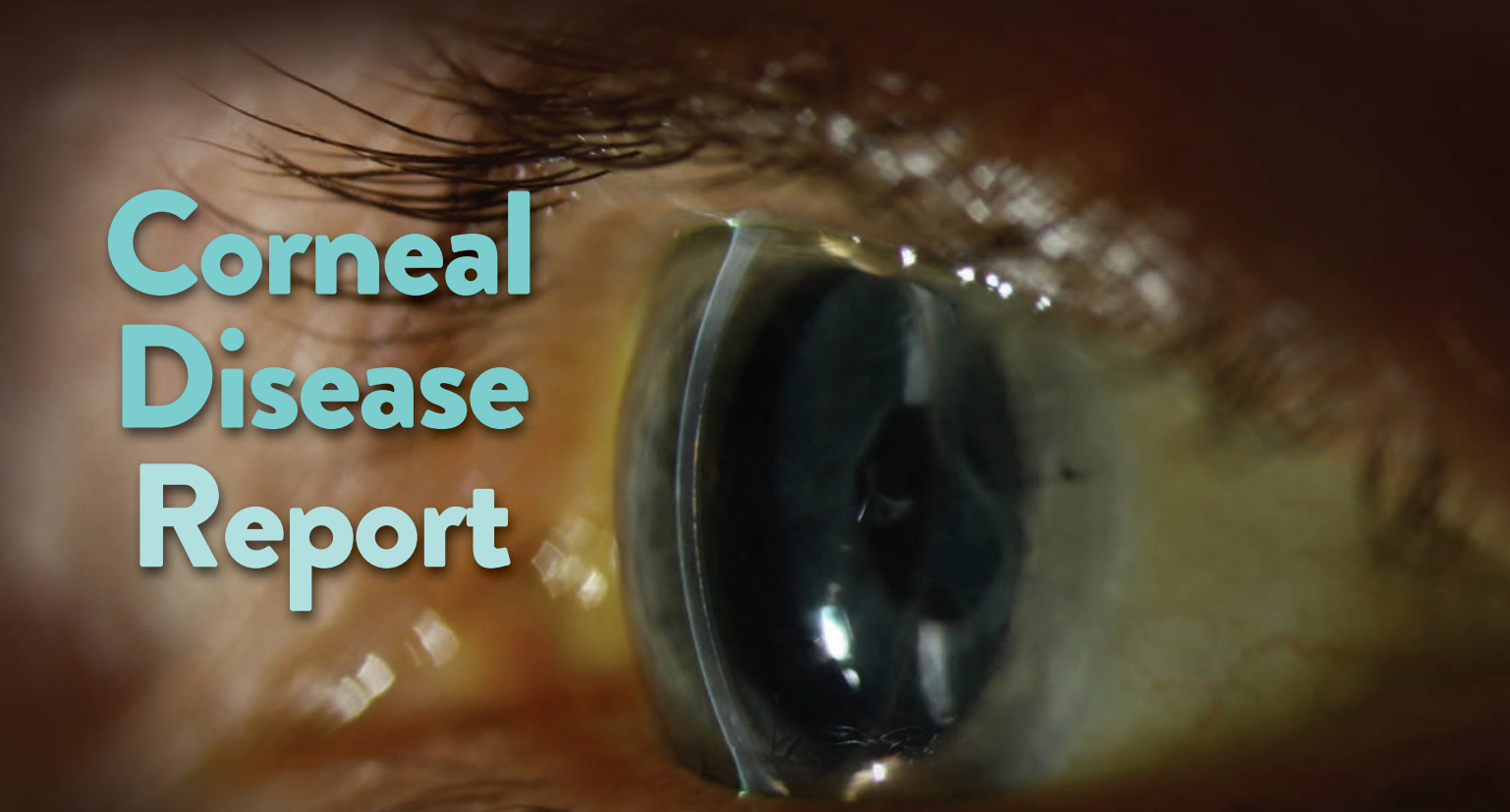
Earn 2 CE Credits: Your Responsibilities in Screening Macular Function, **p. 100**

REVIEW® OF OPTOMETRY

April 15, 2016

www.reviewofoptometry.com



Corneal Disease Report

- Digging Deeper into Superficial Corneal Dystrophies, **p. 36**
- The Ins and Outs of Corneal Wound Healing, **p. 44**
- No Insult To Injury: Treating Corneal Trauma, **p. 56**
- Essential Procedures: Collecting a Corneal Culture, **p. 64**

ALSO INSIDE

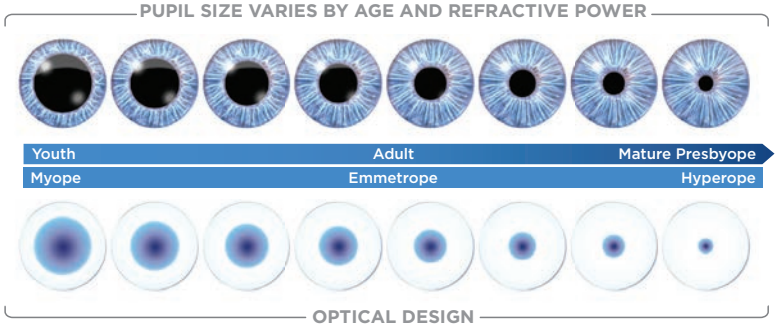
- Glaucoma: Hone Your Differential Diagnosis, **p. 74**
- Seeing Blue: The Impact of Excessive Blue Light Exposure, **p. 88**
- Current and Emerging Therapies for Allergic Conjunctivitis, **p. 94**

Built on the ACUVUE® MOIST Platform—
the #1 prescribed daily disposable brand around the globe*

Now you can **continue excellent care**

1-DAY ACUVUE® MOIST Brand MULTIFOCAL Contact Lenses:
Advancing multifocal lenses with pupil optimization: INTUISIGHT™ Technology

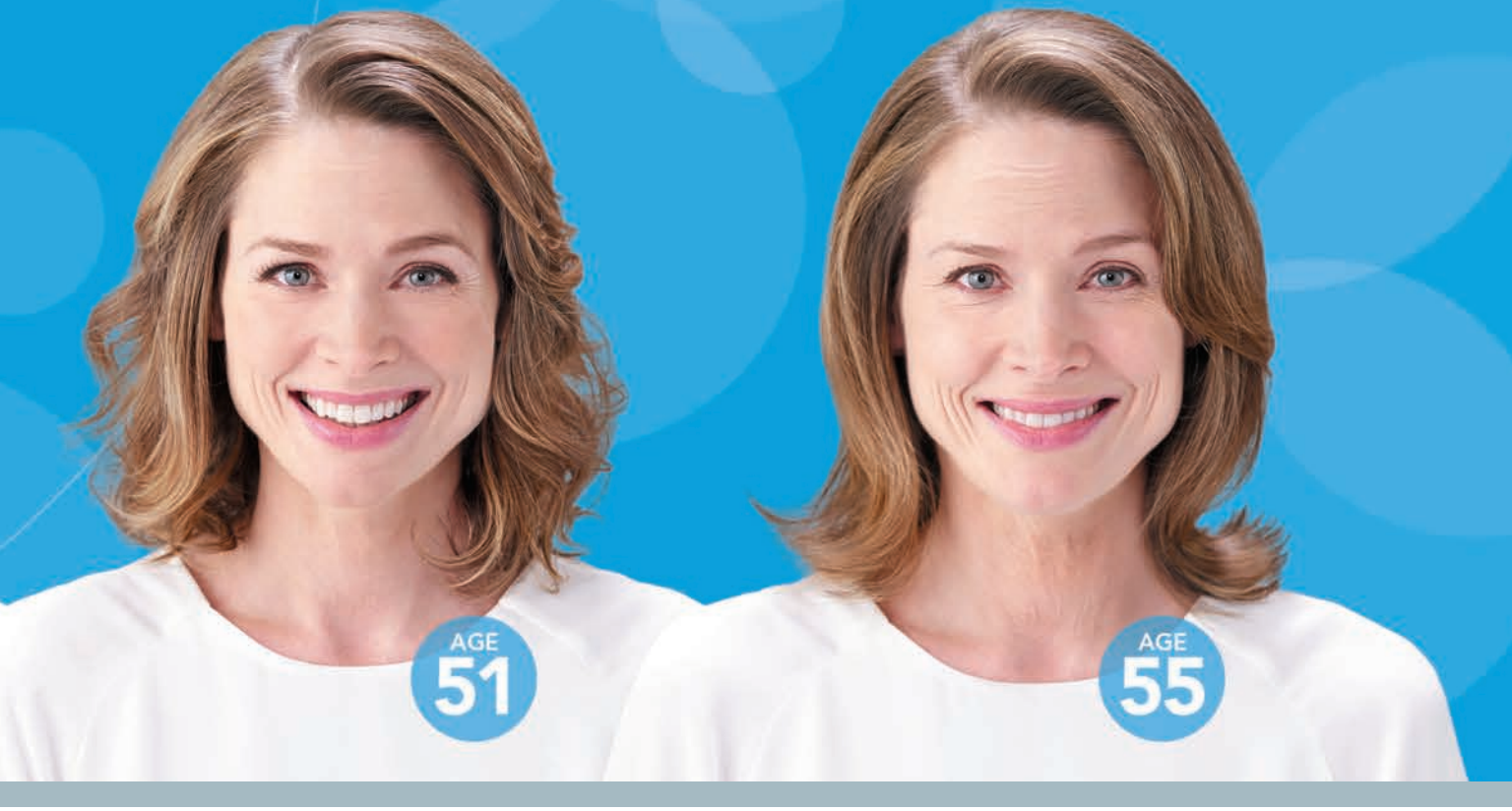
The **ONLY MULTIFOCAL LENS** that uniquely optimizes the optical design to the pupil size for a predictable performance across the refractive range and ADD powers.



