be harder to apply individually. Research gleaned from a combination of RCT and genetic trials may be on the horizon. Pharmacogenomics—the way genes influence response to nutrients and drugs—is unique and different for each individual.[22] As genetic research moves forward, the evolution of personalized recommendations will become more commonplace.

Predicting AMD Pathogenesis

The human genome has been catalogued and genetic variations have been identified as single nucleotide polymorphisms (SNPs), which are considered a measure of genetic similarity used for genotyping or genetic fingerprinting. SNPs associated with AMD are located on genes that affect the biological pathways of the disease, and have been confirmed in the literature. Genes involved with the complement cascade of the immune system have a direct effect on the progression of AMD.[23] Thus, AMD has the strongest genetic contribution of all human multi-genetic diseases.[23]

Additionally, the pathogenesis of AMD may be predicted using a combination of fundus diagnosis and determination of genotype.[24] A currently available, validated genetic test (Arctic Dx) may provide greater sophistication in how we view an individual's future risk of AMD progression.[25] Using genotyping, fundus diagnosis and health care history together, an individualized prediction of advanced AMD risk over time can be generated.[24]

Reanalysis of AREDS-1 Using Genomic Testing

Genetic research has shown that SNPs of human variation complement factor (CFH) and age-related maculopathy sensitivity 2 (ARMS2) each have important roles in AMD.[26]

Dr. Awh, et al., authored a clinical study that obtained statistically significant AREDS-1 data from subjects—including genetic information contained in saliva samples. In a novel twist of methodologies contrasting RCT and genomic testing, investigators did not obtain average population statistics, as is routine in an RCT like AREDS-1. Rather, the authors sought to compare how the original AREDS formula subsets—zinc, antioxidants, and zinc plus antioxidants—would affect progression to AMD when sorted by genotype that were composed of high-risk genes. Dr. Awh was specifically interested in results concerning one or two risk alleles of CFH or ARMS2.

Dr. Awh's study analyzed AREDS-1 data for up to 12 years. Subjects with the ARMS2 allele(s) benefited more from the formulation with zinc alone. Furthermore, these subjects had a higher risk of progression to AMD when they also were treated with antioxidants. Subjects with the CFH risk allele(s) benefited more with antioxidants than with the complete AREDS-1. Interestingly, when this group was treated with zinc, there was an associated increase in the risk to progression of AMD. Those with both one ARMS2 and one CFH alleles showed reduced progression using the original AREDS-1 formula of zinc plus antioxidants. Dr. Awh extrapolated the AREDS-1 data to genotype and predicted that the optimal treatment for 49% of the study patients would be a nutrient combination different from the complete AREDS-1 formulation.

The scientific literature includes some studies that support Dr. Awh's contention that there could be a harmful relationship between CFH and ARMS2 with nutrients in the AREDS-1 formula. A retrospective analysis done in 2008 found that the AREDS supplement may be related to the CFH high-risk SNP.[26] In 2009, researchers found "significant interaction between the number of risk alleles for the CFH Y402H variant and treatment, whereby patients with the (high

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Important Safety Information

Warnings and Precautions: LUMIGAN® 0.01% causes changes to pigmented tissues, mostly increased pigmentation of the iris, eyelid, and eyelashes as long as LUMIGAN® 0.01% is administered. Iris color change may not be noticeable for several months to years. After discontinuation of bimatoprost, iris pigmentation is likely to be permanent, while eyelid and eyelash changes have been reported to be reversible in some patients. Patients should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

LUMIGAN® 0.01% should be used with caution in patients with active intraocular inflammation (eg, uveitis) because the inflammation may be exacerbated. Macular edema, including cystoid macular edema, has been reported with LUMIGAN® 0.01%. LUMIGAN® 0.01% 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. LUMIGAN® 0.01% has not been studied to treat types of glaucoma other than open-angle glaucoma. Remove contact lenses prior to instillation of LUMIGAN® 0.01% and reinsert after 15 minutes.

Adverse Reactions: The most common (25%-45%) adverse event with LUMIGAN® 0.01% was conjunctival hyperemia. Approximately 0.5% to 3% of patients discontinued therapy due to conjunctival hyperemia. Other common events (> 10%) included growth of eyelashes and ocular pruritus.

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

1. LUMIGAN® Prescribing Information. **2.** Katz LJ, Cohen JS, Batoosingh AL, Felix C, Shu V, Schiffman RM. Twelve-month, randomized, controlled trial of bimatoprost 0.01%, 0.0125%, and 0.03% in patients with glaucoma or ocular hypertension. *Am J Ophthalmol.* 2010;149(4):661-671. **3.** Managed Markets Insight & Technology, LLC, database, as of November 2013.

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INDICATIONS AND USAGE

LUMIGAN® 0.01% and 0.03% (bimatoprost ophthalmic solution) is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Pigmentation: Bimatoprost ophthalmic solution has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes. Pigmentation is expected to increase as long as bimatoprost is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of bimatoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long term effects of increased pigmentation are not known.

Iris color change 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. While treatment with **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution) can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes: LUMIGAN® 0.01% and 0.03% may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of lashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation: LUMIGAN® 0.01% and 0.03% 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 during treatment with bimatoprost ophthalmic solution. **LUMIGAN®** 0.01% and 0.03% 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.

Angle-closure, Inflammatory, or Neovascular Glaucoma: LUMIGAN® 0.01% and 0.03% has not been evaluated for the treatment of angle-closure, inflammatory or neovascular glaucoma.

Bacterial Keratitis: There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Use With Contact Lenses: Contact lenses should be removed prior to instillation of **LUMIGAN®** 0.01% and 0.03% 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 with bimatoprost ophthalmic solutions (0.01% or 0.03%) the most common adverse reaction was conjunctival hyperemia (range 25%–45%). Approximately 0.5% to 3% of patients discontinued therapy due to conjunctival hyperemia with 0.01% or 0.03% bimatoprost ophthalmic solutions. Other common reactions (>10%) included growth of eyelashes, and ocular pruritus.

Additional ocular adverse reactions (reported in 1 to 10% of patients) with bimatoprost ophthalmic solutions included ocular dryness, visual disturbance, ocular burning, foreign body sensation, eye pain, pigmentation of the periocular skin, blepharitis, cataract, superficial punctate keratitis, periorbital erythema, ocular irritation, eyelash darkening, eye discharge, tearing, photophobia, allergic conjunctivitis, asthenopia, increases in iris pigmentation, conjunctival edema, conjunctival hemorrhage, and abnormal hair growth. Intraocular inflammation, reported as iritis, was reported in less than 1% of patients.

Systemic adverse reactions reported in approximately 10% of patients with bimatoprost ophthalmic solutions were infections (primarily colds and upper respiratory tract infections). Other systemic adverse reactions (reported in 1 to 5% of patients) included headaches, abnormal liver function tests, and asthenia.

Postmarketing Experience: The following reactions have been identified during postmarketing use of **LUMIGAN®** 0.01% and 0.03% 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 **LUMIGAN®**, or a combination of these factors, include: dizziness, eyelid edema, hypertension, nausea, and periorbital and lid changes associated with a deepening of the eyelid sulcus.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C

Teratogenic effects: In embryo/fetal developmental studies in pregnant mice and rats, abortion was observed at oral doses of bimatoprost which achieved at least 33 or 97 times, respectively, the maximum intended human exposure based on blood AUC levels.

At doses at least 41 times the maximum intended human exposure based on blood AUC levels, the gestation length was reduced in the dams, the incidence of dead fetuses, late resorptions, peri- and postnatal pup mortality was increased, and pup body weights were reduced.

There are no adequate and well-controlled studies of **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution) administration in pregnant women. Because animal reproductive studies are not always predictive of human response **LUMIGAN®** should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether **LUMIGAN®** 0.01% and 0.03% is excreted in human milk, although in animal studies, bimatoprost has been shown to be excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when **LUMIGAN®** is administered to a nursing woman.

Pediatric Use: Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use.

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

Hepatic Impairment: In patients with a history of liver disease or abnormal ALT, AST and/or bilirubin at baseline, bimatoprost 0.03% had no adverse effect on liver function over 48 months.

OVERDOSAGE

No information is available on overdosage in humans. If overdose with **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution) occurs, treatment should be symptomatic.

In oral (by gavage) mouse and rat studies, doses up to 100 mg/kg/day did not produce any toxicity. This dose expressed as mg/m2 is at least 70 times higher than the accidental dose of one bottle of **LUMIGAN®** 0.03% for a 10 kg child.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: Bimatoprost was not carcinogenic in either mice or rats when administered by oral gavage at doses of up to 2 mg/kg/day and 1 mg/kg/day respectively (at least 192 and 291 times the recommended human exposure based on blood AUC levels respectively) for 104 weeks.

Bimatoprost was not mutagenic or clastogenic in the Ames test, in the mouse lymphoma test, or in the *in vivo* mouse micronucleus tests.

Bimatoprost did not impair fertility in male or female rats up to doses of 0.6 mg/kg/day (at least 103 times the recommended human exposure based on blood AUC levels).

PATIENT COUNSELING INFORMATION

Potential for Pigmentation: Patients should be advised about the potential for increased brown pigmentation of the iris, which may be permanent. Patients should also be informed about the possibility of eyelid skin darkening, which may be reversible after discontinuation of **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution).

Potential for Eyelash Changes: Patients should also be informed of the possibility of eyelash and vellus hair changes in the treated eye during treatment with **LUMIGAN®** 0.01% and 0.03%. These changes may result in a disparity between eyes in length, thickness, pigmentation, number of eyelashes or vellus hairs, and/or direction of eyelash growth. Eyelash changes are usually reversible upon discontinuation of treatment.

Handling the Container: Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

When to Seek Physician Advice: Patients should also be advised that if they develop an intercurrent ocular condition (e.g., trauma or infection), have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice concerning the continued use of **LUMIGAN®** 0.01% and 0.03%.

Use with Contact Lenses: Patients should be advised that **LUMIGAN®** 0.01% and 0.03% contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to instillation of **LUMIGAN®** and may be reinserted 15 minutes following its administration.

Use with Other Ophthalmic Drugs: Patients should be advised that if more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes between applications.

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risk) genotype were less likely to benefit from the antioxidant-mineral supplementation than subjects with the TT and CT genotypes.[27] In 2012, researchers demonstrated that a strong association exists between all stages of AMD and the ARMS2 SNP.[28] Two years earlier, Stephen Perkins and colleagues outlined the biological plausibility of the CFH/zinc interaction.[1] This publication points specifically at high-risk CFH alleles and zinc.[30]

Dr. Awh shared his findings about genotype and progression to AMD using AREDS supplements at the American Academy of Ophthalmology's annual meeting in late 2013. Afterward, Dr. Chew offered a dissenting view and reported that his data did not complement hers. As there is no consensus among retina specialists on the matter, a comprehensive scientific review is needed to reconcile the conflicting data.

AREDS-1 was the first glimpse into a nutrient strategy to help combat AMD based on traditional evidence-based science. The extension study, AREDS-2, confirmed that lutein and zeaxanthin are more beneficial and safer than beta-carotene in reducing progression of the disease. Studies on the benefits of omega-3 fatty acids are ongoing, while many practitioners will continue to recommend DHA and EPA in different forms and dosages.

The results of AREDS-2 should be considered against its ethical considerations, including the absence of a control group, design complexity, nutrient interaction, subject sampling issues and the effectiveness of additional nutrients studied. In hindsight, it may have been clinically relevant to analyze more subjects who were less nourished than the individuals reflected in AREDS-2.

The AREDS RCT also opens a new door to clinical genetic trials. Dr. Awh predicated his recent work on a clinically rich time capsule of information from AREDS-1, collected for more than 10 years. Study investigators were able to fast-track more than a decade of data by looking at influences by genotype rather than by an average population.

Certainly, the debate to recommend personalized genetic testing or to use a classical RCT will evolve. Because AMD has the strongest genetic contribution of all human multi-genetic diseases, it seems likely that at least some form of personalized genetic testing will help us better protect our patients from the visual ravages of AMD. ■

Dr. Ruskin is the president of the College of Optometrists of Ontario, and is in private practice in Toronto. He is the current chair of the Ocular Nutrition special interest group within the American Academy of Optometry. He has no direct financial interest in any of the products mentioned in this article.

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Systemic Disease Report

Nutrition and Diabetes: Our Role in Patient Care

If we don't educate our patients about the dangers of poor dietary habits and sedentary lifestyles, the incidence of diabetic eye disease will continue to soar.

By Laurie Capogna, OD, and Barbara Pelletier, OD

Whose responsibility is it to educate our patients about the importance of nutrition, lifestyle and excess weight gain with respect to diabetes management? Historically, we left this task to the patient's primary care physician. However, with escalating rates of obesity and metabolic syndrome in North America—in addition to a rapidly expanding incidence of vision loss secondary to diabetic eye disease—optometrists simply can't sit on the sidelines anymore.

As primary eye care providers, it is our responsibility to educate and motivate our patients to maintain a healthy weight through proper nutrition and lifestyle modification. Ultimately, their vision and systemic well-being depend on our guidance.

Metabolic Syndrome and the Diabetes Epidemic

According to the International Diabetes Federation (IDF), metabolic syndrome is a collective term that encompasses several of the most dangerous risk factors for heart attack, including prediabetes, abdominal obesity, high cholesterol and high blood pressure.[1] Affected individuals have a five-fold risk of developing type II diabetes, and are three times more likely to have a heart attack or stroke than healthy individuals. Currently, the IDF estimates that up to 25% of adults worldwide have metabolic syndrome.[1]

Data from the 2011 National Diabetes Fact Sheet show that nearly 26 million Americans have been diagnosed with diabetes, and another 79 million are considered pre-diabetic.[2] Additionally, seven million Americans suffer from the disease but remain undiagnosed.[2]

Diabetes is the leading cause of new cases of blindness among adults aged 20 to 74. The National Eye Institute reports that nearly half of Americans with diabetes have diabetic retinopathy.[2] Of those, nearly 5% have sight-threatening retinopathy, with significantly higher rates among African, Latino and Native American populations.[2]

However, one of the most alarming aspects of this epidemic is the increasing frequency of both type 1 and type 2 diabetes in American youth. Between 2009 and 2011, the incidence of both conditions increased by more than 20%.[3,4]

This is a real crisis. However, the good news is that we can do something about it. Type 2 diabetes is preventable, and it accounts for 95% of all cases.[2] If we educate our patients about the relationship between weight, exercise, dietary intake and diabetic eye disease, we can reduce the incidence of type 2 diabetes and help prevent associated vision loss.

What's the Solution?

The typical North American diet contains high amounts of processed, calorie-dense foods that offer little nutritional value, and consequently promote weight gain. Serving sizes, both in restaurants and at home, are expanding in direct proportion with the waistlines of millions of Americans.

Further, many people—particularly children—are consuming too many soft drinks and sugary beverages that can promote type 2 diabetes. If these general trends continue into the foreseeable future, more people will experience signs and symptoms of diabetic eye disease at increasingly younger ages.

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Choosing foods that are rich in lutein, zeaxanthin, vitamin C, vitamin E and beta-carotene are highly beneficial for maintaining peak ocular health and visual function.

In our "Eyefoods" plan, we advocate the following vegetable and fruit choices:

- *One daily handful of raw, leafy greens—preferably kale or spinach.*
- *Half-cup cooked leafy greens twice a week.*
- *Half-cup of orange vegetables most days, including squash, raw carrots, pumpkin or sweet potatoes.*
- *Two orange peppers per week—raw and/or cooked.*
- *Half-cup of green vegetables per day, such as raw and/or cooked broccoli, Brussels sprouts, green peas and green beans.*
- *Up to three servings of kiwi, avocado, cantaloupe, citrus fruit or berries per day.*

According to the Diabetes Prevention Program (DPP), lifestyle changes for pre-diabetics have a significant impact on diabetes prevention.[5] The DPP was a two-year, multicenter, randomized clinical trial that was designed to determine if modest weight loss via dietary alteration and increased physical activity could prevent or delay the onset of type 2 diabetes more effectively than treatment with metformin.

Participants began the study being overweight and exhibiting blood glucose levels that were higher than normal, but clinically insufficient for a diagnosis of diabetes. The study results showed that diabetes incidence was reduced by 58% in participants who received intensive training in proper dietary intake, physical activity and behavioral modifications, compared to just 31% who received metformin to lower blood glucose levels.[5]

At 10-year follow-up, the DPP researchers determined that the onset of diabetes could be delayed for at least a decade in patients who continued to eat properly and exercise regularly following the study's conclusion.[6] Considering these results, it is critical to educate our patients about the protective benefits of lifestyle modification.

Weight Control

Excess weight gain is one of the fundamental causes of type 2 diabetes. Indeed, the risk of developing diabetes increases seven-fold in overweight people, and 20- to 40-fold in obese people.[7] The most widely accepted way to determine a patient's weight status is to calculate his or her Body Mass Index (BMI), which is a ratio based upon an individual's weight and height.

Waist circumference is another predictor of diabetes. According to a cohort of the Nurses' Health Study, the risk of type 2 diabetes increased progressively in quintiles of patients with the largest waist circumferences (35 inches or greater in women, and 40 inches or greater in men).[8,9]

Additionally, according to the Harvard School of Public Health, losing 7% to 10% of your current weight can reduce your chances of developing type 2 diabetes by as much as 50%.[10] For patients who don't exercise and/or have poor diets at baseline, this sort of weight reduction goal is relatively easy to achieve. For example, those who weigh 150lbs would have to lose just 10lbs to 15lbs.

Increased Physical Activity

In the DPP, 2.5 hours of exercise per week (i.e., brisk walking) was independently helpful at reducing subjects' risk of diabetes.[5] However, according to another cohort from the Nurses' Health Study, physical activity alone does not eliminate an individual's risk for type 2 diabetes.[8]

It is worth noting that other studies challenge this finding, and indicate that physical activity is indeed an independent factor in diabetes prevention.[11] Specifically, weight control is the most important factor to consider—and certainly, physical activity helps facilitate weight loss.

To achieve optimal health benefits, adults should physically exert themselves for at least 30 minutes per day. Even more importantly, however, children should engage in at least 60 continuous minutes of physical activity each day.[11]

Dietary Control

In order to lose weight, patients need to expend more calories than they consume. A diet that closely adheres to the recommendations made by the Omni-Heart study is a great way to help reduce weight, while ensuring that food intake is of high quality.[12]

Diets constructed in accordance with these suggestions are rich in vegetables and fruits, and low in saturated/trans fats, sodium and added sugar.

A standard 2,100-calorie diet should include 11 servings of vegetables and fruit, as well as one to two servings each of whole grains, low-fat dairy, lean proteins, legumes and nuts. (Every patient's ideal caloric intake level should be calculated by his or her dietitian.)[12]

Closely adhering to such recommendations, however, leaves little room for foods that are rich in sugar, such as processed sweets and soft drinks.

For allergic conjunctivitis[1]

THE POWER TO CALM THE ITCH

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INDICATION AND USAGE

BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% is a histamine H_1 receptor antagonist indicated for the treatment of itching associated with signs and symptoms of allergic conjunctivitis.

IMPORTANT RISK INFORMATION

BEPREVE® is contraindicated in patients with a history of hypersensitivity reactions to bepotastine or any of the other ingredients. BEPREVE® is for topical ophthalmic use only. To minimize risk of contamination, do not touch the dropper tip to any surface. Keep the bottle closed when not in use. BEPREVE® should not be used to treat contact lens–related irritation. Remove contact lenses prior to instillation of BEPREVE®.

The most common adverse reaction occurring in approximately 25% of patients was a mild taste following instillation. Other adverse reactions occurring in 2%-5% of patients were eye irritation, headache, and nasopharyngitis.

Please see the accompanying prescribing information for BEPREVE® on the following page.

Reference: 1. BEPREVE [package insert]. Tampa, FL: Bausch + Lomb, Inc; 2012.

BAUSCH + LOMB

For product-related questions and concerns, call **1-800-323-0000** or visit **www.bepreve.com**.

Made by the trusted eye-care specialists at BAUSCH + LOMB

BEPREVE®
(bepotastine besilate ophthalmic solution) 1.5%

BEPREVE® (bepotastine besilate ophthalmic solution) 1.5%

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% safely and effectively. See full prescribing information for BEPREVE®.

BEPREVE® (bepotastine besilate ophthalmic solution) 1.5%
Initial U.S. Approval: 2009

----------RECENT MAJOR CHANGES----------
Contraindications (4) 06/2012

----------INDICATIONS AND USAGE----------
BEPREVE® is a histamine H1 receptor antagonist indicated for the treatment of itching associated with allergic conjunctivitis. (1)

----------DOSAGE AND ADMINISTRATION----------
Instill one drop into the affected eye(s) twice a day (BID). (2)

----------DOSAGE FORMS AND STRENGTHS--------
Solution containing bepotastine besilate, 1.5%. (3)

----------CONTRAINDICATIONS----------
Hypersensitivity to any component of this product. (4)

----------WARNINGS AND PRECAUTIONS----------
- To minimize the risk of contamination, do not touch dropper tip to any surface. Keep bottle tightly closed when not in use. (5.1)
- BEPREVE should not be used to treat contact lens-related irritation. (5.2)
- Remove contact lenses prior to instillation of BEPREVE. (5.2)

----------ADVERSE REACTIONS----------
The most common adverse reaction occurring in approximately 25% of patients was a mild taste following instillation. Other adverse reactions which occurred in 2-5% of subjects were eye irritation, headache, and nasopharyngitis. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb Incorporated. at 1-800-323-0000, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION

Revised: 10/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% is a histamine H_1 receptor antagonist indicated for the treatment of itching associated with signs and symptoms of allergic conjunctivitis.

2 DOSAGE AND ADMINISTRATION
Instill one drop of BEPREVE into the affected eye(s) twice a day (BID).

3 DOSAGE FORMS AND STRENGTHS
Topical ophthalmic solution containing bepotastine besilate 1.5%.

4 CONTRAINDICATIONS
Bepreve is contraindicated in patients with a history of hypersensitivity reactions to bepotastine or any of the other ingredients *[see Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS
5.1 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.

5.2 Contact Lens Use
Patients should be advised not to wear a contact lens if their eye is red. BEPREVE should not be used to treat contact lens-related irritation.

BEPREVE should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of BEPREVE. The preservative in BEPREVE, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of BEPREVE.

5.3 Topical Ophthalmic Use Only
BEPREVE is for topical ophthalmic use only.

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

The most common reported adverse reaction occurring in approximately 25% of subjects was a mild taste following instillation. Other adverse reactions occurring in 2-5% of subjects were eye irritation, headache, and nasopharyngitis.

6.2 Post Marketing Experience
Hypersensitivity reactions have been reported rarely during the post-marketing use of BEPREVE. Because these reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency or establish a casual relationship to drug exposure. The hypersensitivity reactions include itching, body rash, and swelling of lips, tongue and/or throat.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category C: Teratogenicity studies have been performed in animals. Bepotastine besilate was not found to be teratogenic in rats during organogenesis and fetal development at oral doses up to 200 mg/kg/day (representing a systemic concentration approximately 3,300 times that anticipated for topical ocular use in humans), but did show some potential for causing skeletal abnormalities at 1,000 mg/kg/day. There were no teratogenic effects seen in rabbits at oral doses up to 500 mg/kg/day given during organogenesis and fetal development (>13,000 times the dose in humans on a mg/kg basis). Evidence of infertility was seen in rats given oral bepotastine besilate 1,000 mg/kg/day; however, no evidence of infertility was observed in rats given 200 mg/kg/day (approximately 3,300 times the topical ocular use in humans). The concentration of radio-labeled bepotastine besilate was similar in fetal liver and maternal blood plasma following a single 3 mg/kg oral dose. The concentration in other fetal tissues was one-third to one-tenth the concentration in maternal blood plasma.

An increase in stillborns and decreased growth and development were observed in pups born from rats given oral doses of 1,000 mg/kg/day during perinatal and lactation periods. There were no observed effects in rats treated with 100 mg/kg/day.

There are no adequate and well-controlled studies of bepotastine besilate in pregnant women. Because animal reproduction studies are not always predictive of human response, BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

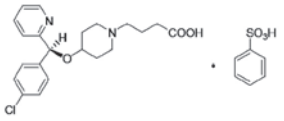
8.3 Nursing Mothers
Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 mcg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection limits. The milk concentration was higher than the maternal blood plasma concentration at each time of measurement.

It is not known if bepotastine besilate is excreted in human milk. Caution should be exercised when BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is administered to a nursing woman.

8.4 Pediatric Use
Safety and efficacy of BEPREVE (bepotastine besilate ophthalmic solution) 1.5% have not been established in pediatric patients under 2 years of age. Efficacy in pediatric patients under 10 years of age was extrapolated from clinical trials conducted in pediatric patients greater than 10 years of age and from adults.

8.5 Geriatric Use
No overall difference in safety or effectiveness has been observed between elderly and younger patients.

11 DESCRIPTION
BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is a sterile, topically administered drug for ophthalmic use. Each mL of BEPREVE contains 15 mg bepotastine besilate.
Bepotastine besilate is designated chemically as (+) -4-[[(S)-p-chloro-alpha -2-pyridylbenzyl]oxy]-1-piperidine butyric acid monobenzenesulfonate.
The chemical structure for bepotastine besilate is:



Bepotastine besilate is a white or pale yellowish crystalline powder. The molecular weight of bepotastine besilate is 547.06 daltons. BEPREVE® ophthalmic solution is supplied as a sterile, aqueous 1.5% solution, with a pH of 6.8.
The osmolality of BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is approximately 290 mOsm/kg.
Each mL of BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% contains:
Active: Bepotastine besilate 15 mg (equivalent to 10.7 mg bepotastine)
Preservative: benzalkonium chloride 0.005%
Inactives: monobasic sodium phosphate dihydrate, sodium chloride, sodium hydroxide to adjust pH, and water for injection, USP.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Bepotastine is a topically active, direct H_1-receptor antagonist and an inhibitor of the release of histamine from mast cells.

12.3 Pharmacokinetics
Absorption: The extent of systemic exposure to bepotastine following topical ophthalmic administration of bepotastine besilate 1% and 1.5% ophthalmic solutions was evaluated in 12 healthy adults. Following one drop of 1% or 1.5% bepotastine besilate ophthalmic solution to both eyes four times daily (QID) for seven days, bepotastine plasma concentrations peaked at approximately one to two hours post-instillation. Maximum plasma concentration for the 1% and 1.5% strengths were 5.1 ± 2.5 ng/mL and 7.3 ± 1.9 ng/mL, respectively. Plasma concentration at 24 hours post-instillation were below the quantifiable limit (2 ng/mL) in 11/12 subjects in the two dose groups.

Distribution: The extent of protein binding of bepotastine is approximately 55% and independent of bepotastine concentration.

Metabolism: *In vitro* metabolism studies with human liver microsomes demonstrated that bepotastine is minimally metabolized by CYP450 isozymes.

In vitro studies demonstrated that bepotastine besilate does not inhibit the metabolism of various cytochrome P450 substrate via inhibition of CYP3A4, CYP2C9, and CYP2C19. The effect of bepotastine besilate on the metabolism of substrates of CYP1A2, CYP2C8, CYP2D6 was not studied. Bepotastine besilate has a low potential for drug interaction via inhibition of CYP3A4, CYP2C9, and CYP2C19.

Excretion: The main route of elimination of bepotastine besilate is urinary excretion (with approximately 75-90% excreted unchanged in urine).

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis and Impairment of Fertility
Long-term dietary studies in mice and rats were conducted to evaluate the carcinogenic potential of bepotastine besilate. Bepotastine besilate did not significantly induce neoplasms in mice receiving a nominal dose of up to 200 mg/kg/day for 21 months or rats receiving a nominal dose of up to 97 mg/kg/day for 24 months. These dose levels represent systemic exposures approximating 350 and 200 times that achieved with human topical ocular use. The no observable adverse effect levels for bepotastine besilate based on nominal dose levels in carcinogenicity tests were 18.7 to 19.9 mg/kg/day in mice and 9.6 to 9.8 mg/kg/day in rats (representing exposure margins of approximately 60 and 20 times the systemic exposure anticipated for topical ocular use in humans).

There was no evidence of genotoxicity in the Ames test, in CHO cells (chromosome aberrations), in mouse hepatocytes (unscheduled DNA synthesis), or in the mouse micronucleus test.

When oral bepotastine was administered to male and female rats at doses up to 1,000 mg/kg/day, there was a slight reduction in fertility index and surviving fetuses. Infertility was not seen in rats given 200 mg/kg/day oral bepotastine besilate (approximately 3,300 times the systemic concentration anticipated for topical ocular use in humans).

14 CLINICAL STUDIES
Clinical efficacy was evaluated in 2 conjunctival allergen challenge (CAC) studies (237 patients). BEPREVE (bepotastine besilate ophthalmic solution) 1.5% was more effective than its vehicle for relieving ocular itching induced by an ocular allergen challenge, both at a CAC 15 minutes post-dosing and a CAC 8 hours post dosing of BEPREVE.

The safety of BEPREVE was evaluated in a randomized clinical study of 861 subjects over a period of 6 weeks.

16 HOW SUPPLIED/STORAGE AND HANDLING
BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% is supplied in a white low density polyethylene plastic squeeze bottle with a white controlled dropper tip and a white polypropylene cap in the following size:
5 mL (NDC 24208-629-02)
10 mL (NDC 24208-629-01)

STORAGE
Store at 15º – 25ºC (59º – 77ºF).

17 PATIENT COUNSELING INFORMATION
17.1 Topical Ophthalmic Use Only
For topical ophthalmic administration only.

17.2 Sterility of Dropper Tip
Patients should be advised to not touch dropper tip to any surface, as this may contaminate the contents.

17.3 Concomitant Use of Contact Lenses
Patients should be advised not to wear a contact lens if their eye is red. Patients should be advised that BEPREVE should not be used to treat contact lens-related irritation.

Patients should also be advised to remove contact lenses prior to instillation of BEPREVE. The preservative in BEPREVE, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of BEPREVE.

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Under license from:
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Osaka, Japan 541-0046

US/BEP/13/0028 4/13

Go for Whole Grain

Processed foods and refined grains comprise a large portion of the average North American's diet. These foods yield high glycemic indices and loads, meaning that they increase blood sugar levels significantly more than healthier, non-processed alternatives.

Whole grains contain more fiber and generally have a lower glycemic index than refined grains.[13] A diet rich in whole grains is associated with a reduced risk of type 2 diabetes, whereas high intake levels of processed foods are directly linked to an increased risk of diabetic disease.[14,15]

Thus, all patients should make an effort to replace refined grains with whole-grain foods. Despite the health benefits of whole grains, their caloric content often can be similar to that of refined grains—so it is important to be mindful of proper serving sizes.

Avoid Sugary Drinks

There is no real cordial way to address this point, but—Americans must stop drinking calorie-laden soft drinks! Soda, sweet tea, blended juice drinks and specialty coffees all contain large quantities of empty calories in the form of simple sugars. They have a high glycemic load and do not provide satiety, so people do not actually consume less food at their next meal.

Multiple studies have shown that women who drank at least one sugar-sweetened soft drink or fruit punch beverage per day were at an increased risk for developing type 2 diabetes.[16,17]

How Can We Help Motivate Our Patients?

Some of our patients know that excess weight gain is directly linked to poor systemic health. However, many of them do not know that high body weight can increase their risk for several serious ocular conditions.

The discussion of weight management often is difficult for optometrists to initiate during an eye exam. In most situations, an individual's body weight can be quite personal, and the practitioner may be fearful of being perceived as judgmental. In addition to this potential stigma, patients generally do not expect this conversation to occur in an eye care setting.

To be effective, you need to approach the patient in a culturally sensitive and age-appropriate manner. Counseling alone will not result in weight loss and lifestyle alteration.

Thus, the ultimate goal is to increase the individual's motivation and confidence. So, how can you achieve this?

Initiate the Conversation

Research shows that patients respond best to objective terms, such as "weight" and "BMI," rather than more pointed terms, such as "overweight" or "obese."

People often view such neutral phrasing as being the most motivating and least disparaging.[18,19]

Here is an example of how to initiate the conversation with your patient, including recommended questions from the American Medical Association:

- *"We define a healthy weight according to body mass index, or BMI, which is based on your height and weight. A healthy BMI is less than 25, overweight is between 25 and 30, and severely overweight is defined as a BMI greater than 30. Based on your height and weight your BMI is 'X.' This can affect the health of your eyes by increasing your risk for diabetic retinopathy and age-related macular degeneration."*

Once the patient is aware of the risks associated with an increased BMI, he or she will be more open to further discussing weight control. Asking permission shows respect and will help the patient feel more comfortable during the conversation.

Here's an example:

- *"I am concerned about your weight and the impact that it may have on your ocular health. I would like to discuss this relationship with you today—is that ok?"*

Recommended Serving Sizes[25]

Many nutrition and diet plans offer serving size suggestions that can be confusing. Serving sizes are important to ensure that patients achieve optimal health benefits from each food while not consuming excess calories. Here are our recommendations from "Eyefoods":

Food	Eyefoods Serving Size	Handy Tips
Raw, leafy green vegetables	One cup	One large handful
Other vegetables	1/2 cup	Size of a small lemon
Fruit	One medium fruit or 1/2 cup	Size of a small lemon
Fish and lean protein	100 grams	Size of a deck of cards
Nuts	16 grams	One small handful
Whole grains	1/2 cup of cooked or one thin slice of bread	Size of a small lemon
Oil	One tablespoon	Preferably olive or canola

Motivational Interviewing

It is important to keep the conversation going to achieve patient motivation. The Yale Rudd Center for Food Policy and Obesity encourages the use of motivational interviewing for improving diet, exercise levels and weight control. Its primary aim is to help empower patients to make their own decisions about behavioral modification. Here are some examples of questions that will help to motivate your patients to make positive lifestyle changes:[20]

- *"How ready do you feel to change your eating patterns and/or lifestyle behaviors?"*
- *"What kinds of things have you done in the past to change your eating habits?"*
- *"What types of physical activity do you enjoy?"*

It's a Team Effort

Once they are ready to make a change, patients will require additional support. Proper guidance is critical to ensure that they achieve healthy, long-term weight loss goals. With the abundance of fad diets and conflicting information on the Internet and television, how can we expect them to sort through it all and make realistic decisions?

The American Diabetes Association educates patients about the importance of their health care team. Consider referring your patients to a registered dietitian, certified diabetes educator and exercise physiologist.

The management of diabetes requires a collective effort, and active communication with the patient's primary care provider is essential for effective long-term care. And don't forget to remind your patients that they are the most important part of their own health care team!

It All Starts With Pediatrics

We need to empower, support and motivate the entire family to inspire children and teens toward a healthier future. But, how can we influence families to change behaviors when increased intake of high-calorie foods and reduced levels of physical activity is becoming the norm in contemporary America? Rather than handing them a prescription on how to achieve and maintain a healthy weight, we need to be more interactive and assume a role of motivator and counselor.[21-24]

Non-judgmental questions combined with attentive listening will help you uncover the beliefs and values of the patients and their parents. The following questions are examples that likely will not cause the individual to become defensive:

- To the child: *"Do you know your approximate weight and height? I am going to use this information to calculate your BMI."*
- To the parent: *"Your child's BMI is very high. It is important that she gains control of her weight before it becomes a bigger problem that also can affect her vision."*

Making a Change

Once the parents are aware of the medical and visual implications of excess weight gain and poor dietary/lifestyle habits, they will be motivated to help their children. The fundamental goal is to achieve permanent, long-term changes, which typically should involve lifestyle modifications for the entire family.

Be sure to reiterate that initial goals should be realistically achievable, and that changes should be made incrementally. Also, stress that even minimal weight loss can decrease diabetes rates in those who are at risk.[21-24]

Asking the parents open-ended questions will help initiate the conversation:

- *"Mrs. Smith, what changes have you made in your family's diet so far?"*

Motivating Children

Your office environment can play an important role in motivating your patients toward a healthier lifestyle. Run in-office and online contests. Start simple, for example, and challenge kids to eat five to 10 fruits and vegetables per day.

Then, instruct them to maintain a log for one month and submit it to your office to enter a prize drawing. Similar contests for at least one hour of physical activity per day also are effective.

Another great initiative is Let's Move, Michelle Obama's campaign designed to help curtail childhood obesity. The initiative's website (www.letsmove.gov) advises that all health care providers include a BMI screening as an aspect of patient care, actively prescribe increased levels of physical activity and healthy eating habits, and to become more involved as a leader in their local communities.

With appropriate education about the value of proper nutrition and lifestyle modification, you can help your patients achieve and maintain a healthy body weight. This, in turn, will help protect them against the onset of debilitating systemic and ocular disease.

Keep in mind that healthy dietary practices often transform into life-long habits. Therefore, the earlier you inspire younger patients to eat nutritiously and engage in regular physical activity, the less likely they will be to develop diabetic eye disease in the future. ■

Dr. Capogna is an active partner at Peninsula Vision Associates in Niagara Falls, Canada, and frequently lectures on nutrition and patient care.

Dr. Pelletier is a partner at IRIS in Welland, Ontario, where she practices primary care optometry and lectures about nutrition and eye health.

Together, they coauthored the top-selling books "Eyefoods: A Food Plan for Healthy Eyes" and "Eyefoods for Kids: A Tasty Guide to Nutrition and Eye Health," as well as developed the website www.eyefoods.com.

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Systemic Disease Report

Obesity Counseling is Within Our Scope

You can no longer afford to ignore the problem or simply hand it off to another clinician. Today, helping patients manage their body weight is one of our fundamental responsibilities. **By Kimberly K. Reed, OD**

Despite widespread awareness of the physical, financial and psychosocial consequences of poor dietary habits and low levels of physical activity, obesity rates among American adults remain alarmingly high.[1]

Currently, 35.7% of all adults living in the US are obese.[2] When adjusting for demographic variations, the highest obesity rates are observed in non-Hispanic black women (58.5%) and the lowest rates are observed in non-Hispanic white women (32.2%).[3]

In 2012, no state had an obesity incidence lower than 20%, as measured by body mass index (BMI).[1] Further, 13 states had an obesity incidence equal to or greater than 30%.[4] To put these figures into context—just 30 years ago, the highest incidence of adult obesity documented in any state's population was still lower than that recorded in the least obese state's population today.[5]

Suffice it to say that contemporary obesity rates in America simply aren't sustainable—either financially or medically.

There is a bit of good news, however. In August 2013, the CDC announced that in 18 states, obesity rates decreased among preschool children from low-income families when compared to 2012 figures.[4] Several states also have independently reported progress in reducing childhood obesity using a multifaceted approach of education, school lunch improvements and increased physical activity levels.[5]

It is also worth noting that since 2005, adult obesity rates have increased more slowly than they did during the two decades prior. In fact, from 2012 to 2013, only one state's obesity level increased (Arkansas), while all others remained unchanged.[5] So, it seems that comprehensive efforts aimed at curtailing obesity-related disease appear to be taking hold—albeit slowly.

But unless your patient base is overwhelmingly healthy, active, fit and young, chances are that obesity rates in your practice mirror those seen in the general US population. Be honest—how often do you discuss weight-related health complications with your patients? If you're like most optometrists, it probably isn't a standard component of your management plan. This approach must change, however, if we are ever going to have a reasonable chance of halting the obesity epidemic.

Obesity's Impact on the Eye and Body

During the last three decades, we've seen a proportionate increase in the incidence of obesity and potentially life-threatening systemic conditions, such as hypertension, carotid artery

For the reduction of IOP in patients with POAG or OHTN

When it's important to consider ocular and systemic side effects...

An alternate route to IOP reduction

- Effective at lowering IOP throughout the day and over the long term[1-3]
- Excellent systemic safety profile including no deleterious effects on CV or pulmonary function in clinical studies[1]
- Established ocular side effects profile: In clinical trials comparing RESCULA and timolol,* both were generally well tolerated regarding ocular adverse events, with similar incidence of hyperemia and similar changes to eyelash length and density[1,4,5]
  - 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]

Please see Brief Summary on reverse and full Prescribing Information, available from your Sucampo representative.

Rescula®
(Unoprostone isopropyl
ophthalmic solution) 0.15%

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.

Marketed by:

Sucampo Pharma Americas, LLC
Bethesda, MD 20814

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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disease, coronary heart disease and stroke, type 2 diabetes, sleep apnea and certain forms of cancer.[5] The association between excess body weight and the aforementioned systemic diseases is well established.

However, until only recently, the vast majority of care providers have not included excess body weight as a primary risk factor in the pathogenesis of several visually devastating ocular conditions. The American Optometric Association Practice Guidelines for Comprehensive Adult Eye and Vision Examination consider patients with diabetes and/or hypertension to be among those "at risk" for significant ocular complications. These patients should undergo a comprehensive evaluation annually, compared to every two years for healthy individuals.[2]

Here's a brief overview of several obesity-related conditions that yield both systemic and ocular complications:

• ***Hypertension.*** More than 75% of hypertension cases can be causally linked to obesity.[6] Hypertension frequently is associated with cardiovascular disease, heart failure, ischemic stroke, intracerebral hemorrhage and chronic kidney disease—primary contributors to morbidity and mortality in US adults.[7]

The American Heart Association's guidelines include a "caution" or "pre-hypertension" category, which is defined as a systolic blood pressure between 120mm Hg and 139mm Hg and/or diastolic pressure between 80mm Hg and 89mm Hg.[8] In recent years, patients in this category are more likely to be placed on antihypertensive therapy rather than instructed to modify their diets and increase exercise levels.[9]

Fortunately, the AHA offers an interactive tool on its website (www.heart.org) that educates patients about the various ways they can reduce their blood pressure via lifestyle modification. Patients can use the program to estimate how much lower their blood pressure would be if they lost five, 10 or even 20 pounds.

The most common ocular manifestations of hypertension include hypertensive retinopathy, retinal vascular occlusions, cranial nerve palsies and optic neuropathy.[10-12] Frequently, patients present with mild hypertensive retinopathy, which is characterized by arteriolar narrowing/constriction, arteriovenous nicking, or other vascular changes that are most evident at the locations of arteriole and venule crossing.[13,14]

Typical optometric management includes documentation in the patient's chart, proper education about the condition, and a recommendation to adhere to their primary care provider's prescribed treatment. In most cases, patients who exhibit these retinal findings also are overweight or obese. Therefore, to reduce the incidence of further disease progression, weight loss strategies must be addressed in the patient's comprehensive management plan.

• ***Diabetes.*** In the early 1990s, approximately 7.8 million Americans had an active diagnosis of diabetes. Today, that figure is approximately 25.8 million.[5] Nearly 40% of US adults currently are diabetic or pre-diabetic, and most of them don't even know it.[5]

Worse yet, by 2020, it is estimated that this figure will climb to 50%, yielding an enormous increase in health care spending to provide care for these patients.[15] So, early intervention for at-risk patients is essential.

There are clear optometric practice guidelines for the management of diabetic retinopathy, the most common retinal vascular cause of vision loss.[16] Clearly, overweight or obese individuals have a much greater likelihood of developing type 2 diabetes.

BMI and Waist Circumference

Body Mass Index, or BMI, is a simple ratio of height to weight. You can calculate BMI by dividing an individual's weight in kilograms by his or her height in meters squared. (Metric measurements not your thing? Don't worry—you can alternatively divide the individual's weight in pounds by his or her height in inches squared, and then multiply the result by a conversion factor of 703.) Additionally, several smartphone apps and online calculators will do the math for you (www.nhlbi.nih.gov/guidelines/obesity/BMI/bmicalc.htm).

Although Body Mass Index is widely used to determine whether patients are overweight (BMI between 25 and 30) or obese (BMI of 30 or greater), the tool has several drawbacks. For example, patients who have a high percentage of muscle mass and very little body fat cannot be evaluated effectively using conventional BMI calculations. Thus, despite excellent metabolic and health profiles, body builders and competitive athletes often would be erroneously classified as obese.

Waist circumference is an alternative method to determine a person's weight status. Measurements greater than 40 inches (102cm) for men and 35 inches (88cm) for women are associated with increased health risks. It is important to note, however, that waist circumference measurements offer no additional diagnostic benefit in patients with a BMI greater than 35.

The Socioeconomics of Obesity

- The costs associated with preventable chronic disease care related to obesity range from $147 billion to nearly $210 billion per year.[33]
- Job absenteeism related to obesity costs about $4.3 billion annually.[34]
- In 2012, more than 35% of adults who did not graduate high school were obese—compared to just 22.1% who graduated from college or a technical school.[5]
- Approximately 33% of adults who earn less than $15,000 a year are obese, compared with 25.4% of those who earn $50,000 or more per year.[5]
- If obesity trends were lowered by reducing the average adult BMI by just 5%, the cost savings would total $29.8 billion in five years, $158 billion in 10 years and $611.7 billion in 20 years.[5]
- On average, obese adults spend 42% more on health care costs than people of a healthy weight.[35]
- Obesity-related hospitalization for children and teenagers cost $125.9 million in 2001 and $237.6 million in 2005.[36]
- An investment of $10 per person in proven, community-based programs to increase physical activity, improve nutrition and prevent tobacco use could save the country more than $16 billion annually over a five-year period—a 560% return on investment.[37]

So, be sure to refer these patients to their primary care provider for evaluation if a year or more has passed since their last physical examination. Also, be especially diligent when examining obese patients for early signs of diabetic eye disease.

• ***Other common conditions.*** Approximately one-third of all cancer deaths are linked to either obesity or a lack of physical activity.[17] And while these cancers aren't always detected as primary ocular tumors, it is still important to inform patients that being overweight or obese can increase their risk for several types of cancer.

Sleep apnea is strongly associated with obesity, especially when the diagnosis is made via measurement of waist and neck circumference.[18,19] Sleep apnea can contribute to several ocular conditions, including glaucoma and keratoconus.

Continuous Positive Airway Pressure (CPAP) is the mainstay of therapy for patients with sleep apnea; however, weight reduction is far more effective at preventing long-term systemic and ocular complications.[18]

Obesity is now recognized as an independent risk factor for age-related macular degeneration.[20,21] Dietary modification can be highly protective against the development and progression of early AMD. At-risk patients should be encouraged to increase their daily intake of leafy greens and brightly colored vegetables (e.g., orange peppers), which are rich in lutein and zeaxanthin.

Additionally, obese patients should be encouraged to lose excess weight through increased physical activity and low-glycemic diets to further protect against AMD. Just keep in mind that nutritional supplementation alone, without comprehensive dietary modification, will not provide optimal protection against macular degeneration.[20,21]

The Psychosocial Impact of Obesity

In America, thinner people frequently stigmatize overweight people. It occurs on television shows, in magazine articles and in day-to-day life. Teachers, college admissions counselors, employers, nutritionists, and even doctors and nurses may ascribe negative attributes to obese people based solely upon their weight.[22-26] Associated stereotypes are prevalent, and overweight and obese individuals often are characterized as lazy, unsuccessful, undisciplined and willless.[27]

The misguided perception that shaming obese people could perhaps motivate them to lose weight secondary to guilt is unsupported. To the contrary, research suggests that such callous regard for overweight individuals poses serious health risks, creates social anxiety, and interferes with more effective efforts to reduce or prevent obesity.[28] Youths who are teased about their weight are more likely to engage in variety of unhealthy behaviors, including binge eating, anorexia or purging.[29,30]

To date, wide-scale public health efforts have been largely successful in curtailing escalating obesity rates in America. Both lay people and health care professionals alike still believe that the condition of obesity is an issue of personal control.[27]

And while dietary choices and lifestyle habits certainly are a primary cause of obesity, the complex and intricate genetic, endocrine, psychological and behavioral drivers for food intake and energy regulation are not completely understood.

Much like patients with an opioid dependency, many people who struggle with obesity exhibit an uncontrollable attraction to food.[31,32] In both instances of addiction, the same areas of the brain are stimulated by similar chemical substances.[31,32] Thus, the



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prevalent belief that overeating is entirely the result of reduced willpower is unsubstantiated. This erroneous generalization impairs obesity intervention efforts and reduces access to quality care, which can create additional psychological stress on the patient.[27]

Connect With Your Patients

Specific, practical and interactive resources are essential when discussing the relationship between obesity and health complications with your patients. Conduct a comprehensive search in your practice area for registered dieticians or other reputable nutrition and wellness coaches. You may find that your community—on a local, county or state level—already has obesity-counseling resources in place.

For example, community centers often offer cooking instruction and exercise classes for those interested in weight loss. Also, walking clubs frequently can be found at indoor shopping malls.

Further, a number of excellent websites are available to provide useful tools and other information regarding healthy weight control strategies, nutritional guidelines and diabetes management. Some of the most helpful sites include:

- www.Heart.org/HEARTORG/Conditions/HighBloodPressure
- www.cdc.gov/healthyweight/index.html
- www.diabetes.org

Obesity Management for Kids and Teens

Considering all of the factors involved, children and teenagers currently are in the best position to slow or even reverse the escalating obesity rate in America. As primary health care providers, optometrists can contribute to these efforts using a sensitive, supportive approach with overweight and obese pediatric patients and their parents.

Several resources are available to help calculate pediatric BMIs (up to age 19)—including the CDC's calculation tool, www.cdc.gov/healthyweight/children. Additionally, this website offers an excellent, printable resource for parents to help their children reach and maintain a healthy weight. Similar information is presented at www.patient.co.uk/health/obesity-and-overweight-in-children, along with a variety of interactive resources from the UK.

Affiliated with the Let's Move initiative, www.healthykidshealthyfuture.org offers free online training, presentations and interactive quizzes for children, parents and health care providers. These materials are designed to emphasize the fundamental importance of healthier lifestyle decisions starting in infancy.

Another useful assessment tool for parents can be found at www.webcalcsolutions.com/Parenting-Assessments/child-obesity-risk. Here, visitors can find a simple, eight-question quiz that's designed to help determine a child's risk of becoming overweight.

Many of the aforementioned websites offer printable brochures and wall charts designed for pediatric education and often include literature on associated lifestyle considerations, such as proper hydration, tobacco avoidance, exercise routines and good sleep habits.

Historically, optometrists largely have been passive observers in the fight against obesity-related disease. Going forward, however, it is imperative that we educate ourselves about the potential ocular and systemic ramifications of obesity, as well as develop the skills necessary to help create effective, individualized management plans for our patients. But, in order to do so, we must first disengage from the outdated notion that weight management is not within our scope of care. ■

Dr. Reed is an associate professor at Nova Southeastern University College of Optometry in Fort Lauderdale, Fla., where she teaches ocular disease, ocular pharmacology and nutrition, and primary clinical care.

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What are the Ocular Manifestations of Hep B?

Eye care professionals may play a role in both the diagnosis and management of a number of conditions secondary to HBV. **By Denh Tuyen, OD, and Andrew S. Gurwood, OD**

Hepatitis B virus (HBV) is the most common cause of liver cancer in the world.[1] Currently, of the two billion people infected with HBV worldwide, 600,000 deaths are anticipated to result annually—either secondary to HBV complications or hepatocellular carcinoma.[2]

Its modes of transmission include sexual contact, needle sharing, blood transfusion and transplacental passage from mother to neonate.[3] Acute HBV infection is associated with general malaise, fever, loss of appetite, vomiting and jaundice.[3] Fulminant presentation of infection involves liver failure accompanied by tissue necrosis.[3] The virus is able to inject itself into the host cell to replicate with a resulting immunological response, causing hepatocellular injury.[4-6] Common ocular sequellae include ischemic retinopathy, pupil sparing third nerve palsy, optic neuritis and uveitis.[7-11]

Pertinent Anatomy

Hepatitis B is a DNA virus.[12] It is comprised of hepatitis B core antigen (HBcAg), hepatitis B e-antigen (HBeAg), DNA polymerase and double-stranded DNA.[13] The entire content of HBV is encapsulated by an envelope that houses the hepatitis B surface antigen (HBsAg).[11]

Viruses are obligate intracellular parasites—they rely solely on host machinery for replication. Viral tropism refers to the ability of viruses to infect specific cells. When the virus latches onto the host cell, it integrates into the cytoplasm in one of three ways: direct translocation, endocytosis or viral fusion to cell membrane.[14] Once inside the cell, viruses start replicating with the help of host enzymes. The newly synthesized viral genome and capsid proteins are assembled into virions, either in the nucleus or cytoplasm, which are then released by budding through the plasma membrane.[14]

Epidemiology

Of the two billion living people who contracted the virus, approximately 400 million still actively suffer from chronic HBV.[15-17] The virus is hyperendemic in regions such as Sub-Saharan Africa, Southeast Asia, China and the West Pacific.[13,18]

Pathogenesis

HBV mainly infects hepatocytes. The virus enters the body following an exposure to the virus particle through either infected blood or bodily fluids. The hepatocyte uncoats itself and transforms into a covalently closed circular form of DNA (cccDNA).[13]

Viral detection by the host

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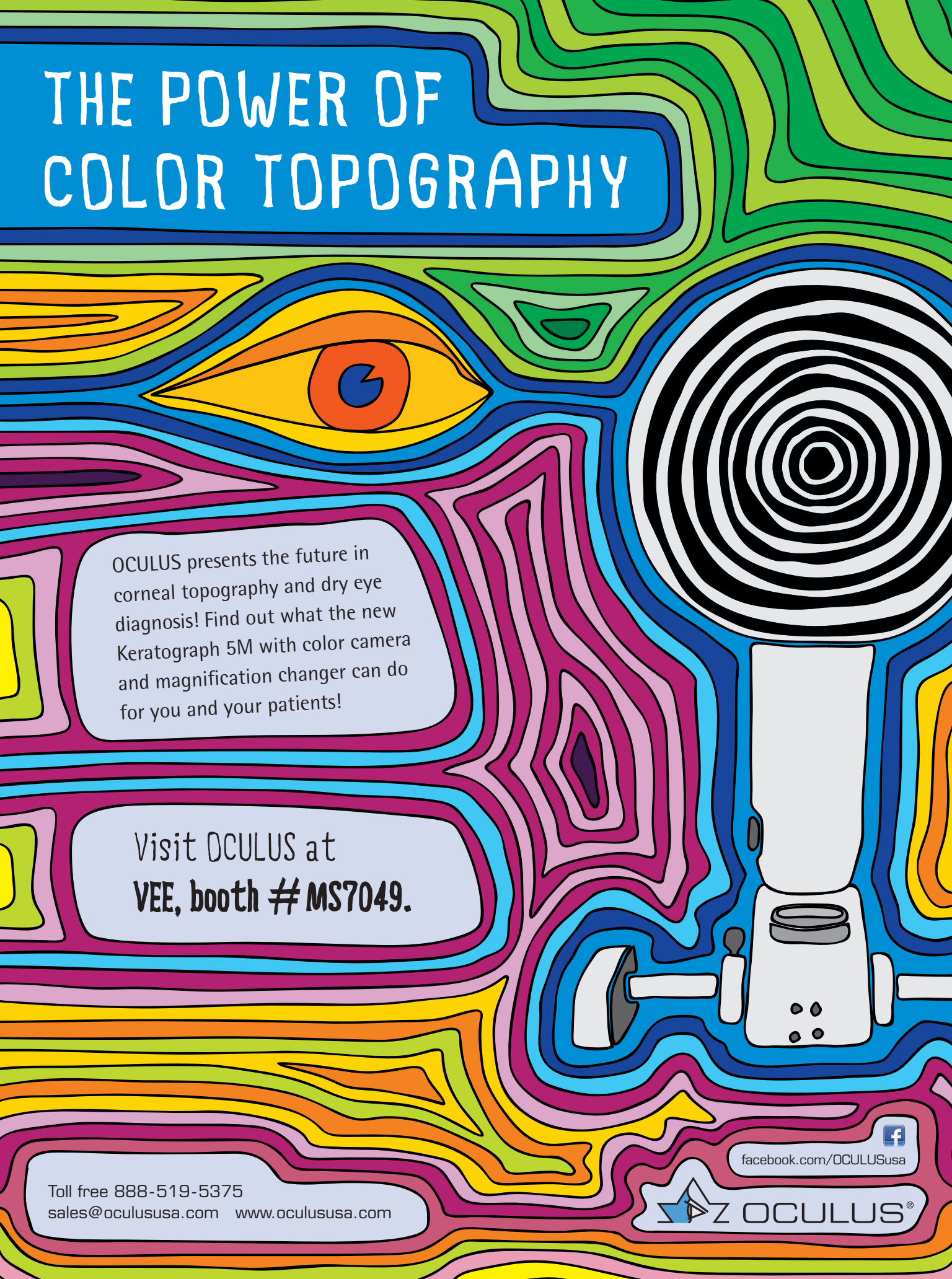

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activates CD8+ T lymphocytes, which directly destroy the infected hepatocyte by apoptosis.[4,5] CD4+ T lymphocytes are also key members of the immune response. They also secrete lymphokines to prompt the activity of B cells, making specific antibodies to fight against foreign antigen, and to amplify the activities of CD8+ T lymphocytes.[4,5]

Lastly, CD8+ cells release cytokines, such as interferon gamma, which summon macrophages. The massive macrophage response then leads to liver damage.[4,5] HBV is not directly cytopathic; instead, it induces an immune reaction that leads to liver injury.[13]

Initially, there is a marked increase in HBsAg and HBcAg upon infection.[14] Once the body detects foreign antigens, antibodies such as immunoglobulin (IgG and IgM) are produced to fight the infection. HBeAg can be detected when viral activity peaks. The infection stage concludes when HBeAg antibodies are formed.[18]

Chronic infection is defined by the presence of HBsAg in the serum for a period lasting longer than six months.[18] During the chronic phase, IgG is still produced to fight the infection—even while the immunity is taxed. In this stage, remaining hepatocyte cells continually divide, and increase the risk for hepatic carcinoma.[6]

Finally, circulating antigen-antibody complexes have the potential to cause further complications by producing vasculitis, glomerulonephritis and cryogloblinemia.[10,19] Ocular manifestations of HBV are the result of these circulating immune complexes, and include various degrees of retinal ischemia, which provoke vasculitis (artery occlusion, vein occlusion, cotton wool spots), pupil sparing third nerve palsy, optic neuritis and uveitis.[7-11]

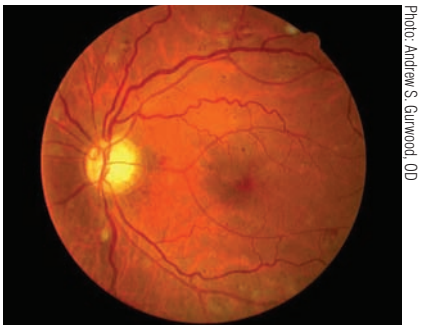

Photo: Andrew S. Gurwood, OD

Optic neuropathy is a potential side effect of interferon use.

Circulating antigen-antibody complexes have the potential to cause further complications by producing vasculitis, glomerulonephritis and cryogloblinemia.[10,19]

Systemic Symptoms

Systemic manifestations of HBV infection during the acute phase of the disease include nausea, vomiting, diarrhea, abdominal discomfort, decreased appetite, fatigue, fever, myalgia, dark urine, and yellowing of the skin and eyes (jaundice).[20,21]

Ocular Manifestations of Infection

• ***Retinal vasculitis.*** The term vasculitis refers to the pathologic inflammation of blood vessels resulting from a buildup of cellular debris secondary to foreign invasion by either virus or bacteria. Retinal vasculitis can be induced by the accumulation of intraretinal inflammatory debris secondary to circulating HBV infection, and the upregulation of cellular elements to eliminate it from the body.[22]

One study indicated that vasculitis was related to an abundance of circulating HBsAg immune complex—namely HBsAg bound to IgM.[22] As retinal vasculitis evolves, blood vessel walls become inflamed, reducing blood flow to tissues. Subsequently, there is a disruption in nutrient and oxygen distribution to affected tissues, giving rise to the classic axonal stasis observed as the cotton wool spot.[23]

Another study determined that hepatitis C virus (HCV) similarly had the potential to induce vasculitis and ischemic retinopathy.[7] A separate research group completed a clinical trial of 85 patients and observed that 51% of individuals with HCV exhibited bilateral ischemic retinopathy.[24] The clinical features of ischemic retinopathy included cotton wool spots (CWS) and retinal hemorrhages.[23] Through their research, they confirmed that the ocular sign of CWS denotes significant ischemia in the affected region. It also provides a palpable sign, indicating ischemic processes are proceeding in the body at large.[7,23,24]

Herpetic retinal vasculitis (acute retinal necrosis [ARN] and progressive outer retinal necrosis [PORN]) and collagen vascular diseases (CVD) share similar presentations.[24] Both of these conditions cause hypoxia secondary to accumulation of inflammatory debris, which impedes retinal

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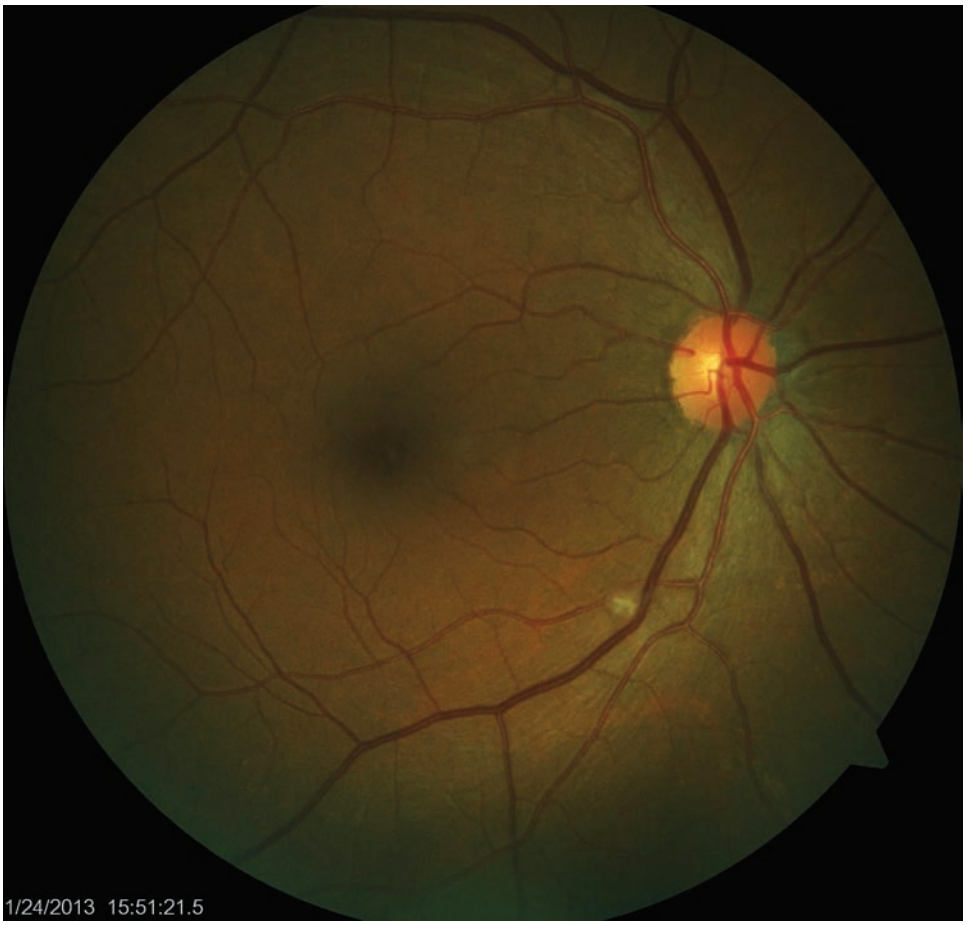
perfusion.[23,24] Examples of CVD include systemic lupus erthromatosis, Beçhet's disease, rheumatoid arthritis, sarcoidosis, Sjögren's syndrome and Reiter's syndrome. Other conditions, such as anemia, giant cell arteritis, antiplatelet antibody syndrome, diabetes and hypertension, also are capable of such vasculopathy.[23]

• ***Pupil-sparing third nerve palsy.*** A literature review uncovered one case in which a 36-year-old man presented with an acute, pupil-sparing third nerve palsy.[8] Evidence of jaundice and darker urine prompted the clinical investigators to perform enzyme linked immuno-assay (ELISA) testing, which uncovered the presence of HBsAg and IgM. The publication concluded that the deposition of circulating immune complexes produced ischemic infarction of the third nerve.[8]

• ***Optic neuritis and uveitis.*** Both optic neuritis and general uveitis have also been observed as consequences of HBV infection.[8,10,11,26] A study conducted in Switzerland indicated that 13% of uveitis cases may, in part, be attributed to HBV infection—with evidence of HBsAg circulating within affected individuals' bloodstreams.[11,26] It is theorized that persistent HBsAg and HBcAg in the system leads to constant production of antibodies, resulting in antigen-antibody complex formation, activating the inflammatory system, and eventually causing tissue destruction.[27] Moorfields Eye Hospital in London has supported the potential for HBV-based uveitis.[11]



Examination of this patient revealed an isolated cotton wool spot. Upon subsequent lab testing, it was confirmed that this patient had hepatits B.

Work-Up

ELISA testing is essential for detecting circulating hepatitis viral proteins—specifically HBsAg, HBeAg and HBeAg antibodies.[18] It is worth noting that the presence of HBsAg in the blood serum for more than six months is an indication of chronicity.[18]

A complete blood count with platelets is also useful for detecting other concurrent systemic diseases. Additionally, prothrombin time (PT) is helpful to assess the coagulability of the blood, and may indicate liver damage.[28]

Liver function tests (LFT) are useful to determine the extent of liver damage.[29] The battery of liver function tests include alanine transaminase (ALT), aspartate transaminase (AST), alkaline phosphatase (ALP), albumin, total proteins, bilirubin, gamma-glutamyltransferase (GGT) and L-lactate dehydrogenase (LD).[29] A number of results may be indicative of liver damage, including:[28]

- Elevated ALT, AST, ALP, bilirubin, GGT and LD.
- Reduced albumin and total protein levels.

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PROVEN EFFICACY AND ESTABLISHED SAFETY[1,2,7]

Indications and Usage

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

Important Risk Information about LOTEMAX® GEL

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

Please see brief summary of full prescribing information on adjacent page.

References: 1. LOTEMAX GEL Prescribing Information, September 2012. **2.** Fong R, Leitritz M, Siou-Mermet R, Erb T. Loteprednol etabonate gel 0.5% for postoperative pain and inflammation after cataract surgery: results of a multicenter trial. *Clin Ophthalmol.* 2012;6:1113-1124. **3.** Shaikh R, Singh TRR, Garland MJ, Woolfson AD, Donnelly RF. Mucoadhesive drug delivery systems. *J Pharm Bioallied Sci.* 2011;3(1):89-100. **4.** Data on file, Bausch & Lomb Incorporated. **5.** Coffey MJ, Davio SR. Viscoelastic and sedimentation characterization of loteprednol etabonate ophthalmic gel, 0.5%. Poster presented at: Association for Research in Vision and Ophthalmology (ARVO); May 6-10, 2012; Fort Lauderdale, FL. Poster #6283/D1143. **6.** Lotemax Prescribing Information, April 2006. **7.** Rajpal RK, Roel I, Siou-Mermet R, Erb T. Efficacy and safety of loteprednol etabonate 0.5% gel in the treatment of ocular inflammation and pain after cataract surgery. *J Cataract Refract Surg.* 2013;39:158-167.

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Brief Summary: Based on full prescribing information.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb at 1-800-323-0000 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

INDICATIONS AND USAGE

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

DOSAGE AND ADMINISTRATION

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

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

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Intraocular Pressure (IOP) Increase

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

Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

Delayed Healing

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

Bacterial Infections

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

Viral Infections

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

Fungal Infections

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

Contact Lens Wear

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

ADVERSE REACTIONS

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

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

USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic Effects: Pregnancy Category C.

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

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

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

Nursing Mothers

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

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment Of Fertility

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

PATIENT COUNSELING INFORMATION

Administration

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

Risk of Contamination

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

Contact Lens Wear

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

Risk of Secondary Infection

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

FOR MORE DETAILED INFORMATION, PLEASE READ THE PRESCRIBING INFORMATION.

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- Prolonged PT, indicating clotting problems.

In the case of optic neuritis and uveitis secondary to immune complex deposition, be sure to test for:[30]

- Titrated levels of IgG, IgA, IgM, C3 and C4 on commercial plates.
- Complement haemolytic activity (CH50).
- C1q binding (C1qBA) and conglutinin binding competition (KgB-CA, CIC) assay.[30] Raised levels of C1qBA and CIC point to an immune complex etiology, which, as mentioned earlier, also is associated with systemic diseases such as vasculitis, arthritis and glomerulonephritis.[30]

If vasculitis is observed, additional tests, such as erythrocyte sedimentation rate (ESR), c-reactive protein (CRP), urine tests, imaging (X-ray, CT and MRI) of larger vessels, angiogram and biopsy, should be ordered.[31]

Treatment for HBV

• ***Interferon therapy is administered subcutaneously.*** It modifies the HBV specific response and reduces viral replication.[13,14] Interferon is a cytokine released by CD8+ T lymphocytes, which recruits macrophages to the site of the insult.[15] Recent clinical trials have indicated that the pegulated form of interferon is the most efficacious.[13] The addition of polyetheylene glycol (PEG) to interferon increases the preparation's half-life and duration of activity.[14] Pegulated interferon is administered weekly for up to 48 weeks.

Side effects include headache, myalgia, alopecia and fatigue.[14] The most common ocular complication associated with interferon therapy is retinal ischemia, which is characterized by CWS, microvascular abnormalities and hemorrhages.[32-34]

Patients placed on the medication should be monitored for fundus changes, visual field abnormalities and retinal nerve fiber layer (RNFL) thickness alterations every three to four months following dosing initiation.[33] Increased RNFL thickness warrants close observation, and any patient who manifests CWS should cease therapy immediaely.[34]

Other, less common conditions associated with interferon use include subconjunctival hemorrhage, retinal detachment, optic neuropathy and elevated intraocular pressure.[29,30,35] Ocular signs typically present from two weeks to six months following therapy initation.[29]

• ***Nucleotide analogs reduce HBV replication by mimicking and inserting themselves as a base upon the viral DNA, effectively halting HBV replication.***[13,14] In comparison to interferon, these agents are administered orally. Current analogs substantially reduce the amount of HBV DNA, but have not demonstrated the ability to completely eradicate the virus.

This catagorizes the medication as a drug for maintaining viral suppression.[13]

Lamivudine is an effective drug for patients with cirrhosis and recurrent hepatitis after liver transplant.[17] The main disadvantage of the medication is viral resistance. Entecavir can be used as an alternative when resistance to lamivudine is detected.[17]

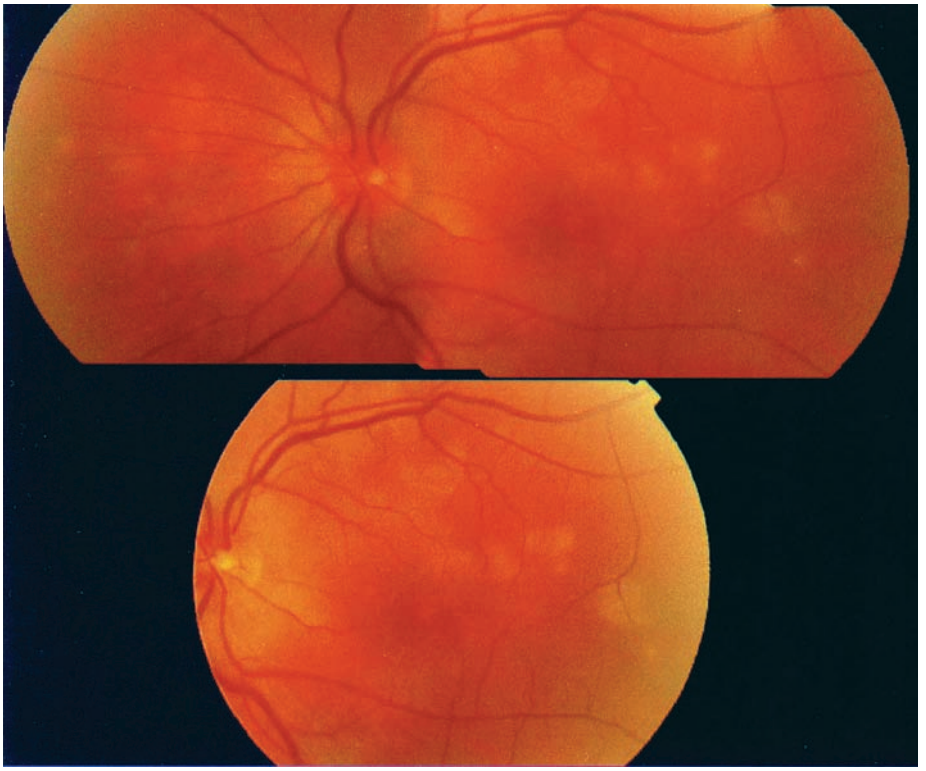
• ***Vaccination has dramatically reduced the prevalence of HBV around the globe.***[13] The vaccination is an effective agent that is safe for administration at birth.[2] The modality can be used prophylactically to prevent perinatal transmission and has been shown to be 89% to 98% effective.[2] Data has shown a large decline in the rate of chronic disease occurrence in the children of Taiwan over a 10-year period (9.8% to 1.3%) following the inception of a successful HBV vaccination program.[13]

Data has shown a large decline in the rate of chronic disease occurrence in the children of Taiwan over a 10-year period (9.8% to 1.3%) following the inception of a successful HBV vaccination program.[13]

The HBV vaccine is comprised of purified HBsAg and is produced via recombinant DNA technology, and typically is administered in three doses.[19] It is is the most widely used vaccine in the world, and is now being considered as the standard of care in the United States.[2] Furthermore, the World Health Organization (WHO) is also pushing for vaccination in hyperendemic areas.[13]

Hepatitis vaccination is not free from potential side effects. There have been a total of 32 uveitis cases resulting from use of the hepatitis B vaccination.[2]

Photo: Gregory D. Foley, OD



This fundus photo demonstrates the active phase of MEWDS, which is typically seen within 24 hours following hepatitis vaccination.

Episodes of acute uveitis relating to immune complex sequellae also have been documented.[36,37]

Many reports of uveitis relating to HBV have been published between 1982 and 2009 from databases like the National Registry of Drug-Induced Ocular Side Effects, The World Health Organization and the FDA.[2] Uveitis is often seen after the first vaccination, and typically the manifestation ensues at day three or later.[2] Recurrence of uveitis after the second and third vaccinations are rare.[2] The ocular treatment for cases of uveitis from this source are standard (cycloplegia and topical steroidal anti-inflammatory drops), with patients typically responding well to the intervention.

Posterior uveitis also has been reported—specifically multiple evanescent white dot syndrome (MEWDS).[34] The condition typically is seen within a window of 24 hours following vaccination.[36] This clinical presentation may be associated with increased levels of IgG and IgM.[34] The ocular treatments for cases of MEWDS from this source are also standard (cycloplegia and topical anti-inflammatory drops), with patients responding well to the intervention.[34]

Other ophthalmological symptoms, such as disc edema, central vein occlusion and optic neuritis, may be seen after vaccination.[34]

HBV infection is the leading cause of liver cancer around the globe. It is hyperendemic, especially in densely populated areas such as Africa, Southeast Asia, China and the West Pacific. The formation of immune complexes due to viral insult can be catastrophic to ocular health, and can result in debilitating diseases, such as vasculitis induced retinal ischemia, optic neuritis, uveitis and pupil sparing third nerve palsy.

Eye care professionals have the potential to play a key role in the diagnosis and management of HBV as well as in its monitoring after treatment by detecting ocular signs such as isolated cotton wool spots and/or retinal hemorrhages. In cases exhibiting these signs where the etiology is unexplained, prompt investigation of the underlying cause through laboratory testing is required. When patients are managed preemptively by vaccination, or currently by medications, close monitoring is warranted, due to risk of ocular complications. The team approach between the eye care professional and the general practitioner is crucial when managing HBV. ■

Dr. Tuyen is on staff at Eye Physicians and Surgeons and is currently a clinical consultant at The Eye Institute. Dr. Gurwood is a professor at Salus University in Elkins Park, Pa.

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Systemic Disease Report

PEER • REVIEWED • PRA • ARTICLE •

Medical Syndromes That Affect Children's Vision

These conditions aren't ordinary—nor should be your evaluation and treatment of these children. **By Marie Bodack, OD**

Most pediatric patients present with problems such as blurred vision, an eye turn or reading difficulties. However, like adults, children may suffer from systemic conditions that affect their vision and ocular health.

In some cases, the child and the parents are aware of the medical condition and are seeking an evaluation for related ocular findings. In other cases, the family is aware of the condition, but is unaware that it can affect the eyes.

And then there are those cases in which the child and family are unaware of the condition, and your exam uncovers an ocular anomaly that leads to the systemic diagnosis.

This article reviews some of the most notable medical conditions with ocular findings that can affect children: Marfan's syndrome, Ehlers-Danlos syndrome, pseudoxanthoma elasticum, osteogenesis imperfecta, Down syndrome and juvenile idiopathic arthritis.

Marfan's Syndrome

• ***Prevalence/characteristics.*** Marfan's syndrome is an autosomal dominant, multisystem, connective tissue disorder with a prevalence of one in 5,000.[1] Patients with Marfan's have a mutation in the FBN-1 gene, located on chromosome 15. FBN-1 encodes for fibrillin-1, a protein involved with the elasticity of connective tissue.[2] Mutations can manifest as severe and fatal neonatal cases, or more minor cases with isolated conditions, such as ectopia lentis (displaced crystalline lens).[3]

• ***Systemic findings.*** Due to a change in the elasticity of connective tissue, patients with Marfan's syndrome have a range of skeletal, cardiac and ocular anomalies. Patients with a "typical" Marfan's appearance are tall and thin with long arms, legs and fingers. They may be very flexible and have stretch marks on their skin without a history of weight loss.[1] Scoliosis (abnormal curvature of the spine) and flat feet (pes planus) may be present. The breastbone is sunken into the chest (pectus excavatum) in some individuals, while it protrudes out (pectus carinatum) in others.

The most serious and potentially fatal complications of Marfan's are cardiac, including aortic root dilation, mitral valve prolapse and aortic dissection or aneurysm formation.[2]

In an effort to help differentiate Marfan's syndrome from other systemic conditions (including familial aortic dilation and/or dissection,

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Goal Statement: Children, like adults, may suffer from systemic conditions that affect their vision and ocular health. This course reviews some of the most notable medical conditions with ocular findings that can affect children. Optometrists can not only manage these patients for ocular problems, but may be the first to recognize a serious condition that leads to an important, possibly lifesaving diagnosis.
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Case Study on Marfan's Syndrome

A 12-year-old male presented for an eye exam for an updated eyeglass prescription. His current Rx was -11.00-1.00x180 OD 20/40, -4.00 sphere OS 20/20. Refraction was stable. No strabismus was present. A dilated exam revealed a lens subluxation superotemporally OD. Fundus evaluation revealed no holes, tears or retinal detachments. Intraocular pressure measured 17mm Hg OD and 18mm Hg OS.

On observation, he appeared tall for his age.

We suspected Marfan's based on the subluxated lens, high myopia and physical appearance. We contacted the patient's pediatrician, who referred the patient to a cardiologist.

The patient returned for a follow-up exam and his guardian reported that the cardiologist said that the child was healthy and "did not answer any questions about Marfan's." The guardian also reported that she had "read up on Marfan's" and mentioned that the patient has flat feet. She requested a second opinion, so we referred him to a pediatric cardiologist in a Marfan's clinic. The results of the evaluation and genetic testing confirmed our suspicion that the patient had Marfan's syndrome. Fortunately, he did not have any cardiac anomalies.

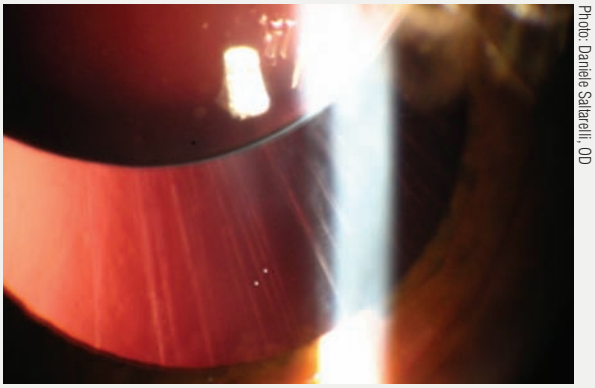


Photo: Daniele Saltarelli, OD

Subluxed lens in another patient with Marfan's syndrome.

We fit the patient with contact lenses, which improved visual acuity to 20/30 OD and 20/20 OS. He also wears protective plano polycarbonate lenses. We educated him on the symptoms of a retinal detachment and lens displacement and told to call as soon as possible if he notices decreased vision, flashes or floaters. Also, we (and the cardiologist) advised him to avoid contact sports. He will follow up with cardiology and optometry annually.

Klinefelter syndrome or homocystinuria), the diagnostic criteria for Marfan's were recently revised to place more emphasis on the cardiac and ocular findings.[4] The current criteria include a family history of Marfan's syndrome, systemic features, genetic testing, and the presence or absence of ectopia lentis and/or cardiac anomalies.

In patients with a positive family history, a diagnosis of Marfan's is confirmed if the individual develops ectopia lentis. If ectopia lentis is not present, evaluation looks next at systemic features, then at the presence or absence of aortic dilation or dissection, and finally, genetic testing.

A variety of systemic findings are assigned a "point value," according to the Marfan's diagnostic criteria. A certain number of points indicates a diagnosis of Marfan's.[5] For example, scoliosis, pes planus and myopia of ≥3.00D each equate to one point. A total score of seven points, along with a positive family history or aortic dilation and/or dissection, confirms the diagnosis of Marfan's.

• ***Ocular findings.*** The most common ocular anomaly in Marfan's is ectopia lentis, affecting approximately 60% of patients.[6] The lens is most commonly subluxed upward, although any direction is possible. In cases of ectopia lentis, the zonules are thinner, fewer in number, irregular in diameter, and have an abnormal attachment to the lens capsule.[7] In some patients, subluxation is slowly progressive, being noted in the first few years of life, or in the late teens to early twenties. However, in the majority of patients, progression of lens displacement is uncommon.[8]

Other ocular findings in patients with Marfan's syndrome include high myopia, cataract, strabismus, glaucoma and retinal detachment.[1,8] Specifically, exotropia has been reported in up to 10% to 19% of patients with Marfan's, while esotropia has been found in approximately 2% of patients.[9] One study of 573 patients with Marfan's found that 5% had glaucoma.[10]

In patients with suspected or confirmed Marfan's syndrome, perform a dilated exam to look specifically for ectopia lentis, retinal detachments, cataracts and glaucoma. In those with ectopia lentis but without a diagnosis of Marfan's, refer the patient to his or her pediatrician or a cardiologist for additional testing. Biomicroscopic evaluation of patients with ectopia lentis should include observing the crystalline lens in multiple positions of gaze to check for movement, which indicates instability.

• ***Treatment/management.*** Treatment for ectopia lentis can include annual monitoring. If the patient is young, or if it is the first time a practitioner is seeing the patient, a dilated exam at six months to monitor for changes to the subluxation may be warranted. In cases when the subluxation is severe (i.e., causing decreased best-corrected vision or at risk for total subluxation), consider referral to a cataract surgeon who has experience with Marfan's patients. Surgical lensectomies are not routinely performed, as the

Types of Ehlers-Danlos Syndrome[11,14]

Type	Prior Type	Major Criteria	Minor Criteria	Inheritance
Hypermobility	III	Joint hypermobility Skin hyperextensibility and/or smooth, velvety feel	Frequent joint dislocations, chronic pain, family history	AD
Classic	I, II	Skin hyperextensibility Atrophic scars Joint hypermobility	Easy bruising, velvety feel to the skin, muscle hypotonia, molluscoid pseudo-tumors (fleshy skin lesions with scars), family history	AD
Vascular	IV	Frequent bruising Thin, translucent skin Characteristic facial appearance Arterial/uterine/intestinal fragility or rupture	Small joint hypermobility, tendon/muscle rupture, early onset varicose veins, easy bruising, pneumothorax, family history	AD
Kyphoscoliotic	VI-A	Joint laxity Severe muscle hypotonia at birth Progressive scoliosis at birth Scleral fragility	Easy bruising, arterial rupture, microcornea, family history	AR
Arthrochalasia	VII-A/B	Joint hypermobility with subluxations Congenital bilateral hip dislocation	Skin hyperextensibility, easy bruising, muscle hypotonia, kyphoscoliosis	AD
Dermatosparaxis	VII-C	Severe skin fragility Sagging in skin	Easy bruising, soft skin	AR
Brittle cornea syndrome*	VI-B	Thin cornea Ocular fragility Blue sclera Keratoconus	Skin and joint hypermobility	AR

AD = autosomal dominant
AR = autosomal recessive
* No longer considered a sub-group of EDS, but included for completeness.

risk of retinal detachments has approached 25% in these patients.[8] A careful refraction is important in these patients because the vision may be reduced or fluctuate, as in cases of subluxation. Additionally, patients with ectopia lentis should use safety glasses and be instructed to refrain from contact sports due to risk of lens migration into the vitreous or anterior chamber.

Ehlers-Danlos Syndrome

• ***Prevalence/characteristics.*** Ehlers-Danlos syndrome (EDS) refers to a group of genetic disorders that affect collagen and extracellular matrix synthesis and structure.[11-13] (*See "Types of Ehlers-Danlos Syndrome," above.*) The estimated prevalence is one in 5,000.[14] Inheritance can be autosomal dominant (AD), autosomal recessive (AR) or X-linked.

Historically, subtypes were classified numerically, so older textbooks may use terms such as "EDS-I" or "EDS-VI." Currently, the preferred classification is descriptive of major and minor diagnostic criteria, such as "classic," "vascular" or "kyphoscoliotic" (abnormal curvature of the spine).

• ***Systemic findings.*** Clinically, patients with EDS bruise easily, have skin hyperextensibility, joint hypermobility and poorly localized pain to varying degrees.[11] The most serious form of the condition is the vascular type, and the most severe complication is spontaneous arterial or organ rupture, which can result in death. Symptoms of spontaneous arterial or organ rupture include chest or abdominal pain, or altered mental status.[11]

Diagnosis of EDS is based on a physical examination and may include collagen typing from a skin biopsy, genetic testing and an echocardiogram.[11,12]

• ***Ocular findings.*** Ocular manifestations include dermatochalasis, keratoconus, microcornea, macrocornea, glaucoma, retinal detachment and myopia.[14] Angioid streaks have been reported in patients with EDS, but are not part of the diagnositic criteria.[15]

A potentially serious ocular complication, especially in the vascular form, is a carotid-cavernous fistula (CCF), an abnormal communication between the arteries and veins in the cavernous sinus. Patients with CCF may present to an optometrist with a complaint of eye pain, chemosis, proptosis and redness of one or both eye(s). They also report hearing a

pulsating sound or noise in their head. Patients may have extraocular motility restrictions and report diplopia. These individuals require referral to a hospital for immediate medical attention.

Both the EDS kyphoscoliotic form (previously Type VI-A) and EDS brittle cornea syndrome form (previously Type VI-B), are autosomal recessive and characterized by joint hypermobility and kyphoscoliosis. Of the subtypes of EDS, corneal fragility is most frequently associated with type VI.[12] These patients may be at risk for glaucoma, ectopia lentis and retinal detachments.[12,15] However, unlike those with the kyphoscoliotic form, patients with brittle cornea syndrome also have craniofacial anomalies, gastrointestinal problems and characteristic hypermobility in the fingers.[12] Keratoconus has also been reported. Currently, brittle cornea syndrome is considered a distinct entity and is not included in most classifications of EDS.[16]

• ***Treatment/management.*** Any patient with EDS should undergo annual eye examinations, including slit lamp examination and dilated fundus examination. The Ehlers-Danlos National Foundation recommends these additional tests at baseline: ocular topography, scanning laser ophthalmoscopy, measurement of corneal thickness and palpebral aperture measurement.[14] In patients who present with joint hyperextendability, a history of easy bruising and corneal findings, consider EDS as a differential. Compile a detailed patient and family history. If you suspect a diagnosis of EDS, be sure to communicate with the patient's primary care physician.

Pseudoxanthoma Elasticum

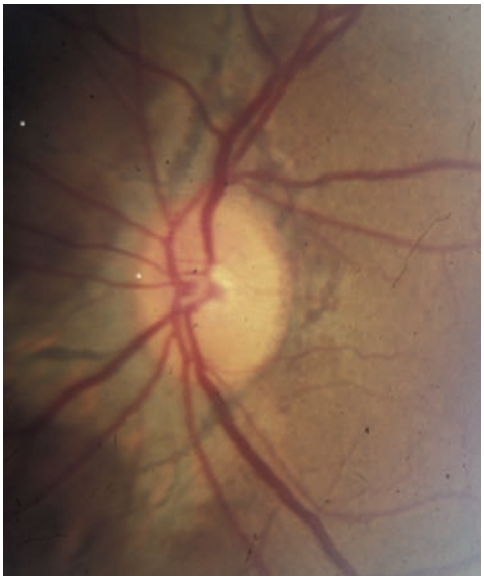
• ***Prevalence/characteristics.*** Pseudoxanthoma elasticum (PXE) is a progressive, primarily autosomal recessive disorder with a prevalence of one in 25,000 to one in 100,000 people.[17] Females are diagnosed twice as often as males.[18] Patients have a defect in the ABCC6 gene, which is involved with the production of multidrug resistance-associated protein 6 (MRP6) whose function is suspected to transport substances across cell membranes.

• ***Systemic findings.*** PXE is characterized by calcium deposits in the elastic fibers of connective tissues. The skin is the primary organ affected, but the cardiovascular system can be affected as well. Patients may have yellowish papules on their skin, especially the neck. The skin develops an orange peel appearance ("peau d'orange") and, over time, the lesions can form plaques and the skin acquires a more wrinkled appearance.[17] Patients can also develop angina pectoris, arteriosclerosis, hypertension, gastrointestinal hemorrhages, renal failure and neurological abnormalities.[19]

Diagnosis is made by biopsy of skin lesions, if present.[17] Genetic testing is also available.

• ***Ocular findings.*** The retina may develop a mottled appearance, also known as "peau d'orange." Areas of chorioretinal atrophy may be present in the mid-periphery.[20]

Angioid streaks, which are breaks in Bruch's membrane that present bilaterally and radiate off the optic disc, are found in 85% of patients.[20] Depending on retinal pigmentation, they may be red to dark brown in color and become darker over time. Angioid streaks have not been reported in children under age eight, and their incidence increases with age.[21] In 50% of cases, angioid streaks are associated with a systemic condition, with PXE being the most common. Other systemic conditions associated with angioid streaks include EDS, Paget's disease and sickle cell retinopathy. Choroidal neovascular membranes (CNVM) may develop in 70% to 86% of patients over time due to breaks in Bruch's membrane.[22]



Angioid streaks in an adult patient.

Neither angioid streaks or peau d'orange retinal appearance affect a patient's visual acuity.

• ***Treatment/management.*** Patients with PXE, even without angioid streaks, should undergo annual dilated eye exams to monitor for the development CNVM. Optical coherence tomography (OCT) testing can also be performed when CNVM is suspected. Provide patients with an Amsler grid to monitor their vision at home.[17] In cases in which neovascularization develops, be certain to refer the patient to a retinal specialist.

Treatment for CNVM is similar to that indicated for patients with macular degeneration, and may include monthly injections of anti-angiogenesis drugs, specifically Lucentis (ranibizumab, Genentech) or Avastin (bevacizumab, Genentech).[23,24] For example, one small study of seven patients who had CNVM associated

Types of Osteogenesis Imperfecta[19,25]

Type	Systemic Findings	Ocular Findings
Type I – Tarda	50% have age-dependent hearing loss, frequent bone fractures, no dental anomalies	Blue sclera, thin central cornea
Type II – Congenital	Lethal form: death from respiratory or cardiac complications in the first few years of life	Blue sclera
Type III	Hearing problems, dental anomalies, scoliosis, short limbs, triangular-shaped face	Blue sclera may be present at birth, then resolves
Type IV	Mild bone deformities, short stature, dental anomalies	Blue sclera may be present at birth, then resolves

with PXE found that, after monthly injections of ranibizumab, best-corrected visual acuity increased from 20/63 to 20/32 on average in one year, with gains maintained at three months post treatment.[24]

As with Marfan's syndrome, patients with PXE should avoid putting their eyes at risk for trauma. Patients who play sports should wear protective goggles.

Osteogenesis Imperfecta

• ***Prevalence/characteristics.*** Osteogenesis imperfecta (OI) is primarily an autosomal dominant multisystem disorder that affects the development of type I collagen fibrils, causing their diameter to be smaller than normal. Mutations in COL1A1 and COL1A2, located on chromosomes 17 and 7, respectively, have been implicated as the origin of the mutations.[19]

Traditionally, there were four types of OI affecting the COL1A1 and 2 genes. (*See "Types of Osteogenesis Imperfecta," above.*) However, up to seven new types of OI affecting different genes, including CRTAP or LEPRE, have been identified. Some of the new forms are autosomal recessive.[26]

Type I is the most common presentation and accounts for 50% of the cases.[25] The exact prevalence is unknown, but an estimated 20,000 to 50,000 Americans have the condition.[25]

• ***Systemic findings.*** Patients suffer from bones that break easily, and they may have scoliosis, dentinogenesis imperfecta (brittle teeth), hearing loss and pulmonary disease.[25] Patients are commonly short in stature and can be prone to nosebleeds.

Diagnosis of OI is based on clinical, dental and radiologic exams. Genetic testing can also be performed.

• ***Ocular findings.*** Patients often have the characteristic "blue sclera," the result of a thin sclera through which the choroid is visible. They may also have a whiter perilimbal region as compared to the surrounding sclera. Scleral rupture has been reported in pediatric patients after a history of trauma or chronic eye rubbing.[27] Keratoconus has also been reported.

• ***Treatment/management.*** Patients should have regular eye exams, with careful evaluation of the integrity of the cornea and sclera. Management of patients includes protective eyewear, particularly during physical activity, to prevent scleral rupture from injury.[27]

Medications for osteoporosis and physical therapy may be used for treating the orthopedic disorders, while the more severe deformities are treated surgically.[28]

Down Syndrome

• ***Prevalence/characteristics.*** Down syndrome is a genetic disorder involving chromosome 21. The most common presentation is trisomy 21, affecting 94% of those with Down syndrome. In 5% of cases, a portion of chromosome 21 is translocated to another chromosome so that there are still 46 chromosomes. One percent of patients have mosaicism, where some cells have 46 chromosomes and others have 47.[29]

• ***Systemic findings.*** Patients with Down syndrome can have multiple systemic conditions, including cardiac disorders such as atrial septal or ventriculoseptal defects. Other possible health problems include gastroenterological blockage, sleep apnea, hearing disorders, hypothyroidism, hip dislocations and dental anomalies.[30]

Physically, patients with Down syndrome have a characteristic appearance including short stature, flattened nasal bridge, small ears, small mouth, upward slanting eyes, epicanthal folds, and short hands and fingers. Some children have delays in mental and social development.

Diagnosis of Down syndrome is frequently based on physical appearance at birth. Genetic testing can be done by amniocentesis during pregnancy, or with blood work (karyotyping) after birth. Echocardiograms and chest X-rays are used to diagnose cardiac anomalies, while X-rays of the abdomen identify gastroenterological anomalies.

• ***Ocular findings.*** Patients with Down syndrome tend to have high refractive errors. One study found that 62% of patients with Down syndrome had hyperopia of ≥2.00D compared with 16% of patients without Down syndrome.[31] In the same study, 60% of patients with Down syndrome had astigmatism vs. only 25% without Down syndrome. Astigmatism tends to be oblique.[32]

Best-corrected visual acuity, even in the absence of pathology or amblyogenic factors, may not be 20/20. The etiology of decreased vision is not known, but optical factors appear to play a role.[33] Numerous studies have found that between 55% to 68% of patients have a significant accommodation lag, even with full correction.[34,35] Subsequent studies have found that up to 65% of patients show improved accommodation with bifocal lenses; in some cases, the child's accommodative ability improves to the point that bifocals are no longer needed.[36,37]

Binocular vision dysfunctions are also common in patients with Down syndrome. The prevalence of strabismus, particularly esotropia, ranges from 19% to 42%.[38-40] Nystagmus has been reported in 10% to 30% of patients.[37,40,41]

Other ocular findings in these patients include blepharitis, cataracts, keratoconus and Brushfield spots. Blepharitis results from eyelid anatomy. Cataracts can be congenital or acquired. Congenital cataracts generally present bilaterally. Some studies report that congenital cataracts are present in 11% to 26% of patients.[40,42] Age-related cataracts appear at an earlier age in these patients compared to the general population. Keratoconus has been reported in 0.5% of patients.[42] Brushfield spots—pale areas of hypoplasia in the peripheral iris—are incidental findings (reported in 1% of adult patients with Down syndrome) that do not require treatment.[42]

• ***Treatment/management.*** When determining a spectacle prescription, be sure to obtain an accurate objective refraction. Testing should also include measurement of accommodative lag with near retinoscopy, such as monocular estimate method (MEM), Nott or Bell retinoscopy, and the prescription of an add when indicated. The recommended bifocal segment is a flat-top 35 set to bisect the pupil, which helps ensure the functional use of the add at near.

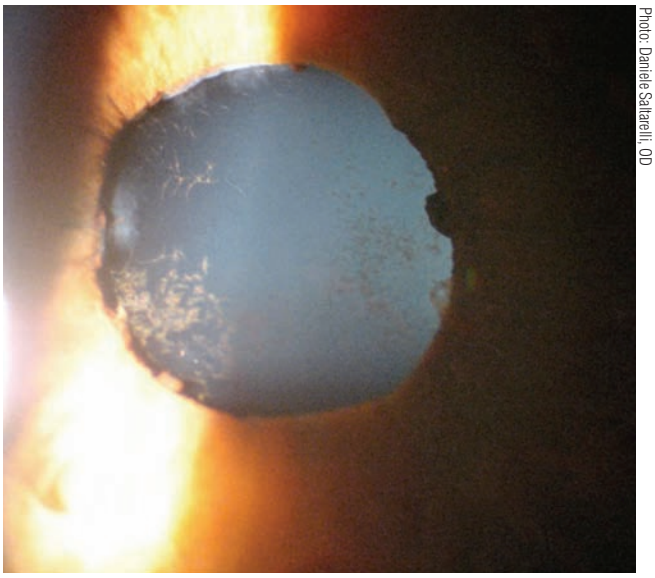


Photo: Danielle Saltarelli, OD

Broken synechaie in a patient with juvenile idiopathic arthritis.

Other conditions are treated as they are in any patient. Strabismus, particularly esotropia, may be accommodative and corrected with spectacles. In cases in which the deviation does not improve with glasses, options include monitoring without intervention, vision therapy or surgery. Treatment considerations should include the magnitude of the deviation, the ability of the child to complete a therapy program and risks of surgery, including anesthesia.

Blepharitis is treated with lid scrubs. Parents should also be educated on the recurrent nature of the condition and need for lid hygiene. Some patients may benefit from a topical antibiotic ointment, such as erythromycin or bacitracin, if they have frequent flare-ups.

Congenital cataracts are generally monitored; but if dense, a surgical consult is warranted.

Patients with keratoconus can wear glasses or may be fit with contact lenses, if indicated. These patients should be monitored for the development of corneal complications, including hydrops.

Juvenile Idiopathic Arthritis

• ***Prevalence/characteristics.*** Juvenile idiopathic arthritis (JIA) refers to a group of autoimmune inflammatory joint conditions that appear in children under age 16. It is considered to result from a combination of genetics and environmental factors. Genes that code for human leukocyte antigen (HLA) have been implicated as a possible risk for developing JIA.[43] Its prevalence is estimated at one in 1,000 children in the United States.[43]

• ***Systemic findings.*** Patients with JIA have a prolonged inflammatory response in one or more joints. Symptoms may include joint pain, morning stiffness, swollen joints and difficulty with motor activities.

The diagnosis of JIA is based on a clinical examination, which frequently includes magnetic resonance imaging (MRI) of the joints.

Types of Juvenile Idiopathic Arthritis[37,38]

Type	Joints Affected	Blood Work	Other Signs
Systemic			Fever for two weeks prior to or concurrent with arthritis, may have a rash, anemia can be present
Oligoarticular	≤4 for 6 months		
RF+ Polyarticular	≥5 for 6 months	+ RF	Resembles arthritis seen in adults
RF- Polyarticular	≥5 for 6 months	- RF	
Psoriatic			Psoriasis (patches of red, irritated skin), abnormalities of fingers and nails
Enthesitis			Tenderness at bones, ligaments and connective tissue, and a greater incidence in boys than girls
Undifferentiated			Do not fit into one category or have multiple characteristics

RF = rheumatoid factor

Blood work includes antinuclear antibody (ANA) and rheumatoid factor (RF).

JIA is classified into seven types: systemic, oligoarticular, RF positive or RF negative, psoriatic, enthesitis-related and undifferentiated. (*See "Types of Juvenile Idiopathic Arthritis," above.*) The classifications are made based on the number of joints affected, signs and symptoms, family history and laboratory test results. Oligoarticular JIA accounts for approximately 50% of cases, while systemic JIA accounts for 10%.[44] With the exception of the enthesitis-related form, girls are affected more than boys.[43]

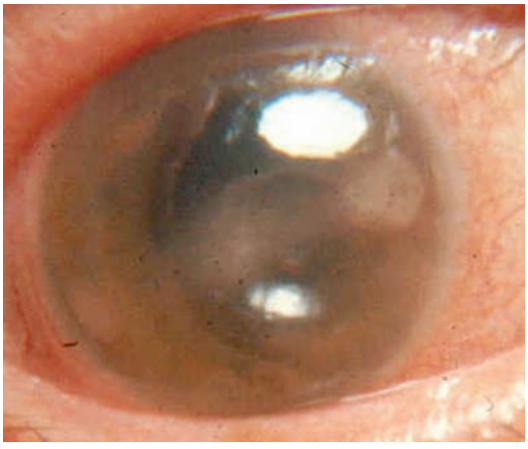


Photo: Danièle Saltarelli, OD

Band keratopathy in patient with JIA.

• ***Ocular findings.*** The most serious ocular side effect of JIA is uveitis. Studies have found that an average of 13% of patients with JIA develop uveitis.[45,46] In patients who are ANA positive, up to 30% may have uveitis.[47] In the majority of cases, the patients are asymptomatic and do not report the classic eye pain or light sensitivity, nor does the parent notice any redness. Patients in whom uveitis goes undiagnosed are at risk of developing synechiae, glaucoma, cataracts and band keratopathy.

It is important to educate parents about the potentially serious ocular complications of JIA and the need for frequent slit lamp eye exams to screen for uveitis.[48] (*See "Recommended Slit Lamp Screening Guidelines for Juvenile Idiopathic Arthritis," page 77.*)

• ***Treatment/management.*** Systemic treatment involves a combination of medications and physical therapy. In the mildest cases, non-steroidal anti-inflammatories (NSAIDs) are first-line treatment. Second-line treatment includes disease modifying anti-rheumatic drugs (DMARDs), like methotrexate, which are administered orally or through injection. In patients who are not responsive to methotrexate, based on joint disease or ocular presentation, biologic-modifying drugs—specifically Humira (adalimumab, AbbVie), Enbrel (etanercept, Amgen), Remicade (infliximab, Janssen Biotech) and Orencia (abatacept, Bristol-Myers Squibb)—may be added or substituted. Clinical trials regarding the most efficacious treatment are ongoing.[43]

As in adult cases, children with uveitis are treated according to the anterior chamber reaction. Pred Forte (prednisolone acetate 1%, Allergan) is the preferred topical steroid, although Durezol (difluprednate 0.05%, Alcon) may also be used. The steroid is dosed frequently initially, then slowly tapered as the uveitis resolves. Patients' intraocular pressure (IOP) should be monitored for a possible steroid response, which can be treated with a topical medication, such as a beta-blocker, to lower IOP. A cycloplegic agent is not routinely used unless the patient is in pain, or there is a greater risk of synechiae.

In cases of uveitis that do not improve with topical treatment, especially within three months, systemic medications may need to be added or adjusted.[49] Therefore, communication with the treating rheumatologist is important.

Treating children can be a rewarding clinical experience. Yet, treating those with an underlying

systemic disease can be exceptionally gratifying because of the changes you can make to a child's quality of life and how they manage their chronic condition.

As primary eye care providers, optometrists may be the first to recognize a serious systemic condition, which could save a patient's life and prevent further deterioration. Furthermore, optometrists can effectively manage these patients for possible ocular complications.

Because many of the conditions discussed in this review are genetic, encourage eye examinations for family members of affected patients, even if they have not been diagnosed with a disorder. ■

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Recommended Slit Lamp Screening Guidelines for Juvenile Idiopathic Arthritis[42]

ANA	Age of onset of JIA (years)	Duration of JIA (years)	Exam Frequency (months)
Positive	≤6	≤ 4	3
Positive	≤6	> 4	6
Positive	≤6	> 7	12
Positive	>6	≤ 2	6
Positive	>6	> 2	12
Negative	≤6	≤ 4	6
Negative	≤6	> 4	12
Negative	>6	N/A	12
Systemic	N/A	N/A	12

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OSC QUIZ

You can obtain transcript-quality continuing education credit through the Optometric Study Center. Complete the test form *(page 79)*, and return it with the $35 fee to: Optometric CE, P.O. Box 488, Canal Street Station, New York, NY 10013. To be eligible, please return the card within one year of publication.

You can also access the test form and submit your answers and payment via credit card at *Review of Optometry* online, www.revoptom.com.

You must achieve a score of 70 or higher to receive credit. Allow eight to 10 weeks for processing. For each Optometric Study Center course you pass, you earn 2 hours of transcript-quality credit from Pennsylvania College of Optometry and double credit toward the AOA Optometric Recognition Award—Category 1.

Please check with your state licensing board to see if this approval counts toward your CE requirement for relicensure.

1. Patients with Marfan's syndrome have been found to have a defect in what gene?
a. ABC6.
b. COL1A1.
c. FBN-1.
d. LEPRE.

2. All of the following are possible systemic complications of Marfan's syndrome EXCEPT:
a. Pes planus.
b. Aortic root dilation.
c. Pectus excavatum.
d. Transverse myelitis.

3. A 12-year-old patient with Marfan's syndrome reports a history of sudden decreased vision after being hit with a "header" during a soccer match. The most likely cause of this patient's symptom is:
a. Rupture of CNVM.
b. Lens subluxation.
c. Hyphema.
d. Optic nerve avulsion.

4. You are examining an adolescent patient with a refractive error of -5.00-1.00x180 OD 20/20 and -7.00-2.50x15 OS 20/20. During dilation, you notice that the left crystalline lens is subluxed superiorly. This patient should be referred to which provider?
a. Cardiologist.
b. Dermatologist.
c. Rheumatologist.
d. Geneticist.

5. The major criteria for the different subtypes of EDS all include:
a. Joint hypermobility or skeletal anomalies.
b. Skin anomalies or hearing loss.
c. Skin anomalies or joint hypermobility.
d. Joint hypermobility or hearing loss.

6. A patient who presents with complaints of eye pain and redness, and who reports hearing a pulsating sound, likely has:
a. Carotid cavernous fistula.
b. Viral conjunctivitis.
c. Scleral rupture.
d. Blepharoconjunctivitis.

7. For the patient in question 6, what systemic condition is the most likely?
a. Marfan's syndrome.
b. Pseudoxanthoma elasticum (PXE).
c. Ehlers-Danlos syndrome (EDS).
d. Juvenile idiopathic arthritis (JIA).

8. Angioid streaks, yellow skin papules and an orange peel appearance in the retina have been associated with which systemic condition?
a. Osteogenesis imperfecta (OI).
b. PXE.
c. EDS.
d. JIA.

9. A patient who presents with dark red streaks radiating off the optic nerve should be educated about the risk of developing:
a. Cataracts.
b. Glaucoma.
c. Paget's disease.
d. Choroidal neovascular membranes.

10. Currently, the treatment for choroidal neovascular membranes that develop from angioid streaks includes:
a. Monitoring.
b. Injection of steroid drugs.
c. Injection of anti-angiogenic drugs.
d. Laser treatment.

11. Osteogenesis imperfecta is a systemic disease characterized by:
a. Frequent bruising.
b. Frequent bone fractures.
c. Mental retardation.
d. All of the above.

12. The most common refractive finding in patients with Down syndrome is:
a. Myopia ≥6.00D.
b. Oblique astigmatism.
c. Regular astigmatism.
d. Hyperopia ≥2.00D.

13. A 12-year-old patient with Down syndrome has a refractive error of +2.00D OD and +2.50D OS. Best-corrected visual acuity using the Snellen chart is 20/40 each eye. The etiology of the decreased vision can be due to:
a. Amblyopia.
b. Brushfield spots.
c. Dense cataracts.
d. Optical factors.

14. When examining a 9-year-old patient with Down syndrome, you find an accommodative lag of +3.50D over her current eyeglasses. The current prescription is +4.00-1.00x180 OU with 20/30 VA each eye. Refraction does not show a change. The most appropriate treatment for this patient is.
a. Rx +4.00-1.00x180 OU.
b. Rx +4.00-1.00x180/+3.00D add.
c. Rx +3.00-1.00x180/+3.00D add.
d. Rx +5.00-1.00x180 OU.

15. Patients with Down syndrome who experience chronic blepharitis may benefit from ophthalmic treatment with which medication?
a. Bacitracin ointment.
b. Polytrim drops.
c. Azithromycin drops.
d. Tobramycin/dexamethasone ointment.

OSC QUIZ

16. An 8-year-old patient who presents with a white and quiet eye with a grade 3+ uveitis should be worked up for which condition?
a. Toxoplasmosis.
b. PXE.
c. EDS.
d. JIA.

17. A patient with JIA who has chronic untreated uveitis can be at risk for:
a. Band keratopathy.
b. Cataracts.
c. Glaucoma.
d. All of the above.

18. Which patient with JIA is at the greatest risk for developing uveitis?
a. ANA positive, age of onset ≤6 years, duration of JIA ≤4 years.
b. ANA positive, age of onset >6 years, duration of JIA ≤4 years.
c. ANA negative, age of onset ≤6 years, duration of JIA >4 years.
d. ANA negative, age of onset >6 years, duration of JIA ≤4 years.

19. What is the recommended slit lamp screening interval for the JIA patient described in question 18?
a. Every month.
b. Every three months.
c. Every six months.
d. Every twelve months.

20. Patients who have JIA may be taking which of the following medications?
a. Adalimumab and methotrexate.
b. Methotrexate and ranibizumab.
c. Oral prednisone and methotrexate.
d. Adalimumab and oral prednisone.

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1.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
2.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
3.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
4.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
5.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
6.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
7.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
8.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
9.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
10.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
11.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
12.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
13.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
14.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
15.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
16.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
17.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
18.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
19.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
20.	Ⓐ	Ⓑ	Ⓒ	Ⓓ

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22. Related to your practice needs: ① ② ③ ④ ⑤
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24. Avoided commercial bias/influence: ① ② ③ ④ ⑤
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27. The difficulty of the course was:
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A Feast of CE at VEE

The Big Apple has everything you need this March to satisfy your appetite for CE.

By Cheryl G. Murphy, OD, Contributing Editor

Vision Expo East, held March 26 to 30, is not just about eyewear. It's a full smorgasbord of education on disease diagnosis and management, clinical application of technology, savvy business solutions, and more.

To Start

One of the most noticeable changes to the course curriculum this year is its early start with the new Global Contact Lens Forum, beginning at 2 p.m. Wednesday, March 26, and running through noon Thursday. This special program of classes serves up seven COPE-approved credit hours and aims to give practitioners sharper strategies for a smoother and more successful contact lens practice.

"The main theme of the forum is the business of contact lenses," says Kirk Smick, OD, co-chairman of the VEE Conference Advisory Board. "The goal is to explore different aspects of the contact lens practice and demonstrate its contribution to the overall primary care optometric practice."

Topics include: the use of technology, Internet and communication with patients; debates on contact lens wearing schedules; the ocular system's response to contacts, and more. The Global Contact Lens Forum is hosted jointly by the British Contact Lens Association and Vision Expo East.

Keep your eyes peeled for Dr. Cheryl Murphy, and you might see yourself on *Review of Optometry*'s Facebook page.

A Sizable Entree

If you're looking for something substantial to sink your teeth into this year at VEE, you'll find the conference CE menu packed with an inviting 19 hours of credits that will satisfy your craving to learn more about glaucoma.

The Special Glaucoma program was successfully offered last year at both Vision Expo East and West. "Its aim is to highlight the most important skills and knowledge that primary eye care optometrists need to regularly treat glaucoma," says Richard Madonna, OD, a member of the VEE Conference Advisory Board.

"Optometry has been granted the privilege to manage glaucoma in almost every state, yet we have been disappointed in the number of ODs who say they actively manage the condition," Dr. Madonna says. "This program highlights the areas in which the practitioner needs to be well versed in order to effectively provide glaucoma care."

He also states that, "the program is taught by practitioners who regularly manage glaucoma, so it provides education that can be used immediately in practice. I believe that the courses have something for everyone, from the practitioner who doesn't regularly manage glaucoma to docs experienced in glaucoma but who wish

Vision Expo East is more than an eyeglass fashion show. This year's meeting offers 325 hours of top-notch continuing education.

to learn a new pearl or two, [as well as those] who just want to be involved in the discussion."

Attending the entire Special Glaucoma program provides practitioners with a comprehensive and thorough view of diagnosing, managing and treating glaucoma, but single classes in the program can be taken a la carte. "While the courses do proceed sequentially from diagnosis to treatment to grand rounds, attendees may wish to take only a few of the courses," Dr. Madonna says.

Courses Galore

Still hungry for more? There are plenty of topics and classes to devour, and the variety is part of Vision Expo's draw. According to Dr. Smick, "more than 4,000 optometrists, opticians, practice managers and office staff come together to take courses at the Vision Expo meetings, [and] Vision Expo educates more eye care professionals than any other meeting in the United States."

Course tracks include clinical, contact lens, optical technology and business topics. Specifically, "clinical subjects related to allergy, retinal disease and ocular emergencies continue to be well attended," says Dr. Smick. "New techniques in refractive surgery and cataract surgery comanagement are always in demand. And, because diabetes is appearing in epidemic waves in our practices, any course dealing with current trends in diabetic management is popular."

Courses that address children's eye conditions are "gaining in popularity as the new Affordable Care Act will bring many underserved children into our practices," he says.

Courses on new lens designs and treatments are once again coming into vogue, as doctors and opticians strive to protect their patients from harmful UV and blue light.

Dr. Smick also notes the importance of continuing education on macular degeneration and nutritional supplements. "Since the completion of the AREDS 2 study, doctors have been looking for the best formula to prescribe to their AMD patients," he says. "Nutraceutical prescribing is at an all-time high because patients are eager to find the right solutions to this overwhelming eye disease."

Also new for 2014 are 12 hours of CE that focus on neuro-ophthalmic disease to ensure that optometrists can diagnose these conditions promptly and manage them properly.

Finally, "Business Solutions is the heart and soul of Vision Expo," says Dr. Smick. "This meeting has come to be known as the business center of the eye care professions." More than 50 hours of business education cover all aspects of staff and practice management, government regulations and audits, as well as dispensary and contact lens business.

Sunday's Cherry on Top

Sunday is the last day of courses at Vision Expo East, and attendees can choose to end it with something sweet by registering for the 12th Annual Ocular Nutrition Symposium, a full-day CE program from the Ocular Nutrition Society. (Attendees must pre-register at www.ocularnutritionsociety.org.)

"The ONS strives to bring in nutrition experts from outside of the eye care industry to discuss the true science behind nutrition," says ONS president Jeffrey Anshel, OD. "Our programs offer insight into how nutrition can bring about positive results for our patients."

Topics include nutrigenetics in eye disease, the role of lutein in visual function and in the brain, early detection of macular degeneration structure and function, evidence-based nutrition and how to bring your newfound nutrition knowledge into practice. The ONS symposium at VEE includes lunch and concludes with "a cabernet, chocolate and chatter" social hour.

Visit www.visionexpoeast.com. ■

Red Eye of Olympic Proportions

Bob Costas's "pink eye" reminds us that the only sure-fire cure for EKC is time.

By Paul C. Ajamian, OD

Q A 42-year-old white female came in on Friday with a red left eye and swollen eyelid. I put her on an antibiotic. But by Monday, the injection and swelling had progressed significantly, so I added a topical steroid. When I saw her again on Tuesday, her eye was even worse; the cornea was uninvolved but the conjunctiva was ballooning out. She's miserable, so I'm referring her to you. Can you help her?

Two problematic cases of epidemic keratoconjunctivitis: One in our patient (above) and one in sportscaster Bob Costas.

A I can diagnose her, but only time will help her.

When I saw this patient on Wednesday, she had a palpable preauricular node on the left side, which told me what I already suspected: epidemic keratoconjunctivitis (EKC).

Oddly enough, this patient presented just a few days before Bob Costas made national news with his debilitating case of "pink eye" during the Winter Olympics.

And, in both cases, the diagnosis was confounded by conjunctival chemosis and swelling of the lids, which is not unusual with EKC. This eyelid involvement and chemosis might steer you toward a diagnosis of allergy or preseptal cellulitis.

Don't be fooled. In preseptal cellulitis, the eye is white and quiet. With EKC, it's red and angry.

So, too, is the patient! Having had it myself, I can attest that EKC makes you miserable and desperate. Bob Costas went off the air, in part, because his photophobia made sitting in front of bright studio lights intolerable. When you have EKC, you'd pay someone a lot of money for the magic bullet to just make it all go away.

No Miracle Pill

Unfortunately, time is the only guaranteed cure. Of course, a miserable EKC patient doesn't want to hear that. They'll go from one doctor to the next, hoping for a better answer.

So, if you have a desperate and disbelieving patient—despite your best efforts to explain otherwise—send him or her for a friendly second opinion. The patient will hopefully stop shopping and let you follow the condition through to resolution on its own.

Having said that, a couple treatments might be worth a try, and palliative measures for comfort are definitely in order.

Some doctors advocate an off-label, one-time, in-office instillation of Betadine 5% Sterile Ophthalmic Prep Solution (povidone-iodine, Alcon), which potentially "nukes" the entire microbial load. Anecdotally, I've found mixed results; sometimes it makes the eye better, sometimes worse.

Early reports have suggested that Zirgan (ganciclovir 0.15%, Bausch + Lomb), which we use for herpetic keratitis, can reduce the recovery time of adenoviral conjunctivitis if used in the first few days.[1] Again, I've found it helped some patients but not others.

More research is needed for both these treatments. Until we have those—or until a drug is approved specifically for adenoviral conjunctivitis—we can offer comfort and reassurance.

To that end, recommend cold compresses and artificial tears. Remove pseudomembranes in office. Because the virus is so contagious and is transmitted by direct contact, educate the patient about strict hygiene measures to prevent infection in the fellow eye as well as in other family members. (This goes for you, too. If you even remotely suspect EKC, use gloves during examination, and try to sterilize everything after the patient leaves.)

When my EKC got to the point that it involved the cornea, I used a bandage contact lens; it helped enough to get me through the day. Also, cycloplegic drops administered two or three times a day might help to reduce the pain and photophobia. ■

1. Tabbara OF. Ganciclovir effects in adenoviral keratoconjunctivitis. Poster (B253) presented at Annual Association for Research in Vision and Ophthalmology (ARVO); April 29-May 4, 2001; Fort Lauderdale, Fla.

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Bugs and Drugs

Does the increasing resistance to antibacterial medications found in a number of organisms pose a threat to your patients? **Edited by Joseph P. Shovlin, OD**

Q Are the new trends in resistance patterns in conjunctivitis and microbial keratitis a concern for contact lens wearers? In particular, what is the status of MRSA-related infection risk in CL wearers?

A To understand the impact of methicillin-resistant *Staphylococcus aureus* (MRSA) as it relates to bacterial keratitis, "it's useful to take a step back and look at what exactly MRSA means and where it came from," says Aaron Bronner, OD, a staff optometrist at the Pacific Cataract and Laser Institute of Kennewick, Wash.

MRSA colonies result from environmental stress brought on by beta-lactam antibiotics. "In these populations, a mutation to the cell wall protein—which drugs like penicillin, methicillin and cephalosporins bind to and act against—rendered these drugs ineffective by eliminating their target," says Dr. Bronner.

In addition to being transmitted vertically from parent cell to offspring, along bacterial cell lineages, these specific mutations are readily transmitted horizontally by plasmids to non-descendant lines of bacteria, Dr. Bronner says, thereby widening the spread of resistance.

Although MRSA species are widely able to resist the effects of many conventional antibiotics, they were less efficient colonizers than many non-MRSA *Staph.* species. As a result, these particular species would not routinely cause pathology—unless such traits were selected for as a result of antibiotic use.

Due to this selectivity, "until the 1990s MRSA was primarily a hospital-borne disease," known more formally as hospital acquired (HA)-MRSA, says Dr. Bronner. "However, beginning in the 1990s, some MRSA strains became more effective colonizers that were able to compete with non-MRSA strains, and so began to show up in the community in individuals with no history of hospitalization or antibiotic use." This is the phenomenon of so-called community acquired (CA)-MRSA.

According to Dr. Bronner, these CA-MRSA isolates are "more virulent and effective growers than HA-MRSA." Despite this fact, they lost some of their resistance during the transformation. As a result, the CA-MRSA isolates are more susceptible to antibiotics.

"As far as resistance within other organisms goes, MRSA and methicillin-resistant *Staph. epidermidis* (MRSE) are discussed with great frequency because they are the primary causative organisms in severe ophthalmic disease," adds Dr. Bronner. A number of other important pathogens, such as *Pseudomonas aeruginosa* and Streptococcal species, are showing resistance patterns as well.

Staph. species causing ocular disease have been shown to exhibit resistance in dramatically increasing numbers. "In fact, MRSA species may replace methicillin-susceptible *Staph. aureus* (MSSA) as the dominant cause of *Staph.*-related eye disease—if this has not already occurred," says Dr. Bronner. Studies currently suggest that between one-third and two-thirds of all *Staph.*-related eye infections are the result of MRSA populations.[1,2]

Pertaining specifically to contact lenses, despite the widely recognized increase in incidence of gram-negative etiologies in the setting of contact lens use in the US, *Staph.* species are still either the first or second most encountered source of contact lens-associated bacterial keratitis, according to Dr. Bronner, so it stands to reason that such patients will have greater exposure to resistant *Staph.* species as well.

"As MRSA is becoming more common among all types of bacterial keratitis, it should be presumed that it will likely become equally more common among contact lens-associated disease," says Dr. Bronner. "Because of the widening distribution of MRSA—as well as the generally prominent role *Staph. aureus* has in ocular disease overall—it can be expected that MRSA infections will become the primary Staphylococcal etiology of both bacterial keratitis as a whole, as well as contact lens-associated bacterial keratitis." ■

1. Asbell PA, Sahm DF, Shaw M, Draghi DC, Brown NP. Increasing prevalence of methicillin resistance in serious ocular infections caused by Staphyloccocs auereus in United States: 2000 to 2005. J Cataract Refract Surg. 2008; 34: 814-8.
2. Hsiao CH, Chuang CC, Tan HY, Ma DH, Lin KK, Chang CJ, Huang YC. Methicillin-resistant Staphyloccus aureus ocular infection: a 10 year hospital based study. Ophthalmology. 2012; 119: 522-7.

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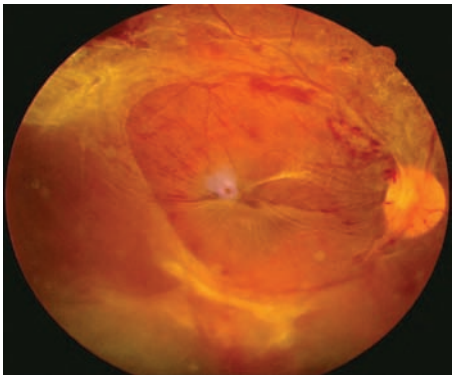
The Interactive Eye

The Review of Systems can be applied many ways, including head-to-toe screenings. What is ROS, and why does it matter? **By Carlo J. Pelino, OD, and Joseph J. Pizzimenti, OD**

The eye does not function in isolation. This has been apparent for a long time. Nineteenth-century physicians skilled in the diagnosis and treatment of eye diseases branched out by adding otology (ear and vestibular diseases), rhinology (diseases of the nose, including the sinuses) and laryngology (diseases of the throat and larynx) to their repertoire. These early EENT physicians viewed the eye and visual system as being closely related to these other organs, so why not treat them all? Optometrists often shared both office space and patients with audiologists, and many still do so today. Several of our optometric colleagues practice in multidisciplinary health settings.

But the connection of the visual system to the rest of the body involves far more than other tissues of the head and neck. As part of the nervous system, the eye interacts with virtually every other organ system. In our bimonthly column, we attempt to illustrate the fact that many systemic conditions have ocular complications, and several ocular diseases—and treatments—have systemic implications.

Optometrists are in a position to team with providers from various other disciplines in the interest of patient health and wellness. A dentist colleague of ours once remarked, "We do the same thing, just in different places. You see diabetic retinopathy; I see diabetic periodontitis. You treat uveitis in a patient with Crohn's disease; I treat their aphthous ulcers (canker sore). You relieve a Sjögren's patient's dry eye; I enhance their diminished saliva production."



Diabetic retinopathy is one of many conditions that require ODs to team with providers from other disciplines.

A True Review

There are ever-growing, high-tech diagnostic methods available to us, but the simple case history usually provides 90% of the useful information, with eye examination and diagnostic tests used to confirm the diagnosis.

The clinical evaluation of any patient, no matter what the discipline, begins with a case history.

We are all familiar with the major elements of the case history, from the chief complaint to medications and allergies. The Problem-Oriented Medical Record (POMR) has proven to be a useful method for documenting medical information.[1] It provides a structure that helps us record our patient notes, and view those notes subsequently in a manner that gives us a good understanding of that patient's history.

The review of systems (ROS) has become a standard element of the history and the POMR. ROS is a list of questions, arranged by organ system, designed to uncover symptoms of dysfunction and disease.[2]

Applying ROS

The ROS can be applied in several ways:

- As a head-to-toe screening tool asked of every patient.
- As additional questions asked only of patients who fall into particular risk categories (e.g., reserving questions designed to uncover pseudotumor cerebri to overweight females of child-bearing age.)
- As a means to describe the likely causes of a presenting symptom (e.g., patients with a chief concern of "unilateral eye and head pain" would merit a detailed headache and neurologic ROS).

Today's clinicians incorporate the ROS into the overall patient care strategy.

Patients' responses should be interpreted within the context of the rest of their profile, including demographics, risk factors, past history, and objective data gained from the examination.

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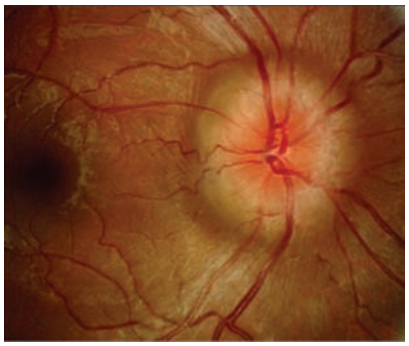

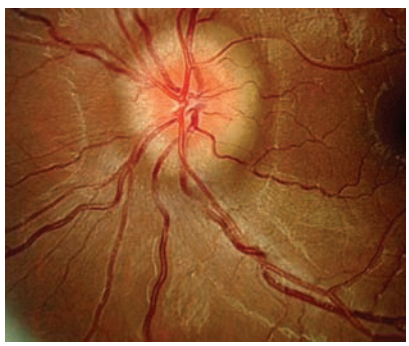

Specific ROS questions can uncover systemtic conditions such as pseudotumor cerebri, pictured here.

The clinician can then come to an informed conclusion about the extent and cause of the patient's symptom(s), and use it to guide their subsequent management.

There are few functions of the human body that operate singularly, and the visual system is no different.

It's just one part of an overwhelmingly complex structure that continually demands our insight and attention.

We owe it to our patients to have a full understanding of how these systems interact so we can provide them with the best treatment and care. ■

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2. Swartz MH. Review of Systems. In: Swartz Textbook of Physical Diagnosis: History and Examination. 4th ed. Philadelphia, PA: WB Saunders; 2002.
3. Bickley L. Review of Systems. In: Bates' Guide to Physical Examination. 7th ed. Philadelphia, PA: Lippincott Williams and Wilkins; 1999.

Review of Systems[2,3]

The ROS can be applied as a head-to-toe, comprehensive screening tool asked of every patient, as additional questions asked only of patients who fall in particular risk categories, or as a means to describe the likely causes of a presenting symptom.

Below are the various organ systems and corresponding ROS. Keep in mind that these are just the more common symptoms and not an exhaustive list.

Constitutional: weight loss or gain, general state of health, wellbeing, and strength

Endocrine: polydipsia, polyuria, hormone therapy, intolerance to heat or cold, weight changes

Integumentary: hair loss, skin eruptions/rashes/growths, sores that grow and/or don't heal, lesions changing in size, shape or color, itching

Immunology: reactions to drugs, food, insects, skin rashes, trouble breathing, anemia, bleeding tendency, lymph node enlargement/tenderness

Musculoskeletal: joint pain, swelling or redness, muscle ache, back pain

Ear/Nose/Throat: pain, mouth sores, change in hearing, poor swallowing, discharge

Respiratory: shortness of breath, chest pain, cough, hemoptysis (coughing up blood), snoring or stop breathing

Cardiovascular: chest pain, palpitations, syncope, dyspnea, edema, heart murmurs, varicosities

Gastrointestinal: appetite changes, indigestion/heartburn, abdominal pain, nausea, vomiting, hematemesis, jaundice, constipation, diarrhea

Genitourinary: urgency, frequency, dysuria, nocturia, hematuria, polyuria, unusual urine, stones, infections, nephritis, hesitancy, incontinence, genital sores, discharge, STD

OB/Gyn/Breast: Chronic or past disease, dysmenorrhea, vaginal discharge, postmenopausal bleeding, dysparenia, number and results of pregnancies, breast mass, pain or discharge

Neurologic: headache, convulsions, paralyses, parathesias, difficulties with memory or speech, sensory or motor disturbances, poor muscular coordination (ataxia, tremor), orientation (place, time, person)

Psychiatric: predominant mood, emotional problems, anxiety, depression, previous psychiatric care, unusual perceptions, hallucinations

Hematology/Oncology: chronic/past hematologic/oncologic disease, abnormal bleeding/bruising, new growing lumps/bumps, hypercoaguability

No Complaint, No Problem. Right?

This relatively asymptomatic patient was referred for a retinal evaluation. Will an underlying condition threaten her vision in the near future? **By Mark T. Dunbar, OD**

A 38-year-old Hispanic female presented at the request of her primary care optometrist. Her eye doctor became concerned when he evaluated her retina, and told her that she needed to see a retina specialist.

Her ocular history was significant for myopia. She reported seeing well with daily disposable contact lenses. Her medical history was unremarkable.

Her best-corrected visual acuity measured 20/20 OU at distance and near with a small myopic correction. Ocular motility testing was normal OU. Confrontation visual fields were full to careful finger counting. Her pupils were equally round and reactive, with no evidence of afferent defect.

The anterior segment examination revealed a clear cornea with a deep and quiet chamber OU. Additionally, she exhibited normal irides and clear lenses.

Dilated fundus exam showed a clear vitreous. Both optic nerves were healthy, with small cups and good rim coloration and perfusion. The maculae appeared normal with a positive foveal light reflex OU.

However, located just outside each macula, we saw peculiar retinal pigment epithelial (RPE) changes that extended along the superior and inferior arcades OU. We took wide-field fundus images of both eyes (*figures 1 and 2*), as well as captured a magnified view along the superior arcade OD (*figure 3*).

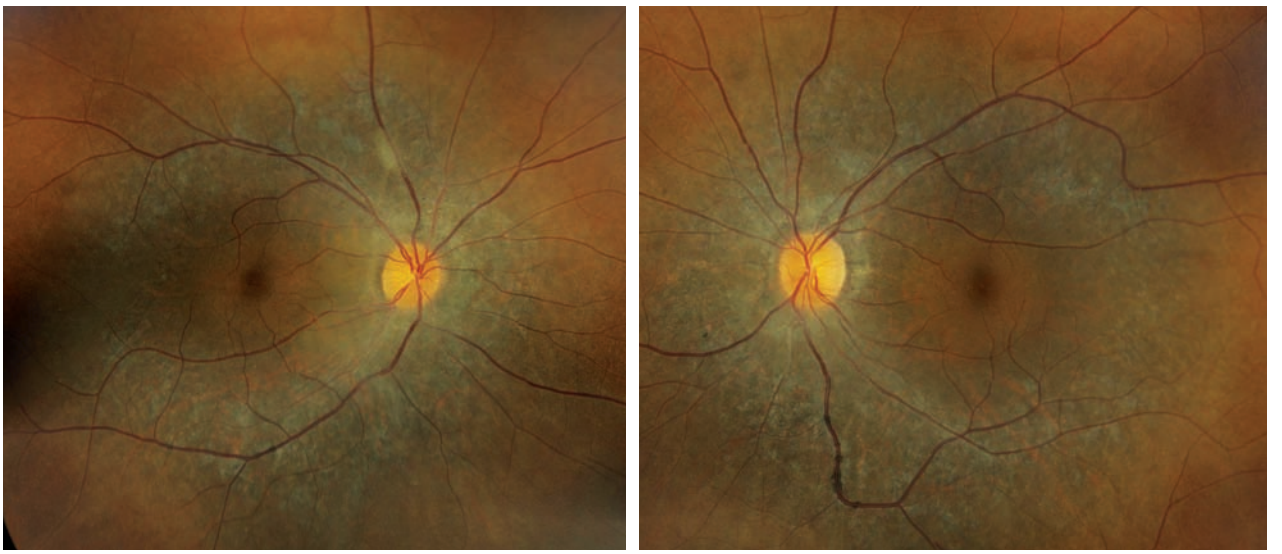
Take the Retina Quiz

1. How would you classify the fundus changes in our patient?
   a. Degenerative.
   b. Tapetoretinal.
   c. Infectious.
   d. Metabolic.

2. What do the small focal changes seen on the magnified fundus view represent?
   a. Drusen.
   b. Crystals.
   c. Calcium.
   d. Lipofuscin.

3. What is the correct diagnosis?
   a. Retinitis pigmentosa.
   b. Stargardt disease.
   c. Cone dystrophy.
   d. Bietti crystalline dystrophy (BCD).

4. Which principal symptom should we expect our patient to report?
   a. Loss of color vision.
   b. Night blindness.



1, 2. Our patient's fundus evaluation revealed obvious changes in both eyes (OD left, OS right). What is the correct diagnosis?

c. Loss of central vision.
d. Blurred vision.

5. What testing would help us best follow this patient?
a. Fluorescein angiography.
b. Visual fields.
c. Electroretinogram (ERG).
d. Both b and c.

For answers, turn to page 114.

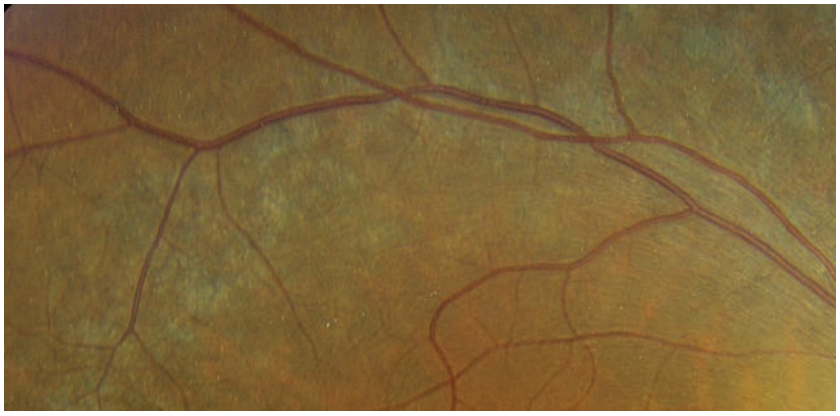
Discussion

The fundus changes seen in our patient are characteristic of a tapetoretinal degeneration—a collective term used to define a nonspecific, hereditary degeneration of the RPE and photoreceptors. Considering that there are several different hereditary retinal degenerations, which one does our patient have?

One clue can be spotted along the superior and inferior arcade where, upon close inspection, you can observe multiple, fine, refractile retinal crystals. Given these findings, we diagnosed our patient with a rare autosomal recessive condition—Bietti crystalline dystrophy. Patients with BCD typically exhibit crystals in the corneal limbus, glistening intraretinal crystals in the presence of RPE atrophy, pigment clumping and choroidal sclerosis.[1]

Interestingly, our patient didn't have corneal crystals. Nonetheless, there are several published reports of BCD patients who presented with the typical retinal findings, but no evidence corneal crystals.[1,2]

Most patients who are diagnosed with BCD develop visual symptoms by the third decade of life. The disease usually progresses very slowly; however, the exact rate can vary based upon the individual's genetic construct. The most commonly reported symptoms are decreased visual acuity and pronounced night blindness (nyctalopia).



3. A magnified view along the right superior temporal arcade.

The natural history of BCD includes progressive vision loss and visual field constriction. It is important to note that advanced age is not always a marker for disease severity and/or progression risk.[1] Therefore, it is reasonable to suggest that environmental factors (e.g., dietary intake) may affect lipid metabolism, or that certain genetic variables might influence phenotypic disease expression.[1,3]

The gene for BCD has been localized to chromosome 4q35. Affected individuals often present with several different mutations of CYP4V2—a member of the cytochrome P450 family, which codes for a 525 amino acid protein.[1] The CYP4V2 gene may play an active role in fatty acid metabolism and has been found in various ocular tissues, such as the retina and RPE.

Biochemical studies have shown that patients with BCD typically experience abnormal lipid metabolism.[1] In one investigational study, BCD patients demonstrated a reduced capacity to convert fatty acid precursors into omega-3 fatty acids and were found to have absent or nonfunctional fatty acid binding proteins.[2]

Our patient was relatively asymptomatic, and still had 20/20 acuity. And while she reported some difficulty seeing at night, she suggested that it did not affect her ability to function properly.

BCD patients should be followed via visual fields and ERG studies. In fact, the clinical grading for BCD has been directly correlated to ERG findings.[1] Patients with RPE atrophy and intraretinal crystals that are confined to the posterior pole tend to show lesser disturbances in the full-field ERG. Indeed, upon testing, our patient had an amplitude reduction in rod (within 20% of the low end of normal), mixed rod/cone (less than 30% of the low end of normal) and cone (between 40% and 50% of the low end of normal) function. Further, visual fields showed very slow progression over a six-year period, with slight constriction superiorly (OD > OS).

Our patient has done very well with this condition. She maintains excellent visual acuity, and is not aware of any associated difficulties. In fact, she wouldn't have even known that she had a problem if it weren't for her myopia. ■

1. Lee KY, Kob AH, Aung T, et al. Characterization of Bietti crystalline dystrophy patients with CYP4V2 mutations. Invest Ophthalmol Vis Sci. 2005 Oct;46(10):3812-6.
2. Mataftsi A. Bietti's crystalline corneoretinal dystrophy: a cross-sectional study. Retina. 2004 Jun;24(3):416-26.
3. Kaiser-Kupfer MI, Chan CC, Markello TC, et al. Clinical biochemical and pathologic correlations in Bietti's crystalline dystrophy. Am J Ophthalmol. 1994 Nov 15;118(5):569-82.

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Physician, Heal Thyself?

While you were sipping eggnog and listening to Bing last Christmas, I was trying to diagnose and treat my own eye infection. **By Alan G. Kabat, OD**

Sir William Osler said, "A physician who treats himself has a fool for a patient." In retrospect, I wish I'd read that quote before last Christmas.

I suppose all physicians are guilty of diagnosing and treating themselves to some degree. I'm not talking about performing your own colonoscopy or suturing your own head wound. But here's a question: Who did your last refraction? I'll bet the majority of you responded, "I did!"

Most of us are probably also guilty of treating our own dry eye or ocular allergy symptoms with samples from the cabinet, rather than seeing a colleague.

Of course, there is a limit to what we can do physically, ethically and legally in terms of self-treatment. And then there's the limit of common sense—which some of us unfortunately fail to recognize before it's too late. Hence, my Christmas story.

A Cornea Carol

This past December 23, I began to feel a burning sensation in my right eye. I was just three days into my winter break from Southern College of Optometry, and was up late watching TV. Figuring it was just my dry eye/blepharitis and lack of sleep, I went to bed.

I awoke on December 24 with a thick mucus discharge and considerable scratchiness in that eye. I actually had to pull my lids apart with my fingers, and recognized this as one of the key diagnostic features of the dreaded "pink eye."

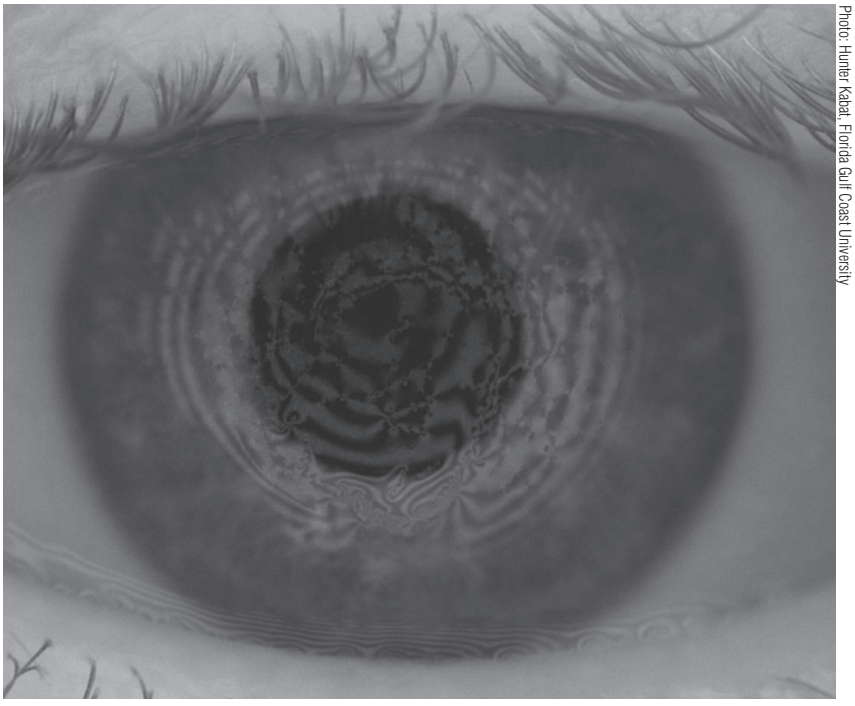

Photo: Hunter Kabat, Florida Gulf Coast University

A self-induced corneal abrasion, reflected in the distorted keratographic mires.

Facing myself in the bathroom mirror, I got a good look at my red, swollen conjunctiva and—despite not having a slit lamp for magnification—confirmed my own preliminary diagnosis. I subsequently posted on my Facebook page, "Oh the irony...I'm suffering from a wicked case of bacterial conjunctivitis!"

Had this been any other time, I likely would have asked a colleague at SCO to take a look. But because this was vacation—and Christmas Eve, no less—I decided it would be a huge imposition to ask someone to evaluate me. Besides, I had a few drug samples in my medicine cabinet for just such an emergency.

Selecting a bottle of TobraDex ST (tobramycin 0.3%/dexamethasone 0.05%, Alcon), I began instilling one drop in my right eye every four hours. In between, I supplemented with artificial tears every half hour or so, and strived carefully not to rub my eyes so as to avoid spreading the infection contralaterally.

Unfortunately, I awoke Christmas morning to find that my left eye was involved as well.

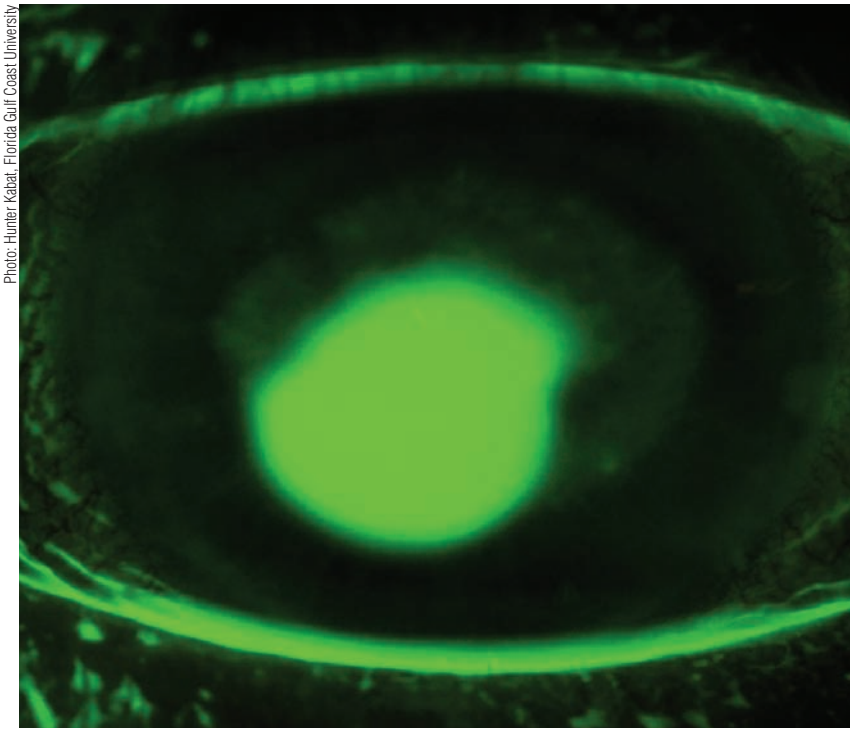

Photo: Hunter Kabat, Florida Gulf Coast University

Fluorescein-enhanced view of my corneal abrasion.

Bilateral Burgeoning

I immediately began treating my left eye with the drops, but the discomfort was twice as severe as that in my right eye. Realizing that both eyes were now involved and there was nowhere else for the infection to spread, I took solace in knowing that I could now wipe my eyes without guilt.

And I did. I unabashedly wiped, rubbed and clawed at my left eye with the all vigor that a flea-ridden mongrel displays while gnawing at his own hindquarters. And as the irritation and swelling in my right eye improved, the pain in my left eye grew more and more severe.

By Christmas evening, I'd exacerbated my simple bacterial conjunctivitis into something far worse.

Artificial tears offered little relief. Doubling up on the dose of TobraDex did not help, either. Unable to keep my eye open and miserable with pain, I resorted to a bottle of hydrocodone pills that I had left over from a prior dental procedure. Eventually, sleep and opioids overcame the discomfort.

Image Thy Father

I awoke on December 26 to find no improvement in my condition. I knew that I needed more urgent attention and appropriate therapy. But, being a Type A personality and the self-proclaimed "world's worst patient," I decided that the only physician in Memphis good enough to diagnose and treat me was…well, me. Formulating my plan, I resolved to go to my clinic; image my eye; and based on those findings, affect a curative course of action.

Realizing that I needed an accomplice to execute this plan, I enlisted the aid of my 19-year-old son, Hunter. I was hopeful that his lack of knowledge regarding optometry would curtail any dissenting opinions or management strategies.

Arriving at the clinic, I proceeded to instill a drop of 0.5% proparacaine in my left eye and give my son a crash course in the operation of the Oculus Keratograph 5M. Between the two of us, we were able to get a couple of decent images of my left eye, which showed a substantial area of corneal erosion.

As the proparacaine began wearing off, I quickly instilled two drops of 5% homatropine and a drop of Durezol (difluprednate, Alcon) to protect against uveitis. I added a drop of Moxeza (moxifloxacin, Alcon) for good measure as prophylaxis against a potential bacterial keratitis.

Finally, I inserted a bandage contact lens approved for overnight wear. I grabbed a few more samples of preservative-free artificial tears, signed out with the security guard and went home to sleep.

Resolution—Just Before New Year's

It took several days for my cornea to heal. The bandage lens improved my comfort level, but my vision was noticeably reduced and it was impossible to use my iPhone or laptop. I ended up sitting on a couch in a darkened room, watching (or rather, listening to) reruns of "Star Trek" and "The Big Bang Theory," and sleeping a lot.

In total, I wore the bandage lens for about 84 hours, all the while instilling Durezol and Moxeza QID.

Even after the erosion resolved, my vision was not 100%. I experienced monocular diplopia and visual discomfort for another 48 hours until things finally returned to normal.

What I recall most about my horrific holiday experience was not only the pain, but also the helplessness of being without functional vision. I've managed literally hundreds of abrasions, erosions and even a laceration or two—but it is impossible to fully comprehend the debilitating distress of a corneal injury until you've experienced it firsthand.

Beyond that, the sheer torment of having useful vision in just one eye was far more distressing than I'd ever imagined. Although I don't think of myself as a developmental optometrist, I have a newfound respect for the value of binocular vision.

As doctors, it's all too easy for us to isolate ourselves emotionally and think of patients simply in terms of a diagnosis and management plan. But when you're on the other side of the exam chair, you literally get a different perspective.

I'm happy to report that I've suffered no long-term effects of my infection or trauma, and that my vision has returned to 20/20 in both eyes. While I wouldn't want to live through it again, my ordeal did help teach me some valuable lessons about myself, and reaffirmed my dedication to caring for the visual welfare of those in need. I'm proud to be in a profession like optometry with such a talented, capable and compassionate group of individuals.

Maybe the next time I have a problem, I'll ask one of you for help. ■

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The Evolution of OCT

Optical coherence tomography could help monitor disease progression in neurological disorders, such as MS. **By Diana L. Shechtman, OD, and Paul M. Karpecki, OD**

Once viewed primarily as an instrument for observation of retinal disease, the clinical use of optical coherence tomography (OCT) has been expanded to include several novel applications in both ophthalmic and neurological settings. For example, the exceptional resolution of OCT allows clinicians to quantify the thickness of the retinal nerve fiber layer (RNFL) and determine the extent of visual damage following optic nerve injury.

More recently, OCT resolution also has made it possible to quantify the thickness of the ganglion cell complex (GCC) in the macular area. Because GCC provides a direct analysis of the integrity of neuronal ganglion cells and ultimately their axons, OCT is increasingly being used to monitor disease progression and treatment efficacy in patients with several neurological disorders—specifically, multiple sclerosis (MS) and optic neuropathy (ON).[1-4]

A Review of MS and ON

• MS is a chronic neurodegenerative disease with inflammatory demyelination that affects the central nervous system (CNS).

Currently, there is no definitive cure. Disease management focuses on prevention of long-term disability by restoring function after attacks and preventing new flare-ups from occurring.

The retinal tissue is an integral part of the CNS, and the RNFL is the most proximal region of the afferent visual pathway, making it an ideal interface to examine the brain. It is also a unique CNS structure as it lacks myelin, which allows for direct assessment of the effect of MS injury on axonal integrity.[5]

• ON involves inflammation of the optic nerve and is strongly associated with multiple sclerosis.

In fact, 30% to 70% of patients with MS will develop an episode of ON (it's the presenting sign in 20% to 30% of cases). Almost half of the patients with ON have white matter lesions consistent with MS.

The five-year risk of developing MS is highly contingent on the number of MRI lesions, but also may occur in patients with an absence of any lesion.[6,7]

Associated OCT Findings

In patients who present with isolated, unilateral ON attack, optical coherence tomography indicates that RNFL thickness decreases over a period of months and stabilizes around six to 12 months, with an average of 20% NFL thickness loss in the affected eye.[8,9]

The extent of damage does not appear to be a predictive factor of MS development, as it is mostly related to the severity of the attack and/or the presence of pre-existing damage secondary to previous optic nerve head injury.[5]

Interestingly, RNFL thinning often develops bilaterally in MS patients—not just in the eye affected by a unilateral attack.

Moreover, MS patients without any known episodes of ON in either eye also show RNFL thinning in both eyes.[2,8,10-13]

Compromised macular thickness also has appeared in MS patients with or without ON. This thinning seems to be concentrated at the level of the inner retina—more specifically, at the level of the GCC, where the degree of thinning correlates with the extent of RNFL loss.[14-17]

This could provide further insight on MS pathophysiology, because RNFL and GCC thinning in an eye without any prior history of ON could be attributed to asymptomatic episodes of subclinical optic neuritis.

Retrograde trans-synaptical degeneration or primary neurodegeneration of the ganglion cells and their axons in the absence of inflammation also has been speculated.[2]

The latter theory suggests that axon and ganglion cell loss may be the result of a direct mechanism of MS affecting these ocular CNS neurons, which makes it possible to use RNFL and macular/GCC thickness as markers for disease progression in MS patients.

The RNFL and ganglion cells also may be used as models to study the role and efficacy of neuroprotective agents in MS care. Furthermore, both RNFL and GCC thinning correlate with visual dysfunction, which opens the first window in establishing a structure/function paradigm in CNS injury. [12,13,17,18]

Diagnostic Applications

One useful OCT application is to aid in the differential diagnosis between neuromyelitis optica (NMO) and optic neuritis associated with MS.

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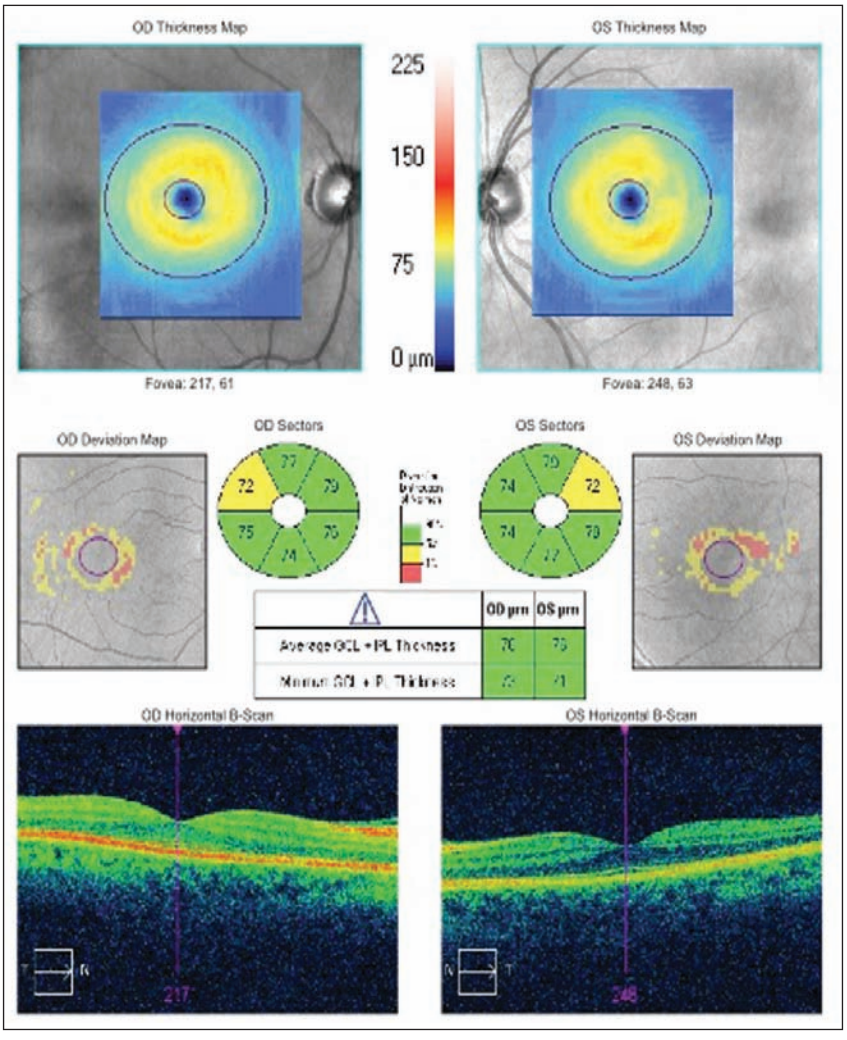
Neuromyelitis optica is a simultaneous inflammation and demyelination of the optic nerve and spinal cord, which also can affect the brain.

Unlike typical optic neuritis associated with MS, management of NMO requires early initiation of immunosuppressive therapy to reduce vision loss and neurological disability, making its early diagnosis crucial. Additionally, NMO patients do not demonstrate RNFL thinning in the non-affected eye. Therefore, it has been suggested that an inter-eye asymmetry in RNFL thickness greater than 15µm three or more months after an ON event should alert the physician to evaluate for NMO-IgG antibody testing to aid in confirming the diagnosis of NMO.[19]

It's important to be aware of recent advancements in OCT technology, as it constitutes a useful tool in the comanagement of patients who present with this potentially disabling disease. Periodic OCT screening of MS patients could provide insights on disease mechanisms by attempting to draw distinctions between thinning due to episodic inflammatory events vs. insidious disease progression. ■

Thanks to Rim Makhlouf, OD, instructor at Nova Southeastern University College of Optometry in Ft. Lauderdale, Fla., for contributing to this column.



This SD-OCT scan of a 43-year-old MS patient shows mild GCIP thinning OU.

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Product Review

Dry Eye

Nighttime Relief

Patients who suffer from severe dry eye may find nighttime comfort and relief with Retaine PM, a preservative-free, oil-based formula by OcuSoft.

Retaine PM is packaged in an economical 5-gram tube, offering 43% more than the traditional 3.5 grams. Retaine PM joins a growing line of branded eye care products for OcuSoft, including artificial tears and nutritional supplements.

Visit www.ocusoft.com/retaine.

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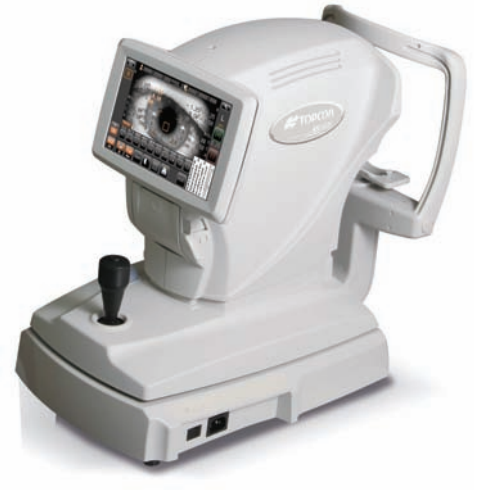
Add subjective visual acuity testing to refine a patient's measurements with Topcon's KR 800S Auto Kerato-Refractometer with Subjective and Glare Testing.



The new 5-in-1 KR-800S incorporates Topcon's Rotary Prism technology for accuracy and consistency and adds on Subjective Visual Acuity testing for good measure.

Check for near and far distance, contrast sensitivity and have access to a grid and glare test. These tools are particularly useful for cataract surgery candidates who complain of poor night vision.

Visit www.global.topcon.com.

Online interface

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Next time you log on to SpecialEyes, you can navigate to the Learning Center to access a prescribing nomogram, custom contact lens fitting guides, horizontal visible iris diameter measuring, optical zone assessment tips and other useful tools.

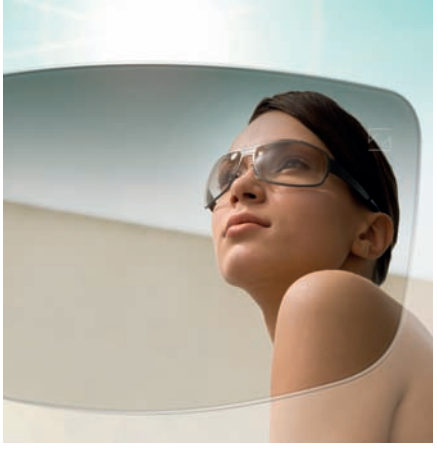
In addition to the website upgrade, the site offers an Arc Length Calculator to accurately calculate arc length of the cornea and an Over-Refraction Calculator, which determines the resultant prescription after a successful in-office over-refraction is performed.

Visit www.specialeyesqc.com.

Lenses

Wrap it Up

If you've been in the market for wrap frames to offer in your dispensary, add Zeiss Progressive Choice Plus Sport to your list of lens choices. Zeiss has extended its line of lenses to include those specifically designed for wrap frames.



Zeiss says the Choice Plus Sport design combines advanced customization for the patient's full prescription with its unique prism compensation method. This combination widens the area of clear vision by as much as 50% over standard lens designs in wrap frames, while dramatically reducing unwanted prism, the company says.

Visit www.vision.zeiss.com.

Eyewear

Sun Collection

Ready for summer? So is Moscot. They've pumped-up four selections from their Moscot Originals collection to create the Governor, Randall, Ellis

and Staten—all infused with rich custom color lenses perfect for summer eyewear.

The company describes the Ellis as chunky and aggressive and the Governor as striking and hefty. As for the Randall and Staten, they are tricked out and full of glamour, respectively.

Visit www.moscot.com.

Cleopatra

Exotic woods are the main feature of Rye & Lye's new collection from Italy. The line features "Cleopatra," a woman's frame with a 1950s chunky cat-eye. The company claims the curves of the temples were specifically designed to enhance the natural grain of the exotic wood.

Other eyewear in the collection includes the butterfly-shaped Ermione and the Edgar for men, with lightweight acetate and aluminum elements and wood trim.

Visit www.rye-lye.it.

Cool Collection

Although best known for high-performance sunglasses and goggles for skaters, surfers and snowboarders, Arnette has now branched out with a frame line that offers a cool-vibe collection for prescription eyeglass wearers.

Most of Arnette Optical's line features unisex frames like the "Dub," a statement model that comes in black, striped Havana, black and grey horn, or blue ice. Other styles follow a rock-star theme: Roadie, Auxiliary, Mixer, Lo-Fi, Sync, Fader, and Frontman.

Visit www.Arnette.com. ■

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March 2014

■ **22-23.** *Spring Conference.* Nova Southeastern University Ft. Myers Campus, Ft. Myers, Fla. Hosted by: Nova Southeastern University. Contact oceaa@nova.edu. Visit http://optometry.nova.edu/ce/index.html.

■ **26-30.** *Vision Expo East.* Javits Center, New York. Hosted by: International Vision Expo. Visit www.visionexpoeast.com.

■ **27-29.** *OAOP Annual Spring Congress.* Embassy Suites Hotel and Conference Center, Norman, Okla. Hosted by: Oklahoma Association of Optometric Physicians. Key faculty: Walt West, OD, Blair Lonsberry, OD, David Talley, OD, Larry Henry, OD, Jason Ellen, OD, Chad Chamberlain, DO, Joyce Ardrey, CPC. CE hours: 18. Contact Heatherlyn Burton at heatherlyn@oaop.org. Visit www.oaop.org.

■ **29-30.** *Conference on Comprehensive EyeCare 2014.* Sheraton Hotel, Niagara Falls, NY. Hosted by: PSS EyeCare. Key Faculty: Joseph Sowka, OD, Paul Ajamian, OD, Anthony Litwak, OD, Deepak Gupta, OD, and Robert Rebello. CE hours: 18. Email Sonia Kumari at education@psseyecare.com. Visit www.psseyecare.com.

April 2014

■ **3-6.** *OptoWest 2014.* Esmeralda Hotel, Indian Wells, Calif. Hosted by: California Optometric Association. Key faculty: Marc Bloomenstein, OD, Sharon Carter, ECOC, Melissa Chun, OD, Laurie Guest, CSP, Lynn Hellerstein, OD, FCOVD, Richard Hom, OD, MPA. CE hours: 40+. Email Rachael Van Cleave at contact@coavision.org. Visit www.coavision.org.

April 3-6, Atlanta

2014 Optometric Business Conference

An international Fulbright Scholar and expert on age-related macular degeneration, a chief economist with Morgan Stanley and a leading authority on the Affordable Care Act are just a few of the presenters who will be at the 2014 Optometric Business Conference, presented by Independent Doctors of Optometric Care (IDOC). The conference, held from April 3-6 at the Loews Hotel in Atlanta, will include sessions on financial management, legal issues, health care reform, reputation management, and several CE and ABO-certified sessions for ODs and their staff.

All independent ODs and staff are offered refundable registration of up to $200 through March 17.

The conference is part of CE and business management education programs held throughout the year by IDOC, the fastest-growing alliance for independent eye care practitioners in the country. In addition to premier business management education, IDOC offers discounts and rebates from more than 65 leading companies in the industry.

Visit www.idoc.net or call 203-853-3333 for information.

■ **4-6.** *NOA Spring Conference.* Embassy Suites Downtown/Old Market, Omaha, Neb. CE hours: 16. Contact Alissa Johnson at (402) 474-7716. Visit www.nebraska.aoa.org/springconference.

■ **11-13.** *New Mexico Optometric Association Annual Convention.* Isleta Resort, Albuquerque, N.M. Hosted by: New Mexico Optometric Association. CE hours: 22. Email Richard Montoya at newmexicooptometry@gmail.com or call (575) 751-7242. Visit www.newmexicooptometry.org.

■ **12-13.** *2014 MOS Primary Care Spring Symposium.* Cincinnati Marriott Northeast, Mason, Ohio. Hosted by: The MidWest Optometric Society and The Ohio State University College of Optometry. Contact Marci at (513) 321-2020. Visit www.midwestoptometricsociety.com.

■ **12-13.** *Symposium on Ocular Disease 2014.* Crowne Plaza, Tyson's Corner, Virg. Hosted by: PSS EyeCare. Key Faculty: Joseph Sowka, OD, Murray Fingeret OD, Deepak Gupta, OD, and Robert Rebello. CE hours: 18. Email Sonia Kumari at education@psseyecare.com. Visit www.psseyecare.com.

■ **23-27.** *American Academy of Optometry-New Jersey Chapter.* Kingston Plantation, Myrtle Beach, SC. Hosted by: New Jersey Chapter. Key faculty: Randall Thomas, OD, Ron Melton, OD, Marc Blumenstein, OD. CE hours: 16. Email Dennis Lyons, OD, dhl2020@aol.com, or call (732) 920-0110.

■ **24-26.** *Mountain West Council of Optometrists Annual Congress.* Caesars Palace, Las Vegas. Hosted by: MWCO. CE hours: 24. Call 1-888-376-6926. Visit www.mwco.org.

■ **24-26.** *59th Annual Education Meeting.* Hilton Savannah DeSoto, Savannah, Ga. Hosted by: Contact Lens Society of America. Key faculty: Patrick Caroline, FAAO, Craig Norman, FCLSA, Michael Ward, FCLSA, Jason Jedlicka, OD, Brooke Messer, OD, Edward Bennett, OD, Stephen Byrnes, OD. CE hours: 22. Email Tina Schott at tinaschott@clsa.info or call (703) 437-5100. Visit www.clsa.info.

■ **24-27.** *KOA 2014 Spring Congress.* Hyatt Hotel & Lexington Convention Center, Lexington, Ky. Hosted by: Kentucky Optometric Association. CE hours: 21. Email Sarah Unger at sarah@kyeyes.org or call (502) 875-3516. Visit www.kyeyes.org.

■ **24-27.** *Arkansas Optometric Association Spring Convention.* The Peabody, Little Rock, Ark. Hosted by: Arkansas Optometric Association. Email aroa@arkansasoptometric.org. Visit www.arkansasoptometric.org.

■ **25-27.** *2014 Annual CE Symposium.* Renaissance O'Hare, Chicago, Ill. Hosted by: The Optometric Society and Optometric CE. Key faculty: James Fanelli, OD, Ernie Bowling, OD, Robert Rebello, Steven Newman, OD. CE hours: 14. Email Joel Rothschild at admin@optometricce.org. Visit www.optometricce.org.

■ **26-27.** *22nd Annual Suncoast Seminar.* Hyatt Regency Clearwater Beach Resort and Spa, Clearwater, Fla. Hosted by: Pinellas Optometric Association. CE hours: 14. Email idoc1@aol.com or call (727) 446-8186. Visit www.optometricce.org.

May 2014

■ **2.** *Berkeley Glaucoma Day - 2nd Annual.* DoubleTree Hotel, Berkeley Marina, Berkeley, Calif. Hosted by: University of California, Berkeley, School of Optometry. Email optoCE@berkeley.edu. Visit awww.aoa.org/events/ucb-glaucoma-day.

■ **2-3.** *Educational Meeting 2014.* Mission Inn, Howey-in-the-Hills, Fla. Hosted by: Florida Chapter of the American Academy of Optometry. Featured speakers: Leo Semes, OD, Albert Woods, OD, and Tim Underhill, OD. CE hours: 10. Contact Arthur T. Young, OD, at eyeguy4123@msn.com.

■ **2-4.** *CE in Italy.* Rome, Italy. Hosted by: James Fanelli, OD. Key faculty: Joe Pizzimenti, OD, Carlo Pelino, OD, James Fanelli, OD. CE hours: 12. Contact James Fanelli, OD, at jamesfanelli@CEinItaly.com or call (910) 452-7225.

■ **2-4.** *May Annual Eye Care Conference & Alumni Reunion.* Nova Southeastern University, Ft. Lauderdale, Fla. Hosted by: Nova Southeastern University. Key faculty: Carlo Pelino, OD. CE hours: 18. Contact Vanessa McDonald at oceaa@nova.edu or call (954) 262-4224.

■ **4-8.** *ARVO Annual Meeting.* Orange County Convention Center, Orlando, Fla. Hosted by: ARVO. Email arvo@arvo.org.

■ **7-8.** *118th Annual Meeting and Spring Seminar.* DeVos Place, Grand Rapids, Mich. Hosted by: Michigan Optometric Association. CE hours: 12. Contact Amy Root at amy@themoa.org or call (517) 482-0616.

■ **10-19.** *AEA Cruises Mediterranean Cruise Seminar.* Athens to Venice. Hosted by: AEA Cruises. Key faculty: Louise Sclafani, OD, Mark Roanova, OD. CE hours: 12. Contact Marge McGrath at aeacruises@aol.com or call (888) 638-6009.

■ **29-31.** *Oregon's Meeting.* Bend Riverhouse Hotel and Conference Center, Bend, Ore. Hosted by: Oregon Optometric Physicians Association. Key faculty: Jane Weissman, MD, Thomas Hwang, MD, Greg Kaultz, OD, Ryan Bulson, OD, Mark Andre, FAAO. CE hours: 11. Contact Lynne Olson at lynne@oregonoptometry.org or call (800) 922-2045.

June 2014

■ **8.** *Resident Forum.* US Berkeley Campus, Berkeley, Calif. Hosted by: University of California, Berkeley, School of Optometry. CE hours: 8. Email mmoy@berkeley.edu or call (510) 642-8802. Visit optometry.berkeley.edu/ce/introduction.

■ **13-14.** *Northwest Residents Conference.* Jefferson Hall on Pacific University Campus, Forest Grove, Ore. Hosted by: Pacific University College of Optometry. CE hours: 10. Email Martina Fredericks at frederim@pacificu.edu or call (503) 352-2207. Visit www.pacificu.edu.

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Surgical **Minute**

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

Let There Be Light

Laser surgery for glaucoma—perhaps overlooked today—still plays an important role.

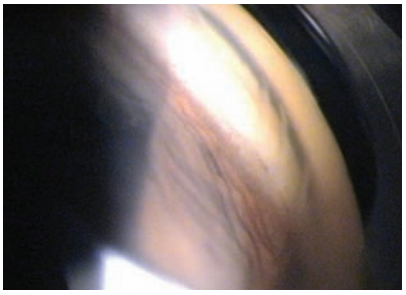
Glaucoma patients, and their doctors, have much cause for optimism in 2014. Many patients can be managed with nothing more than a once-daily topical drug. For those who need more robust IOP lowering, we have a broad swath of surgical options, from the emerging "minimally invasive" class to mainstays like trabs and tubes. Advanced technology, most notably OCT, provides insights into disease progression that would have been unheard of a generation ago, and our burgeoning clinical proficiency has allowed glaucoma management to become routine in optometric practice.

Despite this renaissance in glaucoma care, the role of patient compliance and adherence cannot be overlooked. Noncompliance and non-adherence rates, reported to be at least 25%, continue to undermine our best efforts. Common reasons include inconvenience, forgetfulness, cost and side effects of medications.

Burning Questions

Can laser trabeculoplasty match or beat the results of medical therapy, while also reducing the impact of noncompliance?

Argon laser trabeculoplasty (ALT), introduced in the 1970s, can lower IOP by about 25% to 30%. Though the exact mechanism still is not known, the laser energy may have multiple effects on the trabecular tissue, including a mechanical effect from scar formation at the burn sites and biologic changes in the trabecular endothelial cells.



The surgeon uses a gonio lens to visualize the trabecular meshwork during SLT.

ALT was evaluated in the NEI's Glaucoma Laser Trial (GLT), which compared the procedure's safety and long-term efficacy with that of standard medical therapy for primary open-angle glaucoma. Eyes treated initially with ALT had 1.2mm Hg greater IOP reduction, 0.6db greater visual field improvement and better optic disc status than fellow eyes treated initially with topical medication. Although this trial evaluated argon laser treatment, modern-day glaucoma laser surgery has largely migrated to selective laser trabeculoplasty (SLT) and micropulse laser trabeculoplasty due to their comparable IOP lowering efficacies, but with less damage/scarring and better repeatability.

SLT is an outpatient procedure, performed with a laser-equipped slit lamp. The energy is produced by a specially designed Q-switched, frequency-doubled Nd:YAG laser operating at a 532nm green wavelength, with a potential output of 0.3 to 1.5 millijoules.

Preoperatively, the patient is given one drop of either apraclonidine or brimonidine, plus topical anesthesia. A Goldmann, three-mirror gonio lens is placed on the eye with methylcellulose and the aiming beam is focused onto the pigmented trabecular meshwork. Next, the non-thermal laser is applied using short pulses of relatively low energy with a larger spot size to target and irradiate only the melanin-rich cells in the trabecular meshwork.

Treatment is done in single-burst mode, placing about 50 contiguous but not overlapping 400µm laser spots along 180 degrees. The principle of selective photothermolysis enables the laser to precisely target intracellular melanin granules to activate individual cells without disturbing adjacent non-pigmented cells. The activated cells release cytokines that trigger a targeted macrophage response to the trabecular meshwork cells. The macrophages reactivate the meshwork, reducing fluid outflow resistance and lowering intraocular pressure.

The procedure takes about five minutes per eye, is relatively painless and there are no restrictions afterwards. Postoperatively, patients are prescribed topical NSAIDs or steroids for one week. Clinical improvement may take one to three months to manifest.

Benefits of SLT include proven efficacy as primary, adjunctive or repeat therapy; lack of systemic side effects; protection of the trabecular meshwork; reduced drug costs and improved compliance. Potential side effects include post-op inflammation and IOP spike, which can be controlled with topical meds. ■

References available upon request.

Diagnostic **Quiz**

Dystopian Dystonia

By Andrew S. Gurwood, OD

History

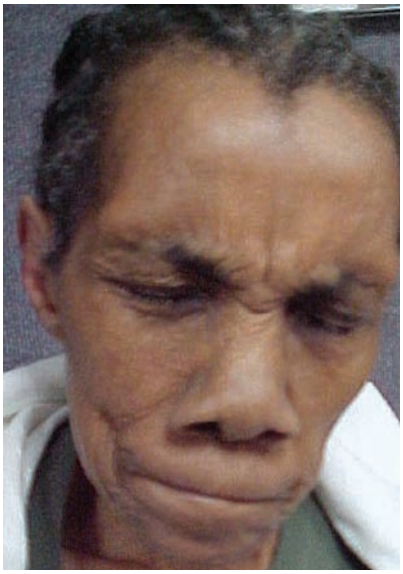
A 67-year-old black female presented for a consultation regarding an unusual facial spasm after being admitted to the hospital 15 days earlier for multiple systemic illnesses. She did not experience any local or generalized head pain, but reported an increase in blinking and "eyelid twitching" as early as five to seven years ago.

Her systemic history was remarkable for medically controlled arrhythmia and hypertension. She reported no known allergies of any kind.

Diagnostic Data

Her best-corrected visual acuity measured 20/20 OU at distance and near. We uncovered no evidence of afferent pupillary defect. Additionally, the external, corneal and internal ocular evaluations were normal.

The dilated fundus examination was normal. Her intraocular pressure measured 14mm Hg OU. The pertinent clinical finding is illustrated in the photograph.



External image of our 67-year-old patient who presented with a facial spasm. What is the most likely diagnosis?

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. ■

Retina Quiz Answers *(from page 90):* 1) b; 2) b; 3) d; 4) b; 5) d.

Next Month in the Mag

April features our Corneal Disease Report.
Topics include:

- *Optometric Study Center: The Pathogens of Corneal Infection* (earn 2 CE credits)
- *The Role of Corneal Pharmacodynamics in Topical Antibiotic Delivery*
- *Endothelial Cell Dystrophy: Causes and Remedies*

Also inside:

- *How Hypertension and High Cholesterol Harm the Eye*
- *Give Your Instruments and Office Equipment a Tune-Up*
- *Visual Field Interpretation: 10 Clues Something is Amiss*

And...

- Don't miss the April issue of *Review of Cornea & Contact Lenses,* devoted to scleral lens topics.

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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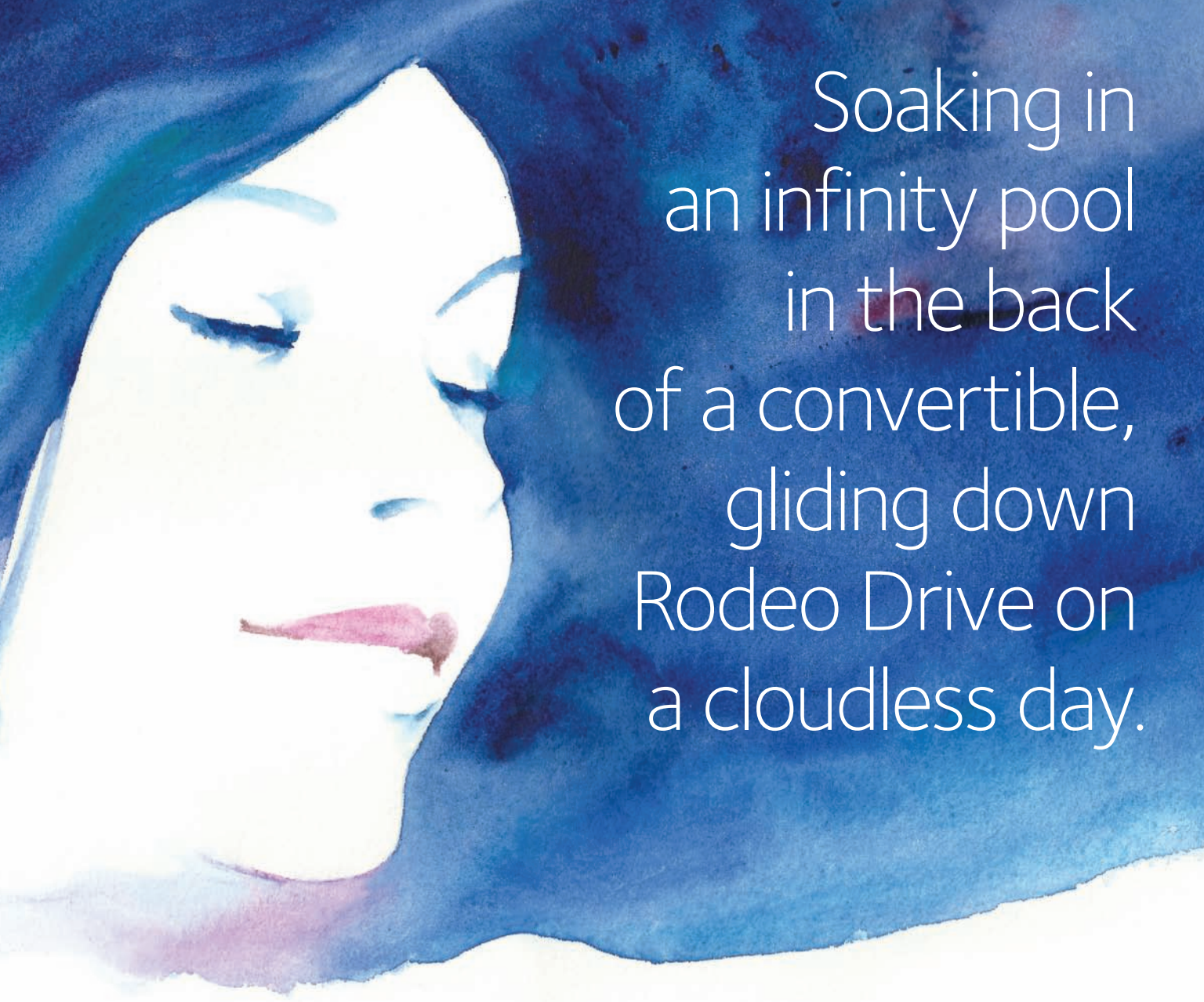

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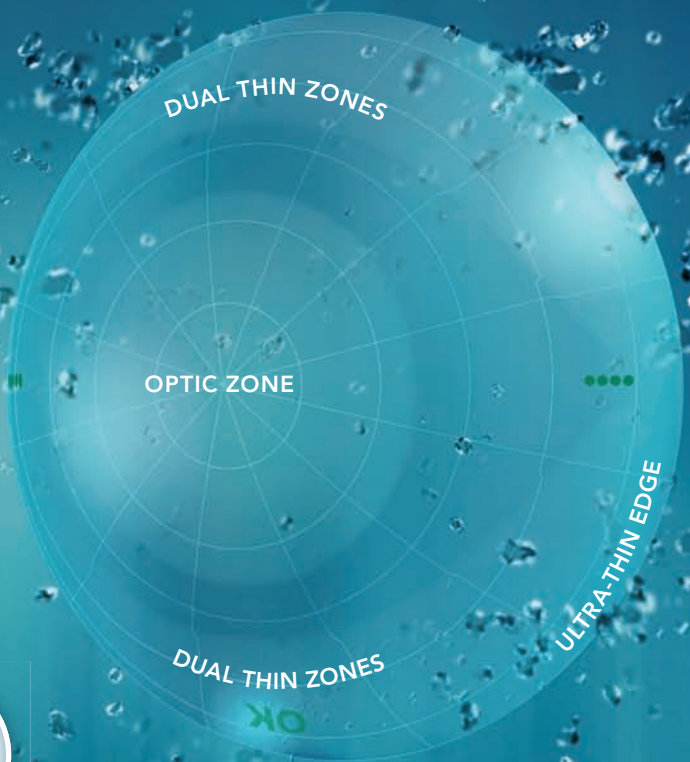

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References: 1. In a subject-masked clinical trial (n=93); Alcon data on file, 2010.

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