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REVIEW® OF OPTOMETRY

February 15, 2016

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INNOVATION IN EYE CARE

All EYES on NEURODEGENERATIVE DISEASE

The eye may harbor biomarkers of Alzheimer's and Parkinson's. New research reveals what to look for, p. 42.

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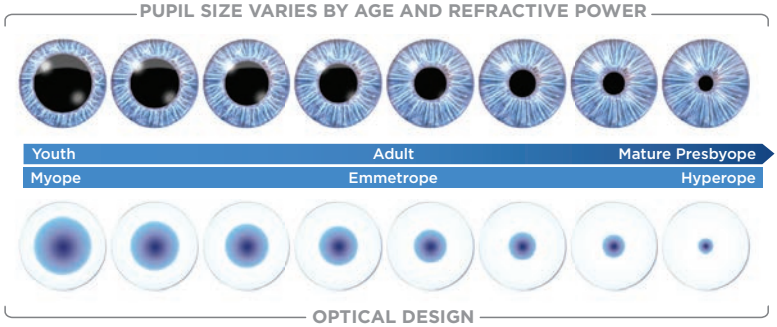

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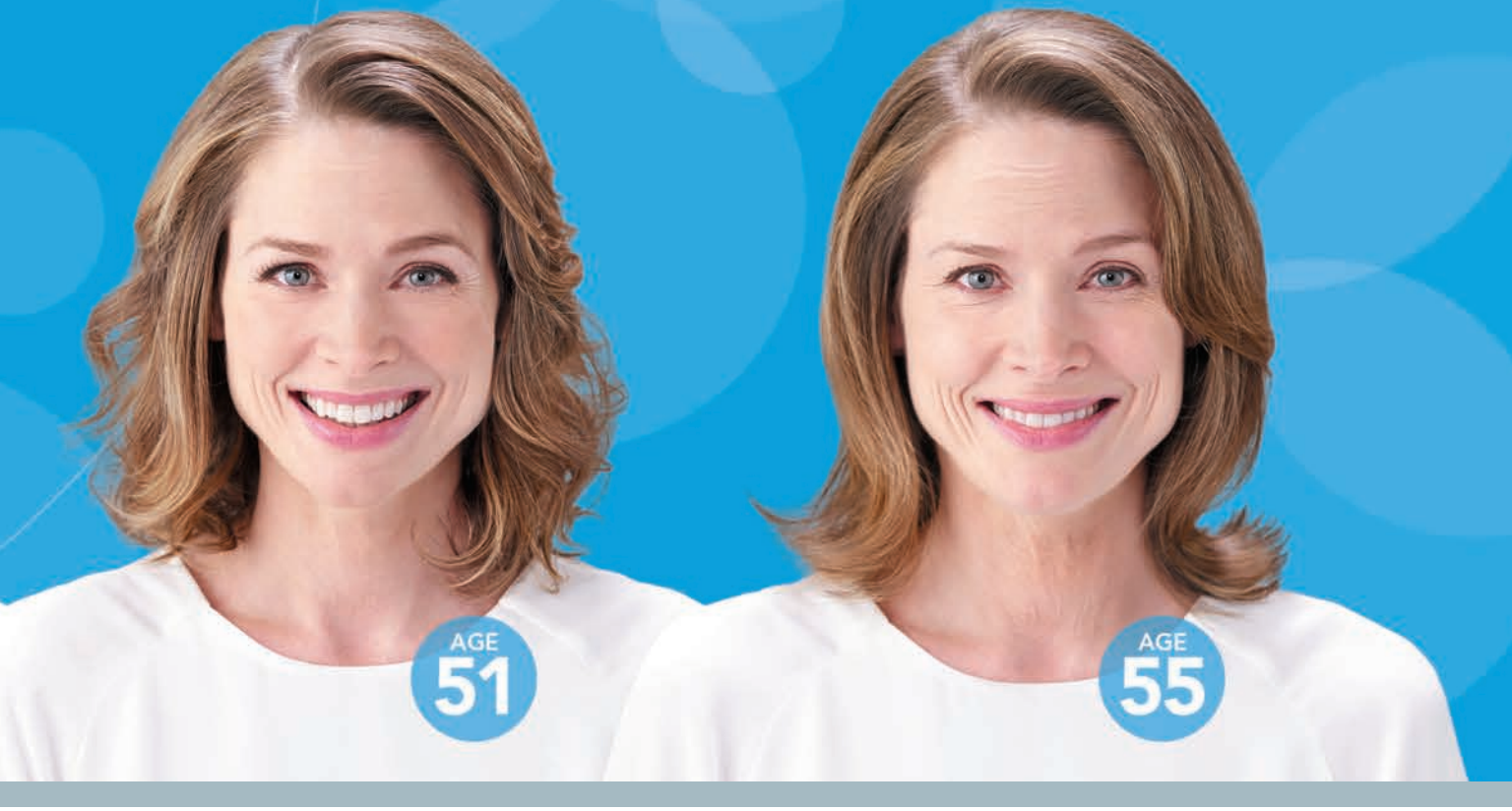

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VOL. 153 NO. 2 ■ FEBRUARY 15, 2016

IN THE NEWS

Researchers have found a rare link between the **varicella zoster vaccine** and corneal inflammation. A review of case studies, presented at the 2015 meeting of the American Academy of Ophthalmology, discovered **20 cases of keratitis** that developed within a month of administration of the vaccine.

Saskatchewan Health Minister Dustin Duncan will **allow ODs to independently treat glaucoma**, against the advice of the College of Physicians and Surgeons. The College feels treatment should be done collaboratively with ophthalmologists, according to associate registrar Bryan Salte in a press release. However, Mr. Duncan is satisfied the Saskatchewan Association of Optometrists (SAO) will ensure members remain **up-to-date on necessary training**—98% are already compliant with recertification.

The **Multi-Ethnic Pediatric Eye Disease Study (MEPEDS)**, the largest study of childhood eye diseases ever undertaken in the United States, confirms that **childhood myopia** among American children has **more than doubled** over the last 50 years, according to a news release. The study was conducted by researchers from the USC Eye Institute at Keck Medicine at USC in collaboration with the National Institutes of Health (NIH).

Researchers at Boston Children's Hospital recently restored some vision in mice with **optic nerve injury** by using **gene therapy** in combination with a **drug cocktail**. They are now testing whether injecting the cocktail of growth factor proteins directly into the eye could be equally as effective as the gene therapy alone.

Keratoconus Risk Factors Revealed

The largest study ever on this disease uncovers some surprises about who may—or may not—be at an increased risk. **By Rebecca Hepp, Senior Associate Editor**

A recent retrospective, longitudinal cohort study has discovered associations between certain sociodemographic factors, common systemic diseases and the risk of keratoconus (KCN). Researchers at the University of Michigan Health System's Kellogg Eye Center and the U-M Institute for Healthcare Policy and Innovation matched 16,053 patients with KCN 1:1 with patients without KCN using billing codes, age, gender and overall health to discover if certain sociodemographic factors and systemic diseases affected the odds of KCN.

"This study is the largest study ever on keratoconus, with over 32,000 subjects," says Andrew Morgenstern, OD, an executive board member of the International Keratoconus Academy of Eye Care Professionals. "This was amongst a large, diverse group of insured individuals; these people have the capability of getting treatment, so these are patients in the chair."

The results of the study show black and Latino patients are at a 57% and 43% increased risk of KCN, respectively, compared with whites, while Asian patients have a 39% reduced risk of a KCN diagnosis compared with whites.

As for systemic diseases, the researchers discovered patients with diabetes mellitus or collagen vascular disease have 20% and 35% lower odds, respectively. Those diagnosed with sleep apnea, asthma and Down syndrome were at increased risk.

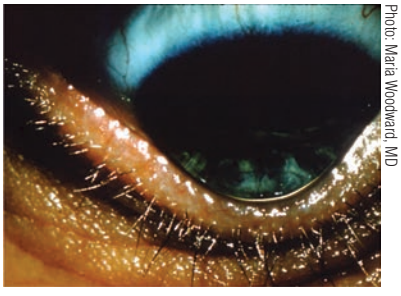

Photo: Maria Woodward, MD

Data from over 32,000 subjects reveals several risk factors for keratoconus.

The study should have a significant impact on clinical practice, Dr. Morgenstern says, considering it identifies specific patient populations that have to be counseled when they are in the office.

"This study is fantastic because it has such a large sample size and it clearly identified common risk factors and sociodemographic issues," Dr. Morgenstern says. "Now that it's out there, it will affect the standard of care for keratoconus screening."

"For example, because of the high rates of obesity in the United States, and because allergens in certain areas of the United States are

(continued on pg. 6)

KCN Screening Implications

(continued from pg. 4)
high, there are higher populations with sleep apnea and asthma now," Dr. Morgenstern says. "The study suggests that if patients have these breathing issues, they have to be counseled on the higher risk of keratoconus."

"As eye care providers, we are qualified to diagnose keratoconus, but a patient with keratoconus should be aware of other conditions that may affect their overall health," says Maria Woodward MD, an assistant professor of ophthalmology at the U-M Medical School and first author of the new study. "We believe the most important thing for practicing eye care providers is to ask about sleep apnea risk factors and asthma for patients with keratoconus."

These findings could go a long way toward improving not only patient education, but also the possibility of newer treatment options, such as corneal crosslinking.

"This study will help promote the understanding of corneal collagen crosslinking and how important it is that the FDA approve this procedure," Dr. Morgenstern says. "If you can identify keratoconus early enough and crosslink it early enough, you can prevent the vision loss in these patients.

"I believe Dr. Woodward and her group at the University of Michigan did a great service to the ongoing understanding of this all too common disease of the cornea," Dr. Morgenstern says.

Woodward MA, Blachley TS, Stein JD. The Association Between Sociodemographic Factors, Common Systemic Diseases, and Keratoconus: An Analysis of a Nationwide Heath Care Claims Database. Ophthalmology. 2015 Dec 16. [Epub ahead of print].

New Genes Associated with POAG

Researchers at Case Western Reserve University School of Medicine, funded by the National Eye Institute (NEI), part of the National Institutes of Health, recently discovered three genes associated with primary open-angle glaucoma (POAG)—possibly opening the door to future advancements in its detection and treatment.

Using data from the NEI Glaucoma Human Genetics Collaboration Heritable Overall Operational Database, investigators compared the DNA of 3,853 people with POAG with 33,480 controls and found that variations in the FOXC1, TXNRD2 and ATXN2 genes were associated with POAG.

FOXC1 had previously been associated with rare cases of severe-onset glaucoma, according to a press release, but the TXNRD2 and ATXN2 associations were a surprise. TXNRD2 helps protect mitochondria against oxidative stress, and its association with POAG "is the first direct report to show the association of a gene linking oxidative damage to glaucoma," Neeraj Agarwal, PhD, a program director at NEI, said in a press release.

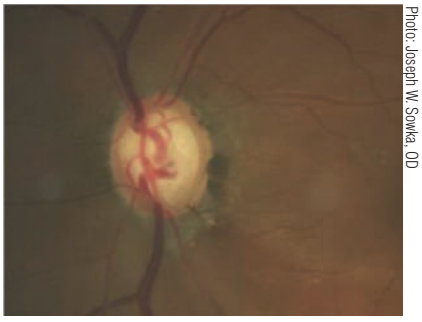

Photo: Joseph W. Sowka, OD

Researchers also discovered both TXNRD2 and ATXN2 are expressed in retinal ganglion cells and the optic nerve head.

"This is a strong step forward to better understanding not only the genetic component of POAG, but also the potential of mitochondrial oxidative stress in the overall pathophysiology of the disease," says Joseph W. Sowka, OD, professor, chief of the Advanced Care Center and director of the Glaucoma Service at Nova Southeastern University College of Optometry. "But it is only a step along our pathway of understanding."

While study authors hope the findings will lead to new therapies, Dr. Sowka has concerns that "once this is widely known, there may be financial incentives for companies to develop a genetic test for glaucoma," he says. "Not very long ago there was a genetic test for glaucoma that imparted very little useful information to assist with the clinical care of patients and it quietly vanished."

But, "at some time in the future, we may have a better understanding of glaucoma genetics and true targeted gene therapy may then become possible," Dr. Sowka says.

Bailey JNC, Loomis SJ, Kang JH, et al. Genome-wide association analysis identifies TXNRD2, ATXN2 and FOXC1 as susceptibility loci for primary open-angle glaucoma. Nature Genetics. 2016. DOI: 10.1038/ng.3482.

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In clinical trials, the most common adverse reaction following the use of RESTASIS® was ocular burning (upon instillation)—17%. Other reactions reported in 1% to 5% of patients included conjunctival hyperemia, discharge, epiphora, eye pain, foreign body sensation, pruritus, stinging, and visual disturbance (most often blurring).

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

Reference: 1. RESTASIS® Prescribing Information.

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News Review

REVIEW® OF OPTOMETRY

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Glaucoma and Yoga: A Good Fit?

Patients diagnosed with glaucoma may be subjected to increased intraocular pressure (IOP) while practicing yoga, particularly during positions in which the head is facing downward, according to researchers from the New York Eye and Ear Infirmary of Mount Sinai.

Patients are encouraged to remain active; however, patients with glaucoma should avoid exercises that could increase IOP such as pushups and lifting heavy weights, said Robert Ritch, MD, senior author of the study, in a press release.

"This new study will help clinicians advise their patients on the potential risk associated with various yoga positions and other exercises that involve inverted poses," Dr. Ritch said.

The study compared the IOP of 10 healthy patients with 10 patients with glaucoma while performing several head-first yoga positions, including standing forward bend, downward facing dog, plow and legs up the wall. The researchers measured baseline IOP, then took measurements after having the groups hold the poses briefly, for up to 120 seconds and during seated resting times of up to 10 minutes.

Measurements of both participant groups revealed a rise in IOP in all of the yoga positions tested, and downward facing dog showed the greatest increase in pressure—IOP increased from 17mm Hg to 28mm Hg in glaucoma patients and 17mm Hg to 29mm Hg in normal patients, according to the study. All yoga poses were associated with a significant increase in IOP within 60 seconds of taking yoga positions and returned to normal within two minutes of returning to the seated position.

Because elevated IOP is an important risk factor for further nerve damage, "the rise in IOP after assuming the yoga poses is of concern for glaucoma patients and their treating physicians," said first author and doctoral student Jessica Jasien, in a press release. She suggested glaucoma patients share their diagnosis with their yoga instructors to allow for proper modification during practice.

Although the study suggests certain aspects of yoga are a cause for concern, some optometrists remain uncertain regarding its clinical impact. "Certain activities do increase IOP while performing them," says James Fanelli, OD, of Cape Fear Eye Institute in Wilmington, NC. "For instance, if you wore a tight necktie 24/7 or were inverted 24/7, then that can realistically increase risk. But activities limited in duration probably do not pose significant risk long-term; however, this would be helpful in cases when a patient is continuing to worsen despite an aggressive treatment approach."

Jasien JV, Jonas JB, de Moraes CG, Ritch R. Intraocular pressure rise in subjects with and without glaucoma during four common yoga positions. PLOS ONE. 2015 Dec. doi:10.1371/journal.pone.0144505.

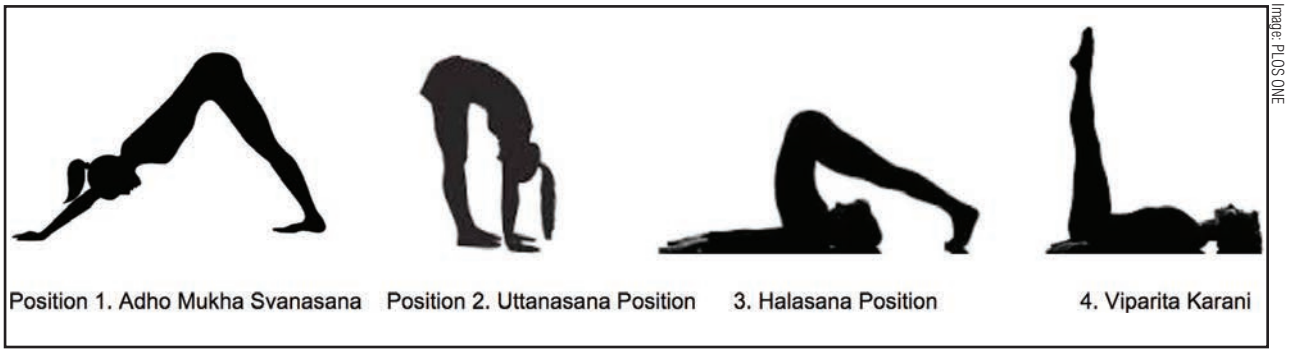

Image: PLOS ONE

Subjects performed several yoga positions, including downward facing dog, standing forward bend, plow and legs up the wall.

Correction

In the article, "ACA Children's Vision Health Benefit: Boom or Bust?" (December 2015), the American Optometric Association was mislabeled as the American Academy of Optometry. The first "Call To Action" point should have read: "Work with the *American Optometric Association*'s (AOA) 'Think About Your Eyes' and 'InfantSEE' programs to publicize the importance of eye health in your community."

Down, Boy.

Help Tame Postoperative Ocular Inflammation and Pain With LOTEMAX® GEL

Indication

LOTEMAX® GEL (loteprednol etabonate ophthalmic gel) 0.5% is indicated for the treatment of post-operative inflammation and pain following ocular surgery.

Important Safety 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.
- 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.
- Use of corticosteroids may result in posterior subcapsular cataract formation.
- 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, and where appropriate, fluorescein staining.
- 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 infection.
- Use 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 exacerbate the severity of many viral infections of the eye (including herpes simplex).
- 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.
- Patients should not wear contact lenses when using LOTEMAX® GEL.
- The most common ocular adverse drug reactions reported were anterior chamber inflammation (5%), eye pain (2%) and foreign body sensation (2%).

Please see brief summary of Prescribing Information on adjacent page.

LOTEMAX® GEL
loteprednol etabonate
ophthalmic gel 0.5%

BAUSCH + LOMB

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to prescribe Lotemax Gel safely and effectively. See full prescribing information for Lotemax Gel.

Lotemax (loteprednol etabonate ophthalmic gel) 0.5%

Rx only
Initial Rx Approval: 1998

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.

Bausch & Lomb Incorporated
Tampa, Florida 33637 USA

US Patent No. 5,800,807

US/LGX/15/0042
Based on 9269100-9269200 Revised: 9/2012

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Review of Optometry February 2016

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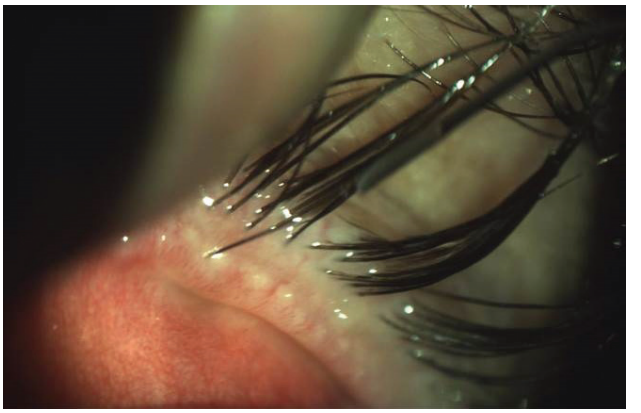

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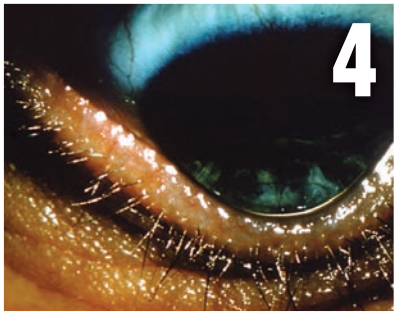

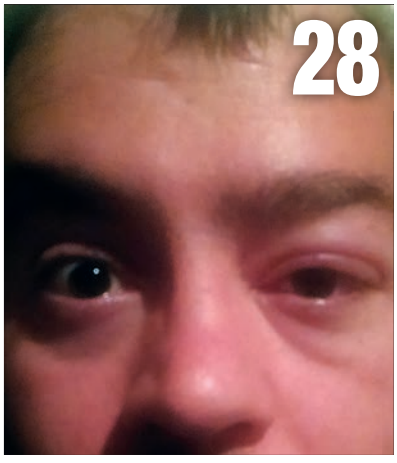

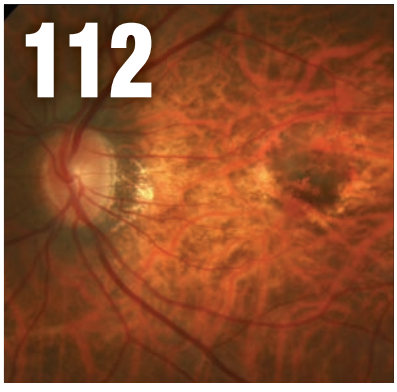

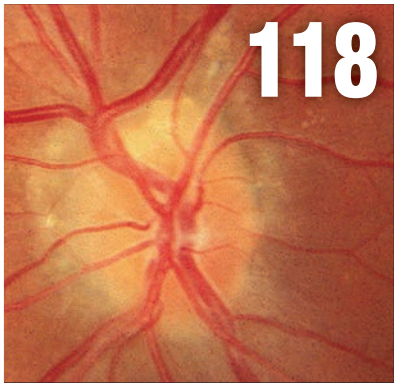

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Focusing on Innovative Choices in Presbyopic Contact Lens Wear

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By
Curtis Frank, OD
Dr. Curtis Frank Vision and Ortho-K Center
Boston, MA

Situated in the heart of Boston's Financial District, my office treats a large number of professionals ages 40 to 50. Most have been wearing single-vision contact lenses for over 20 years, but with Father Time, more and more are shifting to multifocal lenses. Indeed, these baby boomers and Generation X'ers are a part of the new wave of patients with presbyopia.

Significant improvements in materials, designs and parameter ranges make the shift from monovision to multifocal contact lenses more seamless. I'm finding that the PureVision® 2 Multi-Focal Contact Lens for Presbyopia with it's 3-Zone Progressive Design is a great option for my patients. The lenses are easy to fit in most patients and provide clear distance vision along with excellent near clarity that a patient expects when reading or focusing on computer tasks.

Recently, I treated a 57-year-old legal administrator whose current correction—multifocal lenses with two high adds—fell short of her expectations. She was using readers over the lenses and was struggling with poor vision clarity when driving at night. I was able to switch her to the 3-Zone Progressive Design with just a slight adjustment to her current prescription. When she returned for her follow-up visit, she reported that both her distance and near vision were great.

> **"Significant improvements in materials, designs and parameter ranges make the shift from monovision to multifocal contact lenses more seamless."**

Another patient, an avid golfer fitted with a modified monovision lens regimen, had difficulty spotting balls that landed 130 or more yards away from his tee shot. He switched to PureVision® 2 For Presbyopia and was ecstatic with his newfound distance vision. Aside from these two patients, I've also fit a number of emerging presbyopes successfully with this unique progressive lens design.

I have found the fitting guide to provide a predictable fit from the start for many of my patients.

The unique design behind the lens is impressive. Its 3-Zone Progressive Design offers wide near and intermediate zones with gradual power change for focusing on objects like smart phones and computers, while delivering clear vision for distant objects.

We all experience vision changes as we age. But if it's any consolation to contact lens wearers over 40, it's actually a great time to be a presbyope. Recent advances in contact lens technology have given us a host of great options for presbyopic vision correction. The PureVision® 2 contact lenses For Presbyopia with the 3-Zone Progressive Design are a large part of my contact lens arsenal and an excellent "go-to" choice for my presbyopic patients.

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Friends in Low Places

Help spread the word about low vision, a 'niche' that deserves to go mainstream. **By Jack Persico, Editor-in-Chief**

You might think that efforts to help the visually impaired would be an integral part of all optometric offices; however, 'low vision' remains a subspecialty. Still, even those optometrists who don't have the interest or patient population to offer such services can help the broader community by publicizing low vision. February is Low Vision Awareness month, and the NEI's National Eye Health Education Program offers a multitude of educational materials you can share online and in person to spread the word. They're available here: www.nei.nih.gov/nehep/lvam.

As it now stands, too few general optometrists understand how low vision specialists define the condition, and this limits referrals to specialists, according to a poster presented at the 2014 Academy meeting by students from the New England College of Optometry.

You may have been taught that BCVA of 20/70 or worse signified low vision. "The problem with this numeric definition is that it did not take into account the functional problems many individuals with better than 20/70 vision have with conditions that cause glare and/or contrast loss that are not evident during high contrast visual acuity testing routinely performed by eye care providers," says Mark Wilkinson, OD, clinical professor of ophthalmology at the University of Iowa Carver College of Medicine.

To be more inclusive, the NEI defines low vision in functional terms. Its definition encompasses individuals of all ages who have a congenital or acquired impairment of visual acuity or visual field, or other functionally disabling factors, in the better-seeing eye. This loss of vision interferes with the process of learning, vocational or avocational pursuits, social interaction or activities of daily living and is not correctable by standard corrective lenses, medications or surgery.

"Low vision rehabilitation should be part of the continuum of eye care that includes refractive, medical and surgical eye care, which begins at birth and carries forward throughout life," says Dr. Wilkinson, who shares the following patient screening questions developed by Roy Cole, OD, director of the Vision Program Development at Lighthouse Guild in New York:

- *Do you have trouble doing what you want to do because of your vision? For example, reading your mail, watching television, recognizing people, paying your bills, signing your name, climbing stairs, crossing the street or driving?*
- *During the past month, have you often been bothered by feeling down, depressed or hopeless? Do you notice yourself having little interest or pleasure in doing things?*

Refer any patients who answer yes if their difficulties cannot be ameliorated by standard means.

The demographic trends that fuel age-related eye disease are adding to the ranks of the vision impaired *every* month, not just this one. But try to find a little time in February to raise the awareness level of low vision among patients, caregivers, staff—and yourself. ■

Looking deeper
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Words of Wisdom, Or Just Words

It's always fun to revisit how you got where you are today. Unless you're knee-deep in sewage and your wife is saying, "I told you so." **By Montgomery Vickers, OD**

I have decided to kick off my 26th year of Chairside by sharing some random thoughts about this strange and unusual journey:

1. I have always been amused that my colleagues who really don't know me assume many things:

• ***That I am funny.*** Those who know me will tell you that I have my moments, but I am mostly quite a serious fellow. Perhaps spending less time cracking people up when I meet them would help.

• ***That I am bald.*** My hair, which has run the gamut from Ozzy Osbourne to Billy Ray Cyrus to Snoop Dog to Blake Shelton, is all mine, friends. Quit tugging on it to see. And, yes, I add grey streaks to make me look older and wiser.

• ***That I am an expert in everything.*** I have been asked to offer, for example, CE. I guess I could speak on how many useless trips to make to Home Depot before breaking down and hiring a plumber. I could also talk about handling an online CL company's request for an expired Rx while avoiding the fuss of spontaneous combustion. But the newest tool to handle *Demodex*? The best I can come up with is an old ant farm where you fill it with eyelashes so they prefer to live there.

• ***That I am a Democrat.*** To me, global warming just means the property I own in West Virginia will someday be beachfront.

2. How did I get this gig?

A. I toiled to hone my writing skills so I would be ready when luck met opportunity.

B. The publishers of *Review of Optometry* lost a bet.

C. When God was distracted, my grandmother snuck me onto His to-do list.

D. I accepted my neuroses, and the rest his history.

(Answer? B. Never spot anyone 14 points. It got me married!)

3. I was fortunate to have wonderful mentors, and I hope you do as well. All of optometry's concerns are covered by their wise sayings:

- "Make 'em see better." – *Dr. George Bodie, 1980.*
- "If it don't make dollars, it don't make cents." – *Dr. Aaron Vickers, 2006.*
- "If you have to give them their answer today, always say 'No'." — *My Dad, 1969.*
- "Never buy a car that won't hold a few 2x4s." – *Larry Johnson, 2010.*
- "Vickers, write this down. People are no damn good." – *Anon., 1979.* His mom taught me in first grade. You are brilliant and you know who you are, doctor!

4. The first time you fire someone breaks your heart. The second one leaves you kind of numb, but the third time you'll think it's a blast!

5. If you demonstrate a PAL to the patient and they say, "OK, I see how that works," tell them that's the Holy Spirit talking.

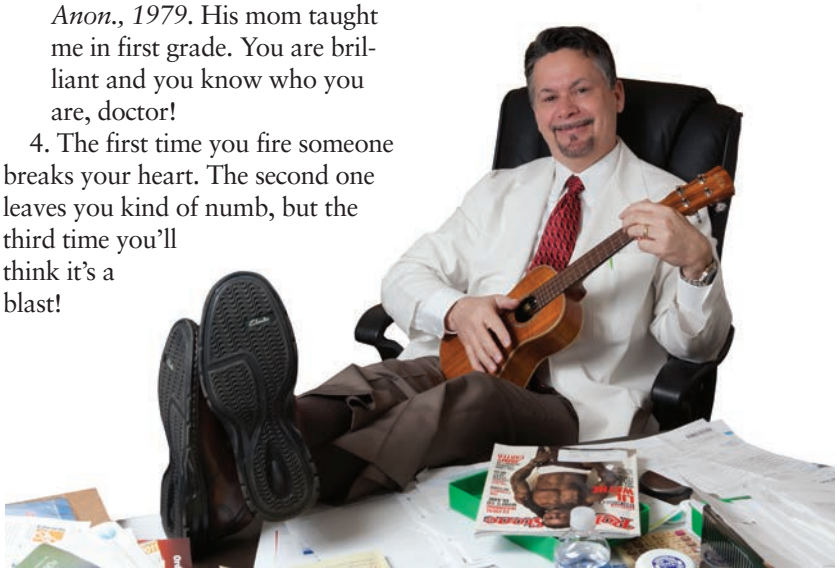
6. My contact lens philosophy is this: If it's in the woods, looks like a horse and has black and white stripes, it's probably a zebra.

7. Patients cannot cancel, they can only postpone. The only one who is allowed to even say the word cancel in the office is me!

8. Contracts only mean some lawyer will make more money.

9. I always assume patients are smarter than I am when it comes to their needs. Start from there and you will be very successful indeed!

10. Optometry is the one profession that requires you to accept yourself completely. Don't keep score. Just have fun taking care of the patient in Room One before moving on to Room Two. That's what a doctor does. ■



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Double Take

When a patient presents with a case of sudden-onset double vision, it's time to think vascular. **Edited by Paul C. Ajamian, OD**

Q A 72-year-old white male presents with a history of sudden-onset horizontal diplopia for the past two days. I cringe when I see people with double vision. Where do I start?

A "Whenever a patient over 50 presents with sudden-onset horizontal and binocular double vision, immediately think cranial nerve six (CN-VI) palsy secondary to a vascular etiology," says Emily Williams, OD, a resident in ocular disease at Omni Eye Services of Atlanta in Georgia.

CN-VI palsy, also know as abducens palsy, is the most common extraocular nerve palsy seen, with an incidence of 11 out of 100,000 patients. While 30% of cases are idiopathic, vascular etiologies represent the most common cause in nearly 35% of cases. In non-traumatic, isolated CN-VI palsies, the most common vascular etiologies include hypertension (28%) and comorbid hypertension and diabetes (17%).[1]

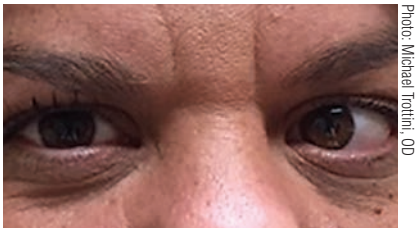

Photo: Michael Trottini, OD

This patient presented to the office with an abduction deficit in the right eye on right gaze.

"Taking a close look at the patient's history is key to narrowing the differential," says Dr. Williams. She adds that practioners should ask about and look for the following:

- Systemic conditions (e.g., hypertension, diabetes and thyroid imbalance).
- Recent illness or trauma.
- Symptoms of Graves' disease and convergence insufficiency.[2]

Dr. Williams says that when communicating with a CN-VI patient, observe for neurological symptoms indicative of prior vascular incidents like stroke. "And, always bear in mind the remote possibility of an etiology consisting in a benign or malignant growth."

The key findings for determining CN-VI etiology typically manifest as the exam progresses. "Visual acuity, IOP, visual field results, pupils and slit lamp measurements should not be affected from an isolated CN-VI palsy," says Dr. Williams. "Cover test will reveal a greater esotropia at distance than near and EOM testing will show the inability of the ipsilateral eye to abduct and will be accompanied by diplopia in that field of gaze."

Dr. Williams also advises performing a dilated fundus examination to rule out specific vascular etiologies such as retinopathy from hypertension or diabetes.

In the absence of abnormal blood pressure, these patients do not need to be sent to the ER. "Educate the patient on the potential etiologies underlying their symptoms. If the patient has diabetes, it is worth mentioning that reoccurrence of the palsy is certainly possible."

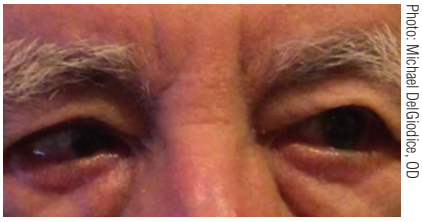

Photo: Michael DelGiodice, OD

When a patient over age 50 presents with sudden-onset horizontal and binocular double vision, immediately think CN-VI palsy secondary to a vascular etiology.

Dr. Williams advises telling patients it is essential to follow up with their PCP or internist to monitor uncontrolled systemic disease such as diabetes and hypertension as was seen in her patient. "This particular patient was sent back to his internist with my recommendation to evaluate for diabetes and to assess the adequacy of the type and dosage of his hypertension medication," Dr. Williams says. The request was ignored and the patient sent for an MRI, which came back negative. His palsy resolved within nine weeks of the intital visit.

She says to inform your patient that if symptoms worsen, new symptoms begin, or if symptoms do not resolve within 12 weeks, head and orbital imaging will be needed. "The patient can return to your office six weeks from the onset of initial symptoms. A second follow up 12 weeks later should be scheduled to confirm resolution of the diplopia." ■

1. Goodwin D. Differential diagnosis and management of acquired sixth cranial nerve palsy. Optometry. 2006; 77(11):534-39.
2. Tasman W. Jaeger E: Abducens Palsies. Duanes: Clinical Ophthalmology Volume 2. 12:3-9.

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CONCIERGE CUSTOMER CARE


JASON MENZO

Sun Ophthalmics is building a "concierge level" of customer care by teaching its sales representatives to be hyperfocused on eye care professionals. "We intend to invest significantly in our reps' training," said Jason Menzo, Vice President of Sales & Marketing, Ophthalmic Business. This training will include a mandatory number of hours each year observing surgery and shadowing eye care professionals in clinic. Furthermore, Sun Ophthalmics' reps will receive training on billing, and reimbursement so they can understand the needs of administrators, and thereby create value-added services for their clients. Moreover, its reps will have fewer targeted doctors in their "call on audience" than the industry standard, so that they can give each one more time and attention and learn about each clinic's operations intimately.

Mr. Menzo believes that thoroughly preparing and educating its reps is the key to differentiating Sun Ophthalmics in the current marketplace. "Within the ophthalmic marketplace today," he explains, "I see that reps have lost some passion and enthusiasm about catering to their customers." He wants to foster loyalty and motivation within the Sun Ophthalmics sales force that will translate to strong relationships with provider-clients. "I want it to be obvious to our customers that Sun Ophthalmics hires ethical, passionate, energetic people who love what they do and the company they work for, because it cares about them and invests in their training."

Mr. Menzo believes that his team's passion for addressing customers' needs is what sets Sun Ophthalmics apart from its competitors. "The partnership between eye care professionals and industry has become more distant in recent years. That is where we see an opportunity to re-energize the space. Our goal is to be seen as the preferred partner by the Ophthalmologists, and Optometrists we serve."

PIPELINE

Sun Ophthalmics plans to launch two novel products in 2016, an ocular drop for managing glaucoma, and one for preventing inflammation after cataract surgery. Both represent improvements over currently available molecules.

The glaucoma product is called Xelpros (latanoprost BAK-free eye drops), which is a unique, preservative-free formulation of latanoprost in a multi-dose bottle. The second product is BromSite (0.075% bromfenac), which features the DuraSite delivery system.

SUN OPHTHALMICS' FORWARD VISION

Mr. Menzo's focus for Sun Ophthalmics in 2016 is to build a national footprint of sales reps. He has assigned key positions within its sales and marketing force in order to have a powerful network in place for the anticipated product launches later this year. With this goal framing its efforts, 2016 promises to be a busy and exciting year for the company. ●

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Put a Lid on Preseptal Cellulitis

How to distinguish potentially life-threatening infections. **By Richard Mangan, OD**

A 31-year-old Caucasian male presented for follow-up after being diagnosed with preseptal cellulitis in his left eye. He claims compliance with his treatment regimen (Bactrim DS BID PO), but feels that his left eyelid has become more swollen and tender. His vision has remained unchanged.

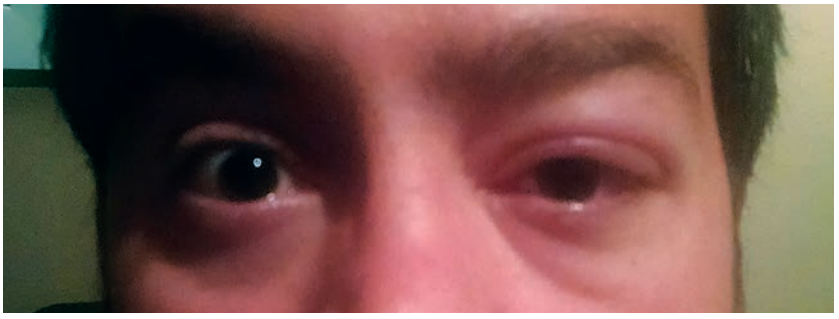
Exam Findings

Entrance BCVA was 20/20 in each eye. While extraocular movements were full in both eyes, the patient reported a pulling sensation in his left eye when looking superior temporal. The left eye appeared slightly proptotic. Retropulsion assessment was inconclusive. Confrontation fields and pupil testing were unremarkable. Dilated funduscopic exam noted no apparent pathology of the posterior pole. Cup-to-disc ratios were 0.3 OU.

Despite having been treated with oral antibiotics, his condition appeared to be worsening. Could it be antibiotic resistance? Does the pulling sensation suggest early orbital cellulitis?

Infection Investigation

Preseptal cellulitis refers to the infectious involvement of the eyelid and periorbital soft tissue anterior to the orbital septum. Conversely, orbital cellulitis is the infectious involvement of tissue posterior to the orbital septum, including the fat and muscle within the bony orbit. The distinction is important because a delay in diagnosing orbital cellulitis may be associated with visual and life-threatening sequelae.



This 31-year-old patient provided poor history for his swollen and tender left eyelid.

Anatomically, the orbital septum is a thin, fibrous, multi-laminated membrane made up of connective tissue that acts as the anterior boundary of the orbit. It extends from the orbital rim to the lids and contains orbital fat.[1] Certain blood vessels and nerves pass through the septum from the orbital cavity to the face and scalp. Venous drainage of the paranasal sinuses and the mid region of the face occur primarily via the orbital veins, which communicate directly with the cavernous sinus. If the cavernous sinus becomes infected, it may adversely affect structures within the sinus (i.e., oculomotor nerve, trochlear nerve, abducens nerve and branches of the trigeminal nerve, internal carotid artery), and extend posteriorly to the pituitary gland and surrounding meninges, and that can be life-threatening.[2]

When confronted with a patient who has lid and periorbital soft tissue erythema and swelling, a detailed case history is warranted. One of the more common causes of preseptal cellulitis is extension from a paranasal sinusitis.[3,4] These patients may report an acute or chronic history of sinus congestion and headache. Other sources of soft tissue infections include skin infections, lid infections (e.g., chalazia, hordeola), dacyrocystitis, trauma (e.g., orbital fracture, foreign body) and insect bites. Preseptal and orbital cellulitis may also be iatrogenic from recent lid, sinus, dental or maxillofacial surgery.[5]

A complete and thorough eye examination should include visual acuity assessment, pupil testing, confrontation fields, extraocular motility assessment, tonometry, slit-lamp biomicroscopy and direct and indirect ophthalmoscopy. In distinct contrast to preseptal cellulitis, eyes with posterior septal involvement may show proptosis, limitation in motility, resistance to retropulsion, orbital pain, an afferent pupillary defect, optic nerve head edema and venous engorgement. A decrease in vision should also raise suspicion for post-septal extension.

Initial treatment of preseptal cellulitis in adults usually consists of empirically prescribed oral antibiotics based on any predisposing risk factors. This is assuming the patient will be compliant. If the adult patient reports a history of acute or chronic sinusitis, then oral antibiotics geared

towards *Staph* and *Strep* (*pneumoniae* and *pyogenes*) species, as well as *H. influenza* and *M. catarrhalis* is warranted. In focal trauma, suspect *Staph aureus*.[2]

Treatment

Antibiotics of choice for preseptal cellulitis include amoxicillin-clavulanate, cefuroxime, gatifloxacin, moxifloxacin and levofloxacin. Patients who report a history of resistant infections will require a more detailed case history to determine which antibiotic is warranted and whether the oral or IV route of administration is most appropriate. Patients who fail to respond or demonstrate clinical worsening while on oral antibiotics should be promptly transitioned to intravenous antibiotics as the possibility of a resistant strain exists. In the case of an immunocompromised patient, also consider a fungal etiology (i.e., *mucormycosis* or *aspergillus*).

When you encounter purulent discharge (i.e., dacyrocystitis, draining lid lesions, etc.), perform culture and sensitivity testing. Attempts to isolate the causative organism through blood cultures or nasal swab may provide conflicting information and is generally not recommended in preseptal cases.

A critical component in the evaluation of a declining preseptal cellulitis or orbital cellulitis is radiographic imaging. Both computed tomography (CT) scans and magnetic resonance imaging (MRI) allow for confirmation of disease extension into the orbit, concurrent sinusitis, as well as orbital or periosteal abscess.[6,7] Contrast dyes help differentiate inflammation from abscess in involved orbital tissue. While MRI provides more detailed information, MRI services may not be readily available at all hours, hindering the clinician's ability to render appropriately prompt therapy. If radiographic imaging confirms post-septal extension on the infection, start the patient on intravenous antibiotics promptly. If culture and sensitivity results are not readily available, empiric treatment is geared towards the most common causative organisms, *Staphylococcus* and *Streptococcus*.

Local hospitalists and specialists in infectious disease will likely have a clear understanding of local trends in antimicrobial susceptibility. Additionally, most hospitals track and maintain infection trends in the form of an antibiogram, which can aid in designing a treatment plan. If local community-acquired MRSA infection rates are high, consider ancillary treatment with IV vancomycin.

When to Opt for Surgery

Surgical intervention is warranted when there is doubt regarding clinical responsiveness to medical treatment. Surgical drainage of an abscess can aid in the response to antibiotics as well as allow one more opportunity to obtain cultures. There are several other situations that may necessitate prompt surgical intervention:

- Retained orbital foreign body
- Iatrogenic foreign body (i.e., scleral buckle or glaucoma drainage device)
- Endophthalmitis
- Dacryocystitis (surgical debulking)
- Fungal infection (surgical debridement)

Follow Up

Our patient was a relatively poor historian. Given this, he reported no history of sinusitis, injury or previous surgery. He also reported no allergies. Based on his assurance that he was compliant with his oral Bactrim DS (sulfamethoxazole and trimethoprim, Roche), a lengthy discussion ensued regarding the need for imaging and consideration of IV antibiotics, as I could not rule out MRSA or similar resistant strain. He was being seen in a remote clinic, so daily monitoring at our clinic was not an option. Instead, we referred him to a co-management center nearby. After a same-day consult, the ophthalmologist decided to add second-line oral antibiotic therapy—Augmentin (amoxicillin and clavulanate, GlaxoSmithKline) 500mg/125mg TID, pending a CT scan of the sinuses and orbit. If the CT scan were to suggest impending or post-septal involvement, IV cefuroxime 1.5g q8h +/- 1g vancomycin Q12h would likely be ordered. Our patient was educated on the importance of compliance with his oral antibiotics, CT imaging and follow-up appointments.

CT imaging (coronal and axial views) of the sinuses and orbits were performed with and without contrast dye. Findings were consistent with a preseptal cellulitis, absent of sinusitis. No post-septal extension was seen. The patient was followed daily for the first three days. Shortly after second-line therapy was initiated, the lid edema and erythema improved and, within two weeks, resolved.

Orbital cellulitis is a true medical emergency. In an era when bacterial resistance is on the rise, even preseptal cellulitis cases warrant close monitoring, especially in patients with predisposing risk factors. Preseptal cases can progress to orbital cellulitis in short order. Knowing the risk factors for orbital cellulitis, as well as the most common causative organisms for such an infection, will put you in a strong position to appropriately care for your patient. ■

1. Koornneef L. Orbital septa: anatomy and function. Ophthalmology. 1979;86(5):876-80.
2. Howe L., Jones N., Guidelines for the management of periorbital cellulitis/abcess. Clin. Otolaryngol. 2004:29;725-8.
3. Jones D, Steinkuller P, Strategies for the initial management of acute preseptal and orbital cellulitis. Trans. Am. Ophthalmol. Soc. 1988;86:94–108.
4. Oxford L, McClay J. Complications of acute sinusitis in children. Otolaryngol. Head Neck Surg. 2005;133:32–7.
5. Cox N, Knowles M, et al. Pre-septal cellulitis and facial erysipelas due to Moraxella species. Clin. Exp. Dermatol. 1994;19:321–3.
6. Eustis H, Mafee M, Walton C, Mondonca J. MR imaging and CT of orbital infections and complications in acute rhinosinusitis. Radiol. Clin. North Am. 1998;36(6):1165–83.
7. Towbin R, Han B, Kaufman R, Burke M. Postseptal cellulitis: CT in the diagnosis and management. Radiology. 1986;158:735–7.

The Ins and Outs of OSD Coding

Keeping your dry eye records in order can provide huge revenue for your practice.

By John Rumpakis, OD, MBA, Clinical Coding Editor

As this month's article "Dealing with DES: In the Present and in the Offing" (p. 34) discusses, dry eye is benefiting from classic and nouveau treatment approaches. Many patients see results with basic treatments; but, if more advanced techniques are required, it is essential to maintain a proper sequence of events in the medical record to establish medical necessity. While specific diagnoses and treatments require specific coding instruction, the vast majority of treatment for ocular surface disease (OSD) is based on the office visit.

The Office Visit

Whether you use the 920X2 intermediate ophthalmic code or a 99201 – 99214 E/M code, remember that medical necessity applies to coding the office visit as well. The Centers For Medicare and Medicaid Services (CMS) are very specific about medical necessity of an office visit, as stated in CMS IOS Publication 100-04, Chapter 12, Section 30.6.1:

"Medical necessity of a service is the overarching criterion for payment in addition to the individual requirements of a CPT code. It would not be medically necessary or appropriate to bill a higher level of evaluation and management service when a lower level of service is warranted. The volume of documentation should not be the primary influence upon which a specific level of service is billed. Documentation should support the level of service reported. The service should be documented during, or as soon as practicable after it is provided in order to maintain an accurate medical record."

Properly perform only the necessary elements of the exam and document them correctly, which will establish the proper office visit code.

Treatment protocols such as artificial tears and ointments, secretagogues, topical anti-inflammatory therapy, Restasis (cyclosporine, Allergan) and nutritional supplements generally don't require any procedure-specific coding and are billed as office visits. OSD is chronic, multifactorial and very commonly requires multiple visits per year; yet, many practitioners do not recognize the value of proper coding and follow-up to manage and track dry eye therapies. This could easily be worth $200 to $350 per year per patient. With conservative numbers showing a natural incidence and prevalence rate of about 25% of the US population, the economics of providing proper dry eye care are quite attractive.[1]

Minor Surgical Procedures

Here are a few minor procedures common in ophthalmic practices and how to code them:

• ***Punctal occlusion.*** Standard rules for coding a minor surgical procedure apply. Any surgical procedure with a global period less than 90 days is considered a minor surgical procedure, and, by definition, the surgical code already contains compensation for an office visit on the day of or the day preceding the procedure in addition to the surgical procedure. Many incorrectly bill an additional office visit with the procedure using modifier -25, putting themselves at risk during an audit.

CPT code 68761 defines the "closure of the lacrimal punctum, by plug, each," so additional modifiers that specify the lid—E1, upper left lid; E2, lower left lid; E3, upper right lid; E4, lower right lid—must be used when coding for punctal occlusion.

Punctal Plug Coding

The various coding sequences for punctal occlusion include:

Two punctal plugs (SAME EYE)
- 68761-E? as one line item
- 68761-51-E? as second line item

Three punctal plugs
- 68761-E?-E? as one line item (2 units)
- 68761-51-E? as second line item (1 unit)

Four punctal plugs
- 68761-50 as one line item
- 68761-50-51 as second line item

There is no difference in coding whether you are using collagen, silicone or hydrogel material to occlude the puncta. CPT 68761 carries a 10-day global period.

E modifiers and the lid designation in the ICD-10 must align properly, otherwise the carrier computers will reject the claim on the basis of a diagnosis mismatch.

• ***Amniotic Membranes.*** CPT code 65778—"Placement of amniotic membrane on the ocular surface; without sutures," with a 10-day global period—is also growing in popularity in ophthalmic practices. With respect to OSD, amniotic membranes are generally

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With CooperVision's largest portfolio of silicone hydrogel 1-day contact lenses you can fit virtually all patients into a 1-day lens that provides high oxygen, comfort and convenience. From the uncompromising performance of MyDay® to the breadth of the clariti® 1 day family, CooperVision is the only one you need to serve your 1-day patients.

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reserved for more advanced disease, as you are not treating the dry eye, but are treating the corneal sequelae of the OSD. Moreover, not all amniotic membranes are created equal, and CMS has noted, in a recent Local Coverage Determination:

"Amnion can be prepared for implantation a number of ways. Heat- or air-dried amniotic membrane loses some of its biologic properties and is not ideal for ocular surface rehabilitation. The tissue can be lyophilized (freeze-dried), which induces minimal change in its properties. Amnion can be preserved in cold glycerol and cryopreserved and stored frozen at -80 degrees. The cryopreservation method allows for greater retention of the membrane's structural, physiological and biochemical properties responsible for its dramatic healing and easier handling intraoperatively."

While it's tempting to use less effective technology to increase profitability, it may not be a wise choice.

For CMS, a separate charge and reimbursement for the supply of the amniotic membrane is not allowed, as it's bundled into the reimbursement for the procedure, not unlike the rationale used for punctal plugs. However, other commercial carriers may have policies that allow for reimbursement of the procedure and the materials. If so, the appropriate HCPCS Level II code is V2790 ("Amniotic membrane for surgical reconstruction, per procedure").

New Tech

Other new technologies, separately identified by either a Level III HCPCS code or a new CLIA-waived procedure, can be coded in addition to the office visit:

• ***CPT code 83516***—immunoassay for analyte other than infectious agent antibody or infectious agent antigen; qualitative or semi-quantitative, multiple step method—is now a CLIA-waived test (be sure to use the modifier –QW on each procedure performed). It can be performed in optometrists' offices that have a clinical lab designation and a physician with the practice has been registered as a clinical lab director. The current national payment amount for this lab test is $15.71 per eye.

• ***0330T***—tear film imaging, unilateral or bilateral, with interpretation and report—is a temporary use or "tracking code" for tear film interferometry. It needs to be reported to the carrier, but is generally a patient payable test. Be aware that there are coordinating rules with CPT code 92285 (anterior segment photography) for this code.

Economic Potential of Dry Eye in the Average OD Practice[2]

Number of Americans with dry eye	78,500,000
Median patient volume in an optometric practice per year	3,100
Overall incidence of combined dry eye	25%
Dry eye patients in an optometric practice per year	775
Average reimbursement for dry eye-related office visit	$73
Typical number of office visits for a dry eye patient per year (non-punctal occlusion)	3
Potential revenue from dry eye office visits per year (non-punctal occlusion)	$164,633.25
Typical revenue from a Medicare punctal occlusion patient	$756.88
Typical revenue from a non-Medicare punctal occlusion patient	$1,336.60
Percentage of patients undergoing punctal occlusion	3%
Potential punctal occlusion revenue from Medicare patients per year (assuming half the practice's volume is Medicare patients)	$8,798.73
Potential punctal occlusion revenue from non-Medicare patients (assuming the other half of the practice's volume is non-Medicare patients)	$15,537.96
Potential revenue due to dry eye per year	$188,969.94
Lifetime economic potential of diagnosing and treating dry eye	$8,503,647

Optometrists basically wrote the book on dry eye. It's a daily occurrence in our patients' lives, and it has nothing but opportunity written all over it when embraced by optometry. It is a growing area of concern, focus of research and service demanded by patients. New technology is always exciting when employed within our practices to provide new avenues to great patient care. But it also requires that we keep up with the appropriate recording and reporting mechanisms that are in place for appropriate compliance. ■

Send questions and comments to ROcodingconnection @gmail.com.

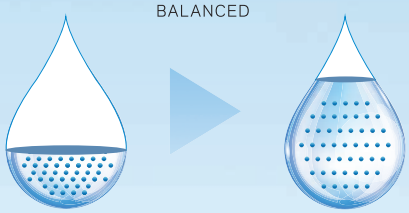
1. Ezuddin NS, Alawa KA, Galor A. Therapeutic strategies to treat dry eye in an aging population. Drugs Aging. 2015 Jul;32(7):505-13.
2. Rumpakis J. Economics of Apathy. Review of Optometry. 2013;150(10):24.

IT'S ENOUGH TO MAKE ANYBODY'S EYES FEEL DRY, GRITTY & UNCOMFORTABLE

A high salt concentration can disrupt the osmolarity balance within the tear film. Elevated tear film osmolarity (osmolarity imbalance or hyperosmolarity) is one of the primary causes of dry eye symptoms.[1]

TheraTears® Dry Eye Therapy with Osmo-Correction™ corrects osmolarity imbalance to restore comfort with a unique hypotonic and electrolyte balanced formula that replicates healthy tears.

THERATEARS® DRY EYE THERAPY
WITH
OSMO-CORRECTION™
HYPOTONIC & ELECTROLYTE BALANCED



HYPEROSMOLARITY

Increased concentration of the tears leads to irritation and potential damage to the ocular surface.

HEALTHY TEAR

TheraTears® Dry Eye Therapy replicates the electrolyte balance of natural tears to restore comfort.

RESTORE + CLEANSE + NOURISH

thera tears®
THERAPY FOR YOUR EYES™

DRY EYE THERAPY

Restores Eyes Natural Balance™

theratears.com

Reference: 1. Research in dry eye report of the Research Subcommittee of the International Dry Eye WorkShop (2007). *Ocul Surf.* Apr 2007; 5(2): 179-193.

AKORN Consumer Health

DEALING WITH DRY EYE:
In the Present and in the Offing

Review the state of the art and glimpse advances expected in the near future.

By Sina Vahedi and Michelle Hessen, OD

An estimated 25% of patients in general eye clinics report symptoms of dry eye syndrome (DES).[1] More than nine million Americans suffer from a moderate to severe form of it. Management of the condition costs United States health care $55.4 billion annually.[2-4] Given the breadth of the condition's impact, the goals of clinicians, researchers, policymakers and industry align: provide relief when needed, and if possible, a lasting cure. This article recaps many successful modalities currently in use by practitioners and looks just over the horizon to some emerging options anticipated for the near future.

Artificial Tears and Ointments

Initial treatment for DES includes artificial tears and ointments. Preservative-free formulations are recommended, especially if dosing more than four times per day is necessary. Preservatives, particularly benzalkonium chloride, are considered cytotoxic to ocular surface epithelia—including conjunctival goblet cells. Phosphate-containing eye drops should be used cautiously as they can promote corneal calcifications especially in the cases of corneal epithelial defects (e.g., corneal erosions or ulcers).[9] Artificial tears are simple in composition and have a low residue time on the ocular surface, limiting their efficacy.

Emulsions containing liquid lipids are also available, and aim to stabilize and better reproduce the tear film. These take the form of charged or uncharged microemulsions and liposomes. Charged microemulsions, such as the cationic Cationorm (carboxymethylcellulose sodium 0.5% ophthalmic solution, Santen Pharmaceutical)—marketed in the United States as Retaine MGD (Ocusoft)—and the anionic Systane Balance (propylene glycol 0.6% ophthalmic solution, Alcon), show improvements in symptoms and corneal staining when compared with aqueous eye drops.[10,11] In a study, 79 patients were randomized to four drops a day of either Cationorm or a polyvinyl alcohol/povidone eye drop.[12] At 28 days, both treatment arms showed improvement in symptoms, and tear-film stability—indicated by tear break-up time (TBUT)—relative to baseline, but Cationorm demonstrated significant improvement in TBUT compared with the aqueous eye drops.[10] Similarly, a trial with 49 participants receiving Systane Balance or saline eye drops for 28 days showed a significantly higher improvement in TBUT with Systane Balance.[11] A liposomal eye spray, Tears Again Advanced Eyelid Spray (OcuSoft), showed greater improvement in inflammation of the lid margin and TBUT compared with hyaluronate artificial tears at four and 12 weeks in a trial of 216 patients.[13]

Defining DES

Recently, the Definition and Classification Subcommittee of the International Dry Eye Workshop redefined DES as "a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface."[5] The etiopathogenetic classification suggested by the Dry Eye Workshop distinguishes two main types of dry eye: an aqueous deficiency state and an evaporative state.

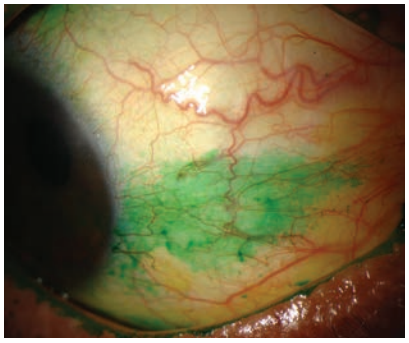


Photo: Michelle Hessen, OD

Conjunctival staining with lissamine green in a dry eye patient.

Uncharged microemulsions like Refresh Optive Advanced (carboxymethylcellulose sodium 0.5%, glycerin 1.0%, polysorbate 80 0.5%, Allergan) contain castor oil as the main lipid component. Treating 191 patients with lipid emulsion eye drops resulted in improvement in symptoms, Ocular Surface Disease Index (OSDI) score and TBUT when compared with baseline at 90 days in patients with mild to moderate DES.[14] The research identified no treatment arm with aqueous tear drops. However, another study that treated 208 patients with either aqueous tear drops (carboxymethylcellulose sodium 0.5%, glycerin 0.9%) or lipid microemulsion eye drops (Refresh Optive Advanced) shows improvement in OSDI and TBUT at 30 days when compared with baseline, and shows no difference between the aqueous or lipid emulsion eye drops.[15]

Artificial tears and emulsions are not as effective as ointments containing semisolid lipids, which—though highly effective—cause blurred vision and have limited use during the daytime. Researchers have created a nanoscale dispersed eye ointment (NDEO) that retains the advantages of ointment in liquid form, and could be used as a drug delivery system for lipophilic drugs. In mice, NDEO treatment reduces corneal fluorescein staining and increases TBUT at day three compared with baseline and a polymer-based artificial tear. Improvement of TBUT started earlier (day three) with NDEO and lasted longer—until day 14—compared with polymer-based artificial tears.[16]

Reducing Tear Drainage

Minimizing tear drainage via placement of punctal plugs or thermal cauterization may contribute to the healing of the ocular surface by extending available lubrication provided by natural and artificial tears. Even punctal plugs alone may improve tear film stability and elongate the TBUT without the need for repeated administration of artificial tears; however, recurrent loss of punctal plugs can be problematic, often limiting the effectiveness of this treatment.[17] Ocular surface inflammation should be addressed with topical medications prior to considering punctal occlusion.

Therapeutic Contact Lenses

Silicone hydrogel soft contact lenses provide high oxygen permeability, making the extended wear modality an acceptable option for assisting with ocular surface repair. Therapeutic bandage contact lenses provide corneal protection from the eyelids' mechanical friction, as well as exposure to the external environment and evaporation of the tear film. Rigid gas permeable scleral lenses create a tear reservoir for constant lubrication of the corneal surface while maintaining necessary oxygen supply. Sclerals also mask surface irregularities, which also contribute to improvement in vision. Results of a retrospective chart review of 49 consecutive patients with ocular surface disease at the setting of various systemic conditions, including Sjögren's syndrome (SS), showed improvement in visual acuity, healing of epithelial defects, reduction in photophobia and improvement in quality of life from scleral lens use.[18]

Secretagogues

Acetylcholine, acting through muscarinic receptors, controls exocrine gland secretion, including lacrimation. Cevimeline and pilocarpine are oral cholinergic agonists that can be used off-label to treat DES. In randomized, prospective, double-blinded trials, oral cevimeline treatment show improvements in tear biometrics (as measured by Schirmer testing, rose bengal and fluorescein staining) and TBUT, as well as subjective patient symptom reporting.[19-21] In a multicenter, placebo-controlled, fixed-dose trial, 373 patients with primary or secondary Sjögren's syndrome and clinically significant dry eyes were randomized to receive either pilocarpine or placebo tablets for 12 weeks.[22] Those receiving 20mg pilocarpine per day experienced significant improvement in dry eye symptoms compared with the placebo group. The drawback—side effects like nausea, abdominal pain, excessive sweating, headache, dizziness and cardiac arrhythmias—limit the use of these drugs.[19,21,22]

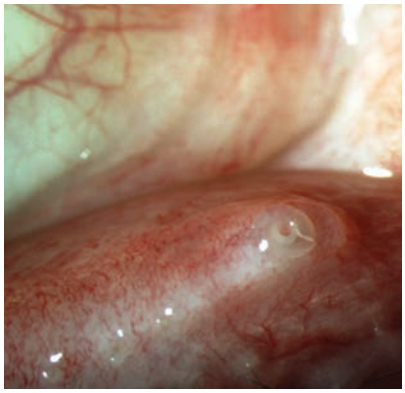


Photo: Alan G. Kabat, OD

Punctal plugs help to increase contact time between the tears and ocular surface, but inflammation must be addressed before considering this option.

Improving Meibum

Oral doxycycline, minocycline and azithromycin are effective in treating DES caused by meibomian gland dysfunction (MGD), likely due to a combination of their ability to reduce inflammation in addition to their role as antibiotics.[23] In a comparative study, a five-day course of oral azithromycin suggested it is more effective than a one-month course of doxycycline in relieving the signs and symptoms of MGD, while causing significantly fewer side effects.[24] Topical azithromycin is also effective in treating evaporative DES and improving the quality of meibomian gland secretions.[25]

Procedures such as Lipiflow and intense pulsed light therapy are also capable of reducing tear evaporation by improving meibum secretions.[26]

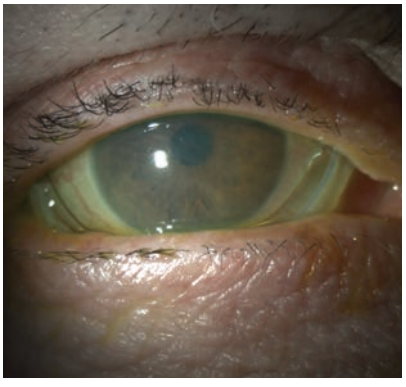


Photo: Alan G. Kabat, OD

Prokera plus in a patient with severe keratoconjunctivitis sicca.

Anti-inflammatory Therapy

It is widely recognized that inflammation plays a significant role in the pathogenesis of dry eye, promoting ocular surface disruption and symptoms of irritation. A number of anti-inflammatory treatments are currently used to treat DES. These may prove exceptionally useful in your treatment of the condition.[27]

• ***Topical NSAIDs.*** These versatile agents are used in the management of many ocular conditions, including allergic conjunctivitis, postoperative ocular pain, cystoid macular edema status post-cataract surgery and DES. NSAIDs treat inflammation by inhibiting different forms of the cyclooxygenase enzyme, thus reducing prostaglandin production—the mediators of inflammation.[28]

Short-term use of NSAIDs can be useful in ameliorating symptoms of ocular discomfort in dry eye; however, they should be used with caution and under close monitoring, and treatment discontinued if the corneal epithelium becomes damaged. NSAIDs—specifically diclofenac—have been shown to reduce corneal sensitivity.[29] This may cause an additional insult to the disrupted epithelium in DES patients. In the literature, several cases of corneal melt associated with topical NSAID use—including diclofenac, ketorolac, nepafenac and bromfenac—show preexisting epitheliopathy.[30-32] Though the exact relationship between corneal melt and topical NSAID use is still not clear, various suggested mechanisms include activation of matrix metalloproteinases, impairment of wound healing and neurotrophic effect resulting from the analgesic action of these drugs.[33]

• ***Topical Corticosteroids.*** More potent than NSAIDs, these agents help reduce ocular inflammation through several mechanisms of action.[34] Topical administration of methylprednisolone 1% ophthalmic solution for several weeks provides moderate to complete relief of DES symptoms and reduces corneal fluorescein staining in patients with SS-related DES, suggests research.[35] Pulse treatment with methylprednisolone for two weeks followed by a taper led to improvement in symptoms starting at two weeks, followed by improved TBUT and Schirmer test scores by the end of taper. After the first pulse treatment, mean drug-free remission time was 56.6 weeks; after the second, it increased to 72.4 weeks. No serious complications, including IOP elevation and cataract formation, occurred during the entire follow-up period.[36]

Loteprednol etabonate (Lotemax, Bausch + Lomb) is a safer topical corticosteroid designed to rapidly break down into inactive metabolites to ensure that it does not circulate systemically at detectable levels. This negates any significant effect on IOP.[37] Recent research following 133 patients who were treated with either loteprednol etabonate 0.1% with hyaluronate artificial tears or fluorometholone 0.1% with hyaluronate artificial tears for two years showed significant improvement in symptoms, Schirmer test scores and fluorescein staining compared with baseline after six months in both groups. The research also showed TBUT improvement in both groups compared with baseline at 12 months. Neither group displayed significant elevation in average IOP at any point in the study.[38]

Topical corticosteroids are also commonly used in combination with Restasis to reduce side effects and improve response to therapy by reducing inflammatory mediators. Patients treated with topical corticosteroids should be monitored closely for known cataract formation risks—glaucoma, corneal thinning and infectious keratitis.[39]

• ***Sutureless Amniotic Membrane.*** In addition to physically protecting the corneal epithelium, amniotic membrane grafts hydrate and oxygenate the regenerating tissue, promote epithelial healing, reduce inflammation and display anti-angiogenic effects.[40] AmbioDisk (IOP Ophthalmics) is a dehydrated, sutureless amniotic membrane graft with no support structure; it is generally applied underneath a bandage

ADD SIMBRINZA® Suspension to a PGA for Even Lower IOP[1]*

INDICATIONS AND USAGE

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

Dosage and Administration

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

IMPORTANT SAFETY INFORMATION

Contraindications

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

Warnings and Precautions

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

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

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

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

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

Adverse Reactions

SIMBRINZA® Suspension

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

Prescribe SIMBRINZA® Suspension as adjunctive therapy to a PGA for appropriate patients

SIMBRINZA® Suspension should be taken at least five (5) minutes apart from other topical ophthalmic drugs

Learn more at myalcon.com/simbrinza

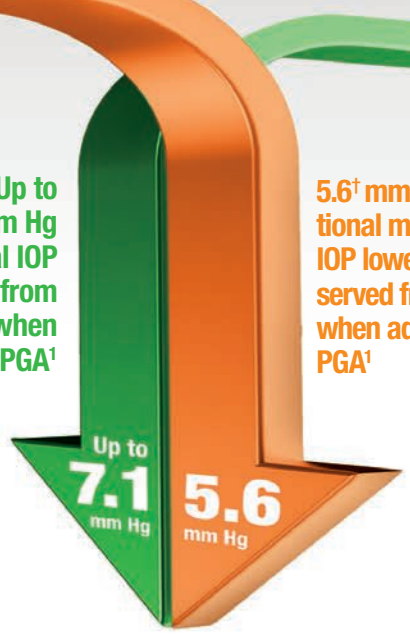
For additional information about SIMBRINZA® Suspension, please see Brief Summary of full Prescribing Information on adjacent page.

Reference: 1. Data on file, 2014.

Alcon
a Novartis company

Up to 7.1 mm Hg additional IOP reduction from baseline when added to a PGA[1]

5.6† mm Hg additional mean diurnal IOP lowering observed from baseline when added to a PGA[1]



		IOP Time Points (mm Hg)[1‡]			
Treatment Arm		8 AM	10 AM	3 PM	5 PM
PGA + SIMBRINZA® Suspension (N=83)	Baseline[§]	24.5	22.9	21.7	21.6
	Week 6	19.4	15.8	17.2	15.6
PGA + Vehicle (N=92)	Baseline[§]	24.3	22.6	21.3	21.2
	Week 6	21.5	20.3	20.0	20.1

‡Least squares means at each Week 6 time point. Treatment differences (mm Hg) and *P*-values at Week 6 time points between treatment groups were: -2.14, *P*=0.0002; -4.56, *P*<0.0001; -2.84, *P*<0.0001; -4.42, *P*<0.0001.
§Baseline (PGA Monotherapy).

		Mean Diurnal IOP (mm Hg)[1‖]
Treatment Arm		
PGA + SIMBRINZA® Suspension (N=83)	Baseline[¶]	22.7
	Week 6	17.1
PGA + Vehicle (N=92)	Baseline[¶]	22.4
	Week 6	20.5

‖Treatment difference (mm Hg) and *P*-value at Week 6 was -3.4, *P*<0.0001.
¶Baseline (PGA Monotherapy).

Study Design: A prospective, randomized, multicenter, double-blind, parallel-group study of 189 patients with open-angle glaucoma and/or ocular hypertension receiving treatment with a PGA. PGA treatment consisted of either travoprost, latanoprost, or bimatoprost. Patients in the study were randomized to adjunctive treatment with SIMBRINZA® Suspension (N=88) or vehicle (N=94). The primary efficacy endpoint was mean diurnal IOP (IOP averaged over all daily time points) at Week 6 between treatment groups. Key secondary endpoints included IOP at Week 6 for each daily time point (8 AM, 10 AM, 3 PM, and 5 PM) and mean diurnal IOP change from baseline to Week 6 between treatment groups.[1]

*PGA study-group treatment consisted of either travoprost, latanoprost, or bimatoprost.
†Treatment difference (mm Hg) and *P*-value at Week 6 was -3.7, *P*<0.0001.

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

BRIEF SUMMARY OF PRESCRIBING INFORMATION
INDICATIONS AND USAGE

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

DOSAGE AND ADMINISTRATION

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

DOSAGE FORMS AND STRENGTHS

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

CONTRAINDICATIONS

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

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

WARNINGS AND PRECAUTIONS

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

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

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

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

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

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

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

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

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

ADVERSE REACTIONS

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

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

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

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

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

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

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

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

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

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

DRUG INTERACTIONS

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

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

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

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

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

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

USE IN SPECIFIC POPULATIONS

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

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

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

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

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

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

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

OVERDOSAGE

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

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

PATIENT COUNSELING INFORMATION

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

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

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

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

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

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

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

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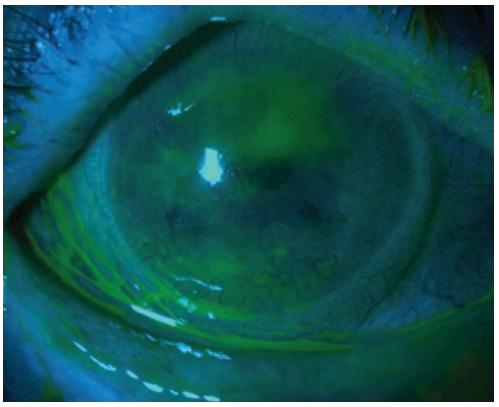
contact lens. ProKera (Biotissue) is a sutureless biological bandage consisting of a cryopreserved amniotic membrane attached to a stabilizing polycarbonate ring; it can be used in cases of severe DES to promote healing and reduce inflammation.[41]

• ***Autologous Serum.*** The patient's own serum contains several anti-inflammatory factors that ultimately inhibit the ocular surface inflammatory cascade responsible for DES. Clinical trials show autologous serum drops improve ocular irritation symptoms, and improve conjunctival and corneal dye staining seen in SS.[42-44] Conversely, greater risk of microbial growth is associated with autologous serum drops, which contain high protein content and are generally nonpreserved.[45]

• ***Nutritional Supplements.*** Omega-3 fatty acids are known to have anti-inflammatory effects.[46] Recent reports find that oral omega-3 supplementation shows promise in DES treatment.[47-49] One trial randomized 259 patients to receive 1g/day of omega-3s or placebo for three months. At the end of this period, the group treated with omega-3s showed significant improvement in symptoms and TBUT.[48] In other research, 496 female contact lens users who complained of dry eyes received 600mg/day of omega-3s or a placebo for six months. The research suggests that the omega-3 treatment improves symptoms, lens comfort levels and TBUT.[47] A third trial randomized 105 patients with DES to receive 2g/day of omega-3s or placebo for three months. Once again, omega-3 supplementation resulted in improved TBUT, OSDI and tear osmolarity compared with placebo.[49]

Research suggests topical omega-fatty acids are beneficial in DES. Mice treated with 0.02% omega-3, 0.2% omega-3, hyaluronic acid (HA) or a mixture of HA and omega-3s. The 0.2% omega-3s alone and those treated with 0.2% omega-3s and HA demonstrated significantly improved corneal irregularity scores. Proinflammatory cytokine levels were reduced much more in the group treated with the omega-3s/HA mixture.[50]

Photo: Alan G. Kabat, OD



This patient with severe keratoconjunctivitis sicca was ultimately treated with topical cyclosporin, autologous serum and amniotic membrane therapy.

• ***Cyclosporin A.*** Topical cyclosporin A (CsA) is frequently used to treat various inflammatory ocular surface disorders.[51] It reduces inflammation by inhibiting T-cell activation and downregulating inflammatory cytokines in the conjunctiva and lacrimal gland. Research suggests the reduction in inflammation via these mechanisms enhances tear production.[52-56] Topical cyclosporine also increases goblet cell density and decreases epithelial cell apoptosis.[57]

Lipids are used as drug delivery systems to deliver CsA to the ocular surface and combat the inflammatory component of DES. Lipids have the advantage of increasing corneal contact time, especially in the case of cationic lipids, which are electrostatically attracted to the mucin layer of the tear film.[58] Restasis (cyclosporine 0.05% ophthalmic emulsion, Allergan) is a well-known example of an anionic microemulsion CsA delivery vehicle. Recently, a cationic microemulsion, Novasorb (Novagali), was shown to deliver three to four times more CsA to rabbit corneas.[58] Novasorb containing 1mg/mL CsA was approved by the European Union under the brand name Ikervis (Santen) and is undergoing Phase III trials in the United States.

In addition to emulsions, other carriers are being investigated as drug delivery systems. Nanocapsules comprised of an oily core surrounded by a polymer shell have been used as delivery systems for CsA. Research shows the nanocapsules delivered a concentration of CsA to rabbit corneas five times greater than with an oily solution of CsA. Corneal CsA levels remained higher for 72 hours following treatment.[59] Yet another nanocapsule delivery system delivered CsA to the cornea at a 10 to 15 times higher concentration than CsA in castor oil, and remained higher for 24 hours.[60]

A CsA-nanocapsule formulation delivered CsA to the cornea at therapeutic concentrations but with less effect on ocular comfort profile.[61] Cationic chitosan nanoparticles loaded with CsA targeted therapeutic doses to the cornea and conjunctiva in rabbits, while avoiding delivery to the inner ocular structures, plasma and blood.[62]

Research suggests polymeric micelles—self-assembling nanocarriers comprised of amphiphilic polymers—are good carriers for CsA delivery to the cornea, leading to a 28-fold increase in CsA levels when compared with an oily solution of CsA.[63] Treatment with CsA-carrying liposomes led to improved amounts of CsA in the tear film, increased

tear formation and lower irritation in rabbit eyes.[64] All these substances show promise for efficient delivery of topical CsA to the cornea.

• ***Lifitegrast.*** A novel integrin antagonist that prevents the binding of lymphocyte function-associated antigen-1 to the intercellular adhesion molecule-1 expressed on inflamed epithelium, lifitegrast disrupts T-cell mediated inflammation seen in DES by preventing T-cell adhesion, migration, activation and cytokine release.[65]

In the first Phase III trial of this agent (OPUS-1), 588 patients with DES received topical lifitegrast 0.5% or placebo twice daily for 84 days. The study met the primary objective endpoint, but not the subjective one. The lifitegrast arm shows significantly improved inferior corneal staining score, but did not show a significant improvement in the visual function subscale score of OSDI, even though patients reported significant improvements in eye dryness and ocular discomfort.[65]

The study design in its next Phase III trial, OPUS-2, was similar to OPUS-1 but was modified to require a minimal level of symptom severity at baseline, and the primary symptom endpoint was changed to eye dryness. Thus, OPUS-2 enrolled patients with moderate to severe DES, while OPUS-1 enrolled patients with mild to moderate DES. This study met its primary symptomatic endpoint but failed to meet its primary objective endpoint, since there was no difference in improvement in inferior corneal staining between the two groups.[66]

Lifitegrast recently concluded a third Phase III efficacy and safety study called OPUS-3, and is now under evaluation by the FDA. The OPUS-3 study, conducted on 711 patients, reveals that lifitegrast significantly improves the symptoms of DES when compared with placebo starting from day 14 and retains improvement until day 84.[67]

Barriers to Topical Treatments

The tear film is the first barrier to the absorption of topical drugs, acting to dilute drug concentration, rapidly clear drugs due to renewal of tear film and blinking reflex, rapidly drain drugs through the nasolacrimal ducts, and inhibit penetration through native barriers such as the ocular surface mucin layer. The tear film is comprised of an outer lipid layer, reducing the evaporation of tears, an intermediate aqueous layer and an inner layer called the glycocalyx, which consists of lysozymes and negatively-charged cell surface mucins.[6,7] Once these are overcome, the cornea presents another barrier to drug absorption due to its highly organized, hydrophobic epithelium and its hydrophilic corneal stroma.[8]

Lacrimal Gland Therapy

Researchers explored transcytosis as a targeted-delivery option from the serum to the lacrimal gland lumen in rabbits and mice. Elastin-like protein polymers were genetically engineered and successfully targeted—transcytosed—to lacrimal glands via the coxsackievirus and adenovirus receptor, a receptor expressed at one of the highest levels in the body by the lacrimal gland.[68] These nanoparticles can be fused with proteins with drug-binding abilities.[69] This is an attractive approach, as it can reduce systemic side effects of the medications and increase treatment compliance and efficacy by creating a drug reservoir in the lacrimal gland.

Gene Therapy

Once the barriers to getting the drug to the ocular surface are overcome, gene therapy can be a viable option to treat dry eye, and delivery systems are crucial to accomplishing the feat. Using well-tolerated nanoparticles, researchers loaded genes coding for MUC5AC—a glycoprotein that plays a key role in tear homeostasis, and which is implicated in several ocular diseases—onto them. Researchers successfully increased expression of MUC5AC, which reduced CD4+ T-cell density, increased goblet cell density, restored tear production and normalized the mucin layer in the inflamed eye.[70]

Conclusion

DES is a common disorder that causes significant discomfort. Treatments aim to replenish and stabilize the tear film and reduce inflammation. Clinicians and patients already have experienced and/or can expect advances on many fronts ranging from improved artificial tears and ointments, light therapy and topical gene therapy via eye drops to restore the mucin layer of the tear film. Targeting inflammation has led to the use of omega-3 fatty acids, ever-improving carrier systems for the delivery of CsA and novel anti-inflammatory compounds.

Treatments comparable to sci-fi are in the offing—soon to be mainstream. With these exciting advancements, we can look forward to the relief they will bring to our patients, and ultimately, millions of dry eye suffers. And, in the meantime, we can use what we have—which themselves are wonderful treatments—to elicit the best outcomes possible for our patients. ■

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1. Doughty MJ, Fonn D, Richter D, et al. A patient questionnaire approach to estimating the prevalence of dry eye symptoms in patients presenting to optometric practices across Canada. Optometry & Vision Science 1997;74(8):624-31.
2. Schaumberg DA, Sullivan DA, Buring JE, et al. Prevalence of dry eye syndrome among US women. American journal of ophthalmology 2003;136(2):318-26.
3. Schaumberg DA, Sullivan DA, Dana MR. Epidemiology of dry eye syndrome. Lacrimal Gland, Tear Film, and Dry Eye Syndromes 3: Springer; 2002:989-98.
4. Yu J, Asche CV, Fairchild CJ. The economic burden of dry eye disease in the United States: a decision tree analysis. Cornea 2011;30(4):379-87.
5. Lemp MA, Foulks GN. The definition and classification of dry eye disease. Ocul Surf 2007;5(2):75-92.
6. Nichols B, Chiappino M, Dawson C. Demonstration of the mucous layer of the tear film by electron microscopy. Investigative ophthalmology & visual science 1985;26(4):464-73.
7. Yañez-Soto B, Mannis MJ, Schwab IR, et al. Interfacial phenomena and the ocular surface. The ocular surface 2014;12(3):178-201.
8. Wilson CG, Tan L. Nanostructures Overcoming the Ocular Barrier: Physiological Considerations and Mechanistic Issues. Nanostructures Overcoming Ocul Barrier Physiol Considerations Mech Issues 2012:173-89.
9. Bernauer W, Thiel M, Kurrer M, et al. Corneal calcification following intensified treatment with sodium hyaluronate artificial tears. British journal of ophthalmology 2006;90(3):285-8.
10. Amrane M, Creuzot-Garcher C, Robert P-Y, et al. Ocular tolerability and efficacy of a cationic emulsion in patients with mild to moderate dry eye disease–A randomised comparative study. Journal Français d'Ophtalmologie 2014;37(8):589-98.
11. Aguilar AJ, Marquez MI, Albera PA, et al. Effects of systane® Balance on noninvasive tear film break-up time in patients with lipid-deficient dry eye. Clinical ophthalmology (Auckland, NZ) 2014;8:2365.
12. Ousler G, Devries DK, Karpecki PM, et al. An evaluation of Retaine™ ophthalmic emulsion in the management of tear film stability and ocular surface staining in patients diagnosed with dry eye. Clinical Ophthalmology (Auckland, NZ) 2015;9:235-43.
13. Khaireddin R, Schmidt K. [Comparative investigation of treatments for evaporative dry eye]. Klinische Monatsblatter fur Augenheilkunde 2010;227(2):128-34.
14. Simmons PA, Carlisle-Wilcox C, Chen R, et al. Efficacy, Safety, and Acceptability of a Lipid-Based Artificial Tear Formulation: A Randomized, Controlled, Multicenter Clinical Trial. Clinical therapeutics 2015;37(4):858-68.
15. Simmons PA, Carlisle-Wilcox C, Vehige JG. Comparison of novel lipid-based eye drops with aqueous eye drops for dry eye: a multicenter, randomized controlled trial. Clinical ophthalmology (Auckland, NZ) 2015;9:657.
16. Zhang W, Wang Y, Lee BTK, et al. A novel nanoscale-dispersed eye ointment for the treatment of dry eye disease. Nanotechnology 2014;25(12):125101.
17. Ferrara JL, Levine JE, Reddy P, et al. Graft-versus-host disease. The Lancet 2009;373(9674):1550-61.
18. Romero-Rangel T, Stavrou P, Cotter J, et al. Gas-permeable scleral contact lens therapy in ocular surface disease. American journal of ophthalmology 2000;130(1):25-32.
19. Fife RS, Chase WF, Dore RK, et al. Cevimeline for the treatment of xerostomia in patients with Sjögren syndrome: a randomized trial. Archives of internal medicine 2002;162(11):1293-300.
20. Ono M, Takamura E, Shinozaki K, et al. Therapeutic effect of cevimeline on dry eye in patients with Sjögren's syndrome: a randomized, double-blind clinical study. American journal of ophthalmology 2004;138(1):6-17.
21. Petrone D, Condemi JJ, Fife R, et al. A double blind, randomized, placebo controlled study of cevimeline in Sjögren's syndrome patients with xerostomia and keratoconjunctivitis sicca. Arthritis & Rheumatism 2002;46(3):748-54.
22. Vivino FB, Al-Hashimi I, Khan Z, et al. Pilocarpine tablets for the treatment of dry mouth and dry eye symptoms in patients with Sjögren syndrome: a randomized, placebo-controlled, fixed-dose, multicenter trial. Archives of internal medicine 1999;159(2):174-81.
23. Liu Y, Kam WR, Ding J, et al. Can tetracycline antibiotics duplicate the ability of azithromycin to stimulate human meibomian gland epithelial cell differentiation? Cornea 2015;34(3):342-6.
24. Kashkouli MB, Fazel AJ, Kiavash V, et al. Oral azithromycin versus doxycycline in meibomian gland dysfunction: a randomised double-masked open-label clinical trial. Br J Ophthalmol 2015;99(2):199-204.
25. Utine CA. Update and critical appraisal of the use of topical azithromycin ophthalmic 1% (AzaSite(®)) solution in the treatment of ocular infections. Clinical Ophthalmology (Auckland, NZ) 2011;5:801-9.
26. Vora GK, Gupta PK. Intense pulsed light therapy for the treatment of evaporative dry eye disease. Curr Opin Ophthalmol 2015;26(4):314-8.
27. Behrens A, Doyle JJ, Stern L, et al. Dysfunctional tear syndrome: a Delphi approach to treatment recommendations. Cornea 2006;25(8):900-7.
28. Vane JR, Bakhle YS, Botting RM. Cyclooxygenases 1 and 2. Annu Rev Pharmacol Toxicol 1998;38(1):97-120.
29. Aragona P, Tripodi G, Spinella R, et al. The effects of the topical administration of non-steroidal anti-inflammatory drugs on corneal epithelium and corneal sensitivity in normal subjects. Eye 2000;14(2):206-10.
30. Asai T, Nakagami T, Mochizuki M, et al. Three cases of corneal melting after instillation of a new nonsteroidal anti-inflammatory drug. Cornea 2006;25(2):224-7.
31. Isawi H, Dhaliwal DK. Corneal melting and perforation in Stevens Johnson syndrome following topical bromfenac use. Journal of Cataract & Refractive Surgery 2007;33(9):1644-6.
32. Prasher P. Acute corneal melt associated with topical bromfenac use. Eye & contact lens 2012;38(4):260-2.
33. Gokhale NS, Vemuganti GK. Diclofenac-induced acute corneal melt after collagen crosslinking for keratoconus. Cornea 2010;29(1):117-9.
34. Hessen M, Akpek EK. Dry Eye: an Inflammatory Ocular Disease. Journal of Ophthalmic & Vision Research 2014;9(2):240-50.
35. Marsh P, Pflugfelder SC. Topical nonpreserved methylprednisolone therapy for keratoconjunctivitis sicca in Sjögren syndrome. Ophthalmology 1999;106(4):811-6.
36. Hong S, Kim T, Chung S-H, et al. Recurrence after topical nonpreserved methylprednisolone therapy for keratoconjunctivitis sicca in Sjögren's syndrome. Journal of ocular pharmacology and therapeutics 2007;23(1):78-82.
37. Bodor N, Buchwald P. Ophthalmic drug design based on the metabolic activity of the eye: Soft drugs and chemical delivery systems. The AAPS Journal 2005;7(4):E820-E33.
38. Jung HH, Ji YS, Sung MS, et al. Long-Term Outcome of Treatment with Topical Corticosteroids for Severe Dry Eye Associated with Sjögren's Syndrome. Chonnam Medical Journal 2015;51(1):26-32.
39. McGhee CN, Dean S, Danesh-Meyer H. Locally administered ocular corticosteroids. Drug Safety 2002;25(1):33-55.
40. Tosi GM, Massaro Giordano M, Caporossi A, et al. Amniotic membrane transplantation in ocular surface disorders. Journal of cellular physiology 2005;202(3):849-51.
41. Suri K, Kosker M, Raber IM, et al. Sutureless amniotic membrane ProKera for ocular surface disorders: short-term results. Eye & contact lens 2013;39(5):341-7.
42. Fox RI, Chan R, Michelson JB, et al. Beneficial effect of artificial tears made with autologous serum in patients with keratoconjunctivitis sicca. Arthritis & Rheumatism 1984;27(4):459-61.
43. Kono I, Kono K, Narushima K, et al. Beneficial effect of the local application of plasma fibronectin and autologous serum in patients with the keratoconjunctivitis sicca of Sjögren's syndrome. Ry machi[Rheumatism] 1986;26(5):339.
44. Tsubota K, Goto E, Fujita H, et al. Treatment of dry eye by autologous serum application in Sjögren's syndrome. British Journal of Ophthalmology 1999;83(4):390-5.
45. Tananuvat N, Daniell M, Sullivan LJ, et al. Controlled study of the use of autologous serum in dry eye patients. Cornea 2001;20(8):802-6.
46. James MJ, Gibson RA, Cleland LG. Dietary polyunsaturated fatty acids and inflammatory mediator production. The American journal of clinical nutrition 2000;71(1):343s-8s.
47. Bhargava R, Kumar P. Oral Omega-3 Fatty Acid Treatment for Dry Eye in Contact Lens Wearers. Cornea 2015;34(4):413-20.
48. Bhargava R, Kumar P, Kumar M, et al. A randomized controlled trial of omega-3 fatty acids in dry eye syndrome. International journal of ophthalmology 2013;6(6):811.
49. Donnenfeld E. Effect of Oral Re-Esterified Omega-3 Nutritional Supplementation on Dry-Eye Disease: Double-Masked Randomized Placebo-Controlled Study. 2015 ASCRS ASOA Symposium and Congress; 2015: Ascrs.
50. Li Z, Choi J-H, Oh H-J, et al. Effects of Eye Drops Containing a Mixture of Omega-3 Essential Fatty Acids and Hyaluronic Acid on the Ocular Surface in Desiccating Stress-induced Murine Dry Eye. Current eye research 2014;39(9):871-8.
51. Utine CA, Stern M, Akpek EK. Clinical review: topical ophthalmic use of cyclosporin A. Ocular immunology and inflammation 2010;18(5):352-61.
52. Pflugfelder SC, Wilhelmus KR, Osato MS, et al. The autoimmune nature of aqueous tear deficiency. Ophthalmology 1986;93(12):1513-7.
53. Stern ME, Gao J, Siemasko KF, et al. The role of the lacrimal functional unit in the pathophysiology of dry eye. Experimental eye research 2004;78(3):409-16.
54. Sall K, Stevenson OD, Mundorf TK, et al. Two multicenter, randomized studies of the efficacy and safety of cyclosporine ophthalmic emulsion in moderate to severe dry eye disease. Ophthalmology 2000;107(4):631-9.
55. Stevenson D, Tauber J, Reis BL, et al. Efficacy and safety of cyclosporin A ophthalmic emulsion in the treatment of moderate-to-severe dry eye disease: a dose-ranging, randomized trial. Ophthalmology 2000;107(5):967-74.
56. Laibovitz RA, Solch S, Andriano K, et al. Pilot trial of cyclosporine 1% ophthalmic ointment in the treatment of keratoconjunctivitis sicca. Cornea 1993;12(4):315-23.
57. Kunert KS, Tisdale AS, Gipson IK. Goblet cell numbers and epithelial proliferation in the conjunctiva of patients with dry eye syndrome treated with cyclosporine. Archives of ophthalmology 2002;120(3):330-7.
58. Daull P, Lallemand F, Philips B, et al. Distribution of cyclosporine A in ocular tissues after topical administration of cyclosporine A cationic emulsions to pigmented rabbits. Cornea 2013;32(3):345-54.
59. Calvo P, Sánchez A, Martínez J, et al. Polyester nanocapsules as new topical ocular delivery systems for cyclosporin A. Pharmaceutical research 1996;13(2):311-5.
60. Yenice , Mocan MC, Palaska E, et al. Hyaluronic acid coated poly- -caprolactone nanospheres deliver high concentrations of cyclosporine A into the cornea. Experimental eye research 2008;87(3):162-7.
61. Khan W, Aldouby YH, Avramoff A, et al. Cyclosporin nanosphere formulation for ophthalmic administration. International journal of pharmaceutics 2012;437(1):275-6.
62. De Campos AM, Sánchez A, Alonso MaJ. Chitosan nanoparticles: a new vehicle for the improvement of the delivery of drugs to the ocular surface. Application to cyclosporin A. International Journal of Pharmaceutics 2001;224(1):159-68.
63. Kuwano M, Ibuki H, Morikawa N, et al. Cyclosporine A formulation affects its ocular distribution in rabbits. Pharmaceutical research 2002;19(1):108-11.
64. Karn PR, Do Kim H, Kang H, et al. Supercritical fluid-mediated liposomes containing cyclosporin A for the treatment of dry eye syndrome in a rabbit model: comparative study with the conventional cyclosporin A emulsion. International journal of nanomedicine 2014;9:3791.
65. Sheppard JD, Torkildsen GL, Lonsdale JD, et al. Lifitegrast Ophthalmic Solution 5.0% for Treatment of Dry Eye Disease. Ophthalmology;121(2):475-83.
66. Tauber J, Karpecki P, Latkany R, et al. Lifitegrast Ophthalmic Solution 5.0% versus Placebo for Treatment of Dry Eye Disease: Results of the Randomized Phase III OPUS-2 Study. Ophthalmology 2015;122(12):2423-31.
67. Shire's OPUS-3 Phase 3 Trial with Lifitegrast Meets Primary and Key Secondary Endpoints, Significantly Reducing Patient-Reported Symptoms for Dry Eye Disease. 2015. (Accessed 1/26/2016, 2016, at https://www.shire.com/newsroom/2015/october/shires-opus-3-phase-3-trial-with-lifitegrast-meets-primary-and-key-secondary-endpoints.)
68. Xie J, Chiang L, Contreras J, et al. Novel fiber-dependent entry mechanism for adenovirus serotype 5 in lacrimal acini. Journal of virology 2006;80(23):11833-51.
69. Hsueh P-Y, Edman MC, Sun G, et al. Tear-mediated delivery of nanoparticles through transcytosis of the lacrimal gland. Journal of Controlled Release 2015;208:2-13.
70. Contreras-Ruiz L, Zorzi G, Hileeto D, et al. A nanomedicine to treat ocular surface inflammation: performance on an experimental dry eye murine model. Gene therapy 2013;20(5):467-77.

All Eyes on Neurodegenerative Disease

The eye can harbor potential early biomarkers for Alzheimer's and Parkinson's disease, and knowing what to look for can aid in early detection and management.

By Jarett Mazzarella, OD, and Justin Cole, OD

Because the retina is often considered an extension of the brain—sharing common features such as anatomical structure, vascular supply and the blood/tissue barrier—retinal imaging offers a unique opportunity to detect and monitor progression of certain neurodegenerative diseases in vivo.[1-8] For example, frequency-doubling perimetry has been shown to detect early changes in ganglion cells and higher visual cortical compromise in neurodegenerative diseases with high sensitivity and specificity.[5,9] Whether the retinal findings in neurodegenerative diseases reflect a local pathogenesis of the disease process or a secondary result of retrograde loss from cortical neurons remains unknown.[10] This article discusses the early signs of neurodegenerative disease in the eye to aid in early diagnosis and prompt management.

Alzheimer's Disease

Dementia, a term for conditions representing a change in mental state due to brain disease or injury, had a global prevalence of 35.6 million in 2010 and is expected to double every 20 years.[11] Damage to nerve cells can affect memory, behavior and the ability to perform routine tasks.[12]

The most common subtype of dementia is Alzheimer's disease (AD), representing 60% to 80% of cases.[12,13] Approximately 50% of patients diagnosed with presumed AD have solely AD, and 50% have mixed types of dementia.[12] Examples of other forms include vascular dementia, frontotemporal lobar degeneration, Parkinson's disease and dementia with Lewy bodies.[12] Neurodegenerative diseases such as AD are exceedingly difficult to study because a definitive diagnosis cannot be made until postmortem histopathological evaluation. Therefore, clinical studies are difficult and often suffer from an increased rate of error.[14]

Disease Impact

Neurodegenerative disorders are a significant socioeconomic burden and a major health care concern.[3] They are typically seen in adulthood, tend to be progressive and share similar mechanisms of pathogenesis.[3,51]

Due to the impact of neurodegenerative diseases on society, researchers are evaluating methods to identify high-risk individuals by screening for biomarkers.[52] To be effective in a primary care setting, biomarker testing must be inexpensive, readily available, rapid, reproducible and well tolerated by the patient.[1] The screening test must have a high sensitivity and specificity for the disease in question, particularly at its earliest stages. It must also have the ability to identify progression prior to significant cognitive loss.[1,11,13,28]

Alzheimer's disease has a prevalence of 6.4% for North Americans age 60 or older.[1] The prevalence increases with age, so that by age 85, 32% are afflicted with AD.[15] It is incurable and leads to progressive neuronal cell death in the brain due to amyloid protein plaques and neurofibrillary tangles that abnormally accumulate in the central nervous system (CNS) and interfere with communication between neurons, resulting in cerebral and hippocampal atrophy.[10,14] The disease progression is typically insidious, with estimates that neuronal damage may be present for up to 20 years prior to cognitive decline.[8,10]

The most common symptom in early disease is short-term memory loss. Symptoms can be grouped into cognitive dysfunction, including, but not limited to, memory loss and language deficits. The two remaining elements include non-cognitive and behavioral symptoms, which can include depression, hallucinations or delusions, among others. Vision and ocular abnormalities are also prevalent in AD (*Table 1*).

A probable diagnosis of AD is made based on a thorough medical history, imaging tests and laboratory workup to rule out other neurodegenerative etiologies. Unfortunately, the diagnosis is often made after the disease has reached an advanced state and significant neuronal damage has occurred.[16] Longitudinal studies postulate that, in early AD, cognitive impairment remains relatively stable.[17] Therefore, early detection of probable AD provides the greatest opportunity for therapeutic intervention and management.

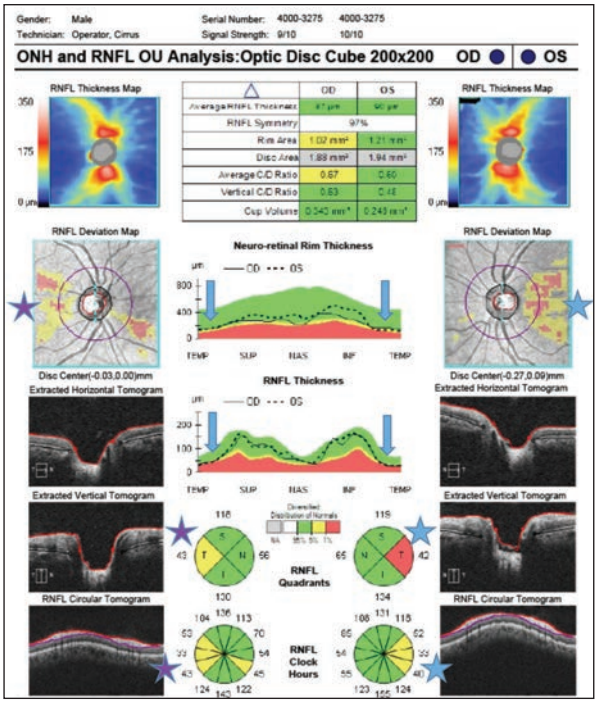

Fig. 1. OCT peripapillary RNFL scan depicting temporal quadrant thinning OU compared with normative data, notated by the purple stars OD and blue stars OS on the deviation maps, quadrant thickness graphs and the clock hour thickness graphs of each eye. The blue arrows mark areas of thinning compared with normative data on the TSNIT graphs in the center of the OCT printout.

Testing for AD includes magnetic resonance imaging (MRI) of the head and a cerebrospinal fluid (CSF) evaluation; the latter tends to be accurate in identifying specific biomarkers for AD.[18] However, CSF testing can be painful and is invasive, which decreases its usefulness as a screening method. Functional MRI has been employed in testing for AD, but variable presentations of the normal aging brain anatomy presents challenges.[19,20] Position emission tomography (PET) scans are currently being evaluated for the detection of AD using compounds that bind amyloid beta peptides known to accumulate in plaques.[21] In combination with genetic testing, PET scans can be highly predictive for the development of AD.[21]

Currently, the only therapies available for AD are palliative. Standard treatment typically consists of neurotransmitter modulators for acetylcholine or glutamate.[22] Other medicinal therapies target behavioral symptoms and may include antidepressants, anxiolytics, anti-Parkinson's medications, beta-blockers, anti-epileptics and neuroleptics.[22,23]

The Eye in Alzheimer's Disease

Alzheimer's disease can affect not only the brain but also the eye. Research on humans and mice indicate that AD pathology occurs in the retina as well as the CNS.[10] Some findings include:

• *Retinal nerve fiber layer (RNFL).* Investigators have noted a significant reduction in RNFL thickness in individuals with AD, as well as those with earlier, prodromal stages of AD with mild cognitive impairment (MCI), compared with normals.[13] Decreased RNFL thickness quantified by optical coherence tomography (OCT) in patients with MCI and AD correlates to loss of retinal neurons and axons.[13] This suggests that the retina may be an early site of damage prior to significant cognitive decline.[13] Investigators noted thinning of the RNFL in all quadrants of AD patients using OCT, which was confirmed with abnormal retinal function testing using pattern electroretinograms.[24] Other researchers evaluated MCI and early AD patients compared with moderate and late-stage AD patients and found RNFL thinning in all

Table 1. Common Ocular Symptoms/Findings of Alzheimer's Disease[1,2,59]

Eye Function	Symptoms	Testing
Visual acuity (VA)	• Blurring • Lack of sharpness • Distortion	• Snellen VA chart
Color vision	• Abnormal appearance of colors • Abnormal perception of colors • Fading or washing out of colors	• Color vision plates • D-15 hue test • 100 hue test • Nerve/macular evaluation
Contrast sensitivity	• Unable to distinguish objects based on changes in light	• Pelli Robson contrast sensitivity chart
Dark adaptation	• Increased time needed to adapt to changes in light level	• Macular photostress test
Visual perceptual abnormality • Visual motion • Visual attention • Visual space construction • Visual memory	• Illusions • Misperceptions • Misidentification	• Visual perceptual workup • Electrodiagnositics
Pupils	• Increased pupil response to cholinergic drops • Altered pupil flash response	• Pharmacological evaluation • Swinging flashlight test
Binocularity • Reduced depth perception • Pursuits • Saccades • Reduced stereopsis	• Double vision • Difficulty focusing and following objects • Eye fatigue	• Extraocular motility testing • Cover test • Saccades • Pursuits • Optokinetic nystagmus testing • Fixation testing
Visual field defects	• No symptoms • Positive scotoma • Negative scotoma	• Confrontational fields • Perimetry/micro perimetry • OCT: RNFL, ganglion cell analysis

quadrants with each group.[10,25,26] Although RNFL thinning occurs in AD, it is non-specific for a particular disease process, and whether it can be used to predict those at high risk for developing AD remains to be seen.[27] Recent studies have focused on longitudinal RNFL thinning in combination with memory measurements to help further define and predict future progression.[28]

• *Macula*. Researchers have found varying results in macular thickness and volume measurements with MCI and AD patients and hypothesize the differences are related to the stage of the disease.[13] Studies report increased macular thickness and volume in some MCI patients, which may be related to the early development of AD.[13,29] In contrast, other researchers found reduced macular thickness and volume measurements in AD patients, with the severity of macular findings related to the degree of cognitive impairment.[4,10,30] Yet others obtained similar results but with no correlation between findings and dementia severity.[4]

Looking more closely at cellular changes in individual retinal layers, research shows significant retinal ganglion cell (RGC) degeneration in AD patients.[10,31] No plaques or tangles were found in the retinal or optic nerve tissue. This supports known evidence that plaques and tangles primarily occur in the hippocampus and limbic areas of the brain in AD, sparing the visual and motor regions of the CNS.[31] Therefore, the researchers hypothesized that RGC loss was most likely related to neurodegenerative disease and not the result of a secondary retrograde process from the CNS.[10,31] The findings showed a 25% reduction in ganglion cell density in the fovea and parafoveal regions, with greatest reduction in the temporal sector of patients with AD.[10,31] Anatomically, these follow the distribution of ganglion cell fibers in the optic nerve forming the papillomacular bundle.

Current research is inconclusive regarding the extent to which changes in macular anatomy and the use of macular imaging can clearly define neurodegenerative pathology in the CNS. Due to the concentration of RGCs in the macula, researchers believe this may represent an area to evaluate both neuronal and axonal degeneration by assessing ganglion cell loss and RNFL thinning, respectively.[10]

• *Optic nerve cupping*. Research suggests retinal ganglion cell loss in AD mimics loss seen in glaucoma at a biochemical level due to neurotoxicity from amyloid deposition.[10]

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Investigators demonstrated a fivefold greater risk of visual field defects and optic disc cupping in patients with AD, as well as a higher prevalence of glaucoma in this population.[32] Researchers also found accelerated visual field loss in glaucoma patients with AD.[10] Differentiating optic nerve pathologies with respect to neurodegenerative diseases continues to present a challenge to clinicians.

Figures 1 and 2 depict a presentation not typical of a glaucomatous process, which mainly affects the inferior and superior neuroretinal rim first, but is more likely associated with a non-glaucomatous neuropathy. However, the exact etiology of the temporal thinning cannot be determined by OCT imaging alone. Visual field testing, serial nerve photography, a thorough history and clinical examination can be adjunctive, but not exclusive, in diagnosing ocular or CNS disease processes. Advancements in disease-specific OCT software will likely improve our ability to identify and differentiate ocular pathologies and correlate findings with neurodegenerative disease.

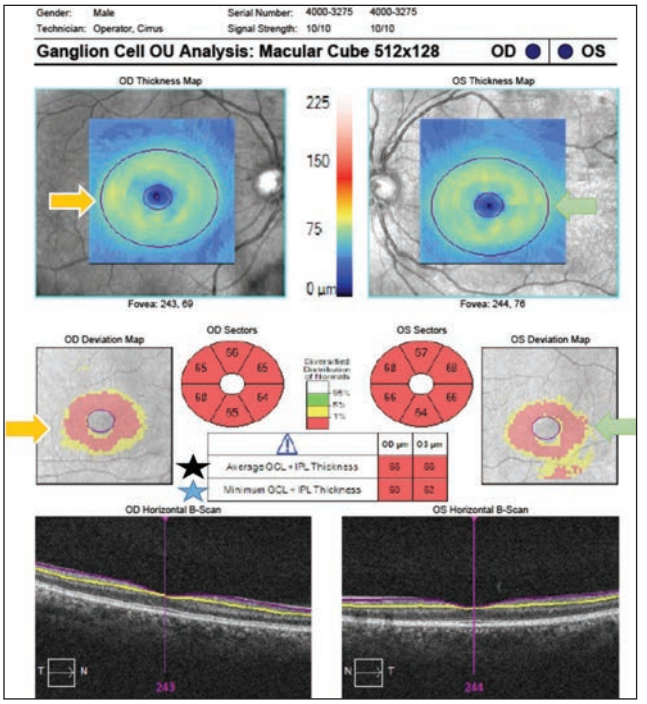

Fig. 2. OCT ganglion cell analysis demonstrating overall ganglion cell/inner plexiform layer thinning compared with normative data. The orange arrows OD and green arrows OS indicate thinning in the thickness and deviation maps for each eye. The black and blue stars notate the data box in the center of the printout showing significant reduction in average and minimum ganglion cell/inner plexiform layer thickness OU.

• ***Microvascular abnormalities.*** Researchers have evaluated retinal photos of patients with *probable* AD and found retinal blood vessel alterations associated with plaque deposits in the brain.[3] These variations consist of venous branching pattern asymmetry, as well as increased arteriolar length to diameter ratio values in AD. Researchers evaluated other measurements such as vascular attenuation, complexity of branching pattern and vessel tortuosity and hypothesized that retinal vasculature morphological changes consist of amyloid deposition extending from the CNS to the retina, resulting in vessel wall destruction.[3] Therefore, detailed funduscopic evaluation and serial retinal photography may present a screening mechanism for earlier AD detection.[3] Using a mouse model, investigators demonstrated microvascular impairment for AD due to amyloid accumulation in small vessels leading to tortuosity and reduction in vessel caliber.[33]

• ***Pupillary abnormalities.*** Currently, investigators are evaluating pupillary abnormalities as potential markers for AD. One particular area of interest is hypersensitivity to pupillary dilation with cholinergic antagonists and agonist medications, such as diluted tropicamide and pilocarpine, respectively.[10] Other research is looking at pupil flash response, which evaluates the pupil's reaction to light of varying intensities and different durations, which is found to be compromised in AD patients.[10]

Parkinson's Disease

A neurodegenerative disorder affecting the basal ganglia of the brain, Parkinson's disease (PD) describes a process that leads to dopamine-producing cell loss and abnormal deposition of protein inside nerve cells, termed Lewy bodies.[8] Other regions of the brain affected by PD include the hypothalamus and the nuclei of the thalamus, as well as the cerebral cortex, amygdala and the hippocampus in advanced disease.[34] A key hormone for signal transmission in the CNS, dopamine's depletion with loss of associated neurons leads to impairment of cognitive, motor and sensory function.[6,35]

This disorder affects more than one million people in the United States, with a peak incidence in the fifth and sixth decade and a prevalence of approximately 1% in the elderly.[36] It is the second most common neurodegenerative disease in the western world; however, its incidence is estimated to be only 1/10 that of AD.[12,37] Symptoms of the disease include, but are not limited to, bradykinesia (slow movement), muscle rigidity on movement,

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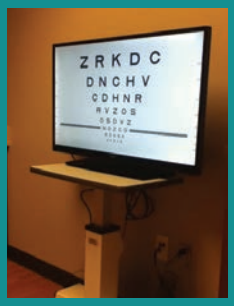
David Lewerenz, OD, FAAO
Clinical Diplomate in Low Vision, American Academy of Optometry
Northeastern State University Oklahoma College of Optometry



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Testing Limitations

Because neurodegenerative disease typically occurs in a diffuse fashion throughout the CNS, the retina—and retinal ganglion cells in particular—only represents a small subset of the CNS and may not fully reflect the extent of neurological damage.[53] Other challenges include normal changes in the retina and optic nerve anatomy with age; namely, thinning of RNFL and loss of ganglion cells.[53] Studies have shown the normal rate of RNFL thinning is approximately 0.2µm per year, and yet the magnitude of RNFL decline with age may be higher in eyes with larger baseline RNFL thickness.[54,55] Furthermore, there is a distinct variability in structural characteristics, which will continue to be an obstacle with current OCT software and normative databases.[56]

Not only is there anatomical variability between normal eyes of different individuals, but the normal findings between the right and left eyes of each patient may differ as well. We must define normal physiological variance between eyes to better define pathological asymmetry. Understanding the variance of normal OCT findings is helpful, considering researchers found that foveal thinning was more pronounced in the eye opposite the side of the body most affected by tremor in PD subjects as well as patients with essential tremor.[42] The organic etiology for asymmetrical laterality in neurodegenerative disease manifestations in some presentations is still poorly understood and further investigation is warranted.

Technological advances in OCT software for cell distinction and disease specificity will determine the role OCT plays in neurological disease diagnosis and monitoring in the future.[42] Evaluating the correlation of RNFL thinning and RGC loss in association with MRI of the brain will help determine the exact association of retinal findings in correlation with CNS manifestations in neurodegenerative disease.[11] Further investigation into the combination of RNFL parameters, macular thickness and macular volume findings may give the highest sensitivity and specificity as a potential biomarker for neurodegenerative states.

resting tremor, posterior instability and altered gait.[7] Additional motor symptoms can include apathy, anxiety, depression, fatigue, memory disturbance, sensory impairment, sleep disorders and autonomic disturbance.[7] PD can have a number of visual symptoms and ocular signs (*Table 2*).

The diagnosis of PD is typically based on motor function symptoms; however, non-motor deficiencies—such as constipation, sleep disturbances, bladder problems and depression—are common in the disease process as well.[35,38] Early diagnosis and prompt therapeutic intervention can increase the likelihood progression of the disease can be slowed.[34] As in AD, no specific test exists to diagnose PD. Typically, a diagnosis is made based on clinical history, symptoms and a neurological examination. Imaging tests such as MRI and PET scans are ordered along with laboratory testing to rule out neurological conditions such as essential tremor, dementia with Lewy bodies, chorea, embolic stroke and others, as differentials.[38,39]

Although the disease is considered incurable, certain medications may help with symptoms and aid in quality of life. Because PD targets dopamine-producing cells, drug therapy is aimed at replacing the neurotransmitter dopamine, since dopamine itself cannot directly penetrate the blood/brain barrier. A common medication prescribed in PD is levodopa, which is able to cross the blood/brain barrier where it is converted to dopamine. Often, levodopa is combined with carbidopa to prevent premature conversion to dopamine, thereby reducing side effects of the drug. In 2015, a carbidopa-levodopa infusion called Duopa (AbbVie) was approved by the FDA. Duopa is administered continuously by a pump directly to the small intestine, which keeps levels constant in the blood stream.[39] Other classes of drugs either mimic dopamine or help prevent the breakdown of dopamine, thereby prolonging the effect.[40,41]

In advanced disease, surgical implantation of a deep brain stimulation device that sends small electric shocks to areas of the brain such as the thalamus and globus pallidus has proven effective in reducing symptoms of tremor, rigidity and stiffness.[38,41] This procedure blocks electrical impulses to targeted CNS regions, but does not damage brain tissue.[38]

The Eye in Parkinson's Disease

Researchers have demonstrated that dopamine, which is commonly found in the retina of normal subjects, is decreased in PD patients.[7] Dopamine deficiency specifically can affect many cells of the retina, including horizontal, amacrine, bipolar and ganglion.[7] These cells may provide a biomarker to detect early disease onset as well as follow its progression.

- ***Retinal nerve fiber layer.*** Researchers first described peripapillary RNFL thinning in PD patients using OCT in 2004.[37,42,43] More recent research has demonstrated variable results showing thinning in the RNFL of PD patients with predominant loss in the temporal peripapillary retina in some studies, while other research is inconclusive.[28] One study found that both RNFL thinning and RGC loss did occur in a cohort of PD patients with correlation to functional reductions in visual acuity, contrast sensitivity, visual fields, color vision and electrodiagnostic tests. They

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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 allergic conjunctivitis.

IMPORTANT SAFETY 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 the eyelids or to any surface. Keep the bottle closed when not in use.
- BEPREVE® should not be used to treat contact lens-related irritation. Remove contact lens prior to instillation of BEPREVE®. Lenses may be reinserted 10 minutes after BEPREVE® administration.
- 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.

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Please see the accompanying full Prescribing Information for BEPREVE® on the following page.

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

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

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(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.

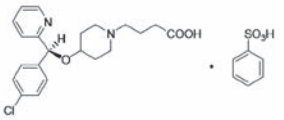
8.3 Nursing Mothers
Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 mcg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection 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 15° – 25°C (59° – 77°F).

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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concluded, however, that macular measurements of the RGC may be more reliable than RNFL thinning to define retinal structural alterations in PD.[44] With no consensus in repeatable longitudinal study findings, RNFL changes associated with PD cannot currently be applied to a screening process.

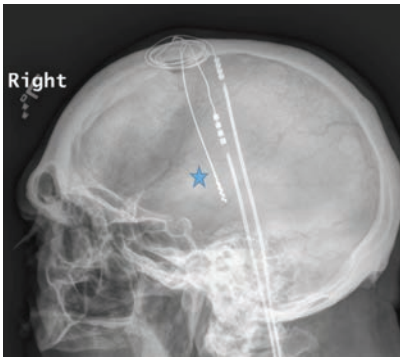
• ***Macula.*** A recent study demonstrated a reduction in central macular thickness and macular volume as well as thinner inner retinal layers in PD patients correlating with reduced motor score testing.[28] Others found a negative correlation between central macular thickness (CMT) and motor scores. These results suggest that depleted dopaminergic cells are not able to communicate with the cone receptors within the fovea, resulting in macular thinning.[28,45] Other investigators found retinal thinning at the edges of the foveal pit in a study cohort of PD patients. They hypothesize this reconstruction of the parafoveal zone may be unique in PD patients and may be related to oxidative stress that occurs to retinal neurons during the disease process.[42,46,47]

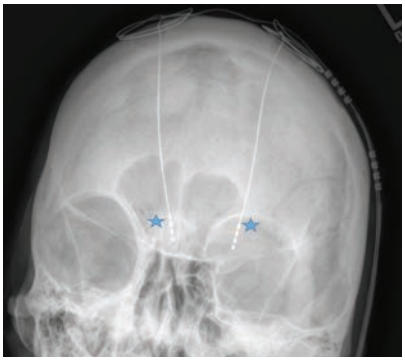
Advanced OCT software has depicted morphological changes in the individual retinal layers of PD patients. The maximal resolution of 3µm to 5µm with SD-OCT limits its ability to define specific cell types.[42] Several studies have found retinal thinning in the nasal and inferior paramacular regions related to PD.[7] These findings are supported by autopsy findings of protein aggregates typical of PD in the inner retinal layers of subjects.[8] Specific evaluation of the ganglion cell, inner nuclear, inner plexiform and outer nuclear layers has also demonstrated thinning related to loss of dopaminergic cells in PD subjects.[8]

Increased volume of the outer plexiform layer has been reported in PD patients using OCT, supported by histopathological evidence of increased autoimmune reactivity to proteins within this layer.[8] Future studies may focus on the parafoveal inner retinal layers, specifically the inner plexiform layer that houses the dopaminergic amacrine cells and innerconnections.[8,36] Specific OCT algorithms for PD are not commercially available, but literature suggests that macula scans may be more accurate than RNFL for defining neurodegenerative loss in PD.[42]

If an accurate ocular biomarker can be established for routine exams, it could aid in possible neuroprotective strategies, disease targeting, anti-inflammatory, immunosuppressive or antioxidative therapies to slow the progression of the neurodegenerative processes.[14] OCT and retinal photography may provide a fast, inexpensive, noninvasive and reproducible means of detecting neurological disease in high-risk patients in the primary optometric setting.[28] Further longitudinal studies will be needed to determine if retinal findings represent a primary retinal degeneration as a part of the neurodegenerative CNS disease process or retrograde manifestation from the CNS.[37] ■

Drs. Mazzarella and Cole are staff optometrists in the Salisbury VA Health Care System, Salisbury, NC.





Figs. 3 and 4. Radiographs of the skull with two deep brain stimulators within the cranium notated adjacent to the blue stars.

1. Ikram MK, Cheung CY, Wong TY, Chen CP. Retinal pathology as biomarker for cognitive impairment and Alzheimer's disease. Journal of Neurology, Neurosurgery, and Psychiatry. 2012;83(9):917-22.
2. Mancil GL. Visual disorders associated with Alzheimer's disease and optometric management. J Am Optom Ass. 1994;65(1):27-31.
3. Frost S, Kanagasingam Y, Sohrabi H, et al. Retinal vascular biomarkers for early detection and monitoring of Alzheimer's disease. Translational Psychiatry. 2013;3:e233.
4. Gao L, Liu Y, Li X, et al. Abnormal retinal nerve fiber layer thickness and macula lutea in patients with mild cognitive impairment and Alzheimer's disease. Archives of Gerontology and Geriatrics. 2015;60(1):162-7.
5. Valenti DA. Alzheimer's disease: screening biomarkers using frequency doubling technology visual field. ISRN Neurology. 2013;2013:989583.
6. Roth NM, Saidha S, Zimmermann H, et al. Photoreceptor layer thinning in idiopathic Parkinson's disease. Movement disorders: official journal of the Movement Disorder Society. 2014;29(9):1163-70.
7. Mailankody P, Battu R, Khanna A, et al. Optical coherence tomography as a tool to evaluate retinal changes in Parkinson's disease. Parkinsonism & Related Disorders. 2015;21(10):1164-9.
8. Chorostecki J, Seraji-Bozorgzad N, Shah A, et al. Characterization of retinal architecture in Parkinson's disease. Journal of the Neurological Sciences. 2015;355(1-2):44-8.
9. Thomas D, Thomas R, Muliyil JP, George R. Role of frequency doubling perimetry in detecting neuro-ophthalmic visual field defects. Am J Ophthalmol. 2001;131(6):734-41.
10. Jones-Odeh E, Hammond CJ. How strong is the relationship between glaucoma, the retinal nerve fibre layer, and neurodegenerative diseases such as Alzheimer's disease and multiple sclerosis? Eye (London). 2015;29(10):1270-84.
11. Larrosa JM, Garcia-Martin E, Bambo MP, et al. Potential new diagnostic tool for Alzheimer's disease using a linear discriminant function for Fourier domain optical coherence tomography. Invest Ophthalmol Vis Sci. 2014;55(5):3043-51.
12. Alzheimer's Association. 2014 Alzheimer's Disease Facts and Figures. Alzheimer's & Dementia. 2014;10(2). www.alz.org/downloads/Facts_Figures_2014.pdf.
13. Ascaso FJ, Cruz N, Modrego PJ, et al. Retinal alterations in mild cognitive impairment and Alzheimer's disease: an optical coherence tomography study. Journal of Neurology. 2014;261(8):1522-30.
14. Sivak JM. The aging eye: common degenerative mechanisms between the Alzheimer's brain and retinal disease. Invest Ophthalmol Vis Sci. 2013;54(1):871-80.
15. Hebert LE, Weuve J, Scherr PA, Evans DA. Alzheimer disease in the United States (2010-2050) estimated using the 2010 census. Neurology. 2013;80(19):1778-83.
16. National Institute of Aging. 2014-2015 Alzheimers Disease Progress Report: Advancing Research Toward a Cure. 2015 December.
17. Lazarczyk MJ, Hof PR, Bouras C, Giannakopoulos P. Preclinical Alzheimer disease: identification of cases at risk among cognitively intact older individuals. BMC medicine. 2012;10:127.
18. Adamczuk K, Schaeverbeke J, Vanderstichele HM, et al. Diagnostic value of cerebrospinal fluid Abeta ratios in preclinical Alzheimer's disease. Alzheimer's Research & Therapy. 2015;7(1):75.

Table 2. Common Ocular Symptoms/Findings of Parkinson's Disease[60,61]

Eye Function	Symptoms	Testing
Visual acuity • Abnormal eye movements	• Reduced VA	• Snellen VA • OCT: macula
Dry eye	• Reduced tear break-up time • Impaired mucin layer • Reduced blink rate and amplitude	Dry eye workup: • Schirmer testing • Tear break-up time • Epithelial staining • Tear evaluation (i.e., osmolarity)

Binocularity/motility	• Convergence insufficiency
	• Eye strain
	• Double vision
	• Hypometric voluntary saccades
	  • Latency and velocity intact
	  • Square-wave jerks; small saccades that affect fixation
		Extraocular motility testing:
		• Near point of convergence testing
		• Vergance testing
		• Saccades
		• Pursuits
		• Fixation testing
		• Optokinetic nystagmus testing

Visual perceptual abnormality	• Visual hallucinations	• History • Dilated exam to rule out ocular pathology • Head imaging to determine organic vs. inorganic nature of symptoms • Neurological workup • Possible neuropsychiatric workup
Eyelid	• Blepharospasm	• Upgaze test to assess fatigability and hypometric movement • Slit lamp examination • Cranial nerve evaluation if hemifacial spasm noted with imaging
Contrast sensitivity	• Abnormal sensitivity with intermediate to high frequency	• Pelli Robson contrast sensitivity chart
Color vision	• Visual blur with colors • May be progressive	• Color vision plates • D-15 hue test • 100 hue test • Red cap desaturation
Visual field	• Field defects may be increased in glaucoma patients	• Confrontational fields • Perimetry • OCT

19. Zhan Y, Chen K, Wu X, et al. Identification of conversion from normal elderly cognition to Alzheimer's disease using multimodal support vector machine. Journal of Alzheimer's disease. 2015;47(4):1057-67.
20. Ferreira LK, Busatto GF. Resting-state functional connectivity in normal brain aging. Neuroscience and Biobehavioral Reviews. 2013;37(3):384-400.
21. Dukart J, Sambataro F, Bertolino A. Accurate prediction of conversion to Alzheimer's disease using imaging, genetic, and neuropsychological biomarkers. Journal of Alzheimer's disease. 2016;49(4): 1143-1159. [Epub ahead of print].
22. Winslow BT, Onysko MK, Stob CM, Hazlewood KA. Treatment of Alzheimer disease. American Family Physician. 2011;83(12):1403-12.
23. Massoud F, Leger GC. Pharmacological treatment of Alzheimer disease. Canadian Journal of Psychiatry. 2011;56(10):579-88.
24. Parisi V. Correlation between morphological and functional retinal impairment in patients affected by ocular hypertension, glaucoma, demyelinating optic neuritis and Alzheimer's disease. Seminars in Ophthalmology. 2003;18(2):50-7.
25. Paquet C, Boissonnot M, Roger F, et al. Abnormal retinal thickness in patients with mild cognitive impairment and Alzheimer's disease. Neuroscience Letters. 2007;420(2):97-9.
26. Kesler A, Vakhapova V, Korczyn AD, et al. Retinal thickness in patients with mild cognitive impairment and Alzheimer's disease. Clin Neurol Neurosurg. 2011;113(7):523-6.
27. Shi Z, Wu Y, Wang M, et al. Greater attenuation of retinal nerve fiber layer thickness in Alzheimer's disease patients. Journal of Alzheimer's Disease. 2014;40(2):277-83.
28. Shi Z, Zhu Y, Wang M, et al. The utilization of retinal nerve fiber layer thickness to predict cognitive deterioration. Journal of Alzheimer's disease. 2015;49:2:399-405.
29. Reichenbach A, Wurm A, Pannicke T, et al. Muller cells as players in retinal degeneration and edema. Graefe's Arch Clin Exp Ophthalmol. 2007;245(5):627-36.
30. Iseri PK, Altinas O, Tokay T, Yuksel N. Relationship between cognitive impairment and retinal morphological and visual functional abnormalities in Alzheimer disease. Journal of Neuro-Ophthalmology. 2006;26(1):18-24.
31. Blanks JC, Hinton DR, Sadun AA, Miller CA. Retinal ganglion cell degeneration in Alzheimer's disease. Brain Research. 1989;501(2):364-72.
32. Bayer AU, Ferrari F. Severe progression of glaucomatous optic neuropathy in patients with Alzheimer's disease. Eye (London). 2002;16(2):209-12.
33. Dorr A, Sahota B, Chinta LV, et al. Amyloid-beta-dependent compromise of microvascular structure and function in a model of Alzheimer's disease. Brain: a Journal of Neurology. 2012;135(Pt 10):3039-50.
34. Jimenez B, Ascaso FJ, Cristobal JA, Lopez del Val J. Development of a prediction formula of Parkinson disease severity by optical coherence tomography. Movement Disorders. 2014;29(1):68-74.
35. Bayhan HA, Aslan Bayhan S, Tanik N, Gurdal C. The association of spectral-domain optical coherence tomography determined ganglion cell complex parameters and disease severity in Parkinson's disease. Current Eye Research. 2014;39(11):1117-22.
36. Adam CR, Shrier E, Ding Y, Glazman S, Bodis-Wollner I. Correlation of inner retinal thickness evaluated by spectral-domain optical coherence tomography and contrast sensitivity in Parkinson disease. Journal of Neuro-Ophthalmology. 2013;33(2):137-42.
37. Stemplewitz B, Keseru M, Bittersohl D, et al. Scanning laser polarimetry and spectral domain optical coherence tomography for the detection of retinal changes in Parkinson's disease. Acta Ophthalmologica. 2015. [Epub ahead of print].
38. National Parkinson Foundation. Nonmotor Symptoms. Accessed December 18, 2015. www.parkinson.org/Understanding-Parkinsons/Non-Motor-Symptoms.
39. Mayo Clinic. Diseases and Conditions: Parkinson's Disease. Accessed December 18, 2015. www.mayoclinic.org/diseases-conditions/parkinsons-disease/basics/symptoms/con-20028488.
40. Tarsly D. Pharmacologic treatment of Parkinson disease. UpToDate. 2015. www.uptodate.com/contents/pharmacologic-treatment-of-parkinson-disease.
41. Tarsly D. Nonpharmacologic management of Parkinson disease. UpToDate. www.uptodate.com/contents/nonpharmacologic-management-of-parkinson-disease.
42. Bodis-Wollner I, Miri S, Glazman S. Venturing into the no-man's land of the retina in Parkinson's disease. Movement Disorders. 2014;29(1):15-22.
43. Inzelberg R, Ramirez JA, Nisipeanu P, Ophir A. Retinal nerve fiber layer thinning in Parkinson disease. Vision Research. 2004;44(24):2793-7.
44. Kaur M, Saxena R, Singh D, et al. Correlation between structural and functional retinal changes in Parkinson disease. Journal of Neuro-Ophthalmology. 2015;35(3):254-8.
45. Altintas O, Iseri P, Ozkan B, Caglar Y. Correlation between retinal morphological and functional findings and clinical severity in Parkinson's disease. Advances in Ophthalmology. 2008;116(2):137-46.
46. Spund B, Ding Y, Liu T, et al. Remodeling of the fovea in Parkinson disease. Journal of Neural Transmission. 2013;120(5):745-53.
47. Slotnick S, Ding Y, Glazman S, et al. A novel retinal biomarker for Parkinson's disease: Quantifying the foveal pit with optical coherence tomography. Movement Disorders. 2015;30(12):1692-5.
48. Wills Eye Hospital. Test Procedures 2015. Accessed December 2, 2015.
49. Armstrong RA. Visual symptoms in Parkinson's disease. Parkinson's Disease. 2011;2011:908306.
50. Lenka A, Hegde S, Jhunjhunwala KR, Pal PK. Interactions of visual hallucinations, rapid eye movement sleep behavior disorder and cognitive impairment in Parkinson's disease: A review. Parkinsonism & Related Disorders. 2015. [Epub ahead of print].
51. Jentsch S, Schweitzer D, Schmidtke KU, et al. Retinal fluorescence lifetime imaging ophthalmoscopy measures depend on the severity of Alzheimer's disease. Acta Ophthalmologica. 2015;93(4):e241-7.
52. National Cancer Institute. Biomarkers 2015. Accessed December 12, 2015.
53. Cheung CY, Ong YT, Hilal S, et al. Retinal ganglion cell analysis using high-definition optical coherence tomography in patients with mild cognitive impairment and Alzheimer's disease. Journal of Alzheimer's Disease. 2015;45(1):45-56.
54. Knight OJ, Girkin CA, Budenz DL, et al. Effect of race, age, and axial length on optic nerve head parameters and retinal nerve fiber layer thickness measured by Cirrus HD-OCT. Archives of Ophthalmology. 2012;130(3):312-8.
55. Leung CK, Yu M, Weinreb RN, et al. Retinal nerve fiber layer imaging with spectral-domain optical coherence tomography: patterns of retinal nerve fiber layer progression. Ophthalmology. 2012;119(9):1858-66.
56. Bussel, Il, Wollstein G, Schuman JS. OCT for glaucoma diagnosis, screening and detection of glaucoma progression. Br J Ophthalmol. 2014;98 Suppl 2:ii15-9.

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A CLOSER LOOK AT PRESBYOPIA CORRECTION

Better corrective lenses and a multitude of surgical approaches give your presbyopic patients more options than ever before. **By Jane Cole, Contributing Editor**

Keen intellects have been trying to tackle the problem of presbyopia at least since the time of Benjamin Franklin, who wrote in 1784 that he was "happy in the invention of double spectacles, which serving for distant objects as well as near ones, make my eyes as useful to me as ever they were." Many people today remain just as happy with modern descendants of that same approach, but that hasn't stopped researchers from continuing to explore innovative approaches, so that the billions of presbyopes in the world can each find a solution that suits them. Here is a look at the latest emerging options to address this all-but-inevitable human need.

Contact Lenses

Data suggests the majority of contact lens wearers prefer to stay in contacts once they become presbyopes; in fact, 91% of contact lens wearers ages 35 to 55 hope to continue wearing contact lenses.[1] "Many presbyopes are interested in occasional contact lens wear, for which daily disposable lenses are an ideal option," says Thomas G. Quinn, OD, of Drs. Quinn, Foster and Associates in Athens, Ohio.

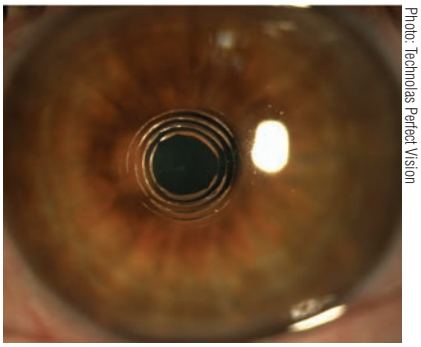


Photo: Technolas Perfect Vision

Clinical view of intrastromal incisions three hours post-Intracor treatment.

The advent of stable lens platforms such as hybrid and scleral lenses is also good news for presbyopes with corneal astigmatism, adds Clark Chang, OD, director of the specialty contact lens service at the Cornea and Laser Eye Institute in Teaneck, NJ. He explains that aspheric optics and reverse geometry in hybrid multifocal lenses allow for an extended range of functional vision, while the ultra-stable nature of scleral lenses provides options for patients with residual cylinder through the concurrent provision of multifocal optics with front toric corrections.

Today's soft disposable multifocals also provide better day-to-day comfort— important in this population, as presbyopes often exhibit drier eyes—while high Dk lens materials combined with plasma treatment make modern hybrid and scleral lenses more ocular surface-friendly than older generations. They may reduce patient dropout due to discomfort even during allergy season, Dr. Chang says, while the new aspheric multifocal hybrids and toric scleral lenses offer a more continuous range of vision than ever before. New lenses in the pipeline to supplement your arsenal include:

• ***Bausch + Lomb's Ultra for Presbyopia.*** Expected to arrive in the second quarter of 2016, this monthly replacement silicone hydrogel lens will combine the three-zone progressive design from the company's Biotrue OneDay multifocal with its Ultra contact lens material. The lens contains polyvinylpyrrolidone, which Bausch + Lomb says enhances wettability to aid in providing better all-day comfort; the lens has the highest Dk/t (163) and lowest modulus (70) among the silicone hydrogels, according

to B+L. Its aspheric optics provide good vision even in low light, and the three-zone design allows for smoother transitions as the patient shifts gaze, the company says.

• ***Brien Holden Vision's extended depth of focus (EDOF) contact lenses.*** These recently received FDA clearance and are scheduled to be available this year. The design uses higher-order aberrations to improve image quality over a wide range of distances while minimizing ghosting and haloes and should perform relatively independent of a patient's natural aberrations and variation in pupil size, the company says.

• ***E-Vision Smart Optics electronic contact lens.*** This device will retain the look and feel of conventional lens, but adds a layer of liquid crystal material that can be "tuned" to different focal lengths via embedded electrodes, allowing the wearer to change prescription in as little as 200 milliseconds, the company says. The first prototype will be available by late 2016, says E-Vision.

• ***Google and Alcon's 'smart' lenses.*** The two companies are partnering to develop a lens that incorporates embedded sensors, microchips and other miniaturized electronics. Alcon expects the lens to provide accommodative vision correction to help restore the eye's natural autofocus on near objects in the form of an accommodative contact lens or intraocular lens (IOL) implanted during refractive cataract treatment.

"The 'smart' lens design offers some promise to be a game changer—if it delivers," suggests Dr. Quinn. "I can't wait to get my hands on it."

Until then, conventional multifocal contact lenses continue to improve with each new generation, and 2016 looks to be a year marked by progress.

Multifocal and Accommodating IOLs: The New Generation

Currently, there are four predominant surgical solutions for presbyopia—multifocal IOLs, monovision, accommodating IOLs and extended depth of focus IOLs—that incorporate intraocular lenses after cataract surgery, says Eric Donnenfeld, MD, clinical professor of ophthalmology at NYU and past president of the American Society of Cataract and Refractive Surgery. Monovision and multifocal lenses have been around for a long time, he notes, but "what is most exciting are the new, lower-add multifocal lenses that reduce the size of haloes and are actually much better tolerated than the older generation of four diopter lenses."

Two of the newest additions are the AcrySof IQ Restor +2.5D IOL (Alcon) and the Tecnis Multifocal +2.75D and +3.25D (Abbott Medical Optics). The FDA approved the former, which uses fewer diffractive zones and a larger central refractive zone than other IOLs for better distance vision, in April 2015.[2] Alcon says it's ideal for patients with "distant-dominant lifestyles." Dr. Donnenfeld notes that a toric version of this intraocular lens should be released shortly.

The one-piece Tecnis multifocal IOL +2.75D improves long intermediate acuity (~50cm theoretical reading distance) while the +3.25D lens improves close intermediate viewing (~42cm distance), AMO says.

Also on the multifocal IOL horizon are three tri-focal lenses currently available in Europe: AcrySof IQ PanOptix trifocal (Alcon), PhysIOL (FineVision) and Lisa Tri 839MP (Carl Zeiss Meditec). While still not available in the United States, Dr. Donnenfeld believes these advancements look promising as future treatment options.

Choosing the Right Presbyopia Correction

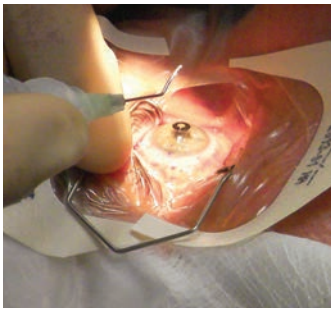
There's no one-size-fits-all approach with presbyopia correction, especially with so many options to choose from. The specific choice is dependent on patient disposition, refractive error, pupil size, habitual environment, visual demands and financial considerations, Dr. Quinn says.

"Communication is everything," says Dr. Freeman. "The eye care provider involved with a patient's care must listen to a patient's goals and expectations of treatment, whether it's glasses or contact lenses, or some type of vision correction surgery," he says.

If surgery is the decided course, the patient and provider need to be on the same page regarding the expected outcome of any surgery, says J. Christopher Freeman, OD. "After a patient's goals and expectations are made known, the providers need to let the patient know what can be delivered. Visual demands, goals for improvement in certain lifestyle or leisure activities, as well as physical and ocular health are a few of the important considerations that should be addressed when developing a treatment plan. If the anticipated outcome is not congruent with the goal, then the patient's goal may need to be adjusted and the expectations reset." Success is much more likely with this approach, Dr. Freeman says.

For Dr. Chang, a thorough understanding of patients' lifestyle and visual habits is essential to guide the decision-making process. For presbyopia patients who are not yet suitable for IOL discussions (i.e., ages 40 to 60), contact lenses and the Kamra inlay can be effective management options for typical day-to-day tasks. If a patient has high demand for near acuity, bifocal GP lenses may still be one of the best options. For those patients who have sufficient crystalline lens change and whose best contact lens corrected vision has been on the decline, then discussing a premium IOL is an excellent option, Dr. Chang says.

Photo: Clark Chang, OD



Intraoperative photo of a patient undergoing Kamra inlay implantation.

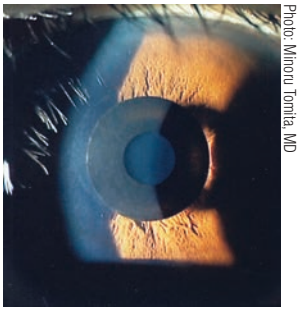


Photo: Minoru Tomita, MD

Slit lamp view of the Kamra inlay in position.

The only FDA-approved accommodative IOL currently available remains the tried and true Crystalens (Bausch + Lomb) and its toric version, Trulign. However, other promising designs are making their way through the pipeline:

• ***Tetraflex (Lenstec).*** This flexible, non-hinged, single-optic IOL features closed-loop haptics angled anteriorly 10°, causing the optic to flex and change curvature with accommodation. A study of functional vision showed improved ability to read 80 words per minute or more at print sizes as small as 20/25 with the Tetraflex.[3]

• ***FluidVision Lens (Power Vision).*** This IOL is an acrylic implant filled with silicone oil that changes curvature with accommodation. As the ciliary muscle contracts and relaxes, energy is transferred to the zonules and lens capsule, where it squeezes fluid from the haptics into the optic to increase its anterior curvature.

• ***Sapphire AutoFocal IOL (Elenza).*** Electroactive optics in this intraocular lens help it change power when accommodation is necessary. A microscopic battery stimulates internal liquid crystals when pupil size decreases.

• ***AMO Tecnis Symfony.*** This extended-depth-of-focus lens takes a different approach to extending a patient's range of vision by addressing the optical property known as chromatic aberration.[4] Dr. Donnenfeld, who was part of the investigative team in an FDA trial of the lens, explains that most subjects tolerated the Tecnis with minimal distance distortion, as well as reduced glare and halo. "You do lose a little bit of contrast, but it's [part of] a whole new generation of lenses that appear to be very interesting," he says, adding that the device is likely to be available in the United States in 2017.

• ***Calhoun Vision Light Adjustable Lens.*** This IOL's power is adjusted after the lens is in place by irradiating the lens's special silicone material with ultraviolet light, which changes the lens's shape and therefore its power.[4] A Phase III study is underway.

• ***AkkoLens Lumina.*** The Lumina is a dual-optic lens that relies on the action of the ciliary body for its effect.[4] The company anticipates receiving the CE mark for the Lumina, and it plans to expand clinical trials in other countries.

• ***Vision Solutions Technologies' LiquiLens.*** Created by optometrist Alan Glazier, this bi-fluidic IOL has a gravity-based mechanism that shifts the focal plane on downgaze by altering interplay of fluids against one another.[4]

• ***AcuFocus IC-8.*** This combination device consists of a small-aperture "mask" and an acrylic IOL lens platform, Dr. Chang says. "The acrylic platform is similar to the other foldable IOLs in use today, so no new surgical delivery technique will be required," he says. The opaque mask component in the center of the IOL optic has an outer diameter of 3.23mm and an inner aperture measuring 1.36mm in size to offer similar benefit of extended depth of focus as in a Kamra inlay (discussed below), he adds. This IC-8 IOL received CE mark in the fall of 2014.

Inlays: The Latest Frontier

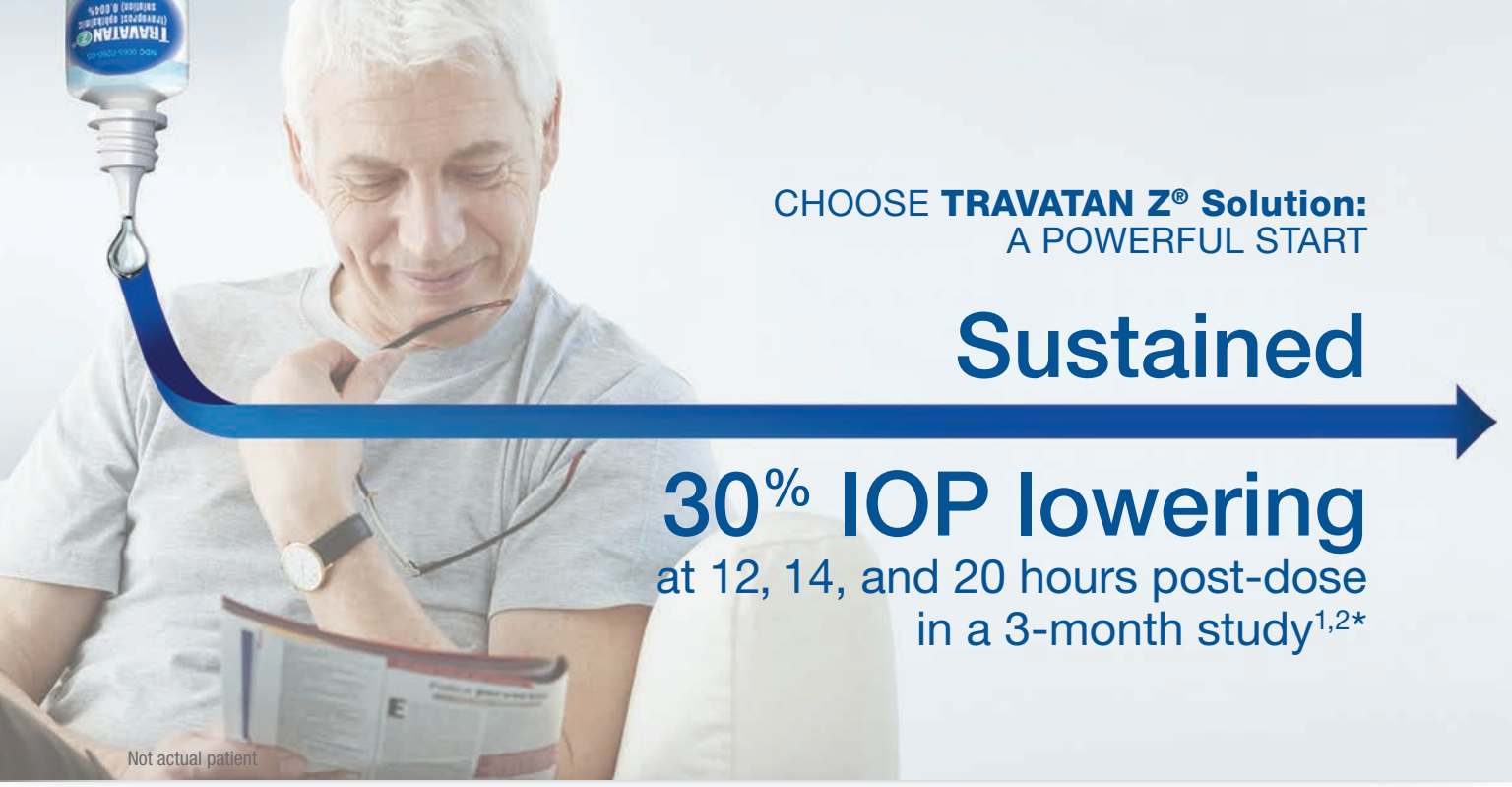
A relatively new approach to presbyopia correction, corneal inlays improve near vision without hindering distance vision in emmetropic presbyopes.

"Corneal inlays serve an exciting niche market for the emmetropic presbyope looking to restore the lifetime of excellent vision that seems to have been stolen from them," says J. Christopher Freeman, OD, of the Landstuhl Regional Medical Center Department of Ophthalmology in Landstuhl, Germany.

In April 2015, the FDA approved the Kamra inlay (AcuFocus) to improve near vision in certain patients with presbyopia. This thin (5µm), small (3.8mm) disc has a 1.6mm central opening that acts like a pinhole to increase the patient's depth of field and improve near vision with little effect on distance vision. Thousands of microperforations in the donut-shaped Kamra inlay allow nutrients to pass through the implant within the cornea, Dr. Freeman says.

The "pseudo-random" distribution pattern of the perforations also ensures the delivery of more focusable light rays to the retinal plane, says Dr. Chang. This allows for better optical regulations by the Kamra inlay and improves visual function in dimmer environments compared to previous generations of small aperture inlays, Dr. Chang says.

"What's nice about the Kamra inlay is that it doesn't distort



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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.

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 the brief summary of Prescribing Information on the adjacent page.

*Study Design: Double-masked, randomized, parallel-group, multicenter non-inferiority comparison of the efficacy and safety of travoprost 0.004% preserved with benzalkonium chloride (BAK) to TRAVATAN Z® Solution after 3 months of treatment in patients with open-angle glaucoma or ocular hypertension. Baseline IOPs were 27.0 mm Hg (n=322), 25.5 mm Hg (n=322), and 24.8 mm Hg (n=322) at 8 AM, 10 AM, and 4 PM for TRAVATAN Z® Solution. At the end of Month 3, the TRAVATAN Z® Solution group had mean IOPs (95% CI) of 18.7 mm Hg (-0.4, 0.5), 17.7 mm Hg (-0.4, 0.6), and 17.4 mm Hg (-0.2, 0.8) at 8 AM, 10 AM, and 4 PM, respectively. Statistical equivalent reductions in IOP (95% confidence interval about the treatment differences were entirely within ±1.5 mm Hg) were demonstrated between the treatments at all study visits during the 3 months of treatment.

References: 1. Data on file, 2013. **2.** Lewis RA, Katz GJ, Weiss MJ, et al. Travoprost 0.004% with and without benzalkonium chloride: a comparison of safety and efficacy. *J Glaucoma.* 2007;16(1):98-103.

TRAVATAN Z®
(travoprost ophthalmic solution) 0.004%

Alcon®
a Novartis company

TRAVATAN Z®
(travoprost ophthalmic solution) 0.004%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE
TRAVATAN Z® (travoprost ophthalmic solution) 0.004% is indicated for the reduction of elevated 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) 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.

Rx Only
U.S. Patent Nos. 5,631,287; 5,889,052, 6,011,062; 6,235,781; 6,503,497; and 6,849,253

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vision," Dr. Donnenfeld explains. "There is no change in refractive index of the cornea, and as with all the inlays, I don't say it's reversible, but removable."

Vance Thompson, MD, of Sioux Falls, SD, who was part of the scientific team in the FDA Kamra inlay clinical trials, says results of the study found, on average, near vision improved from a pre-op Jaeger score of J8 to J2 post-op. "The vast majority [of patients] maintained their uncorrected distance vision at 20/20 or 20/25," he says. "Normally to get that sort of near improvement with monovision, we would have to sacrifice distance much more, so we were amazed at the improvement in near and how distance was preserved."

Dr. Thompson says he was surprised that intermediate vision was maintained or improved following the implantation of the Kamra inlay. This isn't the case with monovision, where more near correction hurts intermediate vision. Also unlike monovision, the overall results post-op didn't lessen with time. "This is very exciting technology for my presbyopic patients with clear lenses," Dr. Thompson says.

Furthermore, adds Dr. Quinn, the procedure itself is relatively quick and leads to minimal patient discomfort. "It saves the patient from the inconvenience of lens application and removal required by contact lens wear." However, "there are some reports of increase glare at night. Challenges with viewing the retina during retinal surgery have been reported when the inlay is in place," Dr. Quinn says.

A few other inlays are moving through the approval process and may be available in the near future:

• ***The Raindrop (ReVision Optics).*** This hydrogel plastic inlay typically is placed within the cornea of the non-dominant eye under a LASIK-style flap created using a femtosecond laser. When in position, it changes the curvature of the cornea so the front of the eye acts like a multifocal contact lens. In November 2015, the FDA accepted the company's premarket approval submission; the product could reach the US by 2017. Dr. Donnenfeld notes patients may sacrifice some quality of distance vision, but overall the loss is minimal.

• ***Flexivue Microlens (Presbia).*** Also pending FDA clearance, this hydrophilic acrylic inlay measures 3.2mm in diameter and 0.015mm/15µ in edge thickness, is offered in powers ranging from +1.5D to +3.5D, in 0.25D increments and implanted in the non-dominant eye. Presbia completed its second stage enrollment of its FDA pivotal study in September 2015. A recent study found that 12 months after implantation, the inlay seems to be an effective method for the corneal compensation of presbyopia in emmetropic presbyopes between the ages of 45 and 60.[5]

• ***Icolens (Neoptics).*** Still in the early stages of development, this hydrophilic copolymer inlay has a diameter of 3.0mm and an edge thickness less than 15µ (depending on refraction). For presbyopia, it offers power ranging from +1.5D to +3.0D (in 0.5D steps).

"Based on my current knowledge of available inlays, I think there may be overlapping clinical indications for each," Perry Binder, MD, writes in a recent issue of *EuroTimes*. "This can only benefit patients' needs. Until we develop a safe and predictable means of replacing the aging dysfunctional lens with a biocompatible intracapsular polymer, the intracorneal inlay in its current iteration and possibly newer alloplastic materials will offer the most predictable, easily removable and safe refractive surgical correction of presbyopia."

Ophthalmic Lenses: Still Making Strides

Spectacles have centuries of familiarity on their side, and progressive addition lenses have been a staple of presbyopia correction for a long time, but recent advances in this category have gone ultra-high tech.

"Spectacle lens technology continues to advance from early progressive addition lenses to today's 'free form' lenses, also known as digital lenses," says Dr. Freeman. These lenses provide an array of computer-calculated, customizable parameters to best suit a given patient's prescription, visual demands and desired frame, he says.

"For example, with advanced computer algorithms, a corridor length can be designed to custom fit a patient's frame of choice, along with the appropriate width of distance or near vision portion of the lens, and can even be optimized to the fitted frame's pantoscopic tilt and face-form wrap. These personalized progressive addition lenses can reduce unwanted distortions, improve adaptation and ultimately increase patient satisfaction," Dr. Freeman says.

Many of the new digital lenses now offer technologies that the companies say will eliminate eye fatigue and boost reading on digital devices. This new era of progressives includes Essilor's Varilux portfolio, which has incorporated technologies that provide sharper vision in all lighting condition, easier transitions between distance and near zones, and a reduction of swim, according to the company.

Other digital lenses include the Shamir's Autograph, inTouch, Spectrum, Element, FirstPal, Creation and Piccolo; Hoya's Lifestyle 2, Mystyle and Summit iQ; and Zeiss' Precision Portfolio and Individual 2. Also from Zeiss is the high-definition Sola HDV. Yet another high-definition lens is the Seiko Supercede from Seiko Optical Products of America.

Other Surgical Techniques

Inlays and new IOLs aren't the only surgical innovations to pique researchers' interests, however:

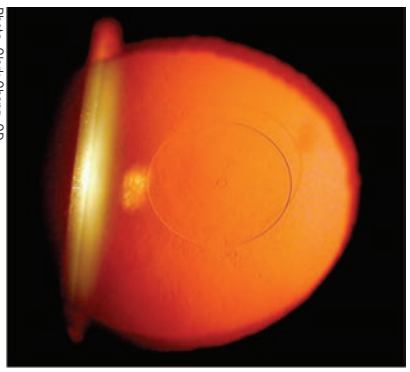
• ***Presby-LASIK.*** This is an aspheric modification of the cornea under a flap using an excimer laser that creates a multifocal cornea by inducing higher-order aberrations that increase depth of focus.[6]

Central presby-LASIK creates a steeper myopic corneal center surrounded by a flat hyperopic periphery, inducing a negative spherical aberration.[6] The pupil constricts with convergence, creating a pinhole effect.[6] Peripheral presby-LASIK induces positive spherical aberration, which increases pseudo-accommodation. The flattened corneal center focuses distance, while the steepened periphery focuses near.[6] Clinical outcomes for both peripheral and central presby-LASIK show promise, but further studies are needed to investigate long-term stability of the procedure and quality of vision under low contrast settings.[7]

Presby-LASIK has been around for a long time in other countries and is especially popular in South America, Dr. Donnenfeld says. However, there are no current active trials in the United States.

• ***Intracor.*** This procedure uses a femtosecond laser to create concentric, intrastromal cylindrical incisions that change the corneal biomechanics to reshape the cornea. Because the procedure is intrastromal, there is no incision of the epithelium, endothelium or Bowman's or Descemet's membrane. The internal rings created by the laser steepen the curvature of a small central zone in the cornea, which increases near vision. The FDA has not yet cleared Intracor for use in the United States, but the presbyopia correction treatment has shown promising results in early studies.[8,9]

Photo: Clark Chang, OD



Flexivue Microlens, within which a 0.5mm central perforation can be seen with retroillumination.

• ***Scleral implants.*** While found to be ineffective in the past, these are back under the microscope, Dr. Donnenfeld says. A newer version of one such device, the VisAbility scleral implant (Refocus Group), uses four small implants placed in scleral tunnels 4mm posterior to the limbus, which the company says restores tension of the posterior zonules, giving the ciliary muscles more efficiency in reshaping the lens in presbyopic patients.[10] Results of a recently completed FDA clinical trial were promising, with 96% of patients seeing J3, 20/40 or better uncorrected at near monocularly. All were better still binocularly.[10]

The concept of scleral expansion to tighten the zonules, increasing their ability to change crystalline lens shape, has been explored for over a decade, Dr. Quinn adds. One caveat, though, is that "tissue barriers are inserted into channels that maintain the scleral expansion. This is somewhat controversial, and the American Academy of Ophthalmology has stated clinical results with scleral expansion 'have been disappointing' and 'leave little support' for it as 'an effective means of presbyopia correction,'" Dr. Quinn says.

• ***LaserAce system (Ace Vision Group).*** This developing technology uses an erbium-YAG laser to create numerous ablation spots through 90% of the scleral depth in an attempt to ease contraction of the ciliary muscle, the company says.

Correction by the Drop

Could your presbyopes one day be able to correct their vision by simply using an eye drop? A few research teams are currently working on this alternative treatment that also creates the pinhole effect as the inlays do, but noninvasively.

• ***Carbachol/brimonidine.*** Last year, researchers in Egypt conducted a double-masked, randomized placebo-controlled clinical trial with 48 naturally emmetropic and presbyopic subjects to investigate the use of a parasympathomimetic drug (carbachol) and an alpha-agonist (brimonidine) to treat presbyopia.[11] "The monocular pharmacologic treatment of presbyopia with one drop a day of carbachol and brimonidine in the non-dominant eye permits acceptable reading vision for many presbyopes, even in older subjects," says lead investigator Almamoun Abdelkader, MD, PhD. "Because of increased depth of focus from the smaller pupil, it does not blur distance or intermediate vision, as does typical monovision therapy, and the perception of normal brightness in the untreated eye eliminates symptoms of dimming from the smaller pupil of the treated eye."

• ***Liquid Vision (Presbyopia Therapies).*** This drop is in Phase II clinical trials as a topical, reversible, short-term treatment for presbyopia. The investigational drug induces a miotic effect on the pupil that lasts approximately eight hours after instillation, developers say.[12] By constricting the pupil and creating a pinhole effect, the drops help to improve near vision performance.

• ***PresbV Tears.*** Columbian researcher Felipe Vejarano, MD, is

leading the investigation of this eye drop for presbyopia correction. Effects of the drop last four to five hours after application and result in increased near vision by three lines without diminished distance vision, Dr. Vejarano says. In some cases, the treatment may improve distance vision by one line, Dr. Vejarano said at the 2015 Academy of Ophthalmology meeting. The drop is applied to both eyes and, because of its pseudo-accommodation, can also improve night vision, he claimed.

Although eye drops can simulate the visual effect of a small-aperture inlay, miotics have a risk of retinal detachment, Dr. Binder notes in *EuroTimes*. "The effect of such drops lasts four to six hours, maximum, and takes time to develop," he writes. "Patients desire instant near acuity and do not wish to wait 15 to 30 minutes before they can read. Having to take frequent drops is not much better than wearing reading glasses." However, the impact of such a topical eye drop on non-small aperture inlays has the potential to enhance their outcomes, he adds.

Dr. Freeman says he is excited that new technology in presbyopia correction is advancing so quickly, and with it, an increase in the options to customize patients' treatments. "Now we are able to address presbyopia with real solutions, and ever-improving ones, to help patients achieve their visual goals."

"Presbyopia is a universal problem that is extremely debilitating to many patients older than 40, and we continue to seek solutions for this," Dr. Donnenfeld says. The optimal solution is "going to be a true accommodating IOL that has no loss of contrast sensitivity," he believes. "They will come eventually." ■

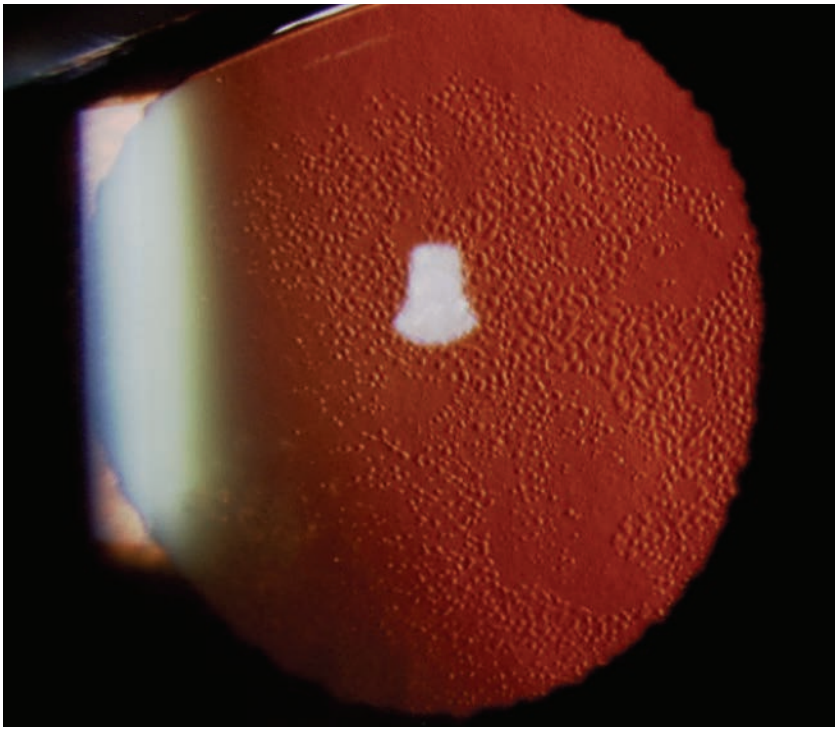
1. Reindel WT, Edmunds FR. A clinical assessment of presbyopic soft contact lens designs: comparing the impact of SofLens multifocal contact lenses and Acuvue bifocal contact lenses on successfully adapted monovision patients. Review of Optometry. 2003 Apr 15;140(4).
2. Saxena V. Alcon intraocular lens gets FDA's stringent PMA approval. Fierce Medical Devices. 2015 Apr 17. Available at www.fiercemedicaldevices.com/story/alcon-intraocular-lens-gets-fdas-stringent-pma-approval/2015-04-17.
3. Bohorquez V, Alarcon R. Long-term reading performance in patients with bilateral dual-optic accommodating intraocular lenses. J Cataract Refract Surg. 2010;36:1880-6.
4. Bethke W. IOL alternatives to multifocality, Review of Ophthalmology. 2015;22(1):32-8.
5. Limnopoulou AN, Bouzoukis DI, Kymionis GD, et al. Visual outcomes and safety of a refractive corneal inlay for presbyopia using femtosecond laser. J Refract Surg. 2013;29:12-8.
6. Crabb A, Krueger, R. The final cut: surgical correction of presbyopia. Review of Cornea and Contact Lenses. 2014 Nov;151(8):20-6.
7. Waring GO, Berry DE. Advances in the surgical correction of presbyopia. International Ophthalmology Clinics. 2013;53:129-152.
8. Khoramnia R, Fitting A, Rabsilber TM, et al. Intrastromal femtosecond laser surgical compensation of presbyopia with six intrastromal ring cuts: 3-year results. Br J Ophthalmol. 2015 Feb;99(2):170-6.
9. Thomas BC, Fitting A, Auffarth GU, et al. Femtosesecond laser correction of presbyopia (INTRACOR) in emmetropes using modified pattern. J Refract Surg. 2012 Dec;28(12):872-8.
10. Stephenson M. The future of presbyopia correction. Review of Ophthalmology. 2015 Feb;22(2):47-9, 71.
11. Abdelkader A. Improved presbyopic vision with miotics. Eye & Contact Lens. 2015 Sept;41(5):323-7.
12. Review of Cornea and Contact Lenses, June 15, 2014. Available at www.reviewofcontactlenses.com/content/c/48838.

ROCKin' a New Treatment Option

Rho-kinase inhibition may soon help glaucoma and some cornea patients. Here's what it does. **By Andrew Rixon, OD, and Andrew S. Gurwood, OD**

As primary eye care practitioners working with a rapidly aging population, our role in glaucoma management is expanding. Unfortunately for patients and practitioners, the pathogenesis of glaucoma is not yet fully understood. A multitude of causal mechanisms have been proposed, including: low cerebrospinal fluid pressure leading to laminar cribrosa non-support, impaired microcirculation and vascular dysregulation, altered immunity, excitotoxicity, oxidative stress and secondary neurodegeneration of retinal neurons and cells from primary neural pathological processes.[1,2]

As we close in on its origin, we may get closer to discovering how to defeat the disease. But for now, what we do know is that intraocular pressure (IOP) is the sole risk factor we can currently modify to alter the characteristic death of retinal ganglion cells seen in glaucoma



A case of Fuch's dystrophy shown in retroillumination. Research now demonstrates the ability of ROCK inhibitor eye drops, in combination with transcorneal freezing, to decrease central corneal thickness and recover corneal clarity in Fuch's cases.

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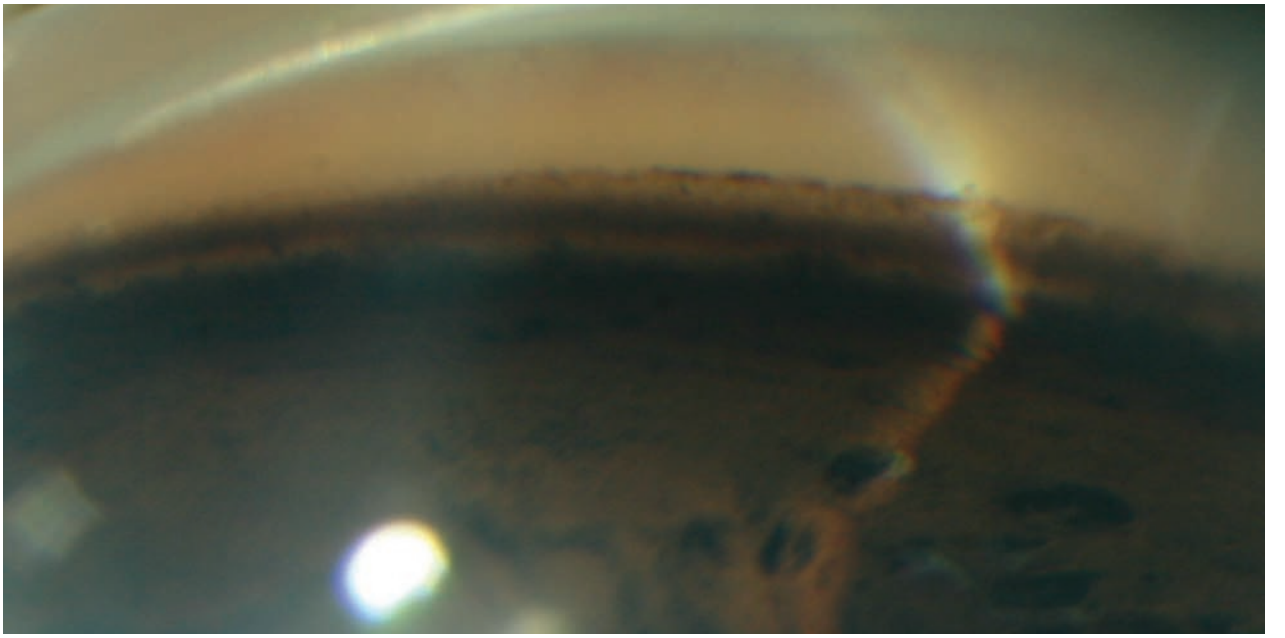

Gonioscopic view of the TM, the initial point of aqueous humor outflow through the conventional outflow pathway and thus a major regulator of IOP. ROCK inhibitors are the first drug class to directly target trabecular outflow, specifically affecting the smooth muscle-like cells of the TM. This novel mechanism results in increased aqueous outflow and subsequent decreased IOP.

patients.[2-6] Often, IOP modification requires surgical intervention.

Extensive scientific research into a non-surgical option has led scientists to pharmacologically target the cells of the trabecular meshwork (TM) to facilitate aqueous outflow.[7] The pharmacological mechanism involved relates to inhibition of Rho GTPase proteins, most notably RhoA, which exists in significantly elevated levels in glaucomatous optic nerve heads (ONH), suggesting they play a role in the disease's pathophysiology.[8]

Clinical research involving Rho-kinase inhibitors (known as ROCK inhibitors) shows promise, one day, to provide additional agents to the topical glaucoma-management armamentarium available in the United States.

TM Outflow Pathway

To understand how ROCK inhibitors work, you first need a little background on the operations of the TM and how, on a cellular level, it provides the mechanism for aqueous outflow.

The TM outflow pathway accounts for up to 90% of aqueous outflow under normal physiological conditions.[9-11] Anatomically, the TM can be separated into distinct regions based on location and function. The regions of the uveal and corneoscleral meshwork consist of arrays of lamellae, which are, themselves, comprised of fenestrated collagen beams. These beams are covered by endothelial-like cells, with loose extracellular matrix (ECM) that occupies the spaces between the cells of the adjacent beams.[12] These spaces decrease in size and the lamellae become flatter as they transition into the area known as the juxtacanalicular (JCT), or cribriform, region. This JCT is composed of cells embedded in a dense network of ECM with narrow intercellular spaces.[13] The ECM provides a channel for aqueous humor (AH) to cross the JCT and exit the anterior chamber through Schlemm's canal, where the AH is eventually drained into the venous circulation. The ECM is an active structure, possessing many bioactive molecules that influence outflow resistance. This activity in the extracellular environment is linked to alterations in the intracellular actin cytoskeleton and vice versa.[13] Resistance to aqueous flow in normals is greatest in the JCT region and/or the inner wall of Schlemm's canal.[9]

Regulation of aqueous outflow in this pathway is primarily controlled by the interaction of two cell types in the JCT region: cells of the TM and Schlemm's canal endothelia. Cells of the TM express smooth muscle-like properties including contractility, electro-mechanical characteristics and expression of actin and myosin specific to smooth muscle tissue.[14] This highly structured cellular actomyosin system affects the overall contractile tone of the tissue,

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1. J.M. Nolan et. al., Exp. Eye Res., 2012; 101:9-15

influencing outflow resistance.[15] Research shows actin depolymerization coupled with decreased cell-ECM interactions and myosin II phosphorylation within cells of the trabecular pathway increase aqueous humor outflow, consequently decreasing IOP.[16,17] The majority of aqueous flowing across the Schlemm's canal endothelia, researchers believe, passes through micron-sized pores.[7] Schlemm's canal cells are highly contractile, and increased contraction greatly increases their cell stiffness. Altered cell stiffness modifies pore formation, ultimately affecting downstream egress of AH from the eye.[7]

Outflow Resistance

Dysfunctional outflow resistance is a concept that is critical to the glaucomatous disease process. A normal reduction of aqueous outflow facility through the TM is approximately 7% to 10% per decade. Primary open angle glaucoma (POAG) patients, however, have increased resistance to outflow.[9] Substantial evidence supports a link between cytoskeletal integrity within the cells of the trabecular pathway and aqueous humor outflow through that route.[16]

Histological changes in POAG patients that may contribute to decreased aqueous outflow include a declining number of TM cells, increased and changed ECM components, deposition of extracellular plaques and stiffening of the TM with decreased contractility force of the elastic fibers.[13,18,19]

Specifically, as the smooth muscle–like properties of TM cells likely facilitate dynamic tissue restructuring, the marked loss of these cells in glaucoma leads to fusion and thickening of the trabecular lamellae, which impairs its function.[14,19] The deposition of extracellular plaques within glaucomatous JXT ECM is similar to the characteristics of the process of fibrosis. These aberrant accumulations adhere to the sheaths of the elastic fibers and their connections to the inner wall endothelium of Schlemm's canal.[13,19]

Researchers believe these increased junctional adherences between the cells of Schlemm's canal and accumulated ECM underlie the increased resistance to aqueous outflow.[20] Bolstering this is the fact that subcortical Schlemm's canal cell stiffness is elevated, by as much as 50%, in glaucomatous eyes.[20] This increased stiffness correlates with decreased pore density, impairing the egress of AH from the eye.[20]

Current Treatment

The current guidelines for POAG treatment suggest first-line medical therapy with hypotensives.[21] Multiple classes of medications are used to lower IOP by affecting both the production and outflow of aqueous humor. These include prostaglandin analogues (PGAs), beta-blockers, carbonic anhydrase inhibitors, alpha adrenergic agonists and miotics.[14]

PGAs are the most efficacious at lowering IOP, with minimal differences amongst medications in that class.[14,22] PGAs work primarily by increasing uveoscleral outflow and, although some studies have shown their ability to alter resistance in trabecular outflow, it is considered minimal.[23-26] Uveoscleral outflow, by direct measurement in humans, accounts for approximately 10% to 20% of outflow under normal conditions.[4]

In the United States, the only currently available medications having a mechanical effect on the conventional outflow pathway are miotics. These agents work by contracting the ciliary muscle, subsequently increasing mechanical pull on the TM, altering the meshwork's parasellar spaces and leading to an enhanced aqueous outflow.[7,16] Due to their significant ocular side effects and frequent dosing schedule, miotics are considered a third-line treatment option.[27] Accordingly, today, they are in limited use.[7] This underscores a need for drugs that might directly target this pathway with less deleterious side effects.[7,28]

Trabecular meshwork outflow tissues are avascular and dependent on the AH to supply antioxidants, growth factors and nutrients. Current first-line therapies that suppress aqueous production or enhance uveal/scleral outflow have the potential to decrease the supply of AH nutrients across the outflow tissues.[29] In the short-term, reduction of IOP protects the optic nerve; but, in the long-term, nutrient deprivation may induce a greater than normal degradation of the trabecular outflow pathway—with deterioration causing a greater risk of increased IOP over time.[29]

A Different Approach

The Rho subgroup of the Ras superfamily is made up of multiple small guanosine triphosphate (GTP)-binding proteins (RhoA, RhoB, RhoC).[14] Rho GTPase, participates in signaling pathways leading to the formation of actin stress fibers and focal adhesions.[30] Rho GTPase is activated in response to growth factors, mechanical stretching, cytokines and extracellular matrix. Rho plays a critical role in a multitude of cellular processes associated with cytoskeletal rearrangements. These include cell morphology, cell motility, cytokinesis, apoptosis and, most notably, smooth muscle contraction.[31,32] Multiple Rho target molecules have been identified as downstream Rho effectors, including Rho-associated coil-forming protein serine/threonine

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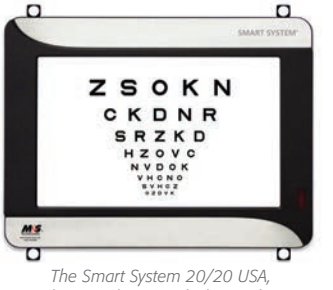

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Compound	Approval/Trial Stage	Developer/Licensee	Mechanism
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AR-13324 (Rhopressa)	Phase III	Aerie Pharmaceuticals	ROCK/NET inhibition
PG-324 (Roclatan)	Phase III	Aerie Pharmaceuticals	Combination ROCK/NET inhibitor and PGA
AMA-0076	Phase II	Amaken Therapeutics, Belgium	ROCK inhibition

Note: A minimum of 8 Rho kinase inhibitor compounds previously in development have been discontinued. This underscores the fact that not all ROCK inhibitors are equally efficacious.[14]

kinases labelled as ROCK-1 and its isoform known as ROCK-2.[33-35] Stimulating the Rho pathway, specifically the aforementioned ROCK-1 and ROCK-2, enhances phosphorylation of the myosin light chain, thus increasing the contractility of those fibers.[16] Upregulation of the Rho pathway has been proposed to play a role in an assortment of diseases, including; asthma, cancer, cardiovascular hypertrophy, diabetes mellitus, erectile dysfunction, hyperproliferative diseases, hypertension, inflammatory diseases, pulmonary hypertension, renal disease and vasospasm.[7]

This has led to substantial research on the physiological consequences of ROCK inhibition on smooth muscle tone and cytoskeletal stability and its subsequent treatment effects.[7]

Rho GTPase in Glaucoma

Activation, and sustained activity of, Rho GTPase in the TM cells and other cell types of the AH outflow pathway increases resistance to aqueous humor drainage.[15,36] This is associated with increased actin stress fibers and cell adhesive interactions, triggering expression of various ECM proteins and cytokines involved in regulating ECM synthesis.[15,36] These changes influence AH drainage working in a feedback response. The discovery of this feedback response uncovered the potential interaction among ECM protein expression, actomyosin contraction and Rho GTPase activity, and their influence on AH drainage through the TM and homeostasis of IOP.[36]

When glaucomatous optic nerve heads were compared with their non-glaucomatous counterparts, significantly elevated levels of RhoA protein were detected, suggesting RhoA plays a role in the pathophysiology of glaucoma.[8] Additionally, endothelin 1 was found in higher concentrations in glaucomatous eyes. Endothelin 1 is a ligand in TM cells that mediates reorganization of the actin cytoskeleton and cell contraction to adjust aqueous outflow. Endothelin 1 is also a major upstream activator of the Rho and Rho-associated protein kinase signaling pathway.[14] These findings led researchers to conclude that pharmacological manipulation of the Rho GTPase signaling pathway could prove useful in relaxing the cellular actomysin system, resulting in cell shape alterations and cellular relaxation that results in a downstream increase in intracellular space and a decrease in the resistance to AH outflow.[7]

ROCK Inhibitors in Glaucoma

Although the probability of glaucoma-related blindness has decreased substantially over the last 45 years, in part due to improvements in medical therapy, no medication with a new mechanism of action has made it to Phase III trials in approximately 20 years.[37,38] Ideally, glaucoma medication should focus on three targets: IOP, outflow facility through the pressure-dependent pathway and retinal ganglion cells (RGC).[39]

Available glaucoma medications focus on aqueous production inhibition and outflow facility improvement through the unconventional pathway.[39] New medications with mechanisms of action that act synergistically with existing therapies could interject added benefits.

The potential role of Rho GTPases in regulating aqueous humor outflow was first proposed in 2001 when western blot analysis revealed the presence of ROCK in human TM cells and bovine ciliary muscle tissue.[30] Now it is understood that the actions of ROCK-1 and ROCK-2 have been shown to alter the cell shape and ECM, increasing the contractility of the TM cells decreasing aqueous humor (AH) outflow facility.[6] Accordingly, when ROCK-1 and ROCK-2 are inhibited, research shows IOP is reduced and outflow facility is increased.[40] Study authors speculate this effect resulted from ROCK inhibitor-induced retraction of TM cell bodies, disruption of actin bundles and impairment of focal adhesion formation.[19]

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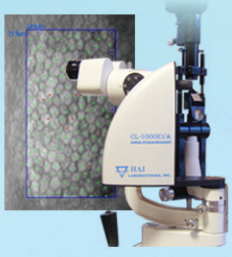

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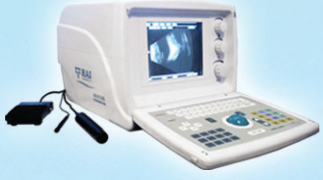

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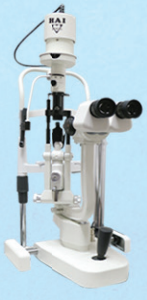

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Additional investigations demonstrate that ROCK inhibitors induce changes in cell-cell junction associated proteins and actin cytoskeleton in Schlemm's canal endothelial cells and cell permeability, leading to improved outflow facility.[41] Succinctly, ROCK-based therapies have a mechanism of action that works via relaxation of the contractile tone of the trabecular tissue in the outflow pathway by altering the cell morphology through cytoskeletal disassembly.[7]

While reducing IOP alone does not seem to halt progressive visual field loss in all patients, specifically those with normal tension glaucoma (NTG) where apoptotic effects may also be in play, reducing damage to the RGCs caused by IOP-independent risk factors might also be useful.[42] ROCK inhibitors are known to enhance the survival of RGCs post ischemic injury.[43] Researchers investigated the effect of K-115, a novel Rho-kinase inhibitor, on the survival of mice RGC after death was induced by optic nerve crush, finding that survival increased by 34% when K-115 was administered orally.[42] Given these results, the authors speculate that suppression of Rho activity has the potential to be a new neuroprotective treatment for glaucoma. ROCK inhibitors may additionally increase blood flow by inhibiting calcium sensitization and relaxing vascular smooth muscles. This effect has been noted in both the conjunctiva and retina and proposed effects directly on the optic disc blood vessels may slow the progression of glaucomatous optic neuropathy.[44]

According to clinical trial registries in the United States, Europe and Japan, seven different selective rho kinase inhibitors have been tested in human clinical trials.[29] ROCK inhibitors have been shown to be

ROCK Inhibition and the Endothelium

Recent research has concentrated on ROCK inhibition's use in corneal disease, specifically endothelial dystrophies.

To maintain transparency, central endothelial cell (CEC) density must remain above 400-500cells/mm^2.[1] In pathological situations such as Fuch's endothelial dystrophy (FD), the rate of cell loss far exceeds that of normal age-related attrition (about 0.6%/year), often terminating with an absolute residual density of 400 cells/mm^2.[1,2]

Pathophysiology

CECs have a severely limited ability to proliferate and, as a result of the dystrophy, undergo compensatory migration and enlargement in an attempt to maintain function.[3,4] The end result of this endothelial decompensation is often irreversible corneal swelling and loss of transparency with an accompanying reduction in vision.[2,5,6] At present, the only curative intervention available is transplantation.[2,5]

Block the ROCK

Endothelial keratoplasty accounted for more than 40% of transplants performed in 2009 and 2010, rising to become the most commonly performed type of keratoplasty in the last three years, approaching 55% in 2014.[6,7]

Although investigators suggest transplantation of cultivated CECs may be a viable intervention for patients with severe endothelial dystrophies, a less-invasive treatment, such as eye drops, would be more appropriate in early stages of endothelial disease.[3] The ROCK inhibitor Y-27632 has shown promise in treating endothelial decompensation, as it works to enhance cell adhesion and accelerate proliferation of the CECs by inhibiting dissociation-induced apoptosis.[4,8-12]

In a study of four patients scheduled for Descemet stripping automated endothelial keratoplasty, researchers demonstrated the efficacy of Y-27632 eye drops, preceded by trans-corneal freezing, in treating central corneal edema caused by late-onset Fuch's corneal dystrophy.[4,12] Y-27632 proved effective for the recovery of corneal transparency and the gradual reduction of corneal thickness for up to six months after treatment, with one patient's vision recovering from 20/100 to greater than 20/20.[4,12] That patient maintained endothelial function and vision for up to 24 months post treatment.[13]

A recent preliminary study has also demonstrated that ROCK inhibitor eye drops can treat post cataract surgical corneal edema.[5] The investigators concluded the development of such drops for acute corneal damage would be useful in reducing the incidence of bullous keratopathy (PBK) and aphakic bullous keratopathy (ABK).[5]

1. Joyce, NC. Proliferative capacity of corneal endothelial cells. Exp Eye Res. 2012;95(1):16–23.
2. Bourne W. Biology of the corneal endothelium in health and disease. Eye. 2003;17: 912-8.
3. Okumura N, Koizumi N, Kay E, et al. The ROCK inhibitor eye drop accelerates corneal endothelium wound healing. Invest Ophthalmol Vis Sci. 2013;54:2493-502.
4. Lee J, Kay E. FGF-2-induced wound healing in corneal endothelial cells requires cdc42 activation and rho inactivation through the phosphatidylinositol 3-kinase pathway. Invest Ophthalmol Vis Sci. 2006;47:1376–86.
5. Okumura N, Inoue R, Okazaki Y, et al. Effect of the Rho-kinase inhibitor Y-27632 on corneal endothelial wound healing. Invest Ophthalmol Vis Sci. 2015;56:6067–74.
6. Anshu A, Price M, Tan D, Price F. Endothelial keratoplasty: a revolution in evolution. Surv Ophthalmol. 2012;57:236-52.
7. Eye Bank Association of America. 2014 Eye Banking Statistical Report. Washington, DC; Eye Bank Association of America;2014.
8. Okumura N, Ueno M, Koizumi N, et al. Enhancement on primate corneal endothelial cell survival in vitro by a ROCK inhibitor. Invest Ophthalmol Vis Sci. 2009;50:3680-7.
9. Koizumi N, Okumura N, Ueno M, Knioshita S. New therapeutic modality for corneal endothelial disease using rho-associated kinase inhibitor eye drops. Cornea 2014;33(Suppl):S25–S31.
10. Okumura N, Nakano S, Kay E, et al. Involvement of cyclin D and p27 in cell proliferation mediated by ROCK inhibitors Y-27632 and Y-39983 during corneal endothelium wound healing. Invest Ophthalmol Vis Sci. 2014;55:318–29.
11. Pipparelli A, Arsenijevic Y, Thuret G, et al. ROCK inhibitor enhances adhesion and wound healing of human corneal endothelial cells. PLoS One. 2013;8:e62095.
12. Koizumi N, Okumura N, Ueno M, et al. Rho-associated kinase inhibitor eye drop treatment as a possible medical treatment for Fuchs corneal dystrophy. Cornea. 2013;32:1167–70.
13. Ljubimov AV, Saghizadeh M. Progress in corneal wound healing. Prog Retin Eye Res 2015;49:17-45.

effective in lowering the intraocular pressure in human trials, with an IOP reduction ranging from 2.9mm Hg to 6.1mm Hg.[29,43,45-48]

ROCK Inhibitors In Use

Since Rho-kinase inhibitors have a different mechanism of action than currently available medications, they may work synergistically with the those options. Research demonstrates ROCK inhibitors work successfully in both fixed-dose combination with and additively to travaprost, latanoprost and timolol respectively.[29,47] IOP reduction ranged from 9mm Hg to 12mm Hg in a fixed combination of Rho-kinase inhibitor/travoprost, and trials where ROCK inhibitors were added independently to current therapies showed a significantly greater change in mean IOP than when placebo was added.[29,47]

The most common side effect of ROCK inhibitors is ocular hyperemia, with an incidence of up to 65% in clinical trials.[29] Hyperemia is due to relaxation of the smooth muscle cells of the conjunctival blood vessels and is transient, resolving in a few hours.[43-46,48] Once-daily dosing at night minimizes this, reducing the incidence of hyperemia to 11% as the hyperemia resolves overnight.[29]

Additional mild to moderate adverse events reported with ROCK inhibitors included: punctate keratitis, photophobia, headache, abdominal pain, mild hepatic dysfunction, asthma and nasopharyngitis.[46,47] Notably, no severe adverse events have been reported in clinical trials. Glanatec (ripasudil, Kowa), K-115, approved for glaucoma and ocular hypertension in September 2014 in Japan, has been shown to induce guttae-like findings.[49] These are due to the formation of protrusions along the

endothlium cell-cell borders. They appear to be transient. Corneal endothelial function markers, corneal thickness and corneal volume have been reportedly unaffected, and no endothelial cell death has been recorded.[49]

Investigators hypothesize that ROCK inhibitors also lower IOP by reducing episcleral venous pressure (EVP). A recent preclinical study has shown that AR-13324, the first of a new class of ocular hypotensive compounds that inhibits both Rho kinase and the norepinephrine transporter, (ROCK-NET) produces a statistically significant lowering of EVP in rabbits.[50] The authors speculate that a similar effect in humans would offer an additional new mechanism of action for patients with glaucoma.

A Phase II study comparing AR-13324 with latanoprost showed AR-13324 to be less effective by approximately 1mm Hg, reducing the IOP by a substantial 5.7mm Hg on average.[51] ROCK-NETs work by inhibiting both Rho kinase and norepinephrine transporter to increase outflow and by decreasing the production of AH.[52] The advancement of this medication to Phase III trials is highly promising and will hopefully yield a novel treatment for patients in the United States.

The potential impact of ROCK-inhibition in the management of glaucoma and FD appears to be promising. These medications, with their novel mechanism of action, will add to the therapeutic collection with the promise of improving vision and quality of life for our patients. ■

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Dr. Gurwood is a professor at Salus University in Elkins Park, Pa.

1. Weinreb R, Aung T, Medeiros F. The pathophysiology and treatment of glaucoma: a review. JAMA. 2014 May;311(18):1901-11.
2. Janssen S, Gorgels T, Ramdas W, et al. The vast complexity of primary open angle glaucoma: disease genes, risks, molecular mechanisms and pathobiology. Prog Retin Eye Res. 2013;37:31-67.
3. Wilson M, Singh K. Intraocular pressure: does it measure up? The Open Ophthalmology Journal. 2009;3:32-7.
4. Alm A, Nilsson S. Uveoscleral outflow: a review. Experimental Eye Research. 2009;88:760-8.
5. Brubaker, R. Targeting outflow facility in glaucoma management. Surv Ophthalmol. 2003;48:Suppl 1: S17-20.
6. Stamer W, Braakman S, Zhou E, et al. Biomechanics of Schlemm's canal endothelium and intraocular pressure reduction. Prog in Retinal Eye Research. 2015;44:86-98.
7. Challa P, Arnold J. Rho-kinase inhibitors offer a new approach in the treatment of glaucoma. Expert Opin Investig Drugs. 2014;23(1):81-95.
8. Goldhagen B, Prola A, Epstein D, Rao P. Elevated levels of RhoA in the optic nerve head of human eyes with Glaucoma. J Glaucoma. 2012;21:530-8.
9. Johnson M. What controls aqueous humor outflow resistance? Exp Eye Res. 2006;82(4):545-57.
10. Tamm E. The trabecular meshwork outflow pathways: structural and functional aspects. Exp Eye Res. 2009;88:648-55.
11. Lutjen-Drecoll E. Functional morphology of the trabecular meshwork in primate. Prog Retin Eye Res. 1999;18:91-119.
12. Tian B, Gabelt B, Geiger B, Kaufman P. The role of the actomyosin system in regulating trabecular fluid outflow. Exp Eye Res. 2009;88:713-7.
13. Keller K, Acott T. The juxtacanalicular region of ocular trabecular meshwork: A tissue with a unique extracellular matrix and specialized function. J Ocul Biol. 2013 June;1(1):3.
14. Wang S, Chang R. An emerging treatment option for glaucoma: rho kinase inhibitors. Clin Ophthalmol. 2014:8;883–90.
15. Pattabiraman P, Maddala R, Rao P. Regulation of plasticity and fibrogenic activity of trabecular meshwork cells by rho GTPase signaling. J Cell Physiol. 2014 July;229(7):927-42.
16. Pattabiraman P, Rao P. Mechanistic basis of rho GTPase-induced extracellular matrix synthesis in trabecular meshwork cells. Am J Physiol Cell Physiol. 2010;298:C749-763.
17. Kaufman P. Enhancing trabecular outflow by disrupting the actin cytoskeleton, increasing uveoscleral outflow with prostaglandins and understanding the pathophysiology of presbyopia: Interrogating Mother Nature: asking why, asking how, recognizing the signs, following the trail. Eye Exp Res. 2008;86(1):3-17.
18. Keller K, Aga M, Bradley J, et al. Extracellular matrix turnover and outflow resistance. Exp Eye Res. 2009;88(4):676-82.
19. Tektas O, Lutjen-Drecoll E. Structural changes of the trabecular meshwork in different kinds of glaucoma. Exp Eye Res. 2009;88(4):769-75.
20. Overby D, Zhou E, Vargas-Pinto R, et al. Altered mechanobiology of Schlemm's canal endothelial cells in glaucoma. Proc Natl Acad Sci USA. 2014;111(38):13876-81.
21. Li T, Lindsley K, Rouse B, et al. Comparitive effectiveness of first-line medications for primary open-angle glaucoma: A systematic review and network meta-analysis. Ophthalmology. 2016 Jan;123(1):129-40.
22. Parrish R, Palmberg P, Sheu W, XLT Study Group. A comparison of latanoprost, bimatoprost, and travoprost in patients with elevated intraocular pressure: a 12-week, randomized, masked-evaluator multicenter study. Am J Ophthalmol. 2003;135(5):688-703.
23. Alm A, Villumsen J. PhXA34, a new potent ocular hypotensive drug. A study on dose-response relationship and on aqueous humor dynamics in healthy volunteers. Arch Ophthlmol. 1991;109(11):1564-8.
24. Toris C, Camras C, Yablonski M. Effects of PhXA41, a new prostaglandin F2, analog on aqueous humour dynamics on human eyes. Ophthalmology. 1993;100:1297-304.
25. Toris C, Gabelt B, Kaufman P. Update on the mechanism of action of topical prostaglandins for intraocular pressure reduction. Surv Ophthalmol. 2008;53(S1):S107-120.
26. Fung D, Whitson J. An evidence-based review of unoprostene isopropyl ophthalmic solution 0.15% for glaucoma: place in therapy. Clin Ophthalmol. 2014;8:543-54.
27. Lee D, Higginbotham E. Glaucoma and its treatment: a review. Am J Health-Syst Pharm. 2005;62:691-9.
28. Tanihara H, Inatani M, Honjo M, et al. Intraocular pressure-lowering effects and safety of topical administration of a selective rock inhibitor, SNJ-1656, in healthy volunteers. Arch Ophthalmol. 2008;126(3):309-15.
29. Kopczynski C, Epstein D. Emerging trabecular outflow drugs. J Ocul Pharmacol Ther. 2014;30(2-3):85-7.
30. Honjo M, Tanihara H, Inatani M, et al. Effects of Rho-associated protein kinase inhibitor Y-27632 on intraocular pressure and outflow facility. Invest Ophthalmol Vis Sci. 2001;42:137-44.
31. Honjo M, Inatani M, Kido N, et al. Effects of protein kinase inhibitor, HA1077, on intraocular pressure and outflow facility in rabbit eyes. Arch Ophthalmol. 2001;119:1171-8.
32. Okumura N, Ueno M, Koizumi N, et al. Enhancement on primate corneal endothelial cell survival in vitro by a ROCK inhibitor. Invest Ophthalmol Vis Sci. 2009;50:3680-7.
33. Ishizaki T, Naito M, Fujisawa K,et al. p160ROCK, a Rho-associated coiled-coil forming protein kinase, works downstream of Rho and induces focal adhesions. FEBS letter. 1997;404:118-24.
34. Leung T, Chen X, Manser E, Lim L. The p160 RhoA-binding kinase ROK alpha is a member of a kinase family and is involved in the reorganization of the cytoskeleton. Mol Cell Biol. 1996;16:5313-27.
35. Amano M, Chihara K, Kimura K, et al. Formation of actin stress fibers and focal adhesion enhanced by rho-kinase Science. 1997;275(5304):1308-11.
36. Zhang M, Maddala R, Rao P. Novel molecular insights into RhoA GTPase-induced resistance to aqueous humor outflow through the trabecular meshwork. Am J Physiol Cell Physiol. 2008;295(5):C1057-70.
37. Malihi M, Moura Filho E, Hodge D, Sit A. Long-term trends in glaucoma-related blindness in Olmsted County, Minnesota. Ophthalmology. 2014;21(1):134-41.
38. Alm A, Camras C, Watson P. Phase III latanoprost studies in Scandinavia, the United Kingdom and the United States. Surv Ophthalmol. 1997;41 Suppl 2:S105-10.
39. Brubaker R. Introduction: Three Targets for Glaucoma Management. Surv Ophthalmol. 2003;48 Suppl 1:S1-2.
40. Tham YC, Li X, Wong TY, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: A systematic review and meta-analysis. Ophthalmology. 2014;121:2081-90.
41. Kameda T, Inoue T, Inatani M, et al. The effect of rho associated protein kinase inhibitor on monkey Schlemm's canal endothelial cell Invest. Ophthalmol Vis Sci. 2012 53(6):3092-103.
42. Yamamoto K, Maruyama K, Himori N, et al. The novel Rho Kinase (ROCK) inhibitor K-115: A new candidate drug for neuroprotective treatment in glaucoma. Invest Ophthalmol Vis Sci. 2014:55(11):7126-36.
43. Williams R, Novack G, van Haarlem T, et al. Ocular hypotensive effect of the rho kinase inhibitor AR-12286 in patients with glaucoma and ocular hypertension. Am J Ophthalmol. 2011;152(5):834-4.
44. Inoue T, Tanihara H. Rho-associated kinase inhibitors: A novel glaucoma therapy. Prog Retin Eye Res. 2013;37:1-12.
45. Tanihara H, Inoue T, Yamamoto T, et al. Additive intraocular pressure-lowering effects of the rho kinase inhibitor ripasudil (K-115) combined with timolol or latanoprost A report of two randomized clinical trials. JAMA Ophthalmol. 2015;133(7):755-61.
46. Tanihara H, Inoue T, Yamamoto T, et al. Phase 1 clinical trials of a selective rho kinase inhibitor, K-115. JAMA Ophthalmol. 2013;131(10):1288-95.
47. Garnock-Jones K. Ripasudil: First global approval. Drugs. 2014;74:2211-5.
48. Inoue T, Tanihara T, Tokushige H, Arale M. Efficacy and safety of SNJ-1656 in primary open-angle glaucoma or ocular hypertension. Acta Ophthalmol. 2015;93(5):e393-5.
49. Okumura N, Okazaki Y, Inoue R, et al. Rho-associated kinase inhibitor drop (ripasudil) transiently alters the morphology of corneal endothelial cells. Invest Ophthalmol Vis Sci. 2015;56(12) 7560-7.
50. Kiel J, Kopczynski C. Effect of AR-13324 on episcleral venous pressure in dutch belted rabbits. J Ocul Pharmacol Ther. 2015;31(3):146-51.
51. Bacharach J, Dubiner H, Levy B, et al. Double-masked, randomized, dose-response study of AR-13324 versus latanoprost in patients with elevated intraocular pressure. Ophthalmology. 2015;122:302-7.
52. Wang R, Williamson J, Kopcyznski C, Serle J. Effect of 0.04% AR-13324, a ROCK and norepinephrine transporter inhibitor, on aqueous humor dynamics in normotensive monkey eyes. J Glaucoma. 2015;24:51–4.

A Peroxide Solution for Gas Permeable Contact Lens Wearers

Bausch + Lomb PeroxiClear® Solution provides a 4-hour disinfection time and comfortable vision for GP lens wearers

By
Stephanie Woo, O.D.
Havasu Eye Center
Lake Havasu City, AZ

Gas permeable (GP) lenses seem to be making a resurgence. This is true for my practice, which sees a large number of specialty contact lens patients. I always talk to my patients about the importance of regular lens care, but with my GP patients, I almost always recommend using a hydrogen peroxide-based solution. For many GP lens-wearers, Bausch + Lomb PeroxiClear® Solution is my peroxide-based cleaning and care solution of choice. My patients seem to do extremely well with PeroxiClear®. I feel comfortable knowing the lenses undergo exceptional disinfection, which is important for GP lenses which some of my patients wear for years..

Many of my patients who use PeroxiClear® Solution say their lenses feel brand new immediately upon insertion and stay moist and clean throughout the day. PeroxiClear® Solution utilizes Triple-Moist Technology®, a unique combination of ingredients that attracts moisture and spreads it across the lens surface, delivering up to 20 hours of moisture.[1] PeroxiClear® Solution is also preservative-free, making it an option for lens wearers with allergies or sensitivities to other GP cleaning solutions.

Bausch + Lomb PeroxiClear® Solution is specially designed for a faster overall disinfection rate compared to other peroxide solutions.[2] I've switched a lot of my patients to PeroxiClear® from Clear Care due to their busy lifestyles and the need for a shorter disinfection time. One of my patients is a 20-year-old college student—a high myopia GP lens-wearer who was using Clear Care solution to clean his lenses. His full class schedule limits him to just five hours of sleep at night. During our first visit, he said it was important that his lenses be ready to wear the minute he woke up. However, each morning he was delayed because his peroxide cleaning solution took six hours to disinfect the lenses. I recommended he try PeroxiClear® Solution, which has a four-hour disinfection cycle that would allow him to wear his lenses sooner.[2] When I saw him again recently, he agreed that the shorter disinfection time was a huge benefit. The same can be said for other patients of mine, who may work shift schedules or have equally busy lifestyles.

There is another practical consideration in choosing Bausch + Lomb PeroxiClear® Solution for GP lens users. Many of my GP patients have severely limited vision, and can only see well when they're wearing their lenses. A 50-year-old keratoconic patient wearing mini-scleral lenses told me she often mixed up the lens for the left eye and the right eye when she tried inserting her lenses in the morning. The problem was that she couldn't distinguish the letter "L" (signifying the left lens) on the lens case that came with her peroxide-based cleaning solution. I suggested she switch to PeroxiClear® Solution, which comes with a specially designed case that makes it easy to recognize the left or right contact lens. The baskets are marked "L" and "R" but are also colored teal and white. She tried PeroxiClear® Solution and happily reported that her contact lens mix-ups were a thing of the past.

I educate my patients about proper contact lens wear, from the initial lens fitting to follow-up appointments to annual exams. For my GP patients, I take particular care in going over the PeroxiClear® regimen for GP lenses, including the need to gently rub the lenses prior to soaking them in the case. Optimal lens performance depends on the synergy of several key factors; among them is maintaining a clean lens surface throughout the life of the contact lens. That's why Bausch + Lomb PeroxiClear® Solution is my go-to hydrogen peroxide solution. With all-day moisture and a shorter disinfection time, PeroxiClear® Solution lends itself to healthy, comfortable GP lens-wearing that fits into patients' busy lifestyles. ■

The lens case for PeroxiClear® Solution features many unique benefits including color-coded baskets that make it easy to differentiate between the right and left lenses.

References: 1. Hoteling A, Nichols W, Schafer J, Orsborn G. Retention of hydrogen peroxide solutions' surfactants on silicone hydrogel lenses. Poster session presented at: American Academy of Optometry (AAO) 92nd Annual Meeting; 2013 Oct 23-26; Seattle, WA. **2.** Results of in vitro study following FDA/ISO stand-alone procedure for disinfecting products. Test solutions were modified with organic soil to create a more rigorous test condition. Primary criteria for effective disinfection are defined as a reduction in the number of bacteria by a minimum of 3logs (99.9%) and a reduction of mold and yeast by a minimum of 1 log (90%) within the recommended disinfection time.

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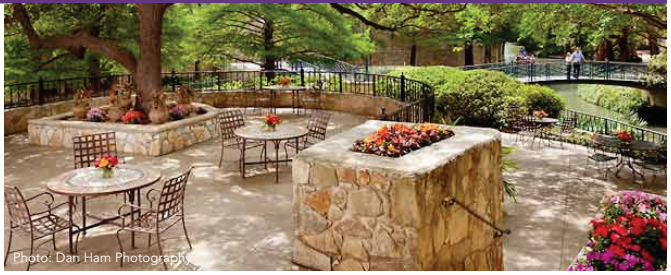

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ADVANCEMENTS IN LASIK

By Paul Karpecki, OD, FAAO, and Derek Cunningham, OD, FAAO

Release Date: February 15, 2016
Expiration Date: February 28, 2017
Goal Statement: After completing this educational activity, participants should be able to select patients for LASIK, confidently comanage LASIK patients and describe the stages of pre- and postoperative care.
Faculty/Editorial Board: Paul M. Karpecki, OD, FAAO, and Derek Cunningham, OD, FAAO
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Disclosure Statement: Dr. Cunningham is a consultant for Abbott Medical Optics, Alcon, Allergan, ArticDx, Bausch + Lomb, Bio-Tissue and TearLab; he received grant/research support from Alcon, Marco, Optovue and Lumenis. **Dr. Karpecki** is a consultant for AcuFocus, Alcon, Abbott Medical Optics, Akorn, Allergan, ArcticDx, Bausch + Lomb, Beaver-Visitec, Bio-Tissue, Bruder Healthcare, Cambium Pharmaceuticals, Eleven Biotherapeutics, Eyemaginations, Eyes4Lives, Fera Pharmaceuticals, Focus Labs, Freedom Meditech, Glaukos, J&J, iCare USA, Konan Medical, Regeneron, Essilor, Eye Solutions, Oculus, OcuSoft, Optometric Medical Solutions, Reichert, Shire Pharmaceuticals, ScienceBased Health, Sightrisk, TearLab, TearScience, TLC Vision, Topcon and Vmax Vision.

THE PAST 10 YEARS have been truly epic in terms of advances in eye care. Innovations in retina, cataract and glaucoma have redefined our profession in this decade—just as LASIK did back in 1999 when the FDA approved its use in the United States, a time when refractive surgery easily stole center stage.

Though other ophthalmic procedures have since earned their own time on eye care's great stage, LASIK surgery still deserves the spotlight, since it has never stopped improving. In fact, LASIK surgery has become so safe, effective and precise that some may have stopped noticing, much less remarking, on the cumulative effect of these technological achievements.

The following continuing education program celebrates LASIK's many advances, detailing the impact they have on our patients in terms of outcomes, safety and satisfaction. It also describes how this era of invention affects optometrists as we rethink our approach to patient selection, education and pre- and postoperative care.

A CLOSER LOOK AT MYOPIA

Year after year, the incidence of myopia continues to rise, impacting optometric practices across the United States (*Figure 1*).

Myopia prevalence is highest among Caucasians and lowest among African Americans, according to the National Eye Institute (*Figure 2*).[1] More than 40% of Caucasians ages 40 to 49 are myopic. Despite these large numbers, myopia is not increasing in the Caucasian population as it is in other races.

While Caucasians have the greatest incidence of myopia, their numbers remain relatively flat for the next 40 years. This is not the case in other races. Most notably, myopia nearly doubles in the next 15 to 25 years among Hispanic Americans and is also growing significantly in African Americans (*Figure 3*).

All of this, of course, comes at a substantial cost. As of 1990, the financial cost of myopia in the United States was estimated at $4.8 billion.[2] When you factor in the increasing prevalence and inflation, the burden is staggering.

By 2030, it is estimated that nearly 40 million people in the United States will have myopia.[1] Whether these patients select contact lenses, eyeglasses or surgery, how we choose to manage them will undoubtedly impact our practices.

HISTORICAL PERSPECTIVES ON CORNEAL REFRACTIVE SURGERY

Refractive surgery reshapes the corneal curvature by removing tissue to alter how light refracts and focuses on the retina. To achieve this, the surgeon has to get the epithelium out of the way so that the stroma can be accessed. The epithelium can't be treated because it's regenerative and dynamic in nature.

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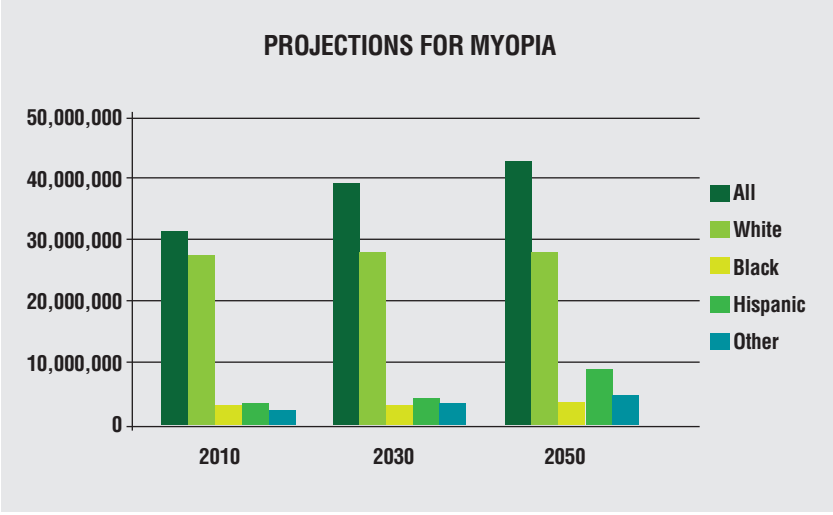

Fig. 1: Although Caucasians have the greatest incidence of myopia, the projected numbers remain relatively flat for the next 40 years. However, the increase in myopia is on the rise in other races. Most notably, myopia nearly doubles in the next 15 to 25 years among Hispanics.[1]

The stroma, on the other hand, is far less capable of regeneration and is not likely to change over time.

Once the surgeon exposes the stroma by creating a hinged flap that can be peeled back, the goal of the refractive procedure is to essentially sculpt it down in much the same way you would grind a prescription onto a spectacle lens.

Not long ago, microkeratomes were the mainstay for flap creation in LASIK refractive surgery, despite challenges with variable bed depths due to the manual nature of the procedure. Many of the complications we saw in practice were directly related to microkeratome use. The shearing effect of a microkeratome can lessen flap stability, resulting in complications such as partial flaps, buttonholes and diffuse lamellar keratitis (DLK). But the main issue with a microkeratome was the highly variable flap thickness, which made the stromal bed depth less predictable and sometimes risked making the cornea too thin.

To minimize complications, three key measurements had to be carefully considered in any patient who wanted LASIK—pupil size, keratometry and pachymetry. Since the early excimer lasers had optical zones of 5mm or less, the size of the pupil was a major factor. Patients with pupils greater than 5mm at that time (circa 1997-2000) would sometimes describe issues related to halos at night. The same could be said for some of the early microkeratomes where, on occasion, a flap that was smaller than 6mm would occur.

Although you should still alert patients with extremely large pupils about possible early postoperative aberrations, use of today's femtosecond lasers for flap creation has made pupil size almost irrelevant.

In addition, there are definite visual benefits to laser-created flaps. Studies have shown that using wavefront-guided LASIK to correct myopia combined with a femtosecond laser flap significantly improves mean night driving visual performance and is a major improvement over traditional non-custom LASIK using a mechanical keratome.[3]

SURGICAL CANDIDACY

The first step in preoperative LASIK care is determining candidacy. Several factors are relevant, including age, corneal thickness and astigmatism.

Myopes and hyperopes with and without astigmatism can be ideal surgical candidates, as are patients who have had issues with their contact lenses. In particular, lens wearers who have struggled with lens intolerance, dry eye, GPC, allergies, meibomian gland dysfunction, CLARE, ulcers or red eyes can often benefit from LASIK. Furthermore, noncompliant contact lens wearers can make excellent LASIK candidates (see "*Contact Lens vs. LASIK Safety Studies*").

Since refractive stability can vary, no set minimum age can be applied to every LASIK case. Generally speaking, low myopes (<4.00D) typically achieve refractive stability by the age of 18 and, as such, can be considered for surgery at that time. However, high myopes may not stabilize until they are 21 or older.

In new patients who are near these age thresholds, consider a second evaluation after six months. At that time, you should not see more than a 0.50D shift in spherical equivalent (not diopter sphere), a 0.25D shift in astigmatism or more than a 10-degree shift in axis.

Like age, corneal thickness is not

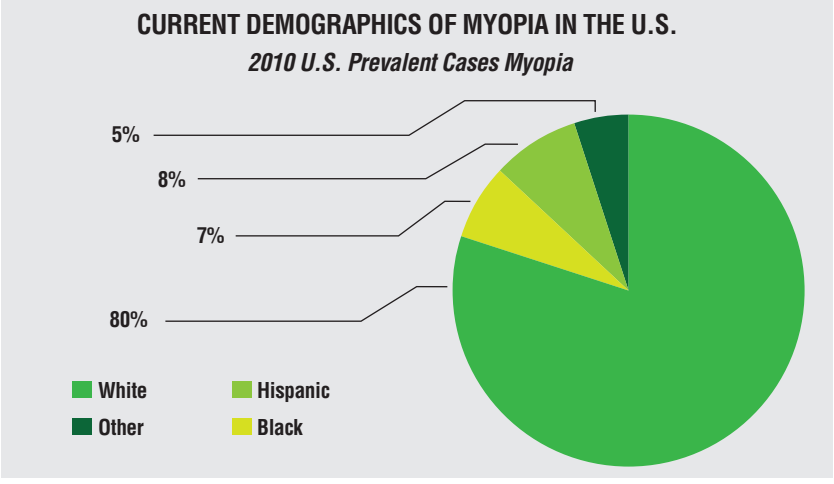

Fig. 2: In the United States, 80% of all myopia cases occur in the Caucasian race.[1]

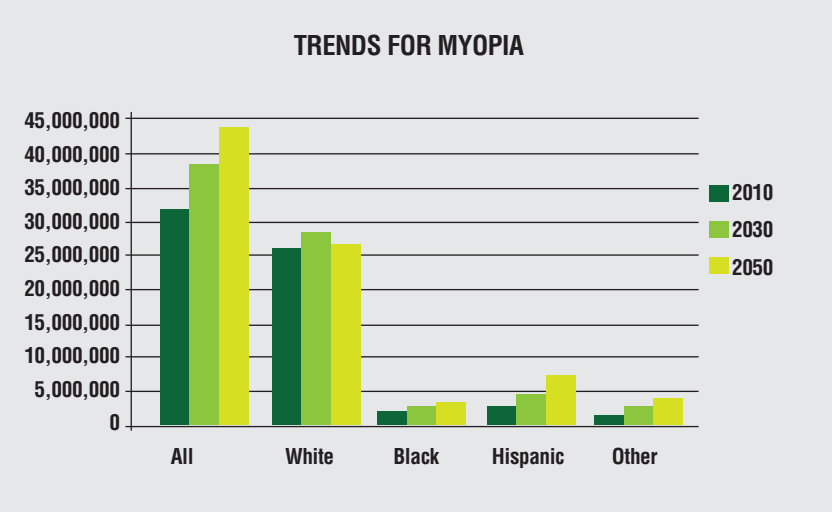

Fig. 3: Overall trends show an increase in myopia across the entire U.S. population. Furthermore, long-term trends show a much greater growth of myopia prevalence in Hispanic and black races compared to Caucasians.[1]

defined by a single, isolated number. Since a patient's refractive error dictates the amount of stroma that will need to be removed, thin corneas alone are not a significant risk factor for refractive surgery. Most surgeons will want at least a 300µm residual stromal bed. However, this will vary from case to case.

LASIK is generally safe in patients with corneas of normal thickness (i.e., anything above 500µm). Anything below 500µm requires greater scrutiny. Patients who are on the border should still be sent to the surgery center because newer measuring technology has shown us that we can safely perform LASIK on many more patients than we thought we could five years ago.

Newer technology has expanded the number of astigmatic patients who can be considered LASIK candidates. The first factor is whether the astigmatism is normal or abnormal, since you need an axis to include in the surgical nomogram. Beyond that, there is the question of symmetry. Not long ago, asymmetry automatically contraindicated LASIK. To some degree this is still the case, since only certain presentations can be treated and the options are fewer; wavefront is a must in these patients. But don't categorically rule out LASIK altogether in patients with asymmetry. Instead, consider reviewing candidacy with your surgeon if there is more than a diopter of asymmetry on vertical keratometry readings or in mean keratometry between the eyes.

The steepness of the cornea is another consideration. Excessively steep corneas should be reviewed for ocular disease. There is no limit to how much a cornea can be flattened, but below 35D (or above 48D for hyperopic ablation) necessitates a conversation with the surgeon.

The LASIK opportunity has also changed for patients with large pupils. With custom wavefront ablations and optical blend zones, pupil size has become an insignificant factor for assessing LASIK candidacy.

Service in the U.S. military is another factor that determines surgical candidacy. The Air Force and Army allow LASIK-treated eyes, and NASA has approved iLASIK (i.e., procedure using the AMO IntraLase FS Laser System) for astronauts. However, service in the Navy and all special forces require surface ablation as opposed to LASIK. Anyone who has an undecided career path prior to entering any service branch should have surface ablation. It's also important to note that any active-duty soldier must check with their command as to the type and timing of surgery.

Ocular disease contraindications include significant cataracts, keratoconus or pellucid marginal degeneration, non-responsive KCS and advanced neurotrophic keratitis.

Of course, other ocular diseases provide reasons to pause and address prior to LASIK. For example, relative ocular disease contraindications include:

- Monocular patients (may indicate amblyopia)
- Dry eye/KCS (treat first)
- Blepharitis (treat first)
- Corneal dystrophies and RCE (consider surface ablation)
- Previous HSV keratitis (prophylactic treatment and dormancy for one year is required)
- Glaucoma (gauge functional loss)
- Retinal disease (gauge functional loss)

No matter how an individual presents clinically, our job as optometrists is to

CONTACT LENS vs. LASIK SAFETY STUDIES[4]

Study	Pts	Comparison	Metric	Outcome
Goldstone, JRS, 2010	22	CRT vs. LASIK	HOA	• Similar induction HOA • CRT greater increase SA
Anera, JRS, 2009	24	CRT vs. LASIK	HOA and CSF	• Greater induction HOA with CRT • Decrease mesopic CSF with CRT
McGee, JCRS, 2009	Review	CL vs. LASIK	Lifetime probability of vision loss	• LASIK as safer or safer than DW SCL • LASIK clearly safer than EW SCL
Chen, JRS, 2007	195	Emmetropes CL/Specs LVC	Quality of life	• Lower with CLs/Specs than emmetropes and LVC • LVC similar to emmetropes
Mathers, Arch Ophth, 2006	Review	CL vs. LASIK	Lifetime probability of vision loss	• LASIK is safer than either EW or DW SCL

let patients know their vision correction options. Furthermore, because patient needs and desires change and technology options continually expand, this conversation should be repeated at every annual exam.

Whenever it seems clinically appropriate, you can begin the conversation by saying something such as, "Your eyes look great. We can correct your vision with glasses, contacts or laser vision solutions. Let's talk about which options are best for you." This ensures that patients view you as a resource for more than just glasses and contacts.

PREPARING PATIENTS FOR LASIK

Stable corneal topography and a low threshold for ocular surface disease are essential prior to LASIK. The need to optimize the ocular surface cannot be overemphasized.

To achieve accurate corneal measurements, discontinue contact lens wear for one week in soft spherical contact lens patients, two weeks for toric soft contact lens wearers and one month for rigid gas permeable (GP) wearers (add an extra month for every decade the patient has worn GPs). Do not consider correction until consecutive corneal measurements show topographic stability.

As you begin to treat ocular surface disease, you may discover that mild amounts of inferior corneal steepening (1D to 2D) may not be keratoconus and could be the result of dry eye. When you aggressively treat dryness with artificial tears, omega-3 supplements, plugs and steroids, the topography can normalize in a matter of weeks.

PATIENT PRECAUTIONS POST-LASIK

- **No eye rubbing for at least a week. All patients should sleep with protective shields. The most common serious complication is a dislodged flap from eye rubbing.**
- **No swimming of any kind (hot tubs, pool, lakes, rivers, etc.) for at least one week.**
- **No excessive exercising for at least one week (especially routines with the head below the heart or those involving the valsalva maneuver).**
- **No eye makeup for one week.**

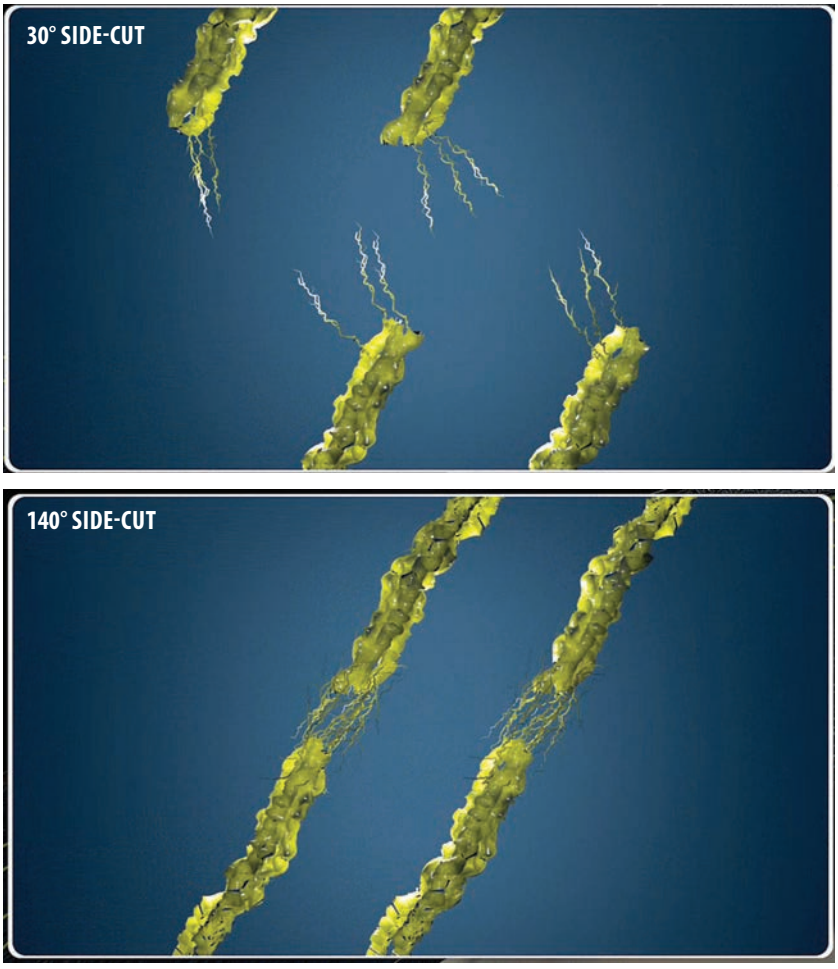

Photo: Abbott Medical Optics

Fig. 4: Microkeratomes used to shear the cornea and pull at the corneal nerves such that, when you put them back down, they didn't heal together quickly. As these images show, the inverted bevel-in side cut up to 150° can have a significant impact on healing and subsequently on postop dry eye.

Giant papillary conjunctivitis (GPC), despite the advent of frequent lens replacement, remains a nuisance for some contact lens wearers and needs to be resolved prior to LASIK. Topical steroids are typically indicated for significant GPC. If the cornea is not excessively altered and the patient can be refracted to 20/20, surgical correction can be considered.

Other common ocular surface findings include general dryness, blepharitis and allergy. Dry eye patients can be effectively treated with artificial tears, nutritional support, punctal plugs, short-term steroids and long-term Restasis.

Blepharitis patients need antibiotic/steroid combinations in the short term, gland maintenance long term and consistent oral omega-3 fatty acids.

For patients with ocular allergies use steroids in the short term preoperatively to shut down the inflammation cascade, and add antihistamines for the long term.

REFERRING PATIENTS

It may seem obvious, but two of the most important things you can do when comanaging LASIK is to let the patient know they're a candidate and let the surgeon know you've made the referral. These communications can play a significant role in your continuing relationships and will help ensure that the patient stays in your practice going forward.

When you make the referral, let the patient know that the surgery center has the advanced imaging necessary to confirm candidacy. Also, reassure

patients that the multi-doctor approach ensures the best possible outcomes and reduces error risk.

If you're not using a referral form provided by the surgery center, make sure your EMR notes include the following:

- Manifest refraction or spectacle prescription
- K readings
- Relevant history
- Cycloplegic refraction
- Results of dilated exam

Always establish a documented relationship before comanaging any patient with a surgeon.

Postoperative communication is essential. Report any postoperative course concerns to the surgery center and request that all patient education materials be shared with you so your patient receives a consistent message.

THE FEMTOSECOND LASER EXPERIENCE

A femtosecond laser emits an infrared beam at a wavelength of 1,053nm. It works by producing photodisruption or photoionization of optically transparent tissue, such as the cornea.

Simply put, femtosecond lasers are like extremely precise scalpels that separate tissue with outstanding consistency and control. They can be focused at any tissue depth that is transparent, and will repeatedly produce the desired effect.

There are several benefits to using a femtosecond laser, including:

- Fewer flap complications
- The ability to vary the size and depth of incisions
- Greater precision
- No moving parts
- Stronger flaps[5]
- Increased contrast sensitivity[6]
- Decreased risk of epithelial ingrowth
- Less IOP rise during procedures[7]
- Less postoperative dry eye[8]

But what's more exciting is how femtosecond lasers work in tandem with advanced technology surgical platforms to create a truly custom experience. We'll use the AMO iLASIK platform as an example, since we can discuss the scope of its capabilities based on our centers' experiences (see "*LASIK: From Start to Finish*"). Other implementations are available in the marketplace as well.

One of the most spectacular features of the laser is its ability to control what the edge of the flap will look like. With advanced customization capabilities such as inverted bevel-in side cut up to 150°, the laser prevents flap slippage and allows for easier flap repositioning. What that means to the optometrist is you'll see increased flap adhesion postoperatively, which translates into optimal wound healing and three times more flap stability compared to a microkeratome-created flap.[9]

The inverted bevel-in side cut up to 150° also improves severed nerve apposition and results in less reduction in corneal sensitivity as well as fewer dry eye symptoms (*Figure 4*)[10] After using this technology, our centers' five-minute postsurgical exams look like our one-day post-ops did before we had this technology. That's how smooth and how well-sealed the results are. It is an absolutely remarkable leap.

This platform also allows surgeons to customize an elliptical flap to avoid some of the long ciliary nerves. By avoiding those nerves, you potentially decrease dry eye issues in at-risk patients.

Other benefits worth mentioning are increased speed, which ensures better accuracy, smoother beds for ablation and a better patient experience.

ADVANCES IN EXCIMER LASERS

The importance of the excimer laser can't be understated; this is truly the workhorse of refractive surgery. Some of the latest advancements in these lasers are positively impacting patient success since, after all, it's the excimer

LASIK: FROM START TO FINISH

As comanaging optometrists, it's extremely helpful to spend a day at the surgery center and walk through all parts of the procedure as they're performed by the surgeon. This will help you make more meaningful connections with your patients and help you better understand the expectations of the surgery center.

In our practices, we frequently use the iLASIK Technology Suite, which is a combination of IntraLase and Advanced CustomVue technologies. Here's how the procedure unfolds:

—1—

An iLASIK procedure begins with a wavefront analysis of the patient's eyes. The WaveScan Wavefront system shines a light into the patient's eye. This light is then reflected back from the retina to the WaveScan system where it is captured and analyzed using Hartmann-Shack technology and Fourier analysis. The result of this analysis is a customized, wavefront-guided treatment based on the total ocular aberrations identified in the patient's eye.

—2—

The second step is the creation of the corneal flap with the IntraLase FS or iFS femtosecond laser. The physician can customize flap parameters—such as depth, diameter, flap shape and edge angle—to meet the unique needs of the patient's eyes. The laser fires thousands of focused laser pulses at a precise depth in an organized, efficient raster pattern to create a resection plane. Pulses are also stacked vertically, or at an angle up to 150°, to create the flap edge. After the flap is cut, the physician manually lifts the flap to expose a smooth lamellar bed for treatment. Flaps are created in less than 18 seconds with minimal energy, resulting in reduced tissue inflammation, reduced total procedure time and improved wound healing.

—3—

In the third step, the patient's wavefront-guided treatment profile is aligned under the excimer laser using iris registration to ensure proper eye tracking. Often, pupils constrict asymmetrically while under the laser, resulting in a pupil centroid shift. Further, the eye can cyclorotate (rotation around the z-axis) when the patient moves from a sitting position to a supine position. Both pupil centroid shift and cyclorotation can result in treatment misalignment and suboptimal results. Engaging iris registration before treatment can overcome these phenomena. The Star S4 IR excimer laser uses variable spot scanning to remove corneal tissue to correct lower- and higher-order aberrations.

—4—

With laser ablation complete, the LASIK flap is replaced on the cornea, completing the procedure.

For a narrated video of this procedure go to: http://www.reviewofoptometry.com/content/c/59107/

laser that determines the prescription. Since most patients have some level of positive spherical aberration, wavefront diagnostic and therapeutic modalities are considered superior to first-generation lasers that did not account for these aberrations.

Wavefront-optimized lasers, as in conventional procedures, use solely the patient's refraction/eyeglass prescription to program the laser. For instance: All -3.00D patients receive the same ablation pattern, regardless of corneal shape, higher-order aberrations, pupil size or location. Higher-order aberrations are not measured or corrected, and all ablation profiles are the same, whether the patient has positive or negative spherical aberrations. These systems take into account the fact that most corneas have positive spherical aberration, and place more pulses in the peripheral area to compensate for energy loss and reflections.

In wavefront-guided laser ablation, information from a wavefront-sensing aberrometer that quantifies aberrations is electronically conveyed to the treatment laser to program the ablation—a departure from conventional excimer laser and wavefront-optimized laser treatments relying on the refraction to program the laser. In this case, higher-order aberrations are measured and incorporated into the treatment plan, and no two treatments will ever be the same.

Both wavefront-guided and wavefront-optimized laser treatments have been found to correct myopia, hyperopia and astigmatism, with more than 90% of eyes achieving 20/40 or better uncorrected visual acuity.[11] However, recent studies have shown wavefront-guided technology to be superior for night vision performance, low-contrast acuity, residual refractive error, uncorrected distance acuity and contrast sensitivity.[12,13] Also, for patients who have neutral or negative spherical aberrations, wavefront-optimized laser treatment can be less optimal since the extra peripheral pulses induce additional negative spherical aberrations.

POSTOPERATIVE CARE

Typically, postop LASIK exams should be scheduled for Day 1, 1 Week, 1 Month and 3 Months (See "*LASIK Postop Schedule*"). The Day 1 exam is most telling clinically. The priority at this visit is proper flap position. Look for macrostriae and inspect the flap edge and gutter flap interface for debris or inflammation, which have a grainy appearance. Potential findings at this visit might include:

- Subconjunctival hemorrhage
- Superficial punctate keratitis (SPK)
- Epithelial abrasion
- Interface debris
- Infection
- Striae

In the event that laser docking results in a subconjunctival hemorrhage, reassure the patient that this routine occurrence does not affect vision and will heal in a time frame consistent with normal bruising.

Patients presenting with interface debris often have meibomian gland secretions. These are rarely visually significant and typically resolve on their own.

DLK is possible any time the body's immune system is set into action. With LASIK, the body responds with interface inflammation, which should start to resolve in 24 to 48 hours. DLK has a grainy appearance, similar to sand, and is non-refractile and opaque. If you see this, you should alert the surgeon or your center director and begin topical steroids immediately. DLK is like a firework—it explodes quickly and then usually fizzles out. The key is to treat it rapidly and aggressively with hourly steroid administration and re-evaluation daily. If visual acuity drops a line or more, the patient should return to the surgeon right away.

DLK is rare with today's technology, but it can require high dosing of topical corticosteroids, as well as the use of oral prednisone. In addition, the surgeon may need to lift the flap and irrigate.

Corneal abrasions are uncommon, but treat them as you would treat any abrasion. Maintain topical antibiotics, monitor daily and be on the alert for epithelial ingrowth. If the abrasion is significant, you can use a bandage contact lens for one day. Because inflammation slightly increases the risk of DLK underneath, increase topical steroid dose.

Visually significant wrinkled flaps are rare and almost always the result of a protective or Fox shield coming off during sleep and the patient inadvertently rubbing their eye. No matter how mild, always alert the surgeon of wrinkles. Microstriae will usually settle out, but the longer you wait, the harder it is for the surgeon to re-lift the flap. If you're looking closely and see microstriae, let the patient's vision be your guide.

Macrostriae, on the other hand, are big folds, and you will almost always see a gutter effect in the periphery. Don't look for staining in the gutter with macrostriae beyond Day 1 postop; the epithelium begins to heal over after 24 hours so staining is not likely. Instead, you'll see an opaque area.

Other elements of the Day 1 exam are patient education and a vision check. It's important to reinforce medication schedules and review eye protection. But, of course, what patients are most eager to discuss on Day 1 is their vision. How you approach these conversations

LASIK POSTOP SCHEDULE

For uncomplicated LASIK procedures, standard postop care should include the following:

- **Day 1** – Ensure proper flap position. Look for macrostriae and flap edge gutter. Inspect the flap interface for debris or inflammation, which will have a grainy appearance. Review eye protection precautions.
- **1 Week** – Ensure proper flap position. Counsel the patient on temporary dry eye symptoms and methods for resolving evening glare, if present.
- **1 Month** – Assess dry eye and any visual symptoms.
- **3 Months** – Assess dry eye and any residual refractive error.

Typically, postop exams can cease after three months, with regular annual or biannual exams occurring thereafter.

will play a significant role in how they perceive the success of their surgery.

At the Day 1 vision check, be careful about what line you leave on the bottom of your chart. If the patient sees your 20/15 line but can't read it, they'll likely feel discouraged. Always have patients start with the big "E" and eyes open. Let the patient know their vision results from the day before for immediate encouragement. Then, let the patient read to the lowest line possible, and blink as needed. As they approach 20/30 or 20/40, compliment them and celebrate.

Though it helps to start with real-word vision, it's equally important to test each eye individually on Day 1, while reassuring the patient that vision will continue to improve.

Next, set the stage for what the patient might expect in the coming weeks. Tell them they will likely see some halos and glare around light, and they may notice some fluctuations in vision. Explain that this is normal and will improve over the course of a month.

Also mention that dryness, particularly in the morning, is normal post-refractive surgery and will improve with time. Daytime dryness is much less common, but continue to assess it at follow-ups. ■

1. Myopia. National Eye Institute. Available at: https://nei.nih.gov/eyedata/myopia (last accessed December 17, 2015).
2. Javitt JC, Chiang YP. The socioeconomic aspects of laser refractive surgery. Arch Ophthalmol. 1994 Dec;112(12):1526-30.
3. Schallhorn SC, Tanzer DJ, Kaupp SE, et al. Comparison of night driving performance after wavefront-guided and conventional LASIK for moderate myopia. Ophthalmology. 2009;116:702-9.
4. Contact Lens vs Spectacles vs LASIK: Summary of Literature. [PowerPoint slides]. Optical Express. Available at: http://www.slideshare.net/beachybidas/contacts-vs-glasses-vs?qid=c36e82ba-92d7-4c81-9918-46661446922c&v=default&b=&from_search=1 (last accessed December 17, 2015).
5. Kim JY, Kim MJ, Kim TI, et al. A femtosecond laser creates a stronger flap than a mechanical microkeratome. Invest Ophthalmol Vis Sci. 2006 Feb;47(2):599-604.
6. Montés-Micó R, Rodríguez-Galietero A, Alió JL. Femtosecond laser versus mechanical keratome LASIK for myopia. Ophthalmology. 2007 Jan;114(1):62-8.
7. Vetter JM, Faust M, Gericke A, Pfeiffer N, et al. Intraocular pressure measurements during flap preparation using 2 femtosecond lasers and 1 microkeratome in human donor eyes. J Cataract Refract Surg. 2012 Nov;38(11):2011-8.
8. Salomão MQ, Ambrósio R Jr, Wilson SE. Dry eye associated with laser in situ keratomileusis: Mechanical microkeratome versus femtosecond laser. J Cataract Refract Surg. 2009 Oct;35(10):1756-60.
9. Knorz MC, Vossmerbaeumer U. Comparison of flap adhesion strength using the Amadeus microkeratome and the IntraLase iFS femtosecond laser in rabbits. J Refract Surg. 2008;24(9):875-8.
10. Donnenfeld E. Preservation of corneal innervation with femtosecond laser inverted sidecut flaps. Invest Ophthalmol Vis Sci. 2010;51:E-Abstract 2855.
11. Wavefront-optimized and wavefront-guided laser ablations. American Academy of Ophthalmology. Available at: http://www.aao.org/bcscsnippetdetail.aspx?id=9338b90c-0b0d-4331-a7e3-56954fe7cb83 (last accessed January 4, 2016).
12. Bower K, Peppers L, Sia R, et al. Visual performance comparison of wavefront-optimized and wavefront-guided laser in situ keratomileusis (LASIK). Invest Ophthalmol Vis Sci 2013;54: E-Abstract 3125.
13. He L, Liu A, Manche EE. Wavefront-guided versus wavefront-optimized laser in situ keratomileusis for patients with myopia: a prospective randomized contralateral eye study. Am J Ophthalmol. 2014 Jun;157(6):1170-8.

CE TEST

1. In early mechanical microkeratome-based LASIK, what measurement(s) must be carefully considered to confirm candidacy for surgery?
a) Pupil size
b) Keratometry
c) Pachymetry
d) All of the above

2. Which of the following is true in modern femtosecond-based LASIK surgery?
a) Pupil size is more relevant than ever
b) Pupil size is almost irrelevant
c) Postoperative aberrations are more likely
d) Flap thickness is predictable to about +/- 40µm

3. If you refer to a center that offers custom wavefront ablations with optical blend zones, which of the following is not a significant factor for assessing LASIK candidacy?
a) Age
b) Pupil size
c) Corneal thickness
d) Astigmatism

4. With respect to age and candidacy, which of the following statements is TRUE?
a) Low myopes typically achieve refractive stability by age 21
b) High myopes can usually be considered for surgery at age 18
c) Low myopes can usually be considered for surgery at age 18
d) Any age is considered fine as long as the refraction has been stable for at least six months

5. Which of the following disqualifies a patient from having femto-based custom wavefront LASIK?
a) An unstable refraction
b) Asymmetric astigmatism
c) Large pupils
d) Plans to enlist in the U.S. Air Force

6. Which of the following ocular diseases are contraindications for LASIK?
a) Significant cataract
b) Pellucid marginal degeneration
c) Non-responsive KCS
d) All of the above

7. To achieve accurate corneal measurements, how long should soft spherical contact lens wearers discontinue contact lens wear?
a) One week for every decade of wear
b) One week
c) Two weeks
d) One month

8. To achieve accurate corneal measurements, how long should toric soft contact lens wearers discontinue contact lens wear?
a) One week for every decade of wear
b) One week
c) Two weeks
d) One month

9. To achieve accurate corneal measurements, how long should RGP wearers discontinue contact lens wear?
a) One week
b) Two weeks
c) One month
d) One month plus an extra month for every decade the patient has worn an RGP

10. When comanaging LASIK, your EMR notes should include the following:
a) Relevant history
b) Cycloplegic refraction
c) Results of dilated exam
d) All of the above

11. A femtosecond laser is an infrared laser with a wavelength of:
a) 1,003nm
b) 1,053nm
c) 1,305nm
d) 1,503nm

12. Which of the following is a benefit to using a femtosecond laser?
a) Increased contrast sensitivity
b) Less IOP rise during procedure
c) Less dry eye
d) All of the above

13. The inverted bevel-in side cut up to 150° feature is frequently associated with:
a) Flap slippage
b) Better flap stability compared to microkeratome-created flaps

CE TEST

c) Decreased flap adhesion postoperatively
d) Slower wound healing

14. Which of the following statements regarding wavefront-guided technology is TRUE?
a) It relies on the prescription/refraction to be inputted into the laser
b) It is identical to wavefront-optimized technology
c) Higher-order aberrations are measured and incorporated into the treatment plan
d) Ablation profiles are based on the assumption that the patient has positive spherical aberrations

15. Which of the following statements regarding wavefront-optimized technology is TRUE?
a) It relies on the prescription/refraction to be inputted into the laser
b) Higher-order aberrations are measured and incorporated into the treatment plan
c) Ablation profiles are the same, whether the patient has positive or negative spherical aberrations
d) A and C

16. The priority at the Day 1 exam is:
a) Proper flap position
b) Residual refractive error
c) Visual symptoms
d) Dry eye symptoms

17. With macrostriae, look for:
a) Staining in the gutter
b) A gutter opaque area
c) Large folds
d) All of the above

18. What percentage of Caucasians ages 40 to 49 are myopic?
a) More than 20%
b) More than 30%
c) More than 40%
d) More than 50%

19. Which of the following statements is TRUE?
a) Trends show an increase in myopia across the entire U.S. population
b) Trends show a much greater growth of the prevalence of myopia in Hispanic and black races compared to Caucasians
c) By 2015 it is estimated that nearly 45 million people in the United States will have myopia
d) All of the above

20. As of 1990, the financial cost of myopia in the United States was estimated to be:
a) $148 million
b) $448 million
c) $4.8 billion
d) $48 billion

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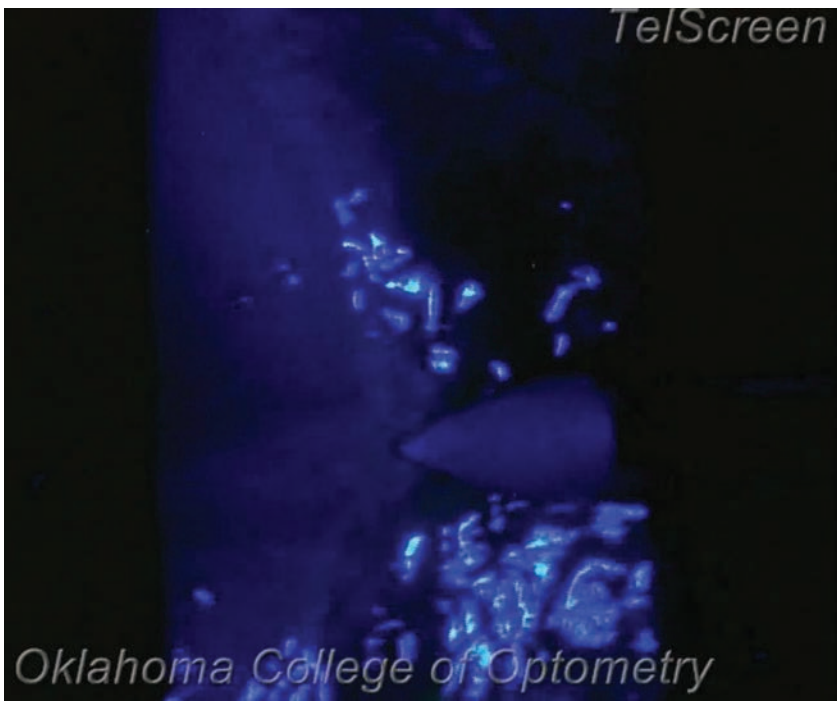
Learn to Burp Corneal Wounds Without a Hiccup

Lower IOP for postoperative cataract patients with this elegant technique.

By Brittany Ellis, OD, and Nathan Lighthizer, OD

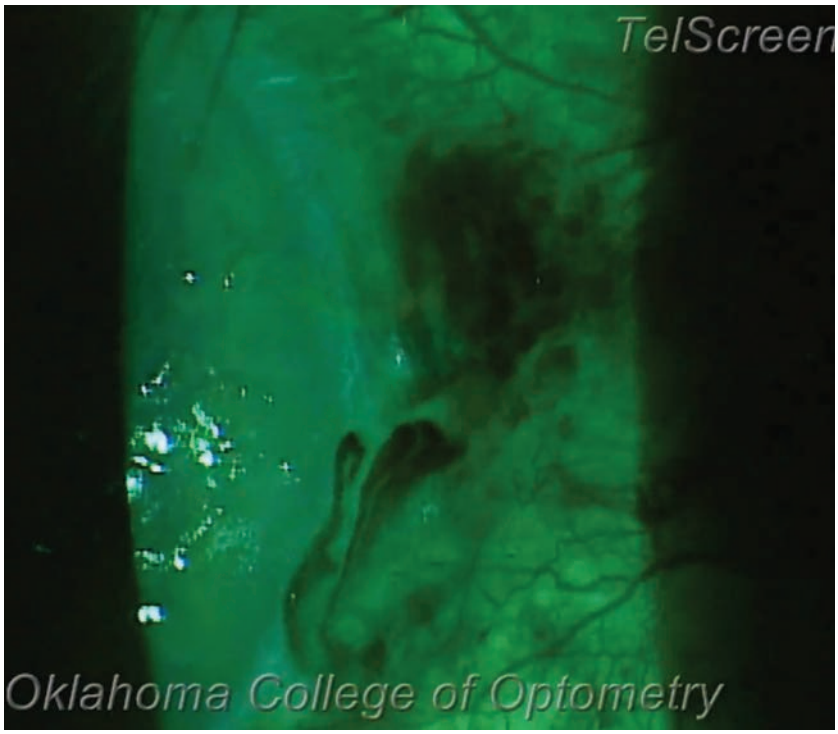
"Doc, I feel miserable this morning. I didn't sleep well at all, my eye is hurting terribly and I've been up vomiting half the night."

These aren't really the first words you want coming out of your patients' mouths the morning after they've had cataract surgery. Your first thought should be, "Is my patient having a pressure spike?" While this certainly can be the cause of the pain, other factors, including corneal abrasion, anesthesia effects and, rarely, retrobulbar hemorrhage, may be the causative factor involved. Our clinical experience has shown that it is often the anesthesia wearing off in the hours after cataract surgery, along with the surgery itself, causing significant ocular

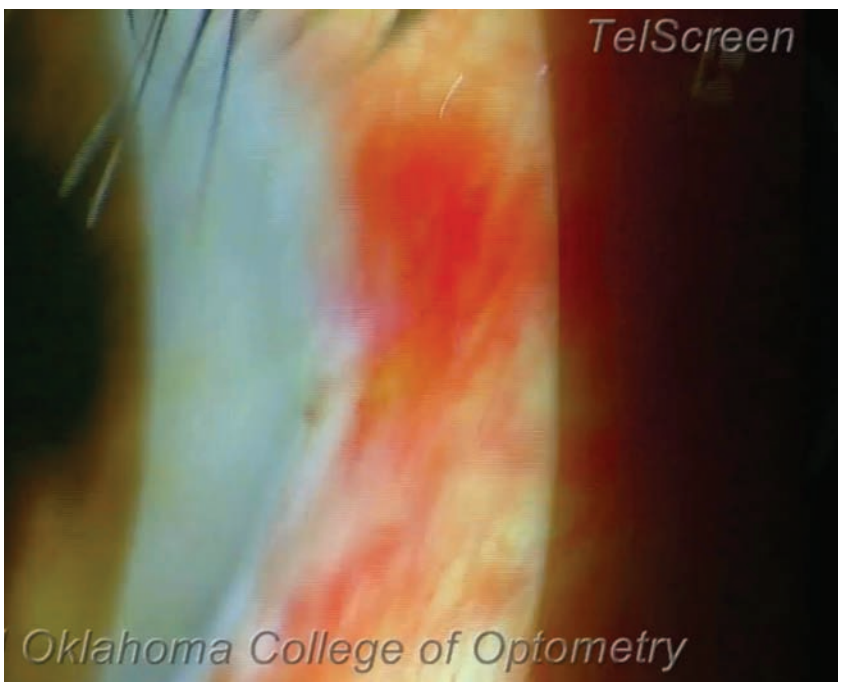


Any time a postoperative cataract patient presents with an IOP greater than 40mm Hg, we opt to burp the wound by taking a device, which can be seen in this image, and pushing just outside the wound to expel excess aqueous. The bright, almost neon blue in this slit lamp image shows the fluid pulsing around the wound.

To see a narrated video of this procedure, visit www.reviewofoptometry.com, or scan this QR code.



In our procedure, we employ an 18-gauge needle to burp the wound, although a spud, cotton swab or Weck-Cel sponge may also be used. In this patient's case, a conjunctival vessel was broken, resulting in the black fluid seen above. Be careful not to confuse this for the fluid you're attempting to expel, as shown on the opposite page. As for the nicked conjunctival vessel, the patient can easily blink away the excess blood, as is seen below.



and periocular pain. If this is the case, the cornea will be intact, IOP will not be elevated, and simple assurance that things will improve in the coming hours is all that is needed, along with possible oral or topical pain relief.

If these other causes of pain, nausea and vomiting are ruled out, and you can confirm that the pressure has elevated significantly, it's time to consider taking action. Fortunately, you have the proper tools in your toolbox to help them feel better.

During a one-day postoperative cataract visit, obtain the patient's visual acuity, and perform a thorough slit lamp examination to assess the corneal clarity, conjunctival injection, iris appearance, anterior chamber inflammatory response, lens position and intraocular pressure (IOP).

If you observe a dramatic rise in IOP, you would expect to see some amount of corneal edema. This increase in IOP could be from some remaining viscoelastic in the anterior chamber, inflammation or red blood cells impeding proper drainage of aqueous humor. In other, less frequent, occurrences it may also be associated with a retained lens fragment either in the anterior or posterior chamber.

Depending on how significant the IOP elevation is, a few different approaches can achieve the necessary decrease in pressure. You can use standard topical ophthalmic drops, such as beta-blockers, carbonic anhydrase inhibitors or alpha-agonists. You can also offer oral acetazolamide, if you deem it necessary.

Another option that can show more immediate results is performing a modified paracentesis.

Paracentesis

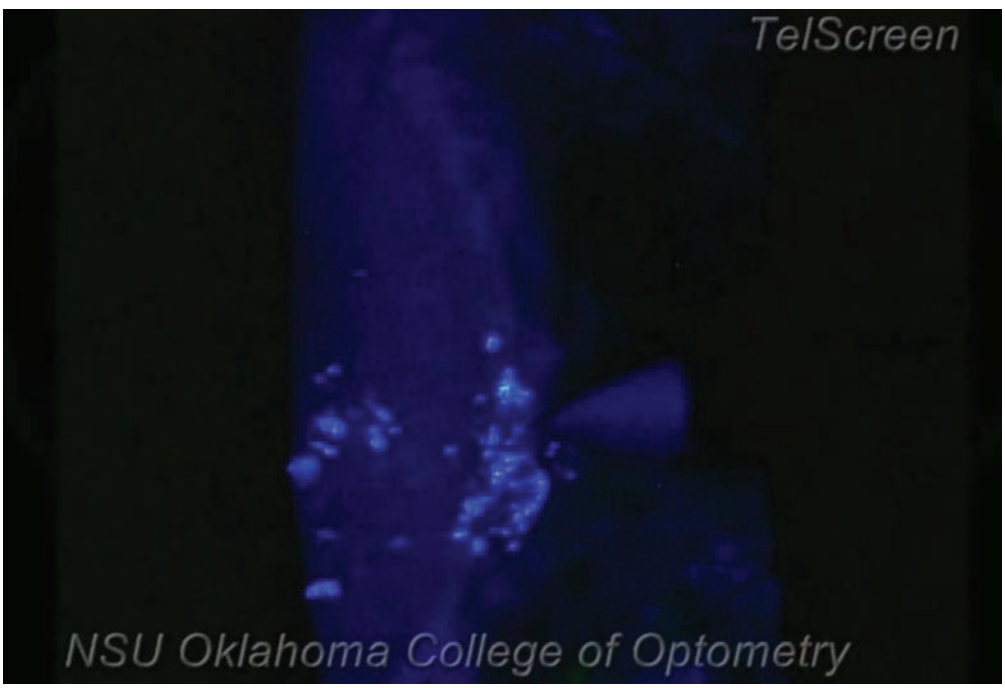
We say it is "modified" because a paracentesis is typically defined as "a surgical puncture of a bodily cavity with a trocar, aspirator or other instrument usually to draw off an abnormal effusion for diagnostic or therapeutic purposes."

In our case, a patient was returning for a one-day postoperative examination, so we did not need to recreate the puncture site; the cataract surgeon has already done this for us. The clear corneal incision provides the ideal site to draw off excess aqueous humor contributing to increased IOP. While the clear corneal incision, or the smaller auxiliary port incisions, is considered a self-sealing wound, within 24 hours of the surgery it can be opened easily to provide immediate and dramatic pressure lowering and symptomatic relief to the patient.

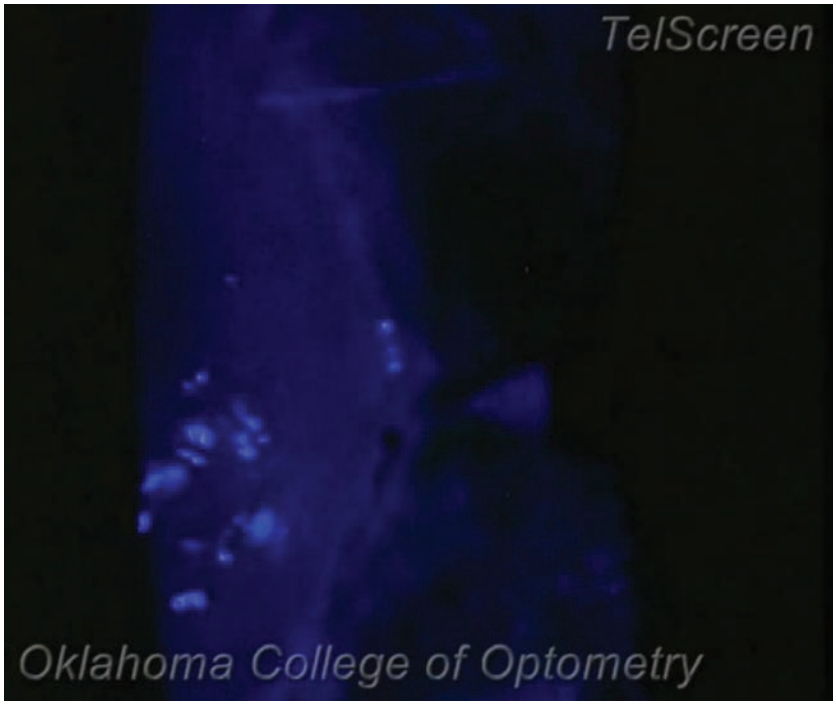
We often refer to this as "burping" the wound, since we are not creating a new puncture site.

Indications

Practitioners should consider a wound burp when a patient presents with an IOP approaching 40mm Hg or greater. Consider the procedure especially when patients experience symptoms similar to those of an acute angle closure. These symptoms include pain,



In this patient's case, we went in nasally; but more commonly, this procedure is performed by pushing just temporal to the limbus. The illuminated area in this image shows the aqueous fluid about to flow out.



The surgeon already did the difficult work by providing the side port used for the surgery. To burp the wound, you just push on the outside of that side port, visible in this slit lamp image.

headache, nausea or vomiting.[1] A significantly hazy cornea with an IOP in the mid 30s or above calls for a wound burp—especially when the aforementioned symptoms are also present.

Another group of patients to strongly consider are currently treated glaucoma patients whose optic nerves already exhibit advanced cupping, and for whom an IOP spike could be detrimental.

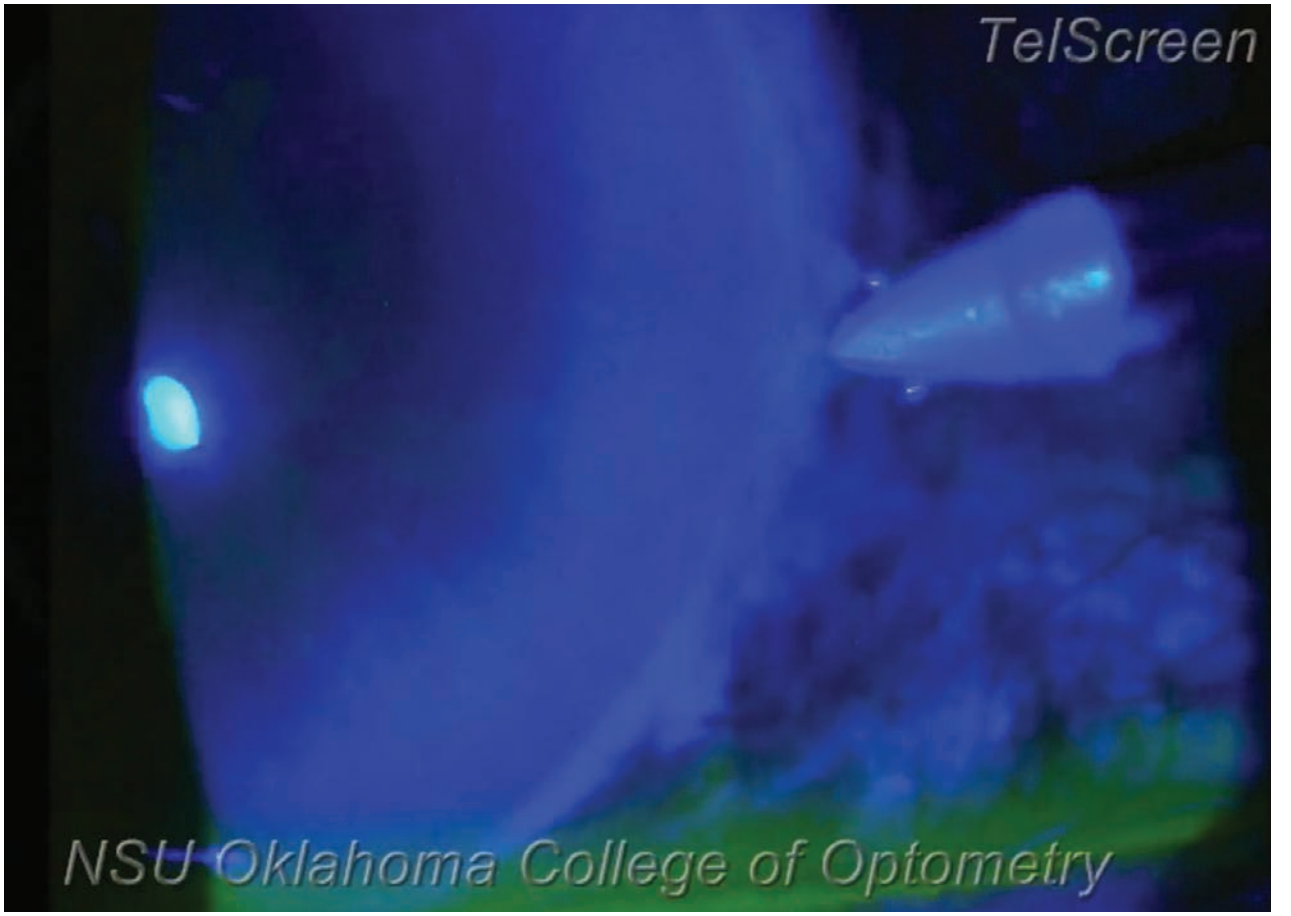
Burping The Wound

Prior to a wound burp, perform an examination, including components such as visual acuities, a thorough slit lamp examination and measurements of IOP. Goldmann tonometry is still the standard, and there is really no reason to check the IOP with any other device. Once you've completed an exam and obtained an accurate IOP, the steps to burping a wound are as follows:

1. ***Numb the eye.*** Instill one or two drops of proparacaine in each eye to improve patient comfort and minimize the blink reflex. If the patient is particularly sensitive, consider an additional drop of Akten (lidocaine gel, Akorn Pharmaceuticals) as well.

2. ***Administer a topical antibiotic.*** Instill one drop of an antibiotic, such as moxifloxacin, gatifloxacin or besifloxacin, to reduce the risk of intraocular infection due to the reopening of the wound. The patient will generally be using a topical antibiotic as part of the postoperative regimen.

3. ***Maximize visualization.*** Instillation of sodium fluorescein may help practitioners better assess the outflow of aqueous humor from the wound. This is a necessary step, as it will be much more difficult to see the flow of fluid out of the wound in the absence of the fluorescein.



As you burp the wound, you'll see the trapped aqueous fluid flow out, through the wound and into the tear lake. It may take several burps—for this patient it took four—but eventually it should lower the IOP. The patient's pressure in this case was lowered to about 18mm Hg after the procedure.

4. ***Position the patient.*** The patient should be aligned comfortably in the slit lamp. Good fixation and head position should be emphasized.

5. ***Select your instrument.*** Some practitioners prefer to use a 25-gauge needle to perform a wound burp, though a Weck-Cel sponge, cotton swab or other blunt tool can also be used.

Our clinical experience has shown that an 18-gauge needle is most appropriate for burping the wound. Weck-Cel sponges and cotton swabs, in our experience, tend to be too large when behind the magnification of the slit lamp and can obstruct your view of the wound and the drainage. The fine, small end of a needle seems to accomplish the task much better and are already nicely packaged for sterility.

6. ***Brace the patient.*** Have the patient look in the direction opposite from the incision site.

7. ***Perform the burp.*** Apply a small amount of pressure just outside of, and perpendicular to, the temporal incision, allowing an opening to the wound that will permit the outflow of aqueous humor. This should appear similar to what one would expect with a positive Seidel sign.

Typically, pressure should be just lateral to the temporal incision site, as that will push the temporal part of the clear corneal incision in and open up the wound.

Our clinical experience has shown that one firm "burp" by the incision for about one second will allow a bolus of fluid to leak out. This tends to lower the IOP by at least 5mm Hg to 10mm Hg, in proportion to the volume of fluid that has been removed. Depending on the practitioner's comfort level and initial patient IOP, it may require multiple burps to lower the intraocular pressure to an adequate level.

When in doubt, check the IOP again before burping to ensure that the IOP has not gone too low into the single digits. Most IOP's of 40mm Hg or greater will come down into the teens after just a couple of burps. Burping should never be done too quickly or too firmly.

8. ***Measure.*** Repeat IOP measurement to ascertain the amount of reduction in IOP achieved.

9. ***Burp again.*** Repeat wound burp until you get the IOP below 20mm Hg.

10. ***Measure again.*** Intraocular pressure should be checked again in 60 minutes to ensure that it is not rising significantly. Further treatment with topical or oral therapies, or even a return trip to the OR, may be deemed necessary if there is a rise in IOP at this time.

11. ***Follow up.*** Have the patient return in one day to ensure the IOP reduction's stability. The patient should continue standard postoperative cataract surgery drops.

Complications

As with any ocular procedure, there are potential complications to educate the patient about. Endophthalmitis is a rare and preventable, but potentially devastating, complication of performing a wound procedure because you are momentarily reopening the eye to the environment. Uncommonly, discomfort or pain during the procedure is possible, as well as bruising or subconjunctival hemorrhage around the site. In patients who have a shallow anterior chambers one should proceed with caution due to the risk of shallowing the chamber further and potentially causing damage to the iris or cornea. The rare patient who has an extremely high IOP and a shallow anterior chamber should be referred back to the surgical center for consultation.

Going Back to The Surgeon

We had one particular patient who had her IOP drop from 50mm Hg down to 18mm Hg after the burping procedure. An IOP check 45 minutes after the burping revealed her IOP back in the high 30s. We burped her again, and again the IOP lowered into the teens. Another 45 minutes later, the IOP was nearly 40mm Hg again. This repeated a couple more times until, finally, the surgeon decided to take the patient back to the OR for an anterior chamber washout of the viscoelastic. This was the ultimate fix as her IOP stabilized in the mid-teens after that and did not elevate again.

Intraocular pressure spikes are commonly seen by practitioners on follow up the day after cataract surgery. This can be both painful and nauseating for the patient. Having the ability to perform a successful wound burp can bring your patient much faster relief than waiting for traditional topical or oral therapies to take effect. By being able to perform this procedure in office, you save the patient a potentially lengthy trip back to the surgeon, a time-consuming office visit, a delay in treatment and avoid potential medical side effects.

In the end, having an IOP that is lowered quickly helps the patient see and feel better, and is a relief to the doctor as well. ■

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1. See JL, Aquino MCD, Chew PT. Angle-Closure Glaucoma. In: Yanoff MD M, Duker MD JS, eds. Ophthalmology. 4th ed: Elsevier, Inc.; 2014.

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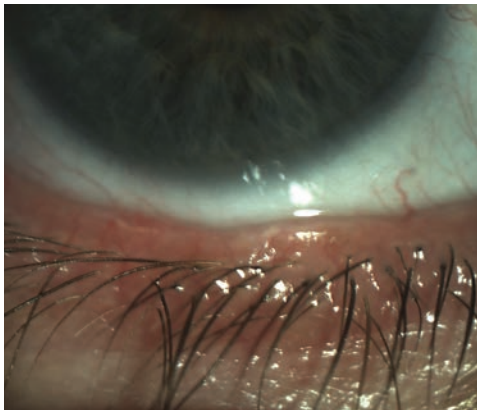
ANTIBIOTICS:
Wonder Drugs For Treating Anterior Segment Infections

Selecting the appropriate medication is essential for optimal success when treating meibomian gland dysfunction, blepharitis and other anterior segment conditions.

By Chandra Mickles, OD, MS

Antibiotics play a vital role in containing and eradicating sight-threatening eye conditions such as eyelid disease, bacterial conjunctivitis and bacterial keratitis. They are also widely used for prophylaxis. Safe and effective use of anti-infective medications is essential for safeguarding the ocular health of our patients. Choosing an antibiotic with antimicrobial efficacy against the suspected bacteria, as well as avoiding sub-lethal dosing, is paramount to success. This article reviews current and emerging antibiotic options for common anterior segment conditions necessitating anti-infective agents.



Scalloped lid margins are indicative of inflammation in meibomian gland dysfunction.

Beyond Lid Hygiene

Meibomian gland dysfunction (MGD) and blepharitis are among the most prevalent problems encountered in the clinical setting.[1] While eyelid hygiene and warm compresses remain first-line therapies, topical and oral antibiotic options have expanded recently to better manage these chronic anterior segment conditions.

Although the etiologies of MGD and blepharitis are poorly understood, the toxic effects of bacteria that colonize the eyelid margin, as well as inflammation, are factors. Research suggests that the pathogenic process is associated with the release of toxic bacterial products that stimulate the production and release of pro-inflammatory cytokines.[2] Therefore, macrolides are an ideal antimicrobial choice due to their antibacterial and anti-inflammatory activity.

Although the macrolide erythromycin has been the mainstay for these conditions, antibiotic resistance may limit its efficacy because of its extensive use.[3] Azithromycin, a second-generation macrolide, has

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Goal Statement: Safe and effective use of antibiotics is essential for safeguarding the ocular health of our patients. Whether treating meibomian gland dysfunction, blepharitis, bacterial conjunctivitis or any other infection in need of antibiotics, choosing the right medication to treat the suspected bacteria, while also avoiding sub-lethal dosing, are the keys to a successful treatment regimen. This article discusses antibiotic treatment options for common anterior segment infections.
Faculty/Editorial Board: Chandra Mickles, OD, MS
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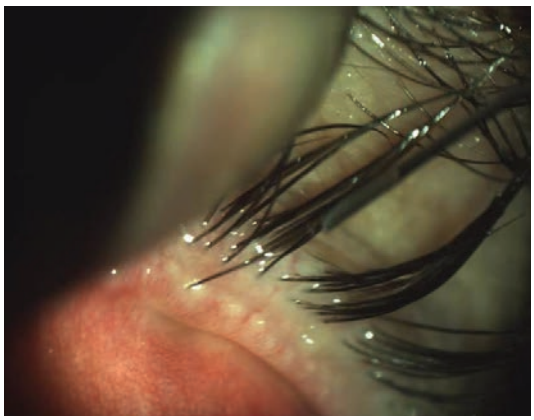

Findings such as obstructed meibomian glands with telangiectasia indicate that conventional eyelid therapy may not be sufficient for MGD management.

recently gained popularity because of its anti-inflammatory properties, excellent ocular tissue penetration and prolonged duration of activity.[4] Topical azithromycin 1% (AzaSite, Akorn) increases retention time, which is believed to be due to its viscous carrier, polycarbophil, that allows for more contact time on the eyelid margin.

Although used off-label for MGD and blepharitis, best success is achieved for these conditions when AzaSite is administered to a closed eyelid with massage twice a day for two days, then daily for a month. Because AzaSite is not approved for patients less than one year of age, erythromycin or bacitracin ointment can be applied at bedtime for up to a month for these younger patients.

When Topicals Aren't Enough

Similar to topical treatments, oral antibiotics with antimicrobial and anti-inflammatory properties are excellent choices for managing refractory cases of MGD and blepharitis. Oral azithromycin and doxycycline are therapeutic options in these cases.[5,6,7] While 50mg doxycycline per day for one to six months is typically used for MGD and blepharitis management, as low as 20mg BID for one month was shown to be equally effective as a four-week treatment of 200mg doxycycline BID.[5] Oral azithromycin can be given as pulsed therapy (500mg per day over three consecutive days in each week for one month) or a five-day treatment of 500mg on day one and 250mg per day thereafter.

While both doxycycline and oral azithromycin have been shown to be effective in MGD and blepharitis treatment, knowing which oral antibiotic has better efficacy in each case can be challenging.[5,7] For treating recalcitrant MGD, researchers found that the five-day oral azithromycin regimen had a significantly better clinical response and fewer side effects than doxycycline 200mg/day for one month.[7] Oral azithromycin's better clinical response and shorter treatment duration suggest it may be the better oral antibiotic option for meibomian gland dysfunction. Investigators recently demonstrated that the greater efficacy of oral azithromycin may be due to its ability to stimulate the meibomian gland epithelial cell function, which is not duplicated by doxycycline and the other tetracyclines.[8]

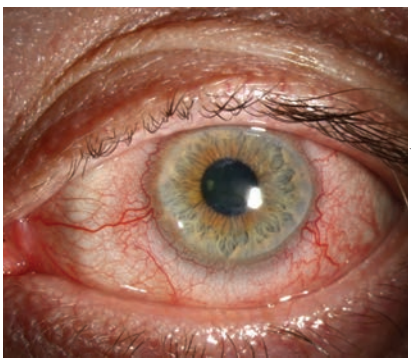

Photo: Christine W. Sindt, OD

Antibiotics can help manage the toxic effects of bacteria that colonize the eyelid margin and cause inflammation, as seen here with rosacea blepharitis.

Both topical and oral antibacterial therapies show promise for effectively managing eyelid disease. Practitioners should also keep in mind that maintenance therapy of eyelid hygiene and warm compresses may be needed in addition to antibiotics in some cases.

Winning the Battle Against Bacterial Conjunctivitis

Bacterial infection is a common cause of infectious conjunctivitis, which is characterized by hyperemia and purulent discharge.[9] Although bacterial conjunctivitis is typically self-limiting, empiric antibiotic therapy can decrease disease transmission and severity, minimize complications and reduce recurrence.[10]

Besivance (besifloxacin 0.6% ophthalmic suspension, Bausch + Lomb) is a highly effective broad-spectrum antibiotic used TID for seven days for bacterial conjunctivitis. It is the first topical chlorofluoroquinolone developed solely for ophthalmic use, and it is effective even against multi-drug resistant *Staphylococci*.[11] Although its lack of a systemic counterpart limits the likelihood of bacterial resistance, overuse is still a concern. Thus, newer generation antibiotics, such as besifloxacin, should be saved for moderate to severe cases of bacterial conjunctivitis.

The use of the earlier generation topical fluoroquinolones in milder cases has been supported, given bacterial conjunctivitis is usually self-limiting and the causative microbe of bacterial conjunctivitis has generally not been methicillin-resistant *Staphylococcus aureus* (MRSA).[12] Other good alternatives for bacterial conjunctivitis management are topical azithromycin and polymyxin

B/bacitracin ointment for children struggling with drop instillation.

Breaking Down Bacterial Keratitis

When faced with a suspected bacterial corneal ulcer, prompt institution of effective therapy is a must to maximize the chances of complete recovery. Unfortunately, this ocular emergency can rapidly cause corneal destruction, leading to potential vision loss. Bacterial keratitis is the most common form of microbial keratitis.[13] Because both gram-negative and gram-positive bacteria are causative pathogens, use of an adequately dosed broad-spectrum antibiotic that covers both gram-positive and gram-negative microorganisms is preferred. Depending on the severity, around-the-clock application of besifloxacin is an excellent choice in most cases. Initially instilling the antibiotic drops in-office can demonstrate the importance of frequent dosing, potentially increase therapeutic compliance and ultimately improve patient outcomes.

The addition of dual broad-spectrum fortified antibiotics, usually a cephalosporin and an aminoglycoside, is indicated for central, large (>2mm) or aggressive bacterial corneal ulcers.[14,15] Infrequently, systemic antibiotics are warranted for bacterial keratitis management. Systemic antibiotics and periocular injections of antibiotics should be considered if corneal perforation is imminent or the infection process has invaded the sclera.

Old Drug, New Trick

The emergence of bacterial resistance and the shortage of new anti-infective agents have driven the reconsideration of older antibiotics as viable therapeutic options. Colistin (Taj Pharmaceuticals) is a polymyxin drug that was used extensively systemically, but was abandoned due to side effects when given parenterally.[16] However, there has been a resurgence in its use due to its activity against antibiotic resistant gram-negative bacteria.[16-20] Topical colistin may be a valuable option for cases of multiple drug-resistant *Pseudomonas* bacterial keratitis. In a recent study, topical colistin 0.19% was found to be safe and effective against multi-drug resistant *Pseudomonas aeruginosa*.[20]

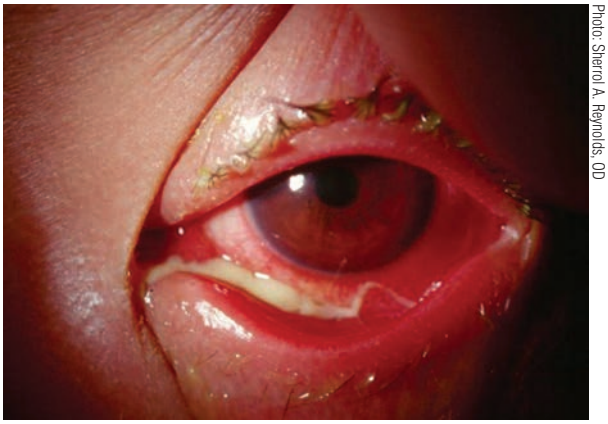

Photo: Sherrol A. Reynolds, OD

Besifloxacin 0.6% ophthalmic suspension, the first topical chlorofluoroquinolone developed solely for ophthalmic use, is often used to treat mucopurulent bacterial conjunctivitis.

The Missing Link

The emergence of antibiotic-resistant pathogens has also prompted the search of alternative techniques that can effectively treat bacterial keratitis. Corneal collagen crosslinking (CXL) is a novel technique that slows the progression of keratoconus and postoperative ectasia. During the standard CXL procedure, the cornea is irradiated with ultraviolet A (UVA) light after application of the photosensitizer riboflavin.[21] This process strengthens the corneal collagen, thereby stabilizing the cornea.

Research has shown riboflavin and UVA irradiation to be bactericidal against gram-negative and gram-positive bacteria, including MRSA.[22,23] UVA has the ability to directly destroy bacteria, while the riboflavin can produce reactive oxygen species toxic to the microorganisms.[24,25] CXL also has a toxic effect on these inflammatory cells, and it increases the cornea's resistance to enzymatic degradation.[26,27] These actions should limit corneal scarring and prevent corneal perforation. Thus, CXL may be a useful alternative treatment option in severe or recalcitrant cases of bacterial keratitis. It may also be beneficial when compliance with conventional antibiotic treatment is an issue.

In several studies, adjunctive CXL therapy, or CXL alone, shortened the healing time and reduced the complication rate of bacterial keratitis when compared to topical antibiotic therapy alone.[22,24,25,28,29] However, in a prospective trial comparing CXL plus conventional topical treatment with antibiotic treatment alone, researchers did not find a difference in healing time between the two groups.[21] Nonetheless, they did find fewer complications in the group treated with both topical antimicrobial therapy and adjunctive CXL.[21]

Despite the reported success of CXL treatment for bacterial keratitis, there are potential safety concerns. The cornea must be a certain thickness for CXL to protect the corneal endothelium from damage, and measuring corneal thickness in the presence of active infection can be difficult.[30] Additionally, it is unknown what effect a corneal infiltrate would have on the penetration

of the riboflavin and UVA.[31] There is not enough data showing the safety of CXL for bacterial keratitis treatment long-term, nor is there an established optimal protocol. Therefore, the use of CXL may be best reserved for severe bacterial keratitis or cases refractory to conventional antibiotic therapy.[21,24,25]

Adjunctive Steroids: Where Do We Stand?

The use of adjunctive topical corticosteroids in the treatment of bacterial keratitis has been a controversial issue in the eye care community. The potential benefits of the corticosteroid—minimizing scarring and ultimately improving visual outcomes—are juxtaposed with concern over exacerbation of infection and delayed healing. The Steroids for Corneal Ulcers Trial (SCUT) attempted to provide evidence for treatment practices for bacterial keratitis by assessing the effect of adjunctive corticosteroids on clinical outcomes.[32] Five hundred participants with culture-positive bacterial keratitis received, as adjunctive therapy, either topical corticosteroids or topical placebo.[33] The results revealed no significant difference in the scar size and visual outcomes between the steroid treatment group and the control group.[33] However, sub-group analyses revealed a modest benefit in visual acuity in steroid-treated participants with central or deep ulcers.[33]

Following these results, questions remained about the long-term outcome of adjunctive steroid use. A 12-month SCUT follow-up study revealed that adjunctive corticosteroids may be associated with improved, long-term clinical outcomes for bacterial ulcers not caused by *Nocardia* species.[32] The best spectacle-corrected visual acuity improved at 12 months for the steroid group.

However, in a recent report of visual outcomes four years following the initial SCUT study, the visual acuity did not significantly change between one year and four years post-treatment in a subset of 50 participants representative of the larger SCUT cohort.[34] This suggests that bacterial keratitis treated with adjunctive steroids may yield improvements in visual acuity 12 months following diagnosis, but improvement thereafter is unlikely.

In light of these results, clinicians should not postpone surgical intervention with corneal transplantation beyond one year for bacterial keratitis cases.[34] A conservative approach is to avoid corticosteroid initiation until the offending pathogen is identified and then provide close follow up if the corticosteroid is introduced. Judicious evidenced-based prescribing and prudent follow up is always warranted.

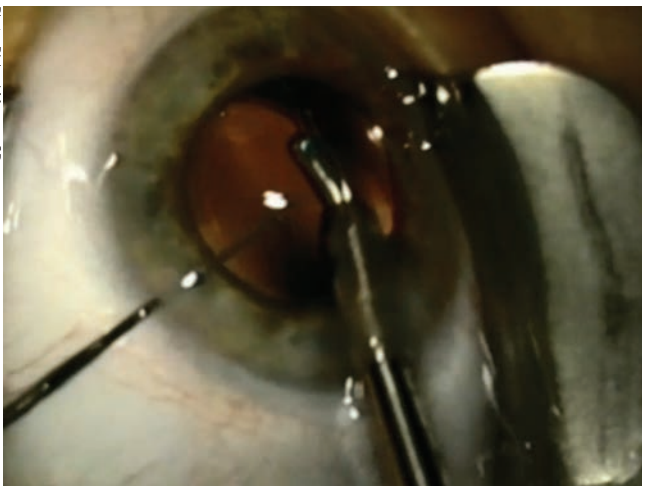

Photo: Richard Mangan, OD

Injecting medication into the posterior chamber after uncomplicated cataract surgery provides sustained therapeutic protection against endophthalmitis and postoperative cystoid macular edema.

Prophylaxis

Antibiotic prophylaxis is also a topic of great debate in the eye care community. Questions remain as to whether or not topical antibiotics are overkill in peri-procedural prophylaxis and if clinicians are using antibiotics excessively in cases of superficial keratitis, viral conjunctivitis and corneal abrasions.

Topical antibiotics are administered perioperatively and peri-procedurally to prevent endophthalmitis. Studies have demonstrated that topical antibiotics, administered under these circumstances, significantly reduce conjunctival bacterial flora.[35,36] However, there is increasing bacterial resistance to the frequently used topical fluoroquinolones. Thus, unwarranted overuse of topical fluoroquinolones for peri-procedural and perioperative prophylaxis is a concern.

The standard use of 5% povidone-iodine with meticulous sterile preparation is an effective prophylactic method for cataract surgery and alone may be enough, particularly with intravitreal injections.[37] Researchers have not shown that perioperative administration of topical antibiotics decreases the risk of endophthalmitis, nor does it reduce bacteria flora beyond that of 5% povidone-iodine alone.[37,38] Further, recent studies suggest that serial, post-injection, topical antibiotics do not reduce endophthalmitis rates, but may actually increase antibiotic resistance.[38]

This has changed the practice patterns specifically for intravitreal injections in which pre-procedure povidone-iodine has been deemed

sufficient.[39] Meanwhile, for more invasive surgical procedures, povidone-iodine alone hasn't been deemed sufficient and alternatives to perioperative topical antibiotic drop instillation are becoming increasingly popular.[39]

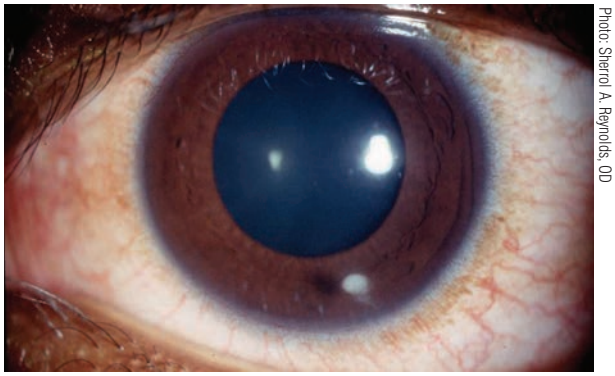

Photo: Sherrol A. Reynolds, OD

A corneal ulcer's location is an important factor in treatment. While controversial, adjunctive corticosteroids may improve outcomes for central or deep bacterial corneal ulcers.

Dropless Perioperative Prophylaxis

Some practitioners are seeking to eliminate topical antibiotic drop instillation for perioperative prophylaxis, which can drive poor patient compliance and antibiotic resistance. Interest in intracameral antibiotics for endophthalmitis prophylaxis for cataract surgery is growing. The European Society of Cataract and Refractive Surgery's study provided evidence for the use of intracameral antibiotics following cataract surgery.[40] The results indicate a fivefold decrease in endophthalmitis following cataract surgery when cefuroxime was injected into the anterior chamber.[40] A large-scale US study also found a significant reduction in postoperative endophthalmitis rates with the use of intracameral cefuroxime.[41]

Although an off-label use, this perioperative prophylactic strategy is now used by an increasing number of ophthalmologists. The challenge is that there currently isn't an FDA-approved injectable for this purpose.[42] There are also safety concerns regarding dilutional and contamination errors because cefuroxime is not commercially available in a preformulated preparation and must be diluted from a powder form in the operating room.[42]

Intravitreal antibiotic and steroid combination use is another alternative strategy for dropless perioperative prophylaxis. Triamcinolone/moxifloxacin (Trimoxi, Imprimis Pharmaceuticals) is a compounded combination medication being used off-label in cataract and LASIK surgery. No formal large-scale randomized studies have been completed investigating this technique. However, a retrospective study of 1575 eyes injected with 15mg/1mg/ml of Trimoxi following intraocular lens implantation found it was effective in preventing inflammation, endophthalmitis and cystoid macular edema.[43] In fact, there were no cases of endophthalmitis.[43]

Intraocular lenses soaked with antibiotics have also been examined as a means to prevent endophthalmitis. Studies show that intraocular lenses presoaked with gatifloxacin and moxifloxacin are capable of delivering clinically significant antibiotic levels in rabbits.[44,45] In a recent study comparing the concentration level of intracameral injection of moxifloxacin to intraocular lenses presoaked with moxifloxacin in rabbits, intracameral antibiotic injections showed a high antibiotic concentration for a short time, but the presoaked IOLs showed slower decrease rates of the antibiotic level in the anterior chamber.[46]

Given these results, dropless strategies of perioperative prophylaxis show promise in the prevention of endophthalmitis, although further work is needed in this area. Protocols that include a steroid component introduce the risk of IOP elevation or transient visual blur.

Prophylactic use of antibiotics for corneal abrasions is less controversial. Despite lack of proven effectiveness for non-infected corneal abrasions, prophylactic antibiotic use persists for corneal abrasions because the compromised cornea is more susceptible to infection than an intact cornea. Broad-spectrum antibiotics are an excellent choice for corneal abrasions and other conditions for which the cornea is compromised. The preservative-free fluoroquinolones Vigamox and Moxeza (moxifloxacin 0.5%, Alcon) have broad coverage and can prevent adverse effects of preservatives on vulnerable corneas.

A Look Ahead

Despite the increase in drug resistance, antibiotic innovation has slowed over the past decade. Thankfully, there are encouraging signs of development. The primary focus has been on therapies that do not drive resistance. Instead of launching an improved antibiotic with the same target profile, the emphasis is on new antibacterial mechanisms of action and delivery methods.

Isothiazoquinolones—novel compounds in the quinolone family—show great promise as future bactericidal agents. They are structurally different from fluoroquinolones, and in addition to targeting bacterial DNA replication enzymes inhibited by fluoroquinolones, they add a distinct mechanism of action by targeting another bacterial DNA replication enzyme, DNA primase.[47] Acting against the DNA primase provides a distinct mechanism of

action and allows the antibiotic to act against bacteria, even in a non-dividing state.[48] Additionally, research shows this added target increases antimicrobial efficacy and decreases the chance of resistance compared to fluoroquinolones.[47-49] Development and commercialization of the isothiazoquinolone ACH-702 (Achillion Pharmaceuticals), an ocular antibacterial of good therapeutic potential, is underway.[50]

In addition to antibiotic resistance, frequent instillation of topical antibiotics, particularly for anterior segment infections, poses a significant challenge to patients. Various anterior segment antibiotic drug delivery systems are being developed to address this issue and should improve patient outcomes. Extended-release antibiotic delivery systems have the potential to maximize the therapeutic effect while minimizing resistance. Several antibiotic delivery strategies have demonstrated some success, such as hyaluron-based ocular sustained delivery of moxifloxacin; a punctal plug delivery system that elutes moxifloxacin; biodegradable implants that deliver levofloxacin; and antibiotic drug-eluting contact lenses.[51-54] These ocular drug delivery systems are in early stages of development, but show promise as safe and effective techniques.

Conclusion

Bacterial infections of the anterior segment can have visually devastating consequences. Fortunately, we have a vast arsenal of antibiotics to manage these conditions and preserve the sight and quality of life of our patients. Nevertheless, the emergence of antibiotic resistance is a serious public health concern. Prudent prescribing, new antibiotics and innovative drug delivery strategies will help combat this growing issue. Antibiotics will remain our 'wonder drug' as an invaluable tool in our anterior segment disease management armamentarium. ■

Dr. Mickles is an associate professor at Nova Southeastern University College of Optometry and a fellow of the American Academy of Optometry.

1. Schaumberg DA, Nichols JJ, Papas EB, et al. International workshop on meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011 Mar;52(4):1922-9.
2. Gerd G, Tauber J, Baudoin C. The international workshop on meibomian gland dysfucntion: report of the subcommittee on management and treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011 Mar 30;52(4):2050-64.
3. John G. A comparative study in the clinical and microbial efficacy of topical besifloxacin ophthalmic suspension 0.6% with erythromycin ophthalmic ointment 0.5% for the management of acute blepharitis. Poster presented at the Annual Meeting of the Association for Research in Vision and Ophthalmology, May 6-9 2012; Fort Lauderdale, FL.
4. Duncan K, Jeng BH. Medical management of blepharitis. Curr Opin Ophthalmol. 2015;26(4):289-94.
5. Foulks GN, Borchman D, Yappert M, Kakar S. Topical azithromycin and oral doxycycline therapy of meibomian gland dysfunction: a comparative clinical and spectroscopic pilot study. Cornea. 2015;32(1):44-53.6. Yoo SE, Lee DC, Chang MH. The effect of low-dose doxycycline therapy in chronic meibomian gland dysfunction. Korean J Ophthalmol. 2005;19:258-63.
6. Greene JB, Jeng BH, Fintelmann RE, et al. Oral azithromycin for the treatment of meibomitis. JAMA Ophthalmol. 2014;132(1):121-2.
7. Kashkouli MB, Fazel AJ, Kiavash V, et al. Oral azithromycin versus doxycycline in meibomian gland dysfunction: a randomised double-masked open-label clinical trial. Br J Ophthalmol. 2015;99(2):199-204.
8. Liu Y, Kam WR, Ding J, Sullivan DA. Can tetracycline antibiotics duplicate the ability of azithromycin to stimulate human meibomian gland epithelial cell differentiation? Cornea. 2015;34(3):342-6.
9. Azari A, Barney NP. Conjunctivitis a systemic review of diagnosis and treatment. JAMA. 2013 Oct 23;310(16):1721-29.
10. Sheikh A, Hurwitz B. Topical antibiotics for acute bacterial conjunctivitis: Cochrane systematic review and meta-analysis update. Br J Gen Pract. 2005;55(521):962-4.
11. Fechner PU, Teichmann KD. The Conjunctiva. In: Fechner PU, Teichmann KD, eds. Ocular therapeutics. Pharmacology and clinical application. New Jersey: Slack Incorporated;1998:285-326.
11. Deschênes J, Blondeau J. Besifloxacin in the management of bacterial infections of the ocular surface. Canadian Journal of Ophthalmology. 2015;50(3):184-91.
12. Asbell PA, Colby KA, Deng S, et al. Ocular TRUST: nationwide antimicrobial susceptibility patterns in ocular isolates. Am J Ophthalmol. 2008;145(6):951-8.
13. Al-Mujaini A, Al-Kharusi N, Thakral A, Wali UK. Bacterial keratitis: perspective on epidemiology, clinico-pathogenesis, diagnosis and treatment. Sultan Qaboos Univ Med J. 2009 Aug;9(2):184-95.
14. Rosenberg JB, Gritz DC. Fluoroquinolones or fortified antibiotics for treating bacterial keratitis: systematic review and meta-analysis of comparative studies. Can J Ophthalmol. 2011;47(6):493-9.
15. Eiferman RA, O'Neill KP, Morrison NA. Methicillin-resistant staphylococcus aureus corneal ulcers. Ann Ophthalmol. 1991 Nov;23(11):414-5.
16. Dijkmans AC, Wilms EB, Kamerling IM, et al. Colistin: revival of an old polymyxin antibiotic. Ther Drug Monit. 2015 Aug;37(4):419-27.
17.Catchpole CR, Andrews JM, Brenwald N, et al. A reassessment of the in-vitro activity of colistin sulphomethate sodium. J Antimicrob Chemother. 1997;39:255-60.
18. Reina R, Estenssoro E, Sáenz G, et al. Safety and efficacy of colistin in acinetobacter and pseudomonas infections: a prospective cohort study. Intensive Care Med. 2005;31:1058-65.
19. Michalopoulos AS, Tsiodras S, Rellos K, et al. Colistin treatment in patients with ICU-acquired infections caused by multi-resistant gram-negative bacteria: the renaissance of an old antibiotic. Clin Microbiol Infect. 2005;11:115-21.
20. Jain R, Murthy SI, Motukupally SR, Jain M. Use of topical colistin in multiple drug-resistant pseudomonas aeruginosa bacterial keratitis. Cornea. 2014 Sept;33(9):923-7.
21. Said DG, Elalfy MS, Gatzioufas Z, et al. Collagen cross-linking with photoactivated riboflavin (PACK-CXL) for the treatment of advanced infectious keratitis with corneal melting. Ophthalmology. 2014;121(7):1377-82.
22. Chan E, Snibson GR, Sullivan L. Treatment of infectious keratitis with riboflavin and ultraviolet-A irradiation. J Cataract Refract Surg. 2014 Nov;40:(11):1919-25.
23. Schier A, Greebal G, Attia H, et al. In vitro antimicrobial efficacy of riboflavin and ultraviolet light on staphylococcus aureus, methicillin-resistant staphylococcus aureus, and pseudomonas aeruginosa. J Refract Surg. 2009 Sep;25(9):799-802.
24. Tabibian D, Richoz O, Hafezi F. PACK-CXL: Corneal cross-linking for treatment of infectious keratitis. J Ophthalmic Vis Res. 2015 Jan-Mar;10(1):77-80.
25. Price MO, Tenkman LR, Schrier A, et al. Photoactivated riboflavin treatment of infectious keratitis using collagen cross-linking technology. J Refract Surg. 2012 Oct;28(10):706-13.
26. Wang F. UVA/riboflavin apoptosis in mouse cornea. Ophthalmologica. 2008;222:369-72.
27. Spoerl E, Wollensak G, Seller T. Increased resistance of the cross-linked cornea to enzyme degradation. Curr Eye Res. 2004;29:35-40.
28. Khan YA, Kashiwabuchi RT, Martins SA, et al. Riboflavin and ultraviolet light a therapy as an adjuvant treatment for medically refractive Acanthamoeba keratitis: report of 3 cases. Ophthalmology. 2011;118:321-31.
29. Makdoumi K, Mortensen J, Sorkhabi O, et al. UVA-riboflavin photochemical therapy of bacterial keratitis: a pilot study. Graefes Arch Clin Exp Ophthalmol. 2012;250:95-102.
30. Spoerl E, Mrochen M, Sliney D, et al. Safety of UVA-riboflavin cross-linking of the cornea. Cornea. 2007;26:385-9.
31 Khan YA, Kashiwabuchi RT, et al. Riboflavin and ultra-violet light A therapy as an adjuvant treatment for medically refractive Acanthamoeba keratitis; report of 3 cases. Ophthalmology. 2011;118:321-31.
32. Srinivasan M, Mascarenhas J, Rajaraman R, et al. The steroids for corneal ulcers trial (SCUT): secondary 12-month clinical outcomes of a randomized controlled trial. Am J Ophthalmol. 2014;157(2):327-33.
33. Srinivasan M, Mascarenhas J, Rajaraman R, et al. Corticosteroids for bacterial keratitis: The Steroids for Corneal Ulcers Trial (SCUT). Arch Ophthalmol. 2012;130(2):143-50.
34. McClintic SM, Prajna NV, Srinivasan M, et al. Visual outcomes in treated bacterial keratitis: four years of prospective follow-up. Invest Ophthalmol Vis Sci. 2014 May;55(5):2935-40.
35. Moss JM, Nguyen D, Liu YI, et al. Comparison of one-day versus one hour application of topical gatifloxacin in eliminating conjunctival bacterial flora. Ophthalmology. 2008 Nov;115(11):2013-6.
36. Ta CN, Egbert PR, Singh K, et al. Prospective randomized comparison of 3-day versus 1 hour preoperative ofloxacin prophylaxis for cataract surgery. Ophthalmology. 2002 Nov;109(11):2036-40.
37. Halachmi-Eyal O, Lang Y, Keness Y, Miron D. Perioperative topical moxifloxacin 0.55 and povidone-iodine 5.0% alone to reduce bacterial colonization in the conjunctival sac. J Cataract Refract Surg. 2009 Dec;35(12):2109-14.
38. Hsu J, Gerstenblith AT, Garg SJ, Vander JF. Conjunctival flora antibiotic resistance patterns after serial intravitreal injections without post-injection topical antibiotics. Am J Ophthalmol. 2014 Mar;157(3):514-8.
39. Auletto F. Where do we stand in the battle against resistant bacteria. Review of Cornea & Contact Lenses. 2013 Nov. Accessed December 15, 2015. http://www.reviewofcontactlenses.com/content/d/disease/c/44959/.
40. ESCRS Endophthalmitis Study Group. Prophylaxis of postoperative endophthalmitis following cataract surgery: results of the ESCRS multicenter study and identification of risk factors. J Cataract Refract Surg. 2007 Jun;33(6):978-88.
41. Shorstein NH, Winthrop KL, Kerinnton LJ. Decreased postoperative endophthalmitis rate after institution of intracameral antibiotics in a northern California eye department. J Cataract Refract Surg. 2013 Jan;39(1):8-14.
42. Montan PG, Wejde G, Setterquist H, et al. Prophylactic intracameral cefuroxime. Evaluation of safety and kinetics in cataract surgery. J Cataract Refract Surg. 2002 Jun;28(6):982-987.
43. Galloway MS. Intravitreal placement of antibiotic/steroid as substitute for postoperative drops after cataract surgery. The Annual ASCRS ASOA Symposium and Congress, April 25-29, 2014. Abstract.
44. Shaw J, Smith EF, Desai RU, et al. Can intraocular lenses

deliver antibiotics intracamerally? J Ocul Pharmacol Ther. 2010 Dec;26(6):587-9.
45. Kleinmman G, Apple DJ, Chew J, et al. Hydrophilic acrylic intraocular lens as a drug-delivery system: Pilot study. J Cataract Refract Surg. 2006 Apr;32(4):652-4.
46. Liptnitzi I, Bronshtein R, Ben Eliahu S, et al. Hydrophilic acrylic intraocular lens as a drug delivery system: Influence of the presoak time and comparison to intracameral injection. J Ocul Pharmacol Ther. 2013 May;29(4):414-8.
47. Shapiro A. In vitro activity of ACH-0139586, a novel isothiazoquinolone, moxifloxacin and gatifloxacin against clinical isolates, including methicillin and fluoroquinolone resistant. Invest Ophthalmol Vis Sci. 2012;53. ARVO e-abstract 6259.
48. Podos SD, Thanassi JA, Leggio M, Pucci MJ. Bactericidal activity of ACH-702 against nondividing and biofilm *staphylococci*. Antimicrob Agents Chemother. 2012 Jul;56(7):3812-8.
49. Pucci MJ, Podos SD, Thanassi JS, et al. In vitro and in vivo profiles of ACH-702, and isothiazoloquinolone, against bacterial pathogens. Antimicrob Agents Chemother. 2011 Jun;55(6):2860-71.
50. Chapin M, Tobaru A, Sandwick V. Leveraging Ex-US Deals. Review of Ophthalmology. 2014. Accessed December14, 2015. www.reviewofophthalmology.com/content/c/50833/.
51. Lee HK, Rafii MJ, Mann B, et al. Hyaluron-based ocular sustained delivery of moxifloxacin. Invest Ophthalmol Vis Sci. 2014 April;55:454.
52. Chee SP. Moxifloxacin punctum plug for sustained delivery. Ocul Pharmacol Ther. 2012 Aug;28(4):340-9.
53. Gao P, Nie X, Zou M, et al. Recent advances in materials for extended-release antibiotic delivery system. J Antibiot. 2011 Sep;64(9):625-34.
54. Hyatt AJ, Rajan MS, Burling K, et al. Release of vancomycin and gentamicin from a contact lens versus a fibrin coating applied to a contact lens. Invest Ophthalmol Vis Sci. 2012 Apr;53(4):1946-52.

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1. Which oral antibiotic has been shown to be effective in meibomian gland dysfunction management?
a. Azasite.
b. Ciprofloxacin.
c. Cefprozil.
d. Doxycycline.

2. What is a fundamental principle of prescribing antibiotics to manage anterior segment infections?
a. Avoid sub-lethal dosing.
b. Choose an antibiotic with antimicrobial efficacy against the suspected bacteria.
c. Prescribe the antibiotic for intermittent use.
d. a and b.

3. The indicated dosing frequency when using besifloxacin for bacterial conjunctivitis is:
a. QD.
b. BID.
c. TID.
d. QID.

4. Which antibiotic does *not* have a systemic equivalent?
a. Besifloxacin.
b. Azithromycin.
c. Moxifloxacin.
d. Ciprofloxacin.

5. Which of the following is the most common microbial keratitis?
a. Viral keratitis.
b. Fungal keratitis.
c. Bacterial keratitis.
d. *Acanthamoeba* keratitis.

6. Typically, when should systemic antibiotics be considered in bacterial keratitis management?
a. Marginal ulcers.
b. When corneal perforation is imminent.
c. When the infectious process has invaded the sclera.
d. b and c.

7. Fortified antibiotics are indicated for which of the following?
a. Recalcitrant MGD.
b. Central, large (>2mm) ulcers.
c. Marginal, small ulcers.
d. Corneal abrasions.

8. Which antibiotic contains a vehicle that increases the drug's retention time?
a. Azasite.
b. Vigamox.
c. Augmentin.
d. Ciloxan.

9. Which of the following is *not* an application of corneal crosslinking discussed in this article?
a. Slowing the progression of keratoconus.
b. Slowing the progression of keratoglobus.
c. Bacterial keratitis.
d. Slowing the progression of postoperative ectasia.

10. Riboflavin and UVA have been shown to be bactericidal against which of the following?
a. Gram-negative and gram-positive bacteria, including MRSA.
b. Gram-positive bacteria only.
c. Gram-negative bacteria only.
d. Gram-negative bacteria and gram-positive bacteria, not including MRSA.

11. In a recent study, topical colistin was found to be effective against which microbe?
a. *Pseudomonas aeruginosa*.
b. *Streptococcus*.
c. *Staphylococcus aureus*.
d. *Listeria*.

12. Which of the following is true regarding the 12-month SCUT follow-up study?
a. Adjunctive topical corticosteroids can improve the clinical outcomes of bacteria ulcers caused by *Nocardia* species.
b. Adjunctive topical corticosteroids may be associated with improved, long-term clinical outcomes for bacterial ulcers not caused by *Nocardia* species.
c. Adjunctive topical corticosteroids should be initiated for all corneal ulcers.
d. Adjunctive topical corticosteroids should be initiated for ulcers caused by *Nocardia* species.

13. Which of the following is true regarding the four-year SCUT follow-up study?
a. The visual acuity significantly changed between one year and four years post treatment.
b. The visual acuity did not significantly change between one year and four years post treatment.
c. a and b.
d. None of the above.

14. Which of the following is true regarding prophylaxis for infections with intravitreal injection?
a. Post-procedure use of antibiotics is preferred.
b. Pre-procedure use of povidone-iodine and post-procedure use of antibiotics are preferred.
c. Pre-procedure use of povidone-iodine is sufficient.
d. Pre-procedure use of antibiotics and

OSC QUIZ

post-procedure use of povidone-iodine is preferred.

15. Which of these is a promising dropless perioperative prophylaxis strategy?
a. Intracameral cefuroxime.
b. Intravitreal triamcinolone/moxifloxacin.
c. Both a and b.
d. None of the above.

16. The European Society of Cataract and Refractive Surgery's study provided evidence for the use of which of the following perioperative prophylaxis strategy?
a. Intraocular lenses presoaked with antibiotics.
b. Preoperative povidone-iodine.
c. Intravitreal antibiotic/steroid combination.
d. Intracameral antibiotics.

17. Corneal abrasions can be treated with which preservative-free fluoroquinolone?
a. Tobrex.
b. Besivance.
c. Vigamox.
d. Zylet.

18. What is the best choice for management of non-infected corneal abrasions?
a. Broad-spectrum antibiotics.
b. Narrow-spectrum antibiotics.
c. Fortified antibiotics.
d. Corneal crosslinking.

19. Which of the following is *false* regarding isothiazoquinolones?
a. They are in the quinolone family.
b. They target bacterial DNA replication enzymes.
c. They provide a distinct mechanism of action.
d. They have a lower antimicrobial efficacy than fluoroquinolones.

20. Which antibiotic is the first topical chlorofluoroquinolone developed solely for ophthalmic use?
a. Moxifloxacin.
b. Ciprofloxacin.
c. Besifloxacin.
d. Ciloxan.

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18.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
19.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
20.	Ⓐ	Ⓑ	Ⓒ	Ⓓ

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Tap Into the Big Picture at SECO 2016

This year's congress has a lot to offer novice and experienced optometrists alike.

By Jane Cole, Contributing Editor

SECO has long been known as the education destination. But this year, the congress revolves around a theme, "The Big Picture, Widen Your Perspective," which is designed to help you and your staff gain a greater perspective on how to implement the latest research and technology into your day-to-day practice.

This year's congress will be held from Feb. 24-28 in Atlanta. SECO 2016 will offer nearly 400 courses and a total of 173 CE credit hours, with a maximum of 35 CE credits available for optometrists.

"SECO is the go-to meeting for those who want the tools to tackle the challenges of today's health care demands," says Paul C. Ajamian, OD, SECO optometric education committee chair. "From groundbreaking sessions to custom-tailored teaching, SECO sets the stage for an unforgettable experience."

Some highlights of this year's congress you don't want to miss include:

Thursday, Feb. 25

• ***Pre- and Post-op Cataract Surgery, 2-4pm.*** During this new learning lab in the exhibit hall, Daryl Mann, OD, Jason Duncan, OD, and Nilou Soltanian, OD, will help you become proficient with pre-op and post-op cataract evaluations, including patient selection, IOL counseling and understanding traditional vs. laser surgery. During the lab, a variety of patients (one day, one week and one month post-surgery) will be available for you to examine to reinforce proper examination protocols. This course is for the novice as well as the experienced doctor.

Photo: SECO

Terry Kim, MD, spoke on cutting-edge cornea during a 2015 Special Session.

Friday, Feb. 26

• ***Understanding Alzheimer's, 7:45-8:45am.*** Leonard Messner, OD, will provide an overview of the pathophysiology and non-ocular and ocular manifestations of Alzheimer's disease. Special attention will be paid to OCT, low contrast acuity and visual motor dysfunction as biomarkers of disease activity and progression.

• ***The Sky's the Limit—Or is It?!, 9-11am.*** This special session will question the underlying assumptions about glaucoma that have been made for decades. It will also propose new mechanisms of disease pathophysiology and introduce new treatment options to help patients. In this exclusive SECO session, John Berdahl, MD, will update the audience on innovations in eye care, what is making news at the ASCRS meetings and special insights into his research with NASA.

• ***Answers about AREDS, 1:45-2:45pm.*** With the understanding that AMD is everywhere and doctors must have a working knowledge of nutritional therapy, this course will discuss AREDS1 from a historical perspective and AREDS2 from a current-day practical perspective to help you implement changes into practice. The course will be presented by Jeffry Gerson, OD.

• ***Heads Up! The Science Behind Concussions and Vision, 5-7pm.*** Christina Master, MD, and Michael Gallaway, OD, will discuss the pathophysiology of concussion injury and acute management strategies. Clinical assessment of the vestibular and oculomotor systems will be described along with approaches to rehabilitation patients with post-concussion vision deficits. Recent data on the prevalence and treatment of visual dysfunction in concussion will be presented as well.

Saturday, Feb. 27

• ***Fresh Look at Fields and OCTs, 9:15-11:15am.*** Nationally-respected expert Don Hood, PhD, will increase your understanding of glaucomatous damage and how to measure it using OCT and adaptive optics during this special session. You'll see the nature of glaucomatous damage to the macula through both visual fields and imaging results, as well as learn methods for improving the detection of glaucomatous damage.

• ***Secrets of an Oculoplastic Surgeon, 1:15-3:15pm.*** Byron Wilkes, MD, will cover the common diagnoses and management of a comprehensive oculoplastic and orbital surgery practice. Dr. Wilkes will describe common eyelid lesions and functional eyelid diagnoses such as entropion, ectropion, dermatochalasis and ptosis. Dr. Wilkes will also discuss cosmetic surgery in a comprehensive ophthalmology practice using pre- and post-op photos.

• ***Amniotic Membranes Learning Lab, 1:15-3:15pm.*** This two-hour wet lab is designed to give the clinician hands-on experience in placing amniotic membranes. Indications for clinical use and proper coding and billing will also be discussed. The course will be presented by Doug Devries, OD, and Dave Kading, OD.

• ***Beyond Ebola and HIV Update, 5-6pm, 6-7pm.*** Presented by infectious disease expert Robert Kalayjian, MD, these two courses will explore genetic and environmental factors that drive new and resurgent epidemics such as ebola, multidrug resistant pathogens and malaria. The benefits and controversies of vaccines in the control of such epidemics will also be discussed. Dr. Kalayjian will also present information on the Zika virus.

• ***Inside MS, 5-7pm.*** Dr. Messner will take the stage again to present this course, which will provide a comprehensive review of the neuro-ophthalmic manifestations of multiple sclerosis (MS), including optic neuritis, brainstem motility disorders, nystagmus and cranial neuropathies. Dr. Messner will also present the epidemiology and pathogenesis of MS, along with an overview of neuro-imaging and OCT findings.

For more information or to register, go to www.seco2016.com. ■

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SCHEDULE

SATURDAY APRIL 9TH

7:30am – 11:45am	REGISTRATION
9:30am – 11:30am	Workshop: Refractive and Cataract Comanagement
11:45am – 12:45pm	Contemporary Irregular Cornea Management Using Contact Lenses
12:45pm – 2:00pm	OCCRS Multi–Sponsor Lunch
2:00pm – 4:00pm	Keratoconus & Corneal Diseases: Corneal Cross linking and More
4:00pm – 4:30pm	Break
4:30pm – 6:30pm	Ocular Surface Disease Update

SUNDAY, APRIL 10TH

7:15am – 8:00am	Breakfast
8:00am – 9:00am	Refractive Surgery Treatment
9:00am – 10:00am	Femtosecond Laser Update
10:00am – 10:40am	Break
10:40am – 12:40pm	Cataract Surgery Update: Diagnosis and Management, and IOL Options

- The Optometric Cornea, Cataract and Refractive Society will sponsor its 13th annual education symposium, bringing together the most notable experts in the field of cornea, cataract and refractive technology to discuss evolving clinical innovations and management of ocular surface disease and other anterior segment complications.
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Eyeing a Dx of IOIS:

Presentation, Diagnosis and Treatment

When a patient presents with eyelid edema, proptosis and even diplopia, it's time to exclude, exclude, exclude—leading you to a diagnosis of orbital pseudotumor.

By Susan Yee, OD

A 29-year-old male was referred to the VA eye clinic for a red and painful left eye. He had noticed a burning sensation in his left eye 10 days earlier, which gradually worsened. His left eyelid became swollen one week after the onset of symptoms. He was diagnosed with conjunctivitis in the emergency department of a local hospital and was given Zymar (gatifloxacin 0.3% ophthalmic solution, Allergan) every six hours and told to follow up with an eye care specialist if the conjunctivitis did not improve. He had no previous history of injury or surgery to his eyes. There was a history of anisocoria and a fixed right pupil due to past traumatic brain injury (TBI); he also had a systemic history of dysarthria and vitamin D deficiency. He was not currently taking any medication and reported no known allergies.

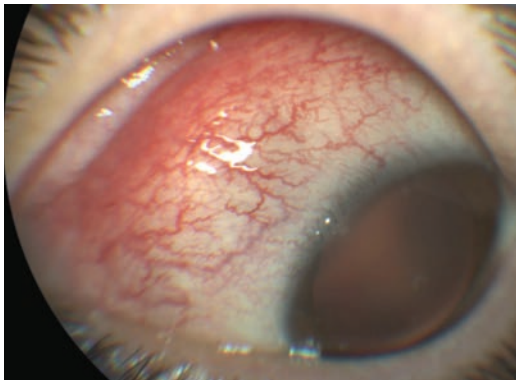

Fig. 1. Nasal and superonasal conjunctival injection.

Diagnostic Data

Uncorrected visual acuity was 20/20 OD and 20/40 OS with no pinhole improvement. Refraction was not attempted at the time. Vital signs were unremarkable. A fixed right pupil was detected with pupillary testing, but no reverse afferent pupillary defect was observed in the left eye. Restriction in upgaze was seen in the left eye during extraocular motility testing, and the patient reported seeing diplopia in upgaze. Visual fields were full and intact to finger confrontation in both eyes. The left conjunctiva was injected in all quadrants (*Figure 1*). Ptosis with mild eyelid edema was seen in the left eye. Retropulsion was equal in both eyes. No proptosis was observed in either eye. All other anterior and posterior segment findings were normal. There was no evidence of iritis, uveitis, vitritis, optic neuritis or pars planitis in either eye. Optic nerves were healthy and pink in color without pallor. Intraocular pressure (IOP) was 15mm Hg OD and 13mm Hg OS.

Given the painful and limited gaze findings, a tentative diagnosis of preseptal cellulitis of the left eye was made, and *stat* computed tomography (CT) of the orbit was ordered to rule out any orbital involvement, including orbital cellu-

Table 1. Differential Diagnosis[1-3]

IOIS	Orbital Cellulitis	Thyroid Eye
Severe pain that is worse on eye movement.	Pain is severe.	Pain is mild.
Usually unilateral, acute onset.	Unilateral, acute onset.	Commonly bilateral with asymmetry; gradual, subacute onset.
Vision is usually normal; can be affected early.	Vision is affected at late stage, unless fungal	Vision usually affected in later stage.
Ocular movement is restricted in field of inflamed muscle.	Ocular movement restricted.	Ocular movement restricted.
Ptosis and eyelid swelling.	Eyelid swelling.	Lid retraction and lag.
Imaging shows muscle enlargement and extension to orbital fat.	Imaging shows sinus disease, bony erosion and venous thrombosis.	Imaging shows muscle enlargement, tendons spared, no extension to orbital fat.
Rapid response to steroids.	Fever and elevated WBC present; history of sinus infections, dental problems and trauma.	Abnormal thyroid function or immunoglobulin studies.

litis and orbital abscess. The patient was started on Tobradex (tobramycin and dexamethasone ophthalmic ointment, Alcon) one drop QID for 10 days in the left eye for possible nonspecific conjunctivitis. He was also started on Augmentin (GlaxoSmithKline) 875mg BID for 10 days. The patient was instructed to sleep with his head elevated 10 to 20 degrees and to apply a cool compress on the left eye for five to 10 minutes twice daily. He was scheduled to return in three to five days for follow-up.

A radiologist at the VA medical center reviewed the *stat* CT of the orbit with contrast. The report stated there was a 9mm by 19mm ill-defined soft tissue mass in the superomedial orbit exerting mass effect on the adjacent globe, along with some diffuse scleral thickening and mild enlargement of the lacrimal gland (*Figure 2*). According to the radiologist, the presentation on CT scan was most indicative of orbital pseudotumor. Lymphoma could be considered in the appropriate clinical setting, while infection was less likely, according to the report.

We referred the patient to our ophthalmology department the same day for further evaluation. Ocular protrusion was measured at 14mm OD and 16mm OS at base of 88 using a Hertel exophthalmometer. All other clinical findings remained unchanged. Baseline blood tests were ordered, and mild leukocytosis was detected with CBC; otherwise, all lab results were negative and within normal limits.

Diagnosis

Based on the clinical presentation, orbital CT and lab results, the patient was diagnosed with orbital inflammation of the left eye by the ophthalmologist, most likely due to idiopathic orbital pseudotumor, also known as idiopathic orbital inflammatory syndrome (IOIS). Orbital cellulitis and thyroid eye disease are most often confused with IOIS, but in this case, diagnosis was not precluded by a misinterpretation of radiologic findings.[1-3]

Treatment and Follow-Up

The patient was started on oral prednisone 60mg daily, since the orbital inflammation was most likely due to orbital pseudotumor.

Other treatment options were presented to the patient, and he declined intravenous antibiotic therapy at the hospital because he had young children at home. Oral antibiotic therapy was not considered. A biopsy was recommended if the orbital mass persisted without resolution.

Two days after starting prednisone, the patient reported subjective overall improvement in his left eye. When he returned to ophthalmology for his two-day follow up, his uncorrected visual acuity was 20/20 OD, 20/30+2 OS with no pinhole improvement. He still had pain with eye movement, but symptoms of diplopia had improved. The patient's left eye still had limited upgaze and ptosis was present secondary to eyelid edema. The conjunctival injection showed slight improvement compared with its initial presentation. The patient was to continue taking 60mg prednisone daily and return to ophthalmology in one week.

Unfortunately, the patient missed his two subsequent appointments. When contacted regarding the condition of his left eye, he said it was doing well. The patient never returned to either the eye clinic or ophthalmology; but, when reviewing his records, we came across an encounter note by a radiologist who saw the patient 10 months later for a CT of the head. The note stated that the patient's right pupil was fixed and non-reactive, his left pupil was reactive and all eye movements were normal.

Discussion

IOIS is a diagnosis of exclusion.[1,4-7] In 1905, researchers described the condition as an "orbital mass clinically mistaken for a neoplasm that was histologically inflammatory."[1] IOIS is a benign, non-infectious and non-neoplastic clinical syndrome that displays a nonspecific inflammatory process.[1,4-6,8] It is an inflammation of the orbit with no known local or systemic etiology, and often occurs between the third and fifth decades of life, without any gender or race preferences. The condition makes up 5% to 8% of all orbital lesions and 16% of all cases of unilateral ptosis in adults.[1,4-7] IOIS occurs in 6% and 17% of the pediatric population; 45% these cases present bilaterally.[1,4-9] It is the third most common orbital disease behind Graves' disease and lymphoproliferative disorders (LPDs).[1,5,10]

Orbital pseudotumor is divided into four histopathological subtypes:

- The *granulomatous* form contains histiocyte infiltration and multinucleated giant cells.
- The *vasculitic* subtype requires a work-up for collagen vascular disease (Wegener's granulomatosis, polyarteritis nodosa).
- The *eosinophilic* form usually occurs when toxic granular proteins are released into the orbital connective tissue.
- The *sclerosing* form is a rare type that has histologic findings similar to other systemic fibroproliferative diseases such as retroperitoneal fibrosis. It is made mostly of dense fibrotic connective tissue with a few inflammatory infiltrates.[1,2,6,9] Sclerosing-associated orbital inflammation, however, is now considered to be a separate disease entity.[10]

While the etiology is unknown, three possible causes exist: upper respiratory infections, immune-mediated and trauma.[1,2,4,5,11] Recent literature suggests IgG4-associated orbital inflammation may also cause the condition.[8,11,12]

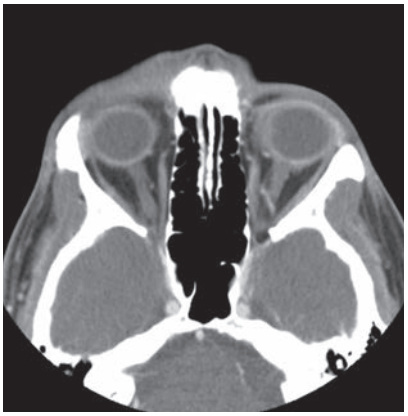

Fig. 2. CT of orbit, ear and fossa without contrast.

IOIS is usually unilateral, and its acute onset may occur within hours or days.[1,4-6,13] The onset can also be subacute (weeks), chronic (months) or recurrent, the last of which occurs more often in cooler months.[1,13] Signs and symptoms of IOIS include:

- Diplopia, pain and photophobia
- Proptosis and eyelid edema
- Conjunctival chemosis and injection in the affected eye[1,7]
- Lack of fever
- Ocular motility restrictions and cranial nerve palsies (III, IV, V1/V2, VI)
- Palpable orbital mass and lacrimal gland enlargement

Less common signs and symptoms include uveitis, elevated IOP, optic nerve swelling/atrophy, retinal edema, choroidal folds, hyperopic shift, posterior scleritis and decrease or loss of vision.[1,4-6,9,10,13,14]

Diagnostic Imaging

Magnetic resonance imaging (MRI) with contrast and CT are the ideal evaluation tools for orbital pseudotumor.[1,4,8,13] The images will show enlarged muscles and tendons, as well as inflammatory infiltrates.[1,4]

Hematologic work-up should include:

- Erythrocyte sedimentation rate (ESR)
- Complete blood count (CBC)
- Blood urea nitrogen (BUN)
- Creatinine and Fasting blood sugar (FBS)
- Angiotensin-converting enzyme (ACE)
- Serum protein electrophoresis (SPEP) and Anti-neutrophil cytoplasmic antibody (ANCA)
- Anti-double stranded DNA (anti-ds DNA)
- Electrolytes and a rapid plasma reagin test[2,6]

Biopsy is usually not indicated unless steroid treatment yields a minimal response, imaging studies show persistent abnormalities, or if the patient presents with progressive neurological deficits.[3,8,15]

Treatment

IOIS is primarily treated with oral corticosteroids.[1,3-5,8,9,13,15] The standard treatment regimen, which typically elicits a quick amelioration of IOIS symptoms, is prednisone 60mg to 100mg daily for two weeks, then a slow taper over weeks to months.[3,6,9,13,16] Pain and proptosis may resolve quickly—in as little as 24 to 48 hours.[3]

Radiation therapy is an alternative treatment option if a patient is unable to tolerate steroid treatment, or is steroid resistant.

Immunosuppressant agents such as methotrexate, cyclophosphamide, azathioprine, cyclosporine and mycophenolate have also been used as treatments for IOIS with some documented success.[1-6,13,15,17] Rituximab, a monoclonal antibody for treatment of B-cell lymphomas, chronic lymphocytic leukemia and rheumatoid arthritis, is emerging as an additional treatment option for IgG4-associated orbital inflamma-

tion, according to recent studies.[8,12,18] Rituximab appears to be effective in treating patients with recurring orbital inflammation and those who were treated unsuccessfully with steroids and immunosuppressants.[8,12,18]

Conclusion

Because IOIS is an idiopathic inflammation of the orbit, it is a diagnosis of exclusion. Imaging studies are a key tool for evaluating and diagnosing this syndrome. Blood work will help rule out any potential systemic conditions. Prednisone remains the primary mode of treatment for IOIS Radiation, immunosuppressants and rituximab are also treatments to consider for this ocular condition. Follow the steps to an appropriate diagnosis and implement the right treatments to yield positive outcomes for your patient's ocular health. ■

Dr. Yee is a staff optometrist at the W. G. Bill Hefner VA Medical Center. Her clinical interest is in ocular disease.

1. Zerilli TC, Burke CL. Orbital pseudotumor after an upper respiratory infection: a comprehensive review. Optometry. 2010;81:638-46.
2. Espinoza G. Orbital inflammation pseudotumor: etiology, differential diagnosis and management. Curr Rheumatol Rep. 2010;12:443-7.
3. Jacobs D, Galetta S. Diagnosis and management of orbital pseudotumor. Curr Opin in Ophthalmol. 2002;13(6):347-51.
4. Guerriero S, Leo ED, Piscitelli D, et al. Orbital pseudotumor in a child: diagnostic implications and treatment strategies. Clin Exp Med. 2011;11:61-3.
5. Deaner J. September 2014 Wills eye resident case series-diagnosis and discussion. Review of Ophthalmology. 2014;21(9):67-9.
6. Swamy BN, McCluskey P, Nemet A, et al. Idiopathic orbital inflammatory syndrome: clinical features and treatment outcomes. Br J Ophthalmol. 2007;91:1667-70.
7. Cooney NL. Orbital pseudotumor. Int J Emerg Med. 2009;2:263.
8. Teke TA, Kaman A, Metin O, et al. Idiopathic orbital inflammation in a child mimicking orbital cellulitis. Clinical Pediatrics. 2015:1-3.
9. Mulvihill A, Smith CR, Buncic JR. Pediatric orbital pseudotumor presenting as a painless orbital and periocular mass. Canadian Journal of Ophthalmology. 2004;39(1):77-9.
10. Pakdaman M, Sepahdari AR, Elkhamary SM. Orbital inflammatory disease: pictorial review and differential diagnosis. World Journal of Radiology. 2014;6(4):106-15.
11. Oles K, Szczepanski W, Skladzien J, et al. IgG4-related inflammatory orbital pseudotumors-a retrospective case series. Folia Neuropathologica. 2015;53(2):111-20.
12. Carbone T, Montes RA, Andrade B, et al. Orbital pseudotumor: uncommon initial presentation of IgG4-related disease. Case Reports in Rheumatology. 2015;1-4.
13. Muqtasid AK, Ali G, Ishrat HD, et al. Orbital pseudotumor. Oman J Ophthalmol. 2009;2(2):96-9.
14. Turkoglu R, Balak N. Atypical presentation of orbital pseudotumor with visual loss as an initial manifestation. J Clin Neurol. 2011;7(1):50-2.
15. Matthiesen C, Bogardus CJ, Thompson SJ, et al. The efficacy of radiotherapy in the treatment of orbital pseudotumor. Int J Radiation Oncology Biol Phys. 2011;79(5):1486-1502.
16. Shen T, Chen J, Lin J, et al. Concomitant idiopathic orbital inflammatory pseudotumor and thyroid-associated ophthalmopathy. Journal of Craniofacial Surgery. 2015;26(6):479-81.
17. Falcini F, Simonini G, Resti M, Cimaz R. Recurrent orbital pain and diplopia in a 12 year old boy. Ann Rheum Dis. 2002;61:93-4.
18. Suhler EB, Lim LL, Beardsley RM, et al. Rituximab therapy for refractory orbital inflammation: results of a phase ½, dose-ranging, randomized clinical trial. JAMA Ophthalmol. 2014;132(5):572-8.
19. Chen T, Figueira E, Lau, OCF, McKelvie PA, Smee RI, Dawes LC, Agar A, Wilcsek G, Francis LC. Successful "Medical" Orbital Decompression with Adjunctive Rituximab for Severe Visual Loss in IgG4-Related Orbital Inflammatory Disease with Orbital Myositis. Ophthal Plast Reconstr Surg. 2014; 30(5): 122-125.
20. Hiraga A, Kuwabara S. Recurrent Alternation Orbital Inflammation. Journal of the Neurological Sciences. 2015;357:288-9.

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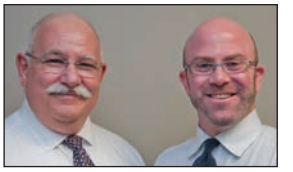

Growing Pains

When measuring pediatric refractive error, subjective is out, objective is in. But when is the child ready to wear glasses? **By Marc B. Taub, OD, MS, and Paul Harris, OD**

To prescribe or not to prescribe? That is the question! Every clinician who treats children on a regular basis frequently faces this dilemma. In the case of most adults, you can simply ask and trust their responses as to whether a new prescription, or a change in their existing one, improves their vision. But for young children, you must rely mostly on objective testing to confirm what the parents, teachers, pediatricians and, yes, the children themselves tell you. Here, we present two cases to shine a spotlight on the gray areas in prescribing for young children.

Case 1

A four-year-old presented for their first exam. The parent reported that the patient had failed a school vision screening, but no documentation was provided to support this. Visual acuity was 20/30 OD, OS, and OU at distance and near with Lea symbols, a shape-based chart. Stereopsis testing showed 30 seconds with the Wirt circles, and the near point of convergence showed a break at 2cm with a recovery at 4cm all three times the test was done. Cover test was orthophoric at distance and near. Amplitude of accommodation was 12 diopters with both the right and left eyes, which was a bit less than expected. Refractive data was:

- *Student's retinoscopy:* +2.25 -1.00x015, +2.25 -1.00x160
- *Cycloplegic retinoscopy:* +3.00 -1.00x010, +2.75 -1.00x160
- *Doctor's retinoscopy:* +1.50 -1.00x015, +1.25 -1.00x160
- *Final Rx:* +1.00 -1.00x015, +0.75 -1.00x160.

The acuity with any of the above was 20/30 OD, OS, OU, at distance and near. What would you do if this child were sitting in your chair?

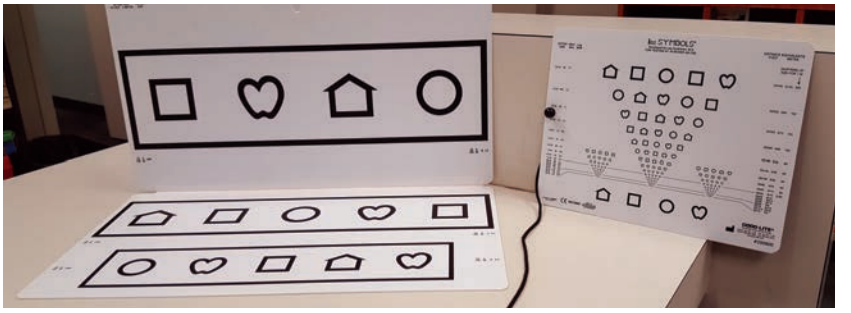

Fig. 1. LEA symbol charts for distance and near.

Table 1. Some Refractive Errors are Amblyogenic Concerns

Isometropia		Anisometropia	
Myopia	Greater than 3.50D	Myopia	Greater than 3.00D
Hyperopia	Greater than 2.00D	Hyperopia	Greater than 1.00D
Astigmatism	Greater than 1.50D	Astigmatism	Greater than 1.00D

Case 2

A five-year-old patient presented for their first examination with the parent reporting that their child failed a school vision screening, but as in the first case, no documentation was provided to support the claim. Visual acuity was 20/50 OD, OS, OU at distance and near with Lea symbols. Testing of stereopsis, near point of convergence and amplitude of accommodation were attempted, but the child did not follow instructions or reply in a way that gave specific clinical data. Cover test was orthophoric at distance and near. The refractive data was as follows:

- *Student's retinoscopy:* +1.50 -1.00x180, +1.50 -1.00x170
- *Doctor's retinoscopy:* +1.50 -1.00x180, +125 -1.00x180
- *Final retinoscopy:* +1.00 -1.00x180, +1.00 -1.00x180
- *Final Rx:* +0.50 -1.00x180, +0.50 -1.00x180

Acuity for each combination was 20/20 OD, OS, OU, at distance and near. What would you do?

Should I Prescribe?

Little evidence-based medicine exists to guide clinicians. The guidelines for refractive amblyopia do not really help us in either case. High refractive error, or that which would be considered an amblyogenic factor, is shown in Table 1. Since both of our pediatric patients' refractive errors fell below the levels of worry for hyperopia and astig-

matism, we had to rely on our own decision-making process.

In case 1, given that the amplitude of accommodation was low and the cover test showed orthophoria at near, a prescription was warranted. The patient was trial-framed in the office and the increase in visual attention to books was instantaneous. You might be thinking we were wrong to prescribe, as acuity did not improve. We caution not to have too much faith in visual acuity in a younger patient. Instead, make a decision based on what you see taking place in the examination room. Since we both fall into the category of "less is more," we attempt to provide the least amount of plus or minus that allows clear, single binocular vision. Since the lower amount of hyperopia led to the same acuities and visual behavior, we prescribed that amount.

When the patient returned several months later, the parent was unsure if the glasses were helping but reported that they were worn constantly and that the she did not take them off and lose them, as many children do! The visual acuity was 20/25 OD, OS, and OU at distance and near. We will see the child for her yearly examination next year.

In case 2, given the improvement in visual acuity and the orthophoric posture on cover test, we once again decided to prescribe glasses for full-time use. Could we have held off, given the visual acuity needs of the child? Yes. At this age, in-school near materials contain larger print and fewer words per page, and writing on a board is quite large. We could have waited until the child was in first grade; however, given the change in acuity observed in-office, we gave the final Rx above. The parent reported good compliance when the child was seen several months later—we typically schedule these types of patients back this soon. While scratched and bent several times, the glasses were well tolerated.

While we decided to prescribe for both these children, arguments can be made to not do so. When evaluating your youngest patients, you must use a mixture of objective and subjective testing if the child is cooperating and you think the child is providing quality responses. Aside from the red-flag amblyogenic refractive errors, judgment lies with the clinician. Keep in mind that once you make the choice to give or hold back a prescription, you can always change your mind at the follow-up visit once more data has been collected. Learn to embrace the art and science of prescribing! ■

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Dry Eye Debacle

A pediatric patient presented with a mysterious case of ocular surface disease. What is the reason? **Edited by Joseph P. Shovlin, OD**

Q I have a seven-year-old white male who presented with a rather unusual dry eye symptoms. His cornea and conjunctiva stained in both eyes with lissamine green. Standard treatments for dry eye have failed. Though I've considered the typical masqueraders, I have failed to identify a cause. Any thoughts on what this is?

A "In all patients, including children, it is critical to obtain a review of systems, including topical and oral medications to rule out any systemic causes of ocular surface disease," says Melissa Barnett, OD, of the UC Davis Eye Center in California. She recommends the patient undergo a general physical exam including laboratory work when indicated; he should also be asked about lifestyle activities, including electronic device use, that could contribute.

Jeffrey J. Walline, OD, PhD, associate dean for research at Ohio State University, agrees, pointing out a number of atypical reasons for a presentation like this in children and adolescents. "Juvenile rheumatoid arthritis may be considered as a relatively common cause of dry eye in children," he says. "Does the child appear nutritionally healthy? A vitamin A deficiency could lead to dry eye issues. Have you considered diabetes? Although the symptoms of diabetes are relatively obvious, the appropriate questions may not have been asked previously."

Use of some medicines like antihistamines, video game use, and sleeping with the eyes open are also potential causes. The sleeping habit in particular is likely to cause a linear pattern of staining, Dr. Walline notes, adding that most of these can be determined by recording a thorough patient history.

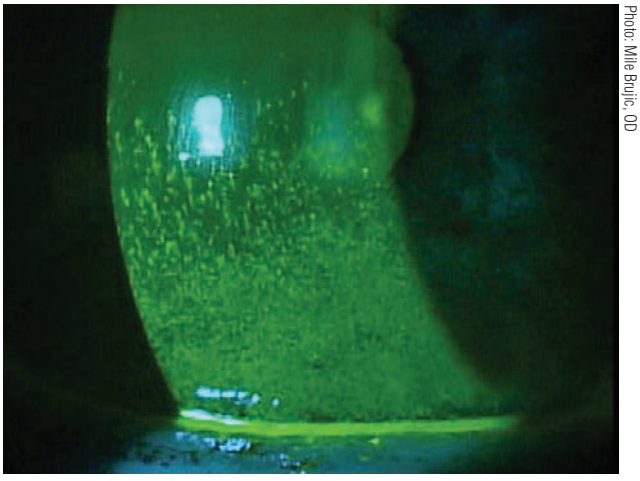


Photo: Mile Brujic, OD

Significant corneal staining in a patient with rheumatoid arthritis.

Mile Brujic, OD, suggests examining the patient's physical features for further signs. "Make sure to assess for any anatomical anomalies, specifically looking for loose lids or incomplete blinks," he says. "Observe the patient to make sure there is not an ocular allergy that may be causing irritation to the eye from itching." Compulsive eye rubbing is a clear sign of a possible allergy.

Additionally, Dr. Brujic suggests ruling out the possibility of mucus fishing syndrome, and paying "particular attention to the lash margin to [eliminate] blepharitis, which at times can be aggressive in young children."

Dr. Barnett agrees, adding that meibomian gland expression is helpful in evaluating the quality of the meibomian glands, and examination of the palpebral conjunctiva, bulbar conjunctiva and cornea can indicate presence of allergies. She suggests implementing dietary supplementation with omega-3 and omega-6 fatty acids and reducing consumption of fried or fatty foods. Fitting the patient with scleral lenses is also an option if the practitioner deems them necessary.

On the medical side, more atypical possibilities like Riley-Day syndrome and celiac disease should also be ruled out. These can be identified via corneal anesthesia with lack of tear reflex present and an evaluation of serum vitamin A levels, respectively. ■

He's Got Some Nerve

Our patient's moderate vision blur developed over several months.

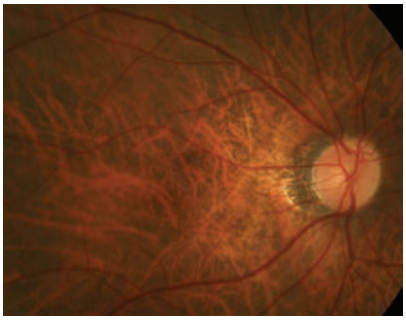
By Mark T. Dunbar, OD, and Leslie Small, OD

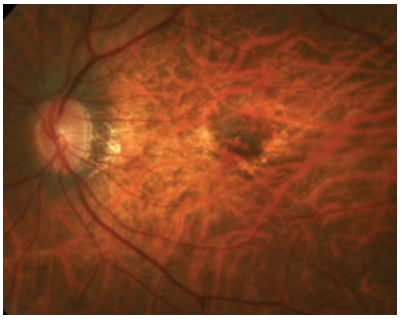
A 44-year-old male presented with a chief complaint of moderate blurred vision in his left eye over several months and requested an updated prescription. He reported that he has needed glasses from a young age. His last eye exam was six months prior. His medical history was unremarkable.

On examination, his best-corrected visual acuity was 20/20 OD and 20/60 OS. The right eye measured -8.50 +0.50 x 175 and the left eye was -9.25 DS.

Extraocular motility testing was normal. Confrontation visual fields were full to careful finger counting OU. Pupils were equally round and reactive, without a relative afferent pupillary defect. The anterior segment was unremarkable. His intraocular pressure measured 17mm Hg OU.

Dilated fundus exam revealed obliquely inserted optic nerves with peripapillary atrophy in both eyes. Images of the right and left eye are available for review (*Figures 1 and 2*). Additionally, SD-OCT and fluorescein angiography was obtained (*Figure 3*). A late frame from the FA is available for review (*Figure 4*).





Figs. 1 and 2. Right and left eye of our patient—note the changes in the posterior pole of the left eye.

Take the Quiz

1. How would you characterize the SD-OCT findings documented in his left eye?
a. Cystoid macular edema.
b. Vitelliform lesion.
c. Choroidal neovascularization type 2.
d. Central serous retinopathy.

2. What additional testing would be helpful in establishing a diagnosis?
a. Visual field.
b. Visual evoked potential.
c. Standardized ultrasound.
d. Multifocal electroretinography.

3. What is the correct diagnosis for this patient?
a. Wet macular degeneration.
b. Macular telangiectasia.
c. Choroidal rupture.
d. Myopic choroidal neovascularization.

4. How should this patient likely be treated?
a. Laser photocoagulation.
b. Photodynamic therapy.
c. Anti-VEGF injection.
d. Combination photodynamic therapy and anti-VEGF therapy.

Diagnosis

Our patient has developed choroidal neovascularization (CNV) as a result of his high myopia. The diagnosis of pathological myopia does not have a universal definition, but is most commonly described as an eye with an axial length greater than 26.5mm and/or at least -6D of refractive error accompanied by degenerative changes of the sclera, choroid and retinal pigment epithelium (RPE) specific to axial elongation.[1-3] These degenerative changes can include a tessellated fundus, posterior staphyloma, RPE atrophy, Fuchs' spots (macular degenerations due to myopia), lacquer cracks (breaks in Bruch's membrane), peripheral retinal thinning (lattice) and detachment, foveoschisis and CNV.[1,3,4] Pathologic myopia is also associated with increased incidence of cataract and optic nerve anomalies.[4]

Pathologic myopic CNV (mCNV) affects 5.2% to 11.3% of pathological myopic patients and is the leading cause of CNV in patients younger than 50 years of age.[1,3,5] mCNV is one of the most visually threatening complications of pathologic myopia, as it diminishes central vision.[1]

When examining a patient with

high myopia, look for predisposing factors for the development of mCNV. These include patchy chorioretinal atrophy over diffuse atrophy, lacquer cracks and posterior staphyloma. On clinical examination, mCNV presents as a small (< 1 disc area), flat, grayish subretinal membrane. A hyperpigmented border is a sign of chronicity.[1,3] Additionally, up to 30% of people with mCNV in one eye will develop mCNV in the other eye, and thus close monitoring of the non-involved eye is indicated.[1]

Optical coherence tomography (OCT) is often enough to confirm and monitor mCNV. The CNV net in mCNV is typically type 2, meaning it is subretinal and located largely above the RPE. Because it is above the RPE a grayish membrane can often be visualized on clinical exam. This is in contrast to age-related macular degeneration, where the CNV net is most commonly sub-RPE (type 1 CNV) and the features of the CNV are not visible.

In our patient, we are able to see the dark circular features of the CNV. This is confirmed on the SD-OCT where a higher reflective lesion is seen above the RPE. Anterior to that, cystoid macular edema has developed.

Fluorescein angiography (FA) for mCNV displays early hyperfluorescence with minimal late leakage, as was the case with our patient.

Treatment

Our patient received an anti-vascular endothelial growth factor (anti-VEGF) intravitreal injection of Avastin (bevacizumab, Genentech). There are several theories as to why anti-VEGF therapy is effective. The most commonly reported is that a break in Bruch's membrane (sometimes called lacquer cracks) induces cellular changes in the RPE that release VEGF.[2] Additionally, *in vitro* studies have shown that the mechanical stretch of RPE cells up-regulates pro-angiogenic factors, including VEGF.[2,4] The REPAIR study, the largest multicenter study for mCNV treated with Lucentis (ranibizumab, Genentech), found that the average improvement of BCVA at 12 months was 13.8 letters.[6] Similar findings were seen with Eylea (aflibercept, Regeneron) and Avastin.[7,8]

Our patient's vision improved and stabilized at 20/30 after three intravitreal Avastin injections. Unfortunately, four years later fluid started to accumulate and vision declined to 20/70. Despite repeated anti-VEGF injections, the vision continued to decline to 4/200 in the left eye. Thankfully, the right has had no significant pathologic myopia complications and remains 20/20. ■

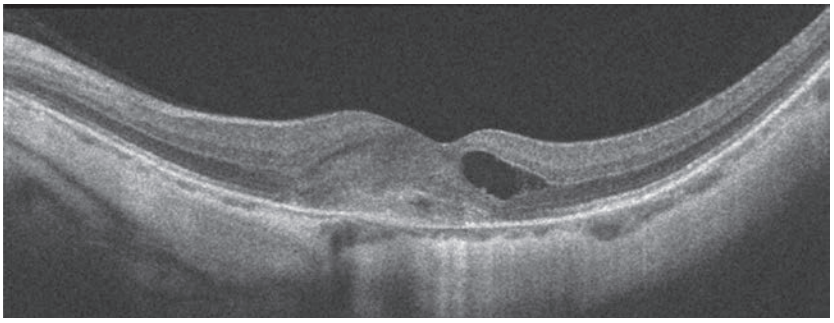


Fig. 3. SD-OCT of the left eye. Can you determine the cause of this presentation?

This case was written by Leslie Small, OD, optometric resident at Bascom Palmer Eye Institute.

1. Chan N, Teo K, Cheung C. Epidemiology and diagnosis of myopic choroidal neovascularization in Asia. Eye Contact Lens 2016;42:48-55.
2. Zhang Y, Han Q, Ru Y, et al. Anti-VEGF treatment for myopic choroid neovascularization: from molecular characterization to update on clinical application. Drug Des Devel Ther. 2015;9:3413-21.
3. Silva R. Myopic maculopathy: a review. Ophthalmologica. 2012;228:197-213.
4. Cho B, Shin J, Yu H. Complications of Pathologic Myopia. Eye Contact Lens. 2016;42:9-15.
5. Munk M, Ruckert R, Zinkernagel M, et al. The role of anti-VEGF agents in myopic choroidal neovascularization: Current standards and future outlook. Expert Opin Biol Ther. 2015.
6. Tufail A, Narendran N, Patel P, et al. Ranibizumab in myopic choroidal neovascularization: the 12-month results from the REPAIR study. Ophthalmology. 2013;120:1944-5.e1.
7. Pece A, Milani P, Monteleone C, et al. A randomized trial of intravitreal bevacizumab vs. ranibizumab for myopic CNV. Graefes Arch Clin Exp Ophthalmol. 2015;253:1867-72.
8. Ikuno Y, Ohno-Matsui K, Wong T, et al. Intravitreal Aflibercept injection in patients with myopic choroidal neovascularization: the MYRROR study. Ophthalmology 2015;122:1220-7.

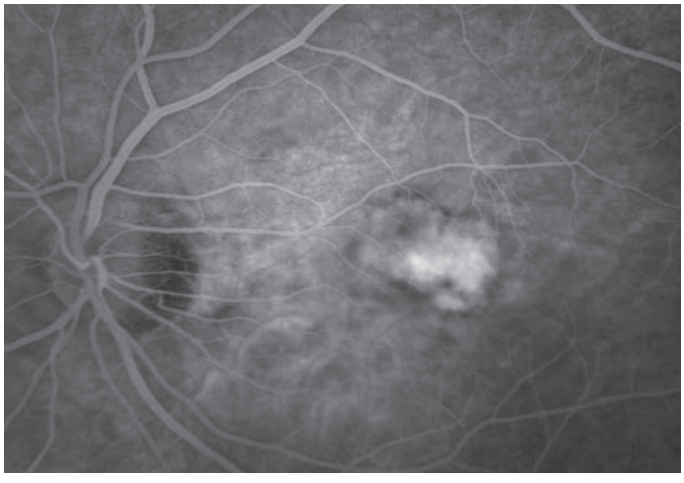


Fig. 4. Late frame of the fluorescein angiogram.

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Sorting Through Med Changes

Medication changes precipitated by insurers complicate the assessment of patients with glaucoma. **By James L. Fanelli, OD**

In 2010, a 38-year-old Caucasian female presented to the office as a new patient with complaints related to visual changes consistent with early presbyopia. She noted that both her distance and near vision had changed gradually over the prior three years, with complaints of strain while performing near tasks.

At this visit, her medications included estradiol QD and Wellbutrin SR QD, and she reported no medication allergies. She reported a family history of glaucoma in her mother, who apparently began drops when she was in her 50s, as reported by the patient. Entering visual acuities through hyperopic astigmatic correction were 20/25- OD and OS.

Examination

A moderate increase in hyperopia was noted on refraction. Best corrected visual acuities were 20/20 OU. Pupils were equal, round and responsive to light and accommodation. We noted no afferent pupillary defect. Extraocular movements were full in all positions of gaze.

A slit lamp examination of her anterior segments was essentially unremarkable. Her angles as estimated at the slit lamp were open grade 2 OU, with no sectoral narrowing. Intraocular pressures (IOP) were 27mm Hg OD and 26mm Hg OS at 10:25am. CCT measured 641µm OD and 635µm OS.

Through dilated pupils, her crystalline lenses were clear in both eyes. Her anterior vitreous was also clear in both eyes. The posterior segment was essentially unremarkable. Specifically, stereoscopic evaluation of her optic discs demonstrated healthy, plush, well perfused neuroretinal rims bilaterally, with relatively small cups estimated to be 0.30 x 0.30 OU. The discs were of normal sizes. The retinal vasculature and macular examinations were all normal, as was the posterior vitreous. Her peripheral retinal evaluation was normal, save for some mild cystoid in each eye.

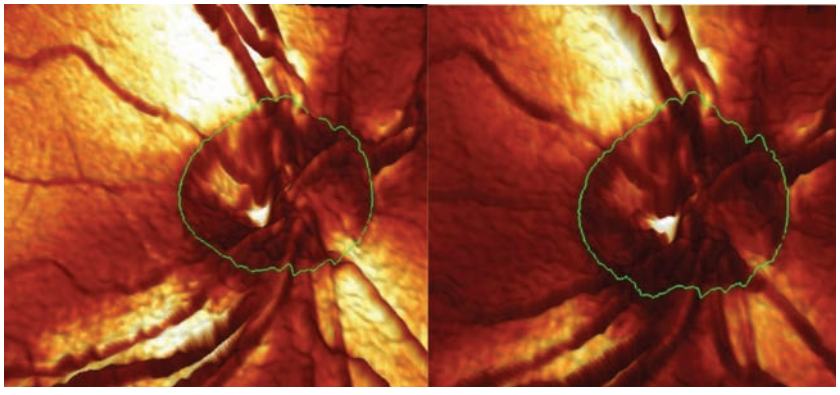


Fig. 1. This image shows the contours of the right optic nerve. Note the change in the neuroretinal rim in the inferotemporal aspect between the baseline (left) and the conversion image (right).

Monitoring

She was determined to be a glaucoma suspect based on the family history of glaucoma, as well as IOP in the mid-to-upper 20s. As such, baseline HRT 3 images and stereo optic disc photos were obtained as baseline. Given her relatively thick pachs and essentially healthy neuroretinal rims, her risk of converting to frank glaucoma was deemed low. She was scheduled for a yearly follow up, pending the results of a baseline threshold field and repeat IOP measurements after three months. She returned as requested for the field study, at which time her IOP was 26mm Hg OU at noon. SAP fields were normal in both eyes with good reliability indices. She was subsequently scheduled for repeat fields, pressure, HRT 3 imaging and optic nerve photos in one year.

She was compliant with scheduled visits yearly. When seen in August 2013, her IOP had risen to 32mm Hg OD and 27mm Hg OS. Her visual field test results were normal, and HRT 3 imaging demonstrated no changes from baseline. Fields performed at this visit were HEP Flicker Defined Form (FDF) threshold fields. Baseline OCTs were performed this day as well, demonstrating a normal

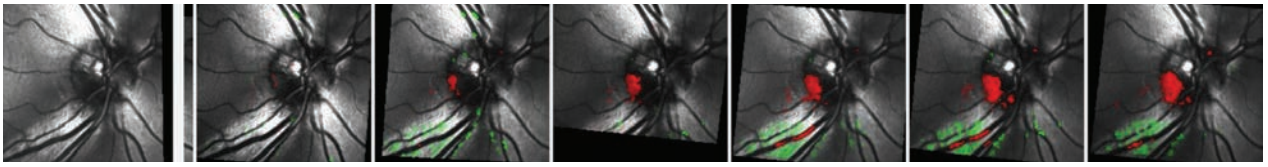


Fig. 2. Progressive structural changes to the inferotemporal neuroretinal rim in the right eye.

RNFL scan. Given the increase in IOP, a follow up was scheduled in six months. At this follow up visit, IOP measured 33mm Hg OD and 26mm Hg OS. HRT 3 imaging demonstrated a small area of change in the inferotemporal sector of the neuroretinal rim as compared with the baseline. HEP FDF fields were stable. Physical examination of the optic nerves demonstrated no apparent change. She was scheduled for a follow up visit in six months.

In October 2014, she presented with IOPs of 32mm Hg OD and 28mm Hg OS. HEP FDF fields demonstrated a slight change in the superior arcuate area in the right eye, and a completely stable field in the left. The HRT 3 imaging demonstrated further progression of the change in the inferotemporal sector of the right nerve and no change in the left. The RNFL circle scan was stable as compared with the baseline. A slight continued change was noted in the neuroretinal rim appearance (*Figure 1*).

Discussion

It appears that both structural and functional changes are occurring in the patient's right eye, whereas the left is remaining stable. We each have our own threshold-to-treat levels, but the evidence at this point is strong that the right eye is beginning to convert. Primarily based upon the patient's relatively young age, I chose to defer treatment, on the outside chance that the changes were merely artifactual. While I didn't necessarily believe this to be the case, I was not yet comfortable committing this patient to a lifetime of treatment. As such, I explained my findings to the patient, couching the conversation in the context of 'appearing to develop glaucoma, but let's be 110% certain before putting you on medications.' Generally, patients are reluctant to begin medications without a compelling reason.

Follow Up

When the patient returned six months later, IOPs remained stable in both eyes, the FDF field remained stable, as did the OCT, but the HRT 3 imaging continued to demonstrate progression (*Figure 2)*. At this point, I was convinced that I had enough evidence to warrant initiating therapy in the right eye. Accordingly, the patient was medicated with Travatan Z (travoprost, Alcon) HS in the right eye only. Her post-treatment IOP was 20mm Hg OD and 25mm Hg OS at 2pm two weeks after initiating therapy. One month following, her IOP was 21mm Hg OD and 26mm Hg OS. Reassured, it appears as though we are achieving a consistent reduction in IOP in the medicated right eye.

In August 2015, her IOP was measured at 20mm Hg OD and 24mm Hg OS. FDF fields demonstrated a slight increase in the field defect previously seen. The OCT remained stable. However, the HRT showed further change in the suspect area of the right optic nerve.

The possibility exists that the continued progression of the structural inferotemporal defect in her right eye may simply be a result of the time lapse from initiation of therapy until the HRT 3 image obtained in August 2015. But, it may also indicate that, although IOP seems to be responding nicely to Travatan Z, we might not necessarily be achieving enough of an IOP reduction to stave off further damage. As is always the case in managing glaucoma, it is imperative that we are certain that things are stable, both structurally and functionally, before we can reassure the patient that they are, in fact, stable. While I was comfortable in thinking that we were on the right track, I was not convinced that the situation was completely stable.

Of course, the benchmark in determining stability is the analysis of structural and functional testing, using whatever specific instruments you are comfortable with or have access to. Not surprisingly, I did not make any changes to her therapy at the August 2015 visit, but did ask her to return in December for repeat testing.

Medications

About one week after the August visit, the patient called the office mentioning that, due to changes in insurance coverage, her branded medication would have a much higher co-pay, and requesting a change to generic latanoprost. Understanding the reality that medications can be cost prohibitive and, subsequently, compliance prohibitive, I OK'd the change to latanoprost. However, this was an inopportune time to change medications, as I was still in the process of

determining whether she was stable. I also had not been given ample time to determine what her IOP variances were post treatment.

Much would hinge on the December 2015 visit: if all was stable, structurally, functionally and with her IOP, then it would be reasonably prudent to continue with the generic medication and move forward with regularly scheduled visit. Conversely, if all was not stable, would it be because the new medication is not controlling IOP as well as the branded medication, or because the disease progressed despite reasonable IOP control?

Unfortunately, there appears to be continued progression of the structural defect in the December 2015 scan (*Figure 2*). And unfortunately, I am back to the same position I was a few months ago in assessing the stability of the situation. It does not appear to be stable. But is she unstable because of the new medication, or would the disease have progressed anyway? As of yet, I don't have the answer to that crucial question.

This case highlights the potential can of worms that may be opened when insurance companies, through financial strong-arming, dictate which medications a patient can take.

But this case highlights the potential can of worms that may be opened when insurance companies, through financial strong-arming, dictate which medications a patient (reasonably and affordably) can take, independent of the clinical judgment of the prescribing physician. Just as I was sorting this case out (and many glaucoma cases take a rather lengthy time to ascertain stability), a wrench is thrown into the gears, requiring further evaluation.

As expected, the patient has been scheduled for yet another structural and functional series of tests to determine, yet still, stability.

Wouldn't it have simply been better to just leave the patient and the doctor alone? I think so. ■

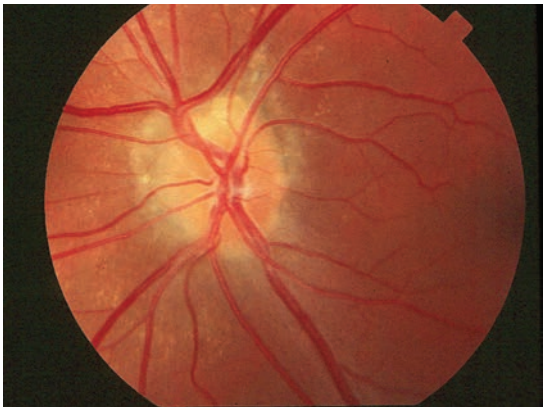

IOP, Drusen and Occlusion

How do we handle these conundrums?

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

Over many years of presenting continuing education courses, we have had the great fortune to meet thousands of our colleagues. We have always fielded questions from the audience and, when the same inquiries come up in several different audiences, we often incorporate them into future lectures. There are two questions involving intraocular pressure (IOP) that we have heard numerous times. The first is whether or not to lower IOP in eyes with optic disc drusen and visual field loss to prevent further neuronal compromise and progression of visual defects. The second is whether or not to lower IOP in ocular hypertensive eyes to prevent a possible retinal vascular occlusion.

In this month's column, we attempt to shed scientific light on these two common conundrums.



This fundus image demonstrates an eye with superficial optic disc drusen.

Disc Drusen

Optic disc drusen (ODD) represent retained hyaline bodies in the optic nerve. Typically, patients with ODD present and remain without symptoms, with the finding disclosed only upon routine ocular evaluation. In some instances, the condition can present with mildly decreased visual acuity and visual field defects.[1-5] An afferent pupillary defect may be noted if the condition is both significant and unilateral or asymmetric.[2]

The classic appearance of ODD involves unilaterally or bilaterally elevated optic discs with irregular or "scalloped" margins, a small or nonexistent cup and unusual vascular branching patterns (i.e., marked bifurcations and trifurcations) that arise from a central vessel core. There may be refractile hyaline deposits visible on the surface of the disc or in the peripapillary area, making the diagnosis clear. In younger patients, the disc elevation tends to be more pronounced and the drusen less calcified and discrete, making them less visible ophthalmoscopically—complicating diagnosis.

Within the optic nerve, the hyaline bodies are confined anterior to the lamina cribrosa and can compress and compromise the nerve fibers and vascular supply, leading to visual field defects and disc hemorrhages.[2-6] Along with slowly developing optic atrophy in extreme cases and possible venous occlusion, disruption of the juxtapapillary tissue can result in choroidal neovascular membrane formation, leading to subretinal hemorrhage, with its attendant complications.[7-9]

While ODD is typically considered a benign condition, it can lead to modest visual compromise and, in rare instances, devastating vision loss.[10-12] Although the condition is typically slow to advance, there is a risk of progressive vision loss or visual field loss over time.

A retrospective analysis of eyes with ODD, both with and without concurrent elevated IOP, reported visual field defects in 91% of ocular hypertensive eyes with ODD and 67% of normotensive ODD eyes, clearly showing that eyes with ODD and concurrent ocular hypertension had a greater prevalence of visual field loss.[10] The researchers concluded that patients with elevated IOP and ODD should remain under close surveillance for disease progression and be treated appropriately to prevent additional visual field loss.[10] Two other small reports also advocated IOP reduction in eyes with ODD and concurrently elevated IOP.[12,13]

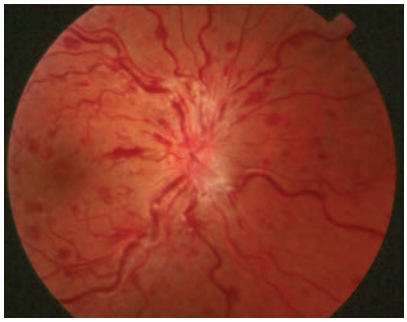
This approach seems reasonable, in that the anomalous nature of the optic discs precludes accurate assessment for glaucoma, and pre-existing retinal nerve fiber layer (RNFL) and visual field loss from ODD can mask damage that may occur from elevated IOP. However, it is unknown if lowering IOP in these cases actually reduces the risk of progression of visual field loss.

Should any eye with significant ODD develop elevated IOP, consider offering the patient prophylactic pressure reduction. In the absence of elevated IOP, there is no evidence that IOP reduction will have any effect on preventing visual morbidity.[10] There are no controlled clinical studies that show a benefit to lowering IOP in any eyes with ODD.

Retinal Vein Occlusion

The etiology of central retinal vein occlusion (CRVO) is thrombotic obstruction of the central retinal vein as it constricts through the lamina cribrosa. This may involve abnormal blood flow or blood constituents, atherosclerosis, vessel anomalies or a combination of these factors. Essentially, properties of blood and the vein itself act in concert to cause thrombus formation with subsequent impedance of venous blood flow from the retina.[14,15]

There are numerous ways that a thrombus forms within the central retinal vein. Blood flow, combined with vessel wall abnormalities, can stimulate vein thrombosis. Additionally, changes in blood constituents, such as hypercoagulability states, elevated viscosity and systemic states of decreased thrombolysis promote thrombus formation. External factors, such as papilledema (causing increased pressure in the optic nerve sheath), may cause further compression and



This fundus image shows an eye with central retinal vein occlusion.

contribute to occlusion.[14,15] Potentially, elevated IOP could cause impedance of blood flow through the retinal veins, subsequently promoting thrombus formation and occlusion. Investigators note that CRVO and hemi-central retinal vein occlusion have a significant association with glaucoma and ocular hypertension; however, they also note that, paradoxically, few patients had high IOP in the eye with the vascular occlusion.[16] In fact, IOP elevation was more likely to occur in the fellow, uninvolved eye.[16] An old adage advocates treating elevated IOP if, for no other reason, to prevent a retinal vascular occlusion. However, it would seem that this practice would negate much of what we have learned from the Ocular Hypertension Treatment Study (OHTS) regarding lowering IOP in ocular hypertensive eyes to prevent glaucoma formation. Do we really want to lower IOP in every ocular hypertensive eye due to fear of retinal vascular occlusion (RVO)?

The most definitive answer to the question of prophylaxis against RVO comes from OHTS. Researchers included 1,636 ocular hypertensive participants—with a mean follow-up of 9.1 years—who had been randomized either to prophylactic IOP reduction or close observation. In a sub-analysis, they noted that 26 RVOs occurred in 23 participants, 15 in the observation group and eight in the medication group. They saw that the 10-year cumulative incidence of RVO was 2.1% in the observation group with untreated ocular hypertension and 1.4% in the medication group. Although the incidence of RVO was higher in the observation group than the medication group, this difference did not attain statistical significance.[17] Based upon this evidence, we cannot justify recommending that ocular hypertension be treated to prevent against RVO. In fact, the 10-year incidence of RVO in ocular hypertensive eyes is really quite low. ■

1. Friedman A, Gartner S, Modi S. Drusen of the optic disc: a retrospective study in cadaver eyes. Br J Ophthalmol. 1975;59(8):413-21.
2. Rosenberg M, Savino P, Glaser J. A clinical analysis of pseudopapilledema: I, population, laterality, acuity, refractive error, ophthalmoscopic characteristics, and coincident disese. Arch Ophthalmol. 1979;97(1):65-70.
3. Katz B, Pomeranz H. Visual field defects and retinal nerve fiber layer defects in eyes with buried optic nerve drusen. Am J Ophthalmol. 2006;141(2):248-53.
4. Lee A, Zimmerman M. The rate of visual field loss in optic nerve head drusen. Am J Ophthalmol. 2005;139(6):1062-6.
5. Purvin V, King R, Kawasaki A, Yee R. Anterior ischemic optic neuropathy in eyes with optic disc drusen. Arch Ophthalmol 2004;122(1):48-53.
6. Wilkins J, Pomeranz H. Visual manifestations of visible and buried optic disc drusen. J Neuroophthalmol. 2004;24(2):125-9.
7. Brown S, Del Monte M. Choroidal neovascular membrane associated with optic nerve head drusen in a child. Am J Ophthalmol. 1996;121(2):215-7.
8. Diduszyn J, Quillen D, Cantore W, Gardner T. Optic disk drusen, peripapillary choroidal neovascularization and POEMS syndrome. Am J Ophthalmol. 2002;133(2):275-6.
9. Romero J, Sowka J, Shechtman D. Hemorrhagic complications of optic disc drusen and available treatment options. Optometry. 2008;79(9):496-500.
10. Grippo TM, Shihadeh WA, Schargus M, et al. Optic nerve head drusen and visual field loss in normotensive and hypertensive eyes. J Glaucoma. 2008;17(2):100-4.
11. Gili Manzanaro P, Yangüela Rodilla J, Rodríguez Caravaca G.,et al. Decreased visual acuity from optic disc drusen. Arch Soc Esp Oftalmol. 2010;85(2):64-9.
12. Morris R, Ellerbrock J, Hamp A, et al. Advanced visual field loss secondary to optic nerve head drusen: case report and literature review. Optometry. 2009;80(2):83-100.
13. Spalding J. Visual-field loss with optic nerve drusen and ocular hypertension: a case report. Optometry. 2002;73(1):24-32.
14. Turello M, Pasca S, Daminato R, et al. Retinal vein occlusion: evaluation of "classic" and "emerging" risk factors and treatment. J Thromb Thrombolysis. 2009 Aug 11. [Epub ahead of print].
15. Yau J, Lee P, Wong T, et al. Retinal vein occlusion: an approach to diagnosis, systemic risk factors and management. Intern Med J. 2008;38(12):904-10.
16. Hayreh S, Zimmerman M, Beri M, Podhajsky P. Intraocular pressure abnormalities associated with central and hemicentral retinal vein occlusion. Ophthalmology. 2004;111(1):133-41.
17. Barnett E, Fantin A, Wilson B, et al. The incidence of retinal vein occlusion in the ocular hypertension treatment study. Ophthalmology. 2010;117(3):484-8.

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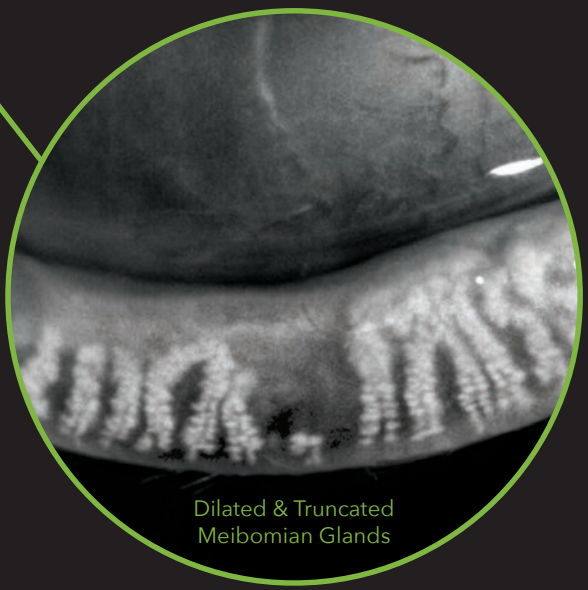

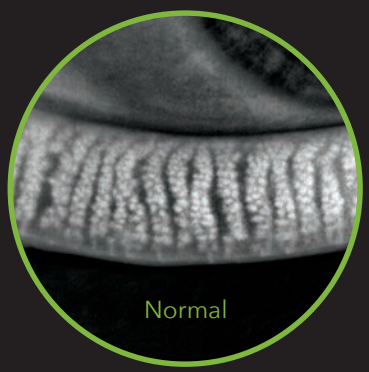

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Fantastic Voyage

3D visualization of live surgery immerses viewers in the retina during vitrectomies.

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

The majority of surgical advancements tend to be subtle and relatively inconspicuous to both patients and their optometrists. One recent advancement, on the other hand, is as big and obvious as it gets. 3D technology in the surgical suite is really straight out of the movies.

Stereoscopic high-definition surgical visualization systems are not brand new in medicine, but they are now starting to permeate various areas of eye surgery. They have been more widely used in cataract and glaucoma surgeries in the last several years, but as this month's Surgical Minute video shows, there are pioneering applications in retina surgery as well. This is not a trivial barrier to cross, as retina surgery is arguably the most delicate ocular surgery out there.

The system uses a three dimensional camera attached to the surgical microscope, and a high-resolution plasma television is placed at the end of the bed. The surgeon and support staff can use 3D glasses to watch the surgery in real time with enhanced stereopsis.

Benefits

Support staff who can see the surgeon's viewpoint can also better anticipate how to help. This video illustrates how a surgeon can successfully perform even the most complex and delicate of retinal surgeries, such as vitrectomy and membrane peel in an eye with proliferative retinopathy. Complicated steps, such as silicone oil tamponade and bimanual manipulation, can been seen in this video.

Anyone in the surgical suite wearing 3D glasses will be able to appreciate the stereopsis and the depth of field that the surgeon's seeing.

For the surgeon, a 3D heads-up display provides significant improvements to traditional surgery. It allows surgeons better visual and ergonomic comfort, as they do not have to bend over and fixate through a microscope. It can also provide enhanced depth of field, leading to more precise surgeries.

Future Advancements

Developing heads-up technologies will provide even more significant surgical refinement, as researchers are testing the use of real-time OCT and other ocular imaging that can be displayed on the screen simultaneously or overlaid on the real-time image. This will give surgeons potentially endless data displayed in their surgical view.

Three dimensional real-time imaging also represents an innovative new platform for education. Surgeons and support staff in training are able to fully appreciate the surgical procedure through the surgeon's view. New surgeons in training can also be evaluated and coached by peripheral mentors.

But the educational opportunities don't end in the OR. Watching three dimensional surgeries affords optometrists a better understanding of techniques and in vivo anatomy. It also reinforces the complexity and delicate nature of ocular surgery. Some surgeons even find this technology beneficial for educating patients about ocular surgery.

3D surgery represents a significant departure from the standardized methods of imaging ocular surgery, so it may come as no surprise that adoption may be slow. Yet, as this technology continues to evolve, we can expect its growth in popularity for surgeons, and better outcomes for patients. ■

To see a narrated video of this procedure, visit www.reviewofoptometry.com, or scan the QR code.

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Practice Management

Tighter EHR Integration

Optometrists can now look forward to more connectivity built into Topcon devices. The company plans to introduce ImageNet Connect, the first product from a new collaboration with EHR software company ifa systems; Topcon recently acquired 50.1% of ifa.

ImageNet Connect is software that connects to all Topcon devices plus various generic ophthalmic devices and systems used in clinics, such as practice management and hospital information systems, says Topcon.

ImageNet Connect is ICD-10 compliant and provides improved patient and workflow efficiency, according to the company.

The product will be made available this spring.

Visit www.topcon.co.jp/en.

Surgery Comanagement Resources

A new educational website may help optometrists interested in increasing their surgical comanagement skills. Quantel Medical's new website educates practitioners on the benefits of using yellow wavelength light during ophthalmic surgeries and promotes the company's 577nm micropulse laser therapy. It also highlights its applications in treating retinal disease.

The website contains studies, presentations and published literature pertaining to the safety and efficacy of micropulse therapy for various ophthalmic applications, according to Quantel.

Visit www.retina-yellow-laser-therapy.com.

Contact Lenses

Specialty Lenses

The Alden Optical line of contact lens products, acquired by Bausch + Lomb in January, provides a greater selection of custom lenses to offer eye care practitioners. Several types of specialty lenses, according to the company, are now available:

- Zenlens, a miniscleral.
- Novakone lenses for keratoconus.
- The Astera multifocal toric lens.

Bausch + Lomb also sells the C-Vue brand contact lenses, licensed by Unilens, which includes aspheric, multifocal and toric options. The company will combine its existing GP contact lenses with the Alden lenses under the new name Bausch + Lomb Specialty Vision Products.

Visit www.bausch.com/our-products.

Toric Soft Lens

CooperVision now offers a new monthly replacement silicone hydrogel lens for astigmatism correction.

The Biofinity XR toric offers a combination of high oxygen permeability and all-day comfort to patients who have both high prescriptions and astigmatism, according to the company.

The new toric lens incorporates a similar uniform horizontal ISO thickness and optimized ballast band as CooperVision's other Biofinity toric lens version, making it an easy-to-fit, stable toric lens with excellent visual acuity, the company says.

The lens will be available in sphere powers from +10.00D to -10.00D (0.50D steps after +/-6.00D), with cylinder powers from -2.75 to -5.75 (0.50 steps) and an axis of 5 degrees to 180 degrees in 5-degree steps, and +8.50D to +10.00D with cylinder powers from -0.75 to -2.25 (0.50 steps) and axis of 5 degrees to 180 degrees in 5-degree steps.

Visit www.coopervision.com/practitioner.

Contact Lens Care

Saline Solution

Optometrists now have a new contact lens rinsing solution to offer their patients. Menicon America's LacriPure offers patients a new alternative to rinsing with tap water. A unit-dose, nonpreserved saline for rinsing contact lenses and lens cases, it is indicated for use with both soft and GP lenses, and is also an approved scleral lens insertion solution, according to Menicon. LacriPure's vials are appropriately sized for all scleral lens diameters and offer single-use bottles to prevent contamination, according to the company. LacriPure is packaged as a convenient seven-week supply, according to Menicon.

Visit store.meniconamerica.com.

February 2016

■ **19-21.** *32nd Annual Palm Beach Winter Seminar.* Hilton West Palm Beach, Florida. Hosted by: Palm Beach County Optometric Association. CE hours: 20+. To register, email PBWinterSeminar@gmail.com or go to www.pbcoa.org.

■ **20-27.** *AEA Cruises Eastern Caribbean Optometric Cruise Seminar.* Aboard NCL Escape, Miami. Hosted by: AEA Cruises. CE hours: 10. To register, email Marge McGrath at aeacruises@aol.com, call (888) 638-6009 or go to www.optometriccruiseseminars.com.

■ **21.** *ICO Winter CE Program.* Illinois College of Optometry, Chicago. Hosted by: Illinois College of Optometry. CE hours: 6. To register, email Elizabeth Grantner at continuinged@ico.edu, call (312) 949-7426 or go to www.ico.edu/alumni/continuing-education.

■ **21.** *Glaucoma Pearls.* Marshall B. Ketchum University, Fullerton, CA. Hosted by: Marshall B. Ketchum University. Key faculty: George Comer. CE hours: 8. To register, email Antoinette Smith at ce@ketchum.edu, call (714) 449-7495 or go to www.ketchum.edu/index.php/ce.

■ **22-23.** *AFOS/SECO 2016.* The Ritz Carlton & Georgia World Conference Center, Atlanta. Hosted by: Armed Forces Optometric Society & SECO. Key faculty: Federal Service Chiefs (Army, Navy, Air Force, VA and IHS) and leading optometric educators. CE hours: 58. To register, email Lindsay Wright at execdir@afos2020.org, call (720) 442-8209 or go to www.afos2020.org.

■ **24-28.** *SECO 2016.* Georgia World Congress Center, Atlanta. Hosted by: SECO International. Key faculty: John Berdahl, Donald Hood, Leonard Messner, Christine Master, Whitney Hauser, Kim Reed. CE hours:175 total, maximum per OD: 35. To register, email Elizabeth Taylor DeMayo at etaylor@secostaff.com, call (770) 451-8206 or go to www.seco2016.com.

■ **25-27**. *MOA Winter Educational Symposium.* Huntley Lodge, Big Sky, MT. Hosted by: Montana Optometric Association. Key faculty: Andrew Morgenstern, Maynard Pohl. CE hours: 13. To register, email Sue Weingartner at sweingartner@rmsmanagement.com, or go to www.mteyes.com.

■ **25-27.** *Third Party/Practice Management Seminar.* Embassy Suites, Portland Airport, Portland, OR. Hosted by: Oregon Optometric Physicians Association. Key faculty: John McGreal, Elizabeth Cottle, Steve Farebrother, Ronald Guerra, Shelly Sneed. CE hours: 15 total, 13 per OD. To register, email Lynne Olson at lynne@oregonoptometry.org, call (800) 922-2045 or go to www.oregonoptometry.org.

■ **28.** *OptoWest South Newport Beach.* Newport Beach Marriott Hotel and Spa, Newport Beach, CA. Hosted by: California Optometric Association. Key faculty: Leo Semes, Todd Severin. CE hours: 12 total, 6 per OD and 6 per staff member. To register, email Sarah Harbin at sharbin@coavision.org, call (916) 266-5022 or go to www.coavision.org.

■ **28.** *IOA Winter CE Series.* Tinley Park Convention Center, Tinley Park, IL. Hosted by: Illinois Optometric Association. Key faculty: Mark Dunbar. CE hours: 6 regular or TQ. To register, email Charlene Marsh at ioabb@ioaweb.org, call (217) 525-8012 or go to www.ioaweb.org.

■ **28-March 4.** *30th Annual Eye Ski Conference.* The Lodge at Mountain Village, Park City, UT. Hosted by: Timothy Kime and James Fanelli. Key faculty: Joe Pizzimenti, Alan Berman, Leonard Messner, James Fanelli. CE hours: 20. To register, email Timothy Kime at tandbkime@bex.net, call (419) 475-6181 or go to www.EyeSkiUtah.com.

■ **29-March 1.** *COVD at SECO.* Omni Hotel at CNN Center, Atlanta. Hosted by: College of Optometrists in Vision Development. Key faculty: Carl Hillier. CE Hours: 13. To register, email penny@covd.org, or go to www.covd.org.

March 2016

■ **3-7.** *VT/Visual Dysfunctions.* 2080 Appleby Line Ste. E6, Burlington, Ontario, Canada. Hosted by: OEP Foundation. Key faculty: Steen Aalberg. CE hours: 35. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org/oepf_calendar.

■ **4-12.** *Tropical CE–Tahiti 2016.* Sofitel Mo'orea Resort and InterContinental Bora Bora Resort and Spa, Mo'orea and Bora Bora, French Polynesia. Hosted by: Tropical CE. Key faculty: Paul Ajamian, Maynard Pohl. CE hours: 20. To register, email Stuart Autry at sautry@TropicalCE.com, call (281) 808-5763 or go to www.TropicalCE.com.

■ **5.** *AZ-AAO Chapter Annual Spring Meeting 2016.* Midwestern University Arizona College of Optometry, Glendale, AZ. Hosted by: American Academy of Optometry Arizona Chapter. CE hours: 6. To register, email Carla Engelke at arizona.aaopt@gmail.com or go to www.aaopt.org/AZChapter.

■ **5-6.** *Borish Symposium.* Bloomington, IN. Host: IU School of Optometry. CE hours: 16. To register, email Cheryl Oldfield at coldfiel@indiana.edu, call (812) 856-3502 or go to www.opt.indiana.edu/ce/seminars.htm.

■ **11.** *ICO Resident Grand Rounds.* Illinois College of Optometry, Chicago. Hosted by: Illinois College of Optometry. CE hours: 4. To register, email Elizabeth Grantner at continuinged@ico.edu, call (312) 949-7426 or go to www.ico.edu/alumni/continuing-education.

■ **12-13.** *Ocular Disease: Part II.* Illinois College of Optometry, Fullerton, CA. Hosted by: Illinois College of Optometry. Key faculty: George Comer, David Sendrowski, Judy Tong. CE hours: 17. To register, email Antoinette Smith at ce@ketchum.edu, call (714) 449-7495 or go to www.ketchum.edu/index.php/ce.

■ **13.** *ICO Winter/Spring CE Program.* Illinois College of Optometry, Chicago. Hosted by: Illinois College of Optometry. CE hours: 6. To register, email Elizabeth Grantner at continuinged@ico.edu, call (312) 949-7426 or go to www.ico.edu/alumni/continuing-education.

■ **17-20.** *VT/Strabismus and Amblyopia.* OEP National Education Center, Timonium, MD. Hosted by: OEP Foundation. Key faculty: Robert A. Hohendorf. CE hours: 28. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org/oepf_calendar. ■

■ **17-22.** *Symposium on Ocular Disease.* Crowne Plaza Hotel, Tyson's Corner, VA. Hosted by: PSS EyeCare. Key faculty: Ron Melton, Randall Thomas, Mile Brujic, William Jones, Elliot Kirstein, Deepak Gupta. CE hours: 18. To register, email Sonia Kumari at education@psseyecare.com, call (203) 415-3087 or go to www.psseyecare.com.

■ **18.** *Binocular Vision and Pediatrics Forum.* Ohio State University College of Optometry, Columbus, Ohio. Hosted by: Ohio State University College of Optometry. Key faculty: Suzanne Wickum. CE hours: 7. To register, email Catherine McDaniel at mcdaniel.547@osu.edu, call (614)688-1425 or go to http://optometry.osu.edu/CE/BVPforum.cfm.

■ **18-20.** *Primary Eye Care Update.* UAB School of Optometry, Birmingham, AL. Hosted by: UAB School of Optometry. CE hours: 18. To register, email Amanda Kachler at uabsoce@uab.edu, call (205) 934-5701 or go to www.uab.edu/optometry/ce.

■ **20.** *Cornea Symposium.* The Colonnade Hotel, Boston. Hosted by: New England College of Optometry. CE hours: 7. To register, email Tony Cavallerano at cavalleranot@neco.edu, call (617) 587-5687 or go to www.neco.edu/academics/continuing-education.

■ **31-Apr. 4.** *Art + Science of Optometric Care.* South Kent Vision Center, Grand Rapids, MI. Hosted by: OEP Foundation. Key faculty: Robert A. Hohendorf. CE hours: 35. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org/oepf_calendar.

April 2016

■ **1.** *ICO Resident Grand Rounds.* Illinois College of Optometry, Chicago. Hosted by: Illinois College of Optometry. CE hours: 4. To register, email Elizabeth Grantner at continuinged@ico.edu, call (312) 949-7426 or go to www.ico.edu/alumni/continuing-education.

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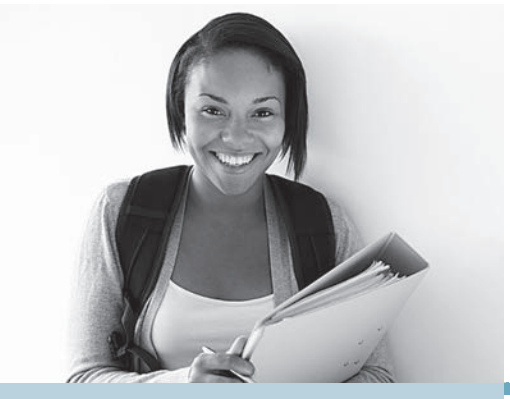

About Rick

Rick Bay served as the publisher of The *Review* Group since 1991.

To those who worked for him, he was a leader whose essence was based in a fierce and boundless loyalty.

To those in the industry and the professions he served, he will be remembered for his unique array of skills and for his dedication to exceeding the expectations of his customers, making many of them fast friends.

Scholarships are awarded to advance the education of students in both ***Optometry*** and ***Ophthalmology***, and are chosen by their school based on qualities that embody Rick's commitment to the profession, including integrity, compassion, partnership and dedication to the greater good.

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Diagnostic **Quiz**

From Bad to Worse

By Andrew S. Gurwood, OD

History

A 66-year-old Caucasian male presented to the emergency department with a chief complaint of lost vision in the right eye. He explained that he woke up with poor vision three days prior but couldn't get anyone to take him to the hospital. As his vision worsened and it became clear he could no longer function, he called the police, who brought him to the emergency department.

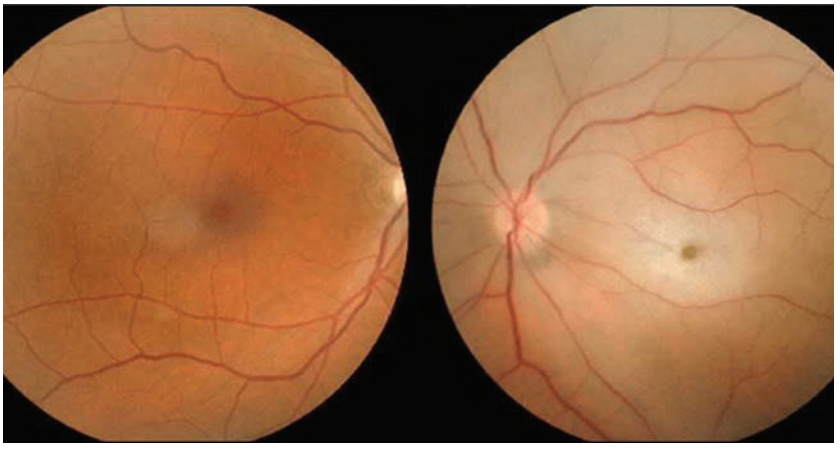
His systemic history was positive for hypertension. His ocular history was remarkable for strabismic amblyopia and corrective muscle surgery in his left eye.

He also recounted that the vision in his left eye was habitually poor since childhood, because of a lazy, crossed eye.

He denied using any medications and reported no known allergies.

Diagnostic Data

His best uncorrected entering visual acuity was no light perception in his right eye and 20/400 OS at distance and near. Pupil testing uncovered a grade IV afferent defect in the right eye. Extraocular muscle movements were full and unrestricted in both eyes with orthophoric position. Confrontation fields were full in all fields of gaze, in the left eye. Slit lamp examination revealed normal and healthy anterior segment structures with no evidence of iris neovascularization in the left eye, with both anterior chambers observed as deep and quiet.



This 66-year-old patient presented to the emergency department with vision loss in the right eye. Can this image combined with his medical history help diagnose him?

Intraocular pressures measured 18mm Hg OU. The pertinent dilated fundus findings are demonstrated in the photograph.

Your Diagnosis

Does this case require additional tests? What does this patient's history tell you about his likely diagnosis? How would you manage this patient? To find out, visit www.reviewofoptometry.com. ■

Retina Quiz Answers *(from page 112):* 1) c; 2) c; 3) d; 4) c.

Next Month in the Mag

In March, *Review of Optometry* will focus on diagnostic skills and techniques. Topics include:

- *OCT Technology: What is Its Role in Optometric Practices?*
- *Pupillary Testing: Implications for Diagnosis*
- *Dilation Dilemma: Why Aren't ODs Dilating Routinely? When Should They?*
- *Optometric Study Center — Automated Perimetry: Visual Field Deficits in Glaucoma and Beyond* (earn 2 CE credits)
- *Essential Procedures: How to Perform a B-Scan Ultrasound*

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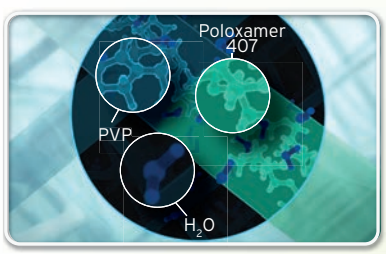

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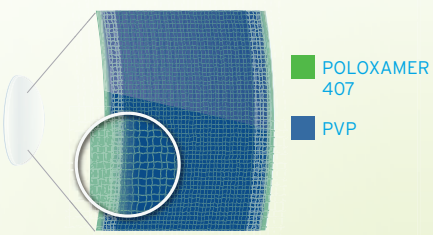

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REFERENCE: 1. Multiple-Packaged Lenses Comparison, Tyler's Quarterly – Professional Edition, September 2013 **2**. Twenty-two subjects participated in a randomized, double masked, contralateral eye study to evaluate water loss of Biotrue ONEday, 1-Day Acuvue Moist, 1-Day Acuvue TruEye contact lenses. After 4,8,12, and 16 hours of wear, lenses were removed and immediately weighed (wet weight). The lenses were then completely dried and reweighed (dry wet). The percent water loss was then calculated for each lens from the wet and dry weights.

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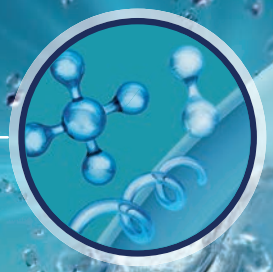

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Reference: 1. Wolffsohn J, Hunt O, Chowdhury A. Objective clinical performance of 'comfort-enhanced' daily disposable soft contact lenses. *Cont Lens Anterior Eye.* 2010;33(2):88-92.

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