For illustrative purposes only.

Competitive lens designs: fixed optical design

Her **Vision** Will Change.
Her **Experience** Won't.



as her vision evolves into presbyopia

Continue providing the care you've always delivered with the multifocal lens you can rely on.

www.acuvueprofessional.com/moist-multifocal-contact-lenses

*Based on independent third-party data, December 2014.

ACUVUE® Brand Contact Lenses are indicated for vision correction. As with any contact lens, eye problems, including corneal ulcers, can develop. Some wearers may experience mild irritation, itching or discomfort. Lenses should not be prescribed if patients have any eye infection, or experience eye discomfort, excessive tearing, vision changes, redness or other eye problems. Consult the package insert for complete information. Complete information is also available by visiting acuvueprofessional.com or by calling 1-800-843-2020.

VOL. 153 NO. 4 ■ APRIL 15, 2016

IN THE NEWS

An update to the Diabetic Retinopathy Clinical Research Network **Protocol T trial** reveals year-two data inconsistent with year-one findings. While year-one data showed Eylea (aflibercept, Regeneron) outperforming both of the other anti-VEGFs for some patients with diabetic macular edema (DME), the year-two results were less conclusive. Researchers found Eylea still outperformed Avastin (bevacizumab, Genentech) at year two, but no longer produced superior results compared with Lucentis (ranibizumab, Genentech). Overall mean VA improvement was 12.8 letters for Eylea, 12.3 for Lucentis and 10.0 for Avastin.

New research from Schepens Eye Research Institute found an **increase in mitochondrial and nuclear DNA damage in Fuchs' endothelial corneal dystrophy (FECD)** and further correlated this with mitochondrial energy production loss. Identifying the cause of cell death in FECD moves research closer to providing alternative and safer treatments options, Ula Jurkunas, MD, principal investigator, said in a press release. Researchers now hope to focus on developing cytoprotective and anti-aging therapies.

We may soon have the technology to **regrow lenses and corneas**, according to two studies in *Nature*. The discovery was made using adult cells genetically reprogrammed to an embryonic stem cell–like state. The first study used rabbit models to achieve **functional lens regeneration** during cataract removal by preserving endogenous lens epithelial stem/progenitor cells. The second study **transplanted lab-grown corneas** into rabbits born without fully formed corneas.

FDA Approves 24-hour IOP Measuring CL

The device may help clinicians monitor glaucoma progression. **By Bill Kekevian, Senior Editor**

In an age of watches that record your heart rate and cell phone apps that track how many calories you burn, it's only natural that eye care would offer its own contribution to the "wearables" movement. After years of development, the Triggerfish system (Sensimed)—a contact lens designed to continuously measure and record ocular changes closely correlated with intraocular pressure (IOP)—was recently cleared for marketing by the FDA.[1]

"This device could conceivably be used to determine the pretreatment fluctuations and impact of nighttime IOP on the clinical picture," says I. Ben Gaddie, OD, president of the Optometric Glaucoma Society. "During treatment, it will help determine true response to medication as well as identify time points when IOP is fluctuating or slipping."

In addition to the one-time-use silicone contact lens outfitted with a micro-sensor, the kit includes an antenna the patient wears around the eye that wirelessly transfers data from the lens to a portable recording device.

It doesn't use the traditional millimeters of mercury to evaluate IOP, but Dr. Gaddie says that's not a problem. He's interested in using the device to monitor patients who are progressing faster than expected

based on in-office IOP measurements. By obtaining a patient's relative pressure over 24 hours, he says, the device could reveal if "the patient is performing activities that are leading to shorter-term elevation of IOP. Being able to identify these triggers and trends will be of tremendous help to the doctor."

The Triggerfish will be loaned to patients by a doctor who will use the data to specify treatment, similar to how cardiologists issue temporary heart monitors.

The company seeks to "work closely with the glaucoma community to design and execute a major post-approval study" that will confirm the device's ability to predict the course of the disease, Senismed CEO David Bailey said in a press release.

1. De Moraes C, Jasien J, Simon-Zoula S, et al. Visual field change and 24-hour IOP-related profile with a contact lens sensor in treated glaucoma patients. Ophthalmology. 2016 April;123(4):744-53.

Introducing the Keeler Z Series Slit Lamp & Digital Tonometer

Keeler Optics...says it all.

The Z Series Slit Lamp is the latest line from Keeler featuring legendary Keeler optics housed in a stylish, contemporary design.

Your choice of 3 or 5 step magnification option in a standard, digital ready, or comprehensive digital capture system.

Check out some of these great features:

- Converging or parallel binoculars
- 14mm Slit length / maximum aperture
- X 6 to x 40 (5 step) or X 10 to X 25 (3 step) magnifications
- Blue, red-free, clear, neutral density and diffuser filters
- 360 degree continuous slit rotation
- Integrated yellow barrier filter
- 1m Square aperture for Uveitis assessment
- LED illumination
- Illumination control mounted next to joystick
- 3 year warranty

Learn more at www.keelerusa.com

Order now and receive a limited edition bronze D-KAT tonometer.

Contact your preferred Keeler distributor for details.

Keeler

Keeler Instruments, Inc. • 456 Parkway • Broomall, PA 19008
Tel: (800) 523-5620 • Fax: (610) 353-7814 • email: keeler@keelerusa.com

Cataract Surgery Disparities Revealed

Substantial geographic disparities in cataract treatment are evinced in a new study from the University of Michigan. Recently published in *JAMA*, the retrospective cross-sectional study used the Clinformatics DataMart database to assess data from 1,050,815 beneficiaries between 2001 and 2011 in 306 US communities.

The study found the median age of patients undergoing cataract surgery for the first time varies by as much as 20 years between some communities—from age 60 in some areas to 80 in others. The variation in the age-standardized cataract surgery rate varies from 7.5% in Honolulu, Hawaii, to 37.3% in Lake Charles, La.

In each of the 306 hospital referral regions included in the study, researchers computed the standard deviations for the age of cataract surgery recipients, then assessed the timing from an individual's first recorded cataract diagnosis to the date of the first extraction. The median time between diagnosis and surgery ranges, for example, from 17 days in Victoria, Texas to 367 days in Yakima, Wash.

"With the increasing number of cataract surgeries, optometrists will be called upon to be more involved in the cataract journey from early diagnosis and preoperative evaluation to education and postoperative care," says Walt Whitley, OD, MBA, director of optometric services at Virginia Eye Consultants. The study "demonstrates the role optometrists have, not just in urban communities, but in rural areas where there are more optometrists available than ophthalmologists."

In addition to the geographical factor, the researchers took into account age, race, socioeconomic status, level of education, UV light exposure, urban vs. rural residency and the number of ophthalmologists or optometrists in a given community. The data reveals racial disparities persisting, with a reduced likelihood for cataract surgery among black patients.

"The most interesting point is regarding the issues with trust and communication with physicians," Dr. Whitley says of the study's look into potential reasons for these racial and socioeconomic disparities. "This is a reminder of the critical role of developing and fostering our relationships with our patients."

While the study is limited by the information provided in claims data, it makes clear the existence of geographic variation in the timing and rates of cataract surgery among different communities. Furthermore, it highlights the need for further exploration into the underlying causes and the patient impact.

Kauh CY, Blachley TS, Lichter PR, et al. Geographic variation in the rate and timing of cataract surgery among US communities. JAMA Ophthalmol. 2016;134(3):267.

Gene Editing May Defeat RP

Scientists used the genomic editing technology CRISPR to correct the gene mutation responsible for retinitis pigmentosa (RP), according to a press release. They used skin samples from patients with RP to generate stem cells that harbored the defective RGPR gene responsible for more than 90% of cases, and then repaired the gene using the bacterial immune system-turned genome-editing tool. By using the patient's own stem cells, researchers hope they can one day transplant them without a concern for tissue rejection.

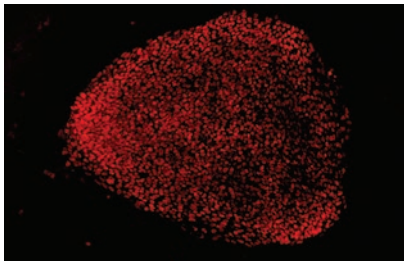


Photo: Vinit Mahajan, UI Health Care

Skin cells were transformed into stem cells, correcting the mutated RPGR gene.

"This particular study proved successful in approximately 13% of the cases," says Steven Ferrucci, OD, of the US Department of Veterans Affairs in North Hills, Calif., and professor at the Southern California College of Optometry at Marshall B. Ketchum University in Los Angeles. "While this number seems low, it is a great improvement over earlier studies, which had success rates hovering around 1%, demonstrating how far the technology has advanced. Certainly more research needs to be done, but this represents a significant step forward in personalized gene therapy for a wide array of retinal disease."

Bassuk AG, Zheng A, Li Y, et al. Precision Medicine: genetic repair of retinitis pigmentosa in patient-derived stem cells. Scientific Reports. 2016 Jan [Epub].

Looking deeper
Exploring innovation

Shire's Vision for Ophthalmics

At Shire, we're a leading biotech with a global track record for our work in rare diseases and specialty conditions.

Now we're expanding our vision and bringing the same commitment to ophthalmics. Pursuing the promise of new therapies in ophthalmics to address patients' unmet needs.

Just watch.

Visit **Shire-Eyes.com**

Shire

Optogenetics Aims to Reverse Blindness

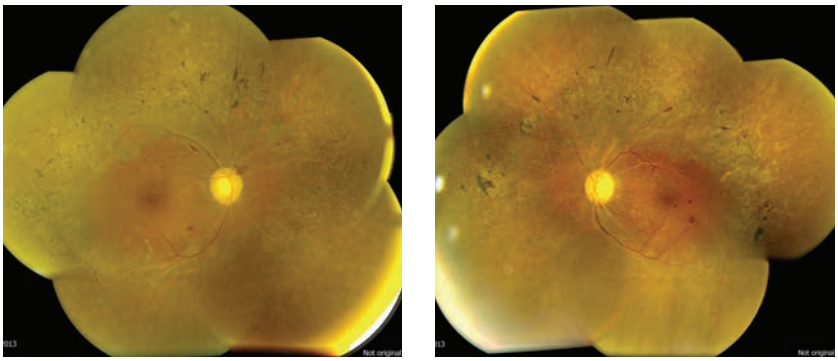
In the first human test of optogenetics—a therapy combining gene therapy and light to control nerve cells—researchers at the Retina Foundation of the Southwest will be injecting DNA from light-sensitive algae into the eyes of patients deemed legally blind from retinitis pigmentosa (RP). The study aims to re-engineer the ganglion cells to respond to light and send signals to the brain, allowing patients to see, if only in blurry black-and-white.

The study will enroll as many as 15 patients with retinitis pigmentosa. The researchers hope the new therapy will allow them to see large objects, or even large letters.

But the therapy has its limitations, as the algae protein only responds to blue light. Researchers expect patients to have monochromatic vision, at best. Still, for blind patients to see even this much would be a huge leap forward.

While the new therapy could revolutionize treatment options for patients with RP, it may also have implications for other disease therapies. According to Antonello Bonci, scientific director of the intramural research program at the National Institute on Drug Abuse in Baltimore, researchers will need more information about which cells to target before it can be used for other diseases such as Parkinson's and severe mental illness. "But that's five years away, not 20 years away," he said in a press release.

"We are hopefully getting closer to identifying another treatment option for RP patients who are at the end stage of the disease with bare to no light perception only. Optometrists should share this positivity and hope with their RP patients," says Ava K. Bittner, OD, PhD, associate professor at Nova Southeastern University. "This clinical trial and a couple of other trials evaluating stem cells for RP are currently recruiting participants in the US, which is exciting since they offer current opportunities for some RP patients who wish to help researchers determine if these approaches might be useful to help improve and/or slow vision loss." ■



Photos: Mark T. Dunbar, OD

The pigment spiculing noted along the arcades and the "moth-eaten" retinal degenerative changes are indicative of retinitis pigmentosa.

REVIEW® OF OPTOMETRY

BUSINESS OFFICES
11 Campus Blvd., Suite 100
Newtown Square, PA 19073

CEO, INFORMATION SERVICES GROUP
Marc Ferrara
(212) 274-7062 • mferrara@jobson.com

PUBLISHER
James Henne
(610) 492-1017 • jhenne@jobson.com

REGIONAL SALES MANAGER
Michele Barrett
(610) 492-1014 • mbarrett@jobson.com

REGIONAL SALES MANAGER
Michael Hoster
(610) 492-1028 • mhoster@jobson.com

VICE PRESIDENT, OPERATIONS
Casey Foster
(610) 492-1007 • cfoster@jobson.com

VICE PRESIDENT, CLINICAL CONTENT
Paul M. Karpecki, OD, FAAO
pkarpecki@jobson.com

PRODUCTION MANAGER
Scott Tobin
(610) 492-1011 • stobin@jobson.com

SENIOR CIRCULATION MANAGER
Hamilton Maher
(212) 219-7870 • hmaher@jhihealth.com

CLASSIFIED ADVERTISING
(888) 498-1460

SUBSCRIPTIONS
$56 a year, $88 (US) in Canada,
$209 (US) in all other countries.

SUBSCRIPTION INQUIRIES
(877) 529-1746 (US only);
outside US, call (847) 763-9630

CIRCULATION
PO Box 2025
Skokie, IL 60076
Tel: (toll free) 1-877-529-1746
Outside US: (847)763-9630
Fax: (847)763-9631

jmi

CEO, INFORMATION SERVICES GROUP
Marc Ferrara

SENIOR VICE PRESIDENT, OPERATIONS
Jeff Levitz

VICE PRESIDENT, HUMAN RESOURCES
Tammy Garcia

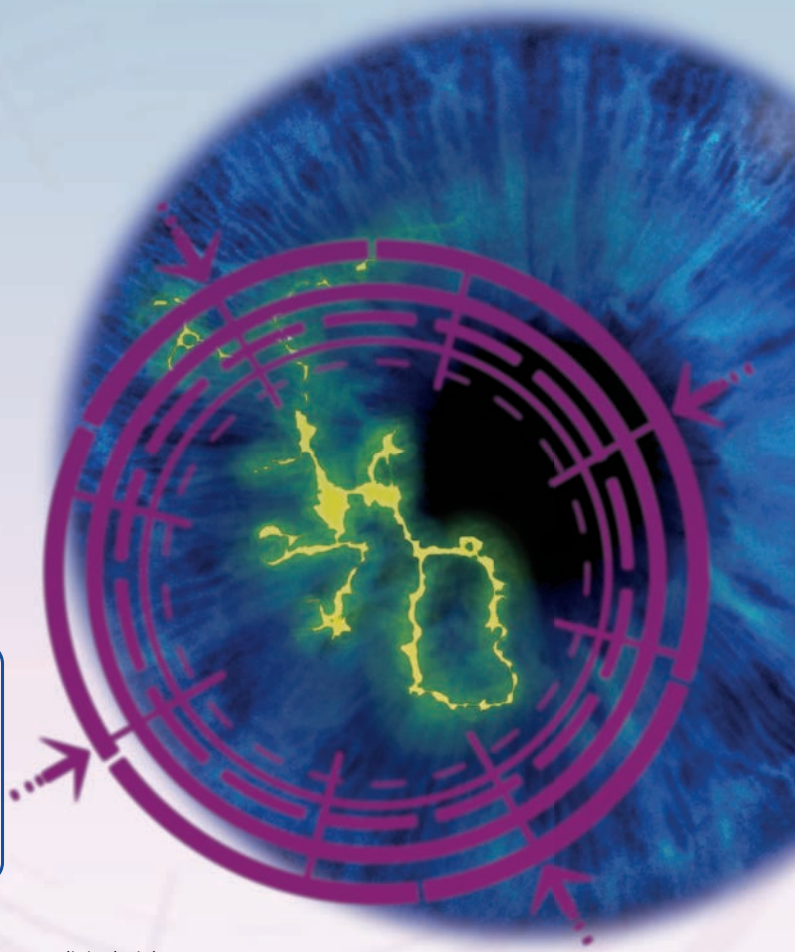
VICE PRESIDENT, CREATIVE SERVICES & PRODUCTION
Monica Tettamanzi

CORPORATE PRODUCTION DIRECTOR
John Anthony Caggiano

VICE PRESIDENT, CIRCULATION
Emelda Barea

Zirgan®
(ganciclovir ophthalmic gel) 0.15%

SELECTIVELY AND EFFECTIVELY TARGET VIRUS INFECTED CELLS



- Inactive in healthy corneal cells[1]
- Up to 77% of dendritic ulcers resolved at Day 7[2,3,*]

*As demonstrated in a phase 3 open-label, randomized, controlled, multicenter clinical trial (N=164) in which patients with herpetic keratitis received either ZIRGAN® or acyclovir ophthalmic ointment 3%, administered 5 times daily until healing of ulcer and then 3 times daily for 1 week. Clinical resolution (healed ulcers) at day 7 was achieved in 77% (55/71) of patients treated with ZIRGAN® versus 72% (48/67) treated with acyclovir (difference, 5.8%; 95% CI, -9.6%-18.3%). ZIRGAN® was noninferior to acyclovir in patients with dendritic ulcers.

Indication

ZIRGAN® (ganciclovir ophthalmic gel) 0.15% is a topical ophthalmic antiviral that is indicated for the treatment of acute herpetic keratitis (dendritic ulcers).

Important Safety Information about ZIRGAN®

- ZIRGAN® is indicated for topical ophthalmic use only.
- Patients should not wear contact lenses if they have signs or symptoms of herpetic keratitis or during the course of therapy with ZIRGAN®.
- Most common adverse reactions reported in patients were blurred vision (60%), eye irritation (20%), punctate keratitis (5%), and conjunctival hyperemia (5%).
- Safety and efficacy in pediatric patients below the age of 2 years have not been established.

Please see brief summary of Prescribing Information on the adjacent page.

References: 1. Foster CS. Ganciclovir gel—a new topical treatment for herpetic keratitis. *US Ophthalmic Rev.* 2008;3(1):52-56. **2.** ZIRGAN Prescribing Information, April 2014. **3.** Croxtall JD. Ganciclovir Ophthalmic Gel 0.15% in Acute Herpetic Keratitis (Dendritic Ulcers). *Drugs.* 2011;71(5):603-610.

BAUSCH + LOMB

Zirgan®
(ganciclovir ophthalmic gel) 0.15%

BRIEF SUMMARY OF PRESCRIBING INFORMATION
This Brief Summary does not include all the information needed to use Zirgan safely and effectively. See full prescribing information for Zirgan.

Zirgan ganciclovir ophthalmic gel 0.15%
Initial U.S. Approval: 1989

1 INDICATIONS AND USAGE
ZIRGAN (ganciclovir ophthalmic gel) 0.15% is indicated for the treatment of acute herpetic keratitis (dendritic ulcers).

2 DOSAGE AND ADMINISTRATION
The recommended dosing regimen for ZIRGAN is 1 drop in the affected eye 5 times per day (approximately every 3 hours while awake) until the corneal ulcer heals, and then 1 drop 3 times per day for 7 days.

3 DOSAGE FORMS AND STRENGTHS
ZIRGAN contains 0.15% of ganciclovir in a sterile preserved topical ophthalmic gel.

4 CONTRAINDICATIONS
None.

5 WARNINGS AND PRECAUTIONS

5.1 Topical Ophthalmic Use Only
ZIRGAN is indicated for topical ophthalmic use only.

5.2 Avoidance of Contact Lenses
Patients should not wear contact lenses if they have signs or symptoms of herpetic keratitis or during the course of therapy with ZIRGAN.

6 ADVERSE REACTIONS
Most common adverse reactions reported in patients were blurred vision (60%), eye irritation (20%), punctate keratitis (5%), and conjunctival hyperemia (5%).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy: Teratogenic Effects
Pregnancy Category C: Ganciclovir has been shown to be embryotoxic in rabbits and mice following intravenous administration and teratogenic in rabbits. Fetal resorptions were present in at least 85% of rabbits and mice administered 60 mg/kg/day and 108 mg/kg/day (approximately 10,000x and 17,000x the human ocular dose of 6.25 mcg/kg/day), respectively, assuming complete absorption. Effects observed in rabbits included: fetal growth retardation, embryolethality, teratogenicity, and/or maternal toxicity. Teratogenic changes included cleft palate, anophthalmia/microphthalmia, aplastic organs (kidney and pancreas), hydrocephaly, and brachygnathia.
In mice, effects observed were maternal/fetal toxicity and embryolethality. Daily intravenous doses of 90 mg/kg/day (14,000x the human ocular dose) administered to female mice prior to mating, during gestation, and during lactation caused hypoplasia of the testes and seminal vesicles in the month-old male offspring, as well as pathologic changes in the nonglandular region of the stomach (see Carcinogenesis, Mutagenesis, and Impairment of Fertility).
There are no adequate and well-controlled studies in pregnant women. ZIRGAN should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers
It is not known whether topical ophthalmic ganciclovir administration could result in sufficient systemic absorption to produce detectable quantities in breast milk. Caution should be exercised when ZIRGAN is administered to nursing mothers.

8.4 Pediatric Use
Safety and efficacy in pediatric patients below the age of 2 years have not been established.

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

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action
ZIRGAN (ganciclovir ophthalmic gel) 0.15% contains the active ingredient, ganciclovir, which is a guanosine derivative that, upon phosphorylation, inhibits DNA replication by herpes simplex viruses (HSV). Ganciclovir is transformed by viral and cellular thymidine kinases (TK) to ganciclovir triphosphate, which works as an antiviral agent by inhibiting the synthesis of viral DNA in 2 ways: competitive inhibition of viral DNA-polymerase and direct incorporation into viral primer strand DNA, resulting in DNA chain termination and prevention of replication.

12.3 Pharmacokinetics
The estimated maximum daily dose of ganciclovir administered as 1 drop, 5 times per day is 0.375 mg. Compared to maintenance doses of systemically administered ganciclovir of 900 mg (oral valganciclovir) and 5 mg/kg (IV ganciclovir), the ophthalmically administered daily dose is approximately 0.04% and 0.1% of the oral dose and IV doses, respectively, thus minimal systemic exposure is expected.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertilty
Ganciclovir was carcinogenic in the mouse at oral doses of 20 and 1,000 mg/kg/day (approximately 3,000x and 160,000x the human ocular dose of 6.25 mcg/kg/day, assuming complete absorption). At the dose of 1,000 mg/kg/day there was a significant increase in the incidence of tumors of the preputial gland in males, forestomach (nonglandular mucosa) in males and females, and reproductive tissues (ovaries, uterus, mammary gland, clitoral gland, and vagina) and liver in females. At the dose of 20 mg/kg/day, a slightly increased incidence of tumors was noted in the preputial and harderian glands in males, forestomach in males and females, and liver in females. No carcinogenic effect was observed in mice administered ganciclovir at 1 mg/kg/day (160x the human ocular dose). Except for histocytic sarcoma of the liver, ganciclovir-induced tumors were generally of epithelial or vascular origin. Although the preputial and clitoral glands, forestomach and harderian glands of mice do not have human counterparts, ganciclovir should be considered a potential carcinogen in humans. Ganciclovir increased mutations in mouse lymphoma cells and DNA damage in human lymphocytes in vitro at concentrations between 50 to 500 and 250 to 2,000 mcg/mL, respectively.
In the mouse micronucleus assay, ganciclovir was clastogenic at doses of 150 and 500 mg/kg (IV) (24,000x to 80,000x human ocular dose) but not 50 mg/kg (8,000x human ocular dose). Ganciclovir was not mutagenic in the Ames Salmonella assay at concentrations of 500 to 5,000 mcg/mL. Ganciclovir caused decreased mating behavior, decreased fertility, and an increased incidence of embryolethality in female mice following intravenous doses of 90 mg/kg/day (approximately 14,000x the human ocular dose of 6.25 mcg/kg/day). Ganciclovir caused decreased fertility in male mice and hypospermatogenesis in mice and dogs following daily oral or intravenous administration of doses ranging from 0.2 to 10 mg/kg (30x to 1,600x the human ocular dose).

14 CLINICAL STUDIES
In one open-label, randomized, controlled, multicenter clinical trial which enrolled 164 patients with herpetic keratitis, ZIRGAN was non-inferior to acyclovir ophthalmic ointment, 3% in patients with dendritic ulcers. Clinical resolution (healed ulcers) at Day 7 was achieved in 77% (55/71) for ZIRGAN versus 72% (48/67) for acyclovir 3% (difference 5.8%, 95% CI - 9.6%-18.3%). In three randomized, single-masked, controlled, multicenter clinical trials which enrolled 213 total patients, ZIRGAN was non-inferior to acyclovir ophthalmic ointment 3% in patients with dendritic ulcers. Clinical resolution at Day 7 was achieved in 72% (41/57) for ZIRGAN versus 69% (34/49) for acyclovir (difference 2.5%, 95% CI - 15.6%-20.9%).

17 PATIENT COUNSELING INFORMATION
This product is sterile when packaged. Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the gel. If pain develops, or if redness, itching, or inflammation becomes aggravated, the patient should be advised to consult a physician. Patients should be advised not to wear contact lenses when using ZIRGAN.

Revised: April 2014

Bausch & Lomb Incorporated
Tampa, FL 33637

US/ZGN/15/0005
Based on 9224702 (flat)-9224802 (folded)

Contents

Review of Optometry April 2016

ANNUAL CORNEAL DISEASE REPORT

36 Digging Deeper into Superficial Corneal Dystrophies

New discoveries in genetic mutations can help you diagnose and manage these conditions. **By Sherry Bass, OD**

44 The Ins and Outs of Corneal Wound Healing

Learn the science and clinical key points of corneal wound healing and adjunct modalities like amniotic membranes to help your patients. **By Tarah N. Lee, OD**

56 No Insult To Injury: Treating Corneal Trauma

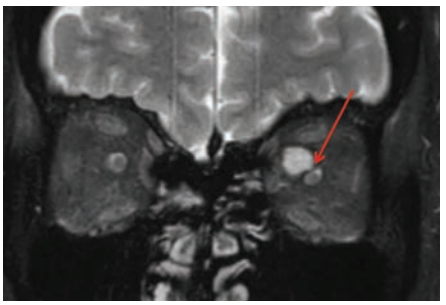
Learn to treat corneal injuries—from abrasions to burns—and help patients on the road to recovery. **By Lori Vollmer, OD**

64 ESSENTIAL PROCEDURES: Collecting a Corneal Culture

When guesses and hunches won't do, get the facts.
By Jessica Robinson, OD, Jason Ellen, OD, Brandon Hadel, OD, and Nathan Lighthizer, OD

74 Glaucoma: Hone Your Differential Diagnosis

Discovering the true diagnosis can be challenging when patients present with glaucoma-like findings. Here are some differentials to look out for.
By Justin Cole, OD, and Jarett Mazzarella, OD

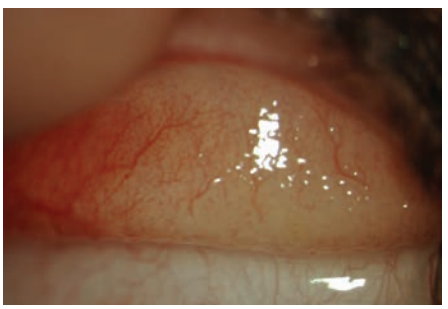


88 Seeing Blue: The Impact of Excessive Blue Light Exposure

The blue light in our lives is a cause for concern. Learn the science and clinical key points to help educate—and ultimately protect—your patients.
By Heather Flint Ford, OD

94 Current and Emerging Therapies for Allergic Conjunctivitis

With so many tools at your disposal, knowing the right treatment strategy can be challenging.
By Stephanie Fromstein, OD



100 EARN 2 CE CREDITS Are You Clear on Your Macular Function Screening Responsibilities?

How the latest technologies can change how you practice.
By Sherrol Reynolds, OD

Departments

Review of Optometry April 2016

4 News Review

20 Letters to the Editor

22 Outlook
Silicon Meets Silicone
JACK PERSICO

24 Chairside
On Next: Optometry Live
MONTGOMERY VICKERS, OD

26 Clinical Quandaries
An Evil Clinical Twin
PAUL C. AJAMIAN, OD

28 Focus on Refraction
When Astigmatism Goes Off-Key
PAUL HARRIS, OD, AND MARC B. TAUB, OD, MS

30 Urgent Care
Urgent Flashes and Floaters
RICHARD MANGAN, OD

49 Coding Connection
Amniotic Membrane—The Perfect Cover
JOHN RUMPAKIS, OD, MBA

110 Cornea + Contact Lens Q+A
What's That Gut to Do With It?
JOSEPH P. SHOVLIN, OD

112 Retina Quiz
Doctor, I Can See These Halos
MARK T. DUNBAR, OD, AND NABILA GOMEZ, OD

116 Glaucoma Grand Rounds
It Happens...Conversion, That Is
JAMES L. FANELLI, OD

120 Therapeutic Review
Irresponsible Education
JOSEPH W. SOWKA, OD, AND ALAN G. KABAT, OD

125 Products

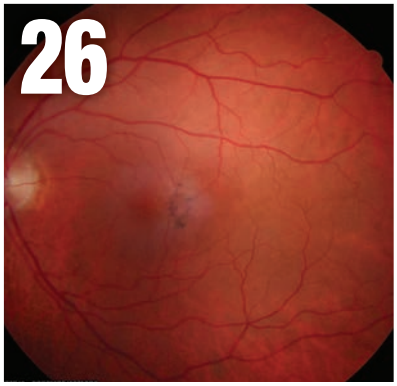
126 Classifieds

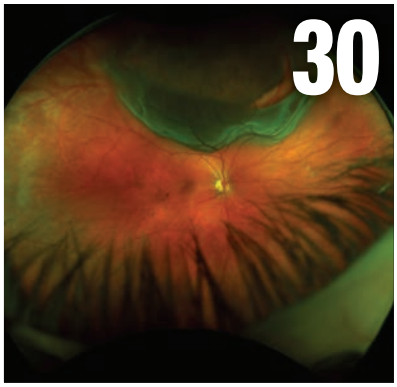
134 Meetings + Conferences

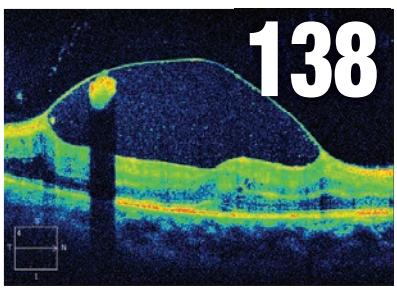
135 Advertisers Index

136 Surgical Minute
Tightening the Lid
WALTER O. WHITLEY, OD, MBA AND DEREK N. CUNNINGHAM, OD

138 Diagnostic Quiz
Changes to the System
ANDREW S. GURWOOD, OD







On The Web »
and more

Check out our multimedia and continuing education online at: *www.reviewofoptometry.com*

Digital Edition

Left your copy of *Review of Optometry* at the office? No problem! Access *Review* on your computer or mobile device!

Go to www.reviewofoptometry.com and click on the digimag link for the current issue.

Facebook and Twitter

For daily updates, "Like" our page on Facebook or "Follow" us on Twitter!

- www.facebook.com/revoptom
- http://twitter.com/#!/revoptom

Look for augmented content and special offers from *Review* and our advertisers. Specified pages work in conjunction with your smartphone or other mobile device to enhance the experience. With Layar, interactive content leaps off the page!

Step1: Download the free Layar app for iPhone or Android.

Step 2: Look for pages with the Layar Logo. layar INTERACTIVE PRINT

Step 3: Open the Layar app, hold the phone above the page and tap to scan it. Hold the phone above the page to view the interactive content.

The first 150 app downloads and completed forms will be entered into a drawing for a complimentary registration to one of *Review*'s 14-hour CE meetings, valued at $495.

INTRODUCING

Smart Blue Filter™

Blue Light protection in a clear lens and at no additional cost.

Harmful Blue Light is all around us. Exposure happens outdoors from the sun and, increasingly, indoors from LED lighting and digital devices. Smart Blue Filter feature is available in select premium lenses from Essilor.
Visit Essilor booth #LP7434 at Vision Expo East for more information!

Available With:

VARILUX® Eyezen™ + Transitions®

Combine with Crizal® No-Glare lenses for the most comprehensive eye protection.

2016 MEETINGS

REVIEW OF OPTOMETRY®
EDUCATIONAL MEETINGS OF CLINICAL EXCELLENCE

New Technologies and Treatments in Vision Care 2016

SAVE THESE DATES!

3 WAYS TO REGISTER

www.reviewofoptometry.com/conferences

Email **Lois DiDomenico**:
ReviewMeetings@Jobson.com

Call: **866-658-1772**

REGISTER EARLY

Program Chair:
Paul Karpecki, OD

San Antonio
Marriott Riverwalk
May 20 - 22, 2016

Bermuda
The Fairmont Hamilton Princess
June 9 - 12, 2016

Image courtesy of Hamilton Princess & Beach Club, A Fairmont Managed Hotel

Interactive CE Workshops

Philadelphia
Philadelphia Marriott Downtown
October 7 - 9, 2016

16-19 CE Credits
(COPE approval pending)

Administered by
Review of Optometry®

cope®
Approval pending

Treating Allergic Conjunctivitis in Today's Cost-Conscious Managed Care Environment

BEPREVE® (bepotastine besilate ophthalmic solution) 1.5%, for itch due to allergic conjunctivitis, and ALREX® (loteprednol etabonate ophthalmic suspension 0.2%), for seasonal allergic conjunctivitis, have demonstrated efficacy, and are made more affordable to eligible patients via the Bausch + Lomb Access Program.

KATHERINE M. MASTROTA, OD, & WALTER WHITLEY, OD, MBA

Ocular allergy affects an estimated 15% to 20% of the general US population.[1] Despite its high prevalence and morbidity, allergic conjunctivitis is often overlooked by patients and clinicians.[1] The managed care environment can be a hurdle when it limits access to therapies, which is why it's important to tell patients that we are prescribing the medications we believe are most appropriate for them and inform them of any patient access programs.

Allergic Conjunctivitis

Allergic conjunctivitis symptoms may negatively impact vision in the short term (Figure 1). In the long term, chronic inflammation from allergic conjunctivitis can induce structural changes and impair visual function.[2]

Because allergic conjunctivitis affects the ocular surface, it can interfere with successful contact lens wear.[3] More than 30 million Americans wear contact lenses, and ocular allergies may cause many to discontinue use of contact lenses.[4,5] Ocular allergy is also a risk factor for regression and haze after PRK and can disqualify a patient from LASIK until symptoms resolve.[6,7]

To Diagnose, Be Proactive

Itching is a hallmark symptom of allergic conjunctivitis. Inquire as to whether these patients have other known allergies. Ask patients about

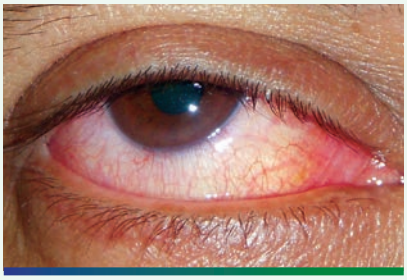


Figure 1 Allergic conjunctivitis.
(Image courtesy of Randall K. Thomas, OD, MPH, and Ron Melton, OD.)

Indication

BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% is a histamine H1 receptor antagonist indicated for the treatment of itching associated with signs and symptoms of allergic conjunctivitis.

Important Safety Information for BEPREVE®

- 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.

Indication

ALREX® (loteprednol etabonate ophthalmic suspension) 0.2% is indicated for temporary relief of the signs and symptoms of seasonal allergic conjunctivitis.

Important Safety Information for ALREX®

- ALREX® (loteprednol etabonate ophthalmic suspension 0.2%) 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 the ocular structures. ALREX® is also contraindicated in individuals with known or suspected hypersensitivity to any of the ingredients of this preparation and to other corticosteroids.
- Prolonged use of ALREX® is associated with several warnings and precautions, including glaucoma with optic nerve damage, defects in visual acuity, cataract formation, secondary ocular infections, exacerbation or prolongation of viral ocular infections (including herpes simplex), delay in wound healing and increase in bleb formation.
- If this product is used for 10 days or longer, intraocular pressure should be monitored. The initial prescription and renewal of the medication order beyond 14 days should be made by a physician only after examination of the patient with the aid of magnification.
- Ocular adverse reactions occurring in 5-15% of patients treated with loteprednol etabonate ophthalmic suspension (0.2%-0.5%) in clinical studies included abnormal vision/blurring, burning on instillation, chemosis, discharge, dry eyes, epiphora, foreign body sensation, itching, injection, and photophobia.

the seasonality of their condition and proactively prescribe therapy for patients prior to allergy season. Many allergy sufferers seen over the winter months may not be currently suffering but would like our recommendation on how to treat their seasonal allergies.

Look carefully at the presentation of allergic conjunctivitis. Are the signs and/or symptoms mild, moderate, or severe? Keep in mind that the signs and symptoms of allergic conjunctivitis are typically bilateral.[2] Typically, ocular allergy presents in conjunction with other systemic atopic manifestations, including rhinoconjunctivitis (or hay fever), rhinosinusitis, asthma, urticaria, or eczema.[2]

Strength Against Ocular Itch

We like the antihistamine/mast cell stabilizer BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% because it offers relief in minutes, is a selective H1 blocker with no significant binding affinity for adrenergic or muscarinic receptors, and has demonstrated efficacy in severe ocular itch.[8] In two double-masked, randomized, placebo-controlled trials, 68% of BEPREVE®-treated eyes (n = 104 eyes) in patients with severe ocular itch achieved complete relief of ocular itch vs 3% of placebo treated eyes (n = 98 eyes; $P \leq 0.001$) (Figure 2).[9] And BEPREVE®, patients can instill one drop in the morning and one drop at night before they go to sleep.[7]

A final key feature we appreciate about BEPREVE® is comfort. In fact, 92% of BEPREVE treated patients indicated feeling no discomfort on a 0 to 3 ocular comfort scale in an analysis of >6400 assessments of both eyes.[10]

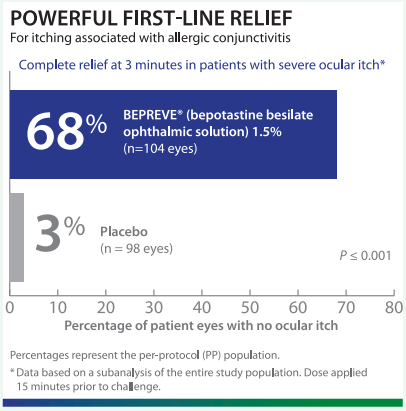


Figure 2 First-line relief. *(Meier reference 12.)*

More than Ocular Itch

If the patient is already on an antihistamine/mast cell stabilizer and presents with multiple signs or symptoms associated with seasonal allergic conjunctivitis, we may prescribe ALREX® (loteprednol etabonate ophthalmic suspension 0.2%).

We recommend ALREX® (loteprednol etabonate ophthalmic suspension 0.2%) for patients with seasonal allergic conjunctivitis because it is a c-20 ester-based corticosteroid; has demonstrated efficacy in treating the following SAC symptoms: itching, burning/stinging, discomfort, foreign body sensation, tearing, and redness; and because the incidence of IOP elevation with ALREX® is comparable to placebo.[11] In a randomized, double-masked, placebo-controlled trial (n = 133), ALREX® was superior to placebo in treating seasonal allergic conjunctivitis ($P < .001$).[12] In two 42-day clinical trials, 1 out of 133 patients treated with ALREX® experienced IOP elevations ≥ 10 mm Hg compared to 1 out of 135 patients treated with placebo.[11] If this product is used for 10 days or longer, IOP should be monitored.

Affordability

Thanks to copay assistance programs from Bausch + Lomb, eligible patients can limit their copay on either their BEPREVE® or ALREX® prescriptions. Often, we can print coupons while patients are still in the office by going to Bausch.com. Ask your Bausch + Lomb Sales Representative for more information.

A patient or pharmacist may inquire about a generic version of BEPREVE® or ALREX®. We let them know that there is no generic equivalent for either medication. Patients need to understand that as their eye care practitioner, we are aware of the therapeutic options available to treat their condition and have chosen to prescribe BEPREVE® or ALREX® for specific reasons.

Katherine M. Mastrota, MS, OD, FAAO, is Regional Practice Ambassador/Director Dry Eye Center of Excellence, Omni Eye Surgery New York. Dr. Mastrota is a consultant or advisor to Allergan, Alcon, B+L, NovaBay, Ocusoft, Paragon-BioTeck, and Shire.

Walter O. Whitley, OD, MBA, FAAO, is Director of Optometric Services at Virginia Eye Consultants in Norfolk, Virginia. Dr. Whitley is a speaker and advisory board member for Alcon, Allergan, Bausch + Lomb, Beaver-Visitec, Bio-Tissue, Ocusoft, Shire, and TearLab.

REFERENCES

1. Rosario N, Bielory L. Epidemiology of allergic conjunctivitis. *Curr Opin Allergy Clin Immunol.* 2011;11:471-6.
2. Bielory L. Ocular allergy overview. *Immunol Allergy Clin North Am.* 2008;28:1-23.
3. Wolffsohn JS, Emberlin JC. Role of contact lenses in relieving ocular allergy. *Cont Lens Anterior Eye.* 2011;34(4):169-72.
4. Centers for Disease Control and Prevention. Fast Facts (January 2014). CDC Website. http://www.cdc.gov/contactlenses/fast-facts.html. Accessed January 22, 2015.
5. Asthma and Allergy Foundation of America. Eye allergy survey results. AAFA Website. http://www.aafa.org/display.cfm?id=7&sub=100&cont=688. Accessed January 22, 2015.
6. Yang HY, Fujishima H, Toda I, et al. Allergic conjunctivitis as a risk factor for regression and haze after photorefractive keratectomy. *Am J Ophthalmol.* 1998 Jan;125(1):54-8.
7. Bielory BP, O'Brien TP. Allergic complications with laser-assisted in-situ keratomileusis. *Curr Opin Allergy Clin Immunol.* 2011 Oct;11(5):483-91.
8. BEPREVE [package insert]. Tampa, FL: Bausch & Lomb Incorporated; 2012.
9. Meier EJ, Torkildsen GL, Gow JA, et al; for Bepotastine Besilate Ophthalmic Solutions Study Group. Integrated phase III trials of bepotastine besilate ophthalmic solution 1.5% for ocular itching associated with allergic conjunctivitis. *Allergy Asthma Proc.* 2012;33:265-274.
10. Data on file. Clinical study report CL-SAF 04-0507-P. NDA 22-288. Ista Pharmaceuticals, Inc. October 27, 2008.
11. ALREX [package insert]. Tampa, FL: Bausch & Lomb Incorporated; 2013.
12. Dell SJ, Lowry GM, Northcutt JA, et al. A randomized, double-masked, placebo-controlled parallel study of 0.2% loteprednol etabonate in patients with seasonal allergic conjunctivitis. *J Allergy Clin Immunol.* 1998 Aug;102(2):251-5.

Please see Brief Summary of Prescribing Information for ALREX® and Full Prescribing Information for BEPREVE® on the following pages.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use Alrex® (loteprednol etabonate ophthalmic suspension 0.2%) safely and effectively. See full prescribing information for Alrex.

Alrex®

loteprednol etabonate
ophthalmic suspension 0.2%

Sterile Ophthalmic Suspension

Rx only

INDICATIONS AND USAGE
ALREX Ophthalmic Suspension is indicated for the temporary relief of the signs and symptoms of seasonal allergic conjunctivitis.

CONTRAINDICATIONS
ALREX, 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. ALREX is also contraindicated in individuals with known or suspected hypersensitivity to any of the ingredients of this preparation and to other corticosteroids.

WARNINGS
Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision, and in posterior subcapsular cataract formation. Steroids should be used with caution in the presence of glaucoma.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

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

PRECAUTIONS
General: For ophthalmic use only. The initial prescription and renewal of the medication order beyond 14 days 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.

If signs and symptoms fail to improve after two days, the patient should be re-evaluated.

If this product is used for 10 days or longer, intraocular pressure should be monitored.

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.

Information for Patients: This product is sterile when packaged. Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the suspension. If redness or itching becomes aggravated, the patient should be advised to consult a physician.

Patients should be advised not to wear a contact lens if their eye is red. ALREX should not be used to treat contact lens related irritation. The preservative in ALREX, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses **and whose eyes are not red,** should be instructed to wait at least ten minutes after instilling ALREX before they insert their contact lenses.

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, (1500 and 750 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender.

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 (85 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 (15 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 postimplantation 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 (15 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. ALREX Ophthalmic Suspension 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 ALREX is administered to a nursing woman.

Pediatric Use: Safety and effectiveness in pediatric patients have not been established.

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

Ocular adverse reactions occurring in 5-15% of patients treated with loteprednol etabonate ophthalmic suspension (0.2% - 0.5%) in clinical studies included abnormal vision/blurring, burning on instillation, chemosis, discharge, dry eyes, epiphora, foreign body sensation, itching, injection, and photophobia. Other ocular adverse reactions occurring in less than 5% of patients include conjunctivitis, corneal abnormalities, eyelid erythema, keratoconjunctivitis, ocular irritation/pain/discomfort, papillae, and uveitis. Some of these events were similar to the underlying ocular disease being studied.

Non-ocular adverse reactions occurred in less than 15% of patients. These include headache, rhinitis and pharyngitis.

In a summation of controlled, randomized studies of individuals treated for 28 days or longer with loteprednol etabonate, the incidence of significant elevation of intraocular pressure (≥10 mm Hg) was 2% (15/901) among patients receiving loteprednol etabonate, 7% (11/164) among patients receiving 1% prednisolone acetate and 0.5% (3/583) among patients receiving placebo. Among the smaller group of patients who were studied with ALREX, the incidence of clinically significant increases in IOP (≥10 mm Hg) was 1% (1/133) with ALREX and 1% (1/135) with placebo.

DOSAGE AND ADMINISTRATION
SHAKE VIGOROUSLY BEFORE USING.
One drop instilled into the affected eye(s) four times daily.

Revised: August 2013.

Bausch & Lomb Incorporated, Tampa, Florida 33637

Based on 9007904-9005504
US/ALX/15/0004 Issued: 02/2015

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*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Contamination of Tip and Solution
5.2 Contact Lens Use
5.3 Topical Ophthalmic Use Only
6 ADVERSE REACTIONS
6.1 Clinical Trial Experience
6.2 Post-Marketing Experience
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis and Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
17.1 Topical Ophthalmic Use Only
17.2 Sterility of Dropper Tip
17.3 Concomitant Use of Contact Lenses

*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.

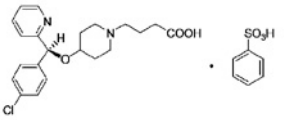
8.3 Nursing Mothers
Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 mcg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection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

Manufactured by: Bausch & Lomb Incorporated
Tampa, FL 33637
Under license from:
Senju Pharmaceutical Co., Ltd.
Osaka, Japan 541-0046

Letters to the Editor

A former real estate salesman in Los Angeles advertising low vision services bought a truck, filled it with magnifiers and CCTVs and drives to the homes of people with low vision.

*Low vision patients are **that** desperate for care.*

An Idea Whose Time Has Come

To quote the February edition's Outlook column, "Friends in Low Places" (an editorial piece that looked at the low vision subspecialty), yes, "you might think that efforts to help the visually impaired would be an integral part of all optometric offices," but, we're finding that's not the case.

The culture of eye care is: diagnosis, treatment and prevention of vision loss. However, once patients have lost significant vision, they are basically abandoned by eye doctors. As a low vision diplomate for more than 25 years and former clinical director of New York Lighthouse Upstate Clinics, I have heard thousands of low vision patients ask, "Why didn't my eye doctor tell me about low vision?"

Unfortunately, we are teaching our doctors to say, "Nothing more can be done." At a recent optometric conference, one of the lecturers summed up a presentation of a macular edema case by stating, "We got the patient to 20/80 but that was all we could do." To which I emphatically retort: *No, it isn't!* In a private conversation with the speaker after the presentation, he told me he refers to low vision all the time. Saying it in private is not enough—it must be said in front of an audience of ODs, over and over again!

Your editorial was wonderful, but it is not enough to change the culture. The leaders in eye care need to teach why, when and how to refer to low vision. It must be taught in CE courses, in optometry schools, in journals and magazines and anywhere else eye doctors get together. We need to use one and two hour CE courses to teach doctors the benefits of low vision referring. Low vision is a subspecialty that requires substantial time and commitment to learn. The organizers of the event mentioned above have since promised to add low vision to future programs. That's a great start toward changing the culture.

As founder of the International Academy of Low Vision Specialists, I'm pleased to note that we have 35 highly trained low vision optometrists located throughout the United States and Canada ready to present a one-hour COPE approved CE course called "Transforming the Phrase, 'Nothing More Can Be Done'" to teach ODs why, when and how to refer. I sent a request to present this course to every optometric CE administrator in the United States for the past two years. Not one has scheduled it.

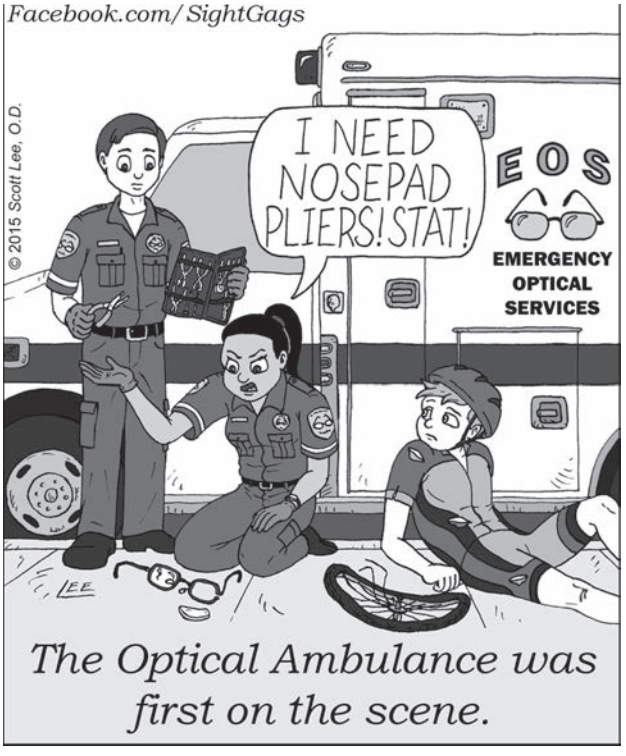
Review of Optometry publishes a Conference Planner each year listing over 200 CE events. Look at the 2016 planner and you can count the number of low vision CE hours being offered on one hand.

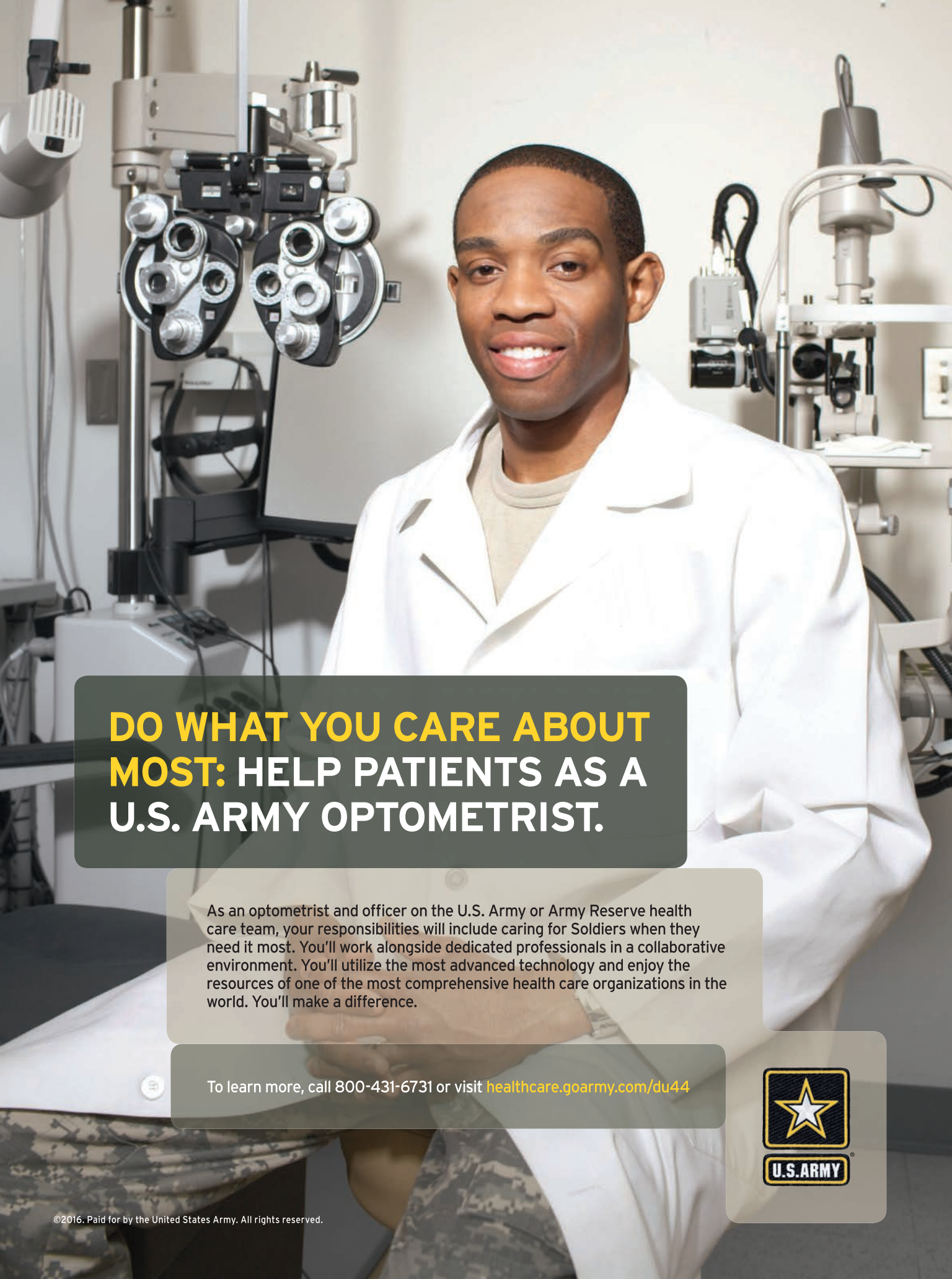
There's a former real estate salesman in Los Angeles advertising low vision services. He bought a truck, filled it with magnifiers and CCTVs and drives to the homes of people with low vision. Low vision patients are *that* desperate for care.

I have declared low vision an 'idea whose time has come.' Any help you can provide will be greatly appreciated.

—Richard J. Shuldiner, OD, FAAO
Low Vision Diplomate, American Academy of Optometry; Founder, International Academy of Low Vision Specialists; Clinical director, Low Vision Optometry of Southern California

Sight Gags By Scott Lee, OD





DO WHAT YOU CARE ABOUT MOST: HELP PATIENTS AS A U.S. ARMY OPTOMETRIST.

As an optometrist and officer on the U.S. Army or Army Reserve health care team, your responsibilities will include caring for Soldiers when they need it most. You'll work alongside dedicated professionals in a collaborative environment. You'll utilize the most advanced technology and enjoy the resources of one of the most comprehensive health care organizations in the world. You'll make a difference.

To learn more, call 800-431-6731 or visit healthcare.goarmy.com/du44

U.S.ARMY

REVIEW OF OPTOMETRY

PRINTED IN USA

FOUNDING EDITOR, FREDERICK BOGER
1891-1913

EDITORIAL OFFICES
11 CAMPUS BLVD., SUITE 100
NEWTOWN SQUARE, PA 19073

WEBSITE • WWW.REVIEWOFOPTOMETRY.COM

SUBSCRIPTION INQUIRIES
1-877-529-1746

CONTINUING EDUCATION INQUIRIES
1-800-825-4696

Outlook

By Jack Persico, Editor-in-Chief

Silicon Meets Silicone

US optometrists now have access to a contact lens that tracks IOP. Other smart lenses are in the works, too.

I reacted with wry amusement when a bit of junk mail recently popped up on my Apple Watch with the subject line, "Man and machine are merging even more than before." My watch tapped me on the wrist to share that with me, as it does all day long for texts, emails, news alerts and other notifications. Smart watches may not yet have gone mainstream the way other new tech platforms have, but the potential is clear. Connected devices worn on the body will be able to share data continuously, in both directions, if we'll let them.

Will we? Intentionally or not, we seem wary of "merging even more than before" with technology. Smart watches still feel like a niche rather than a necessity. The much-ballyhooed Google Glass flopped and was withdrawn. Now, virtual reality headsets—long a staple of sci-fi—are on the cusp of reality, as Facebook preps its Oculus Rift headset for launch. Although VR fires up the imaginations of tech geeks (yours truly included), the concept does create unease. A creepy photo of Mark Zuckerberg striding through a room full of headset-wearing drones made headlines in February about the dystopian future it may portend. If that's what the merging of man and machine looks like, plenty of people will be inclined to take a pass.

But can smart contact lenses succeed where other platforms have struggled? Many in eye care cheered the recent release of the Triggerfish contact lens, which monitors eye movements believed to be analogs for intraocular pressure fluctuation. A microchip embedded in a silicone contact lens records circumferential changes in corneoscleral shape; the data allows doctors to view a diurnal curve of a glaucoma patient to refine the approach to therapy.

Great idea, so-so execution. The strictly utilitarian Triggerfish set-up won't win any fashion awards. The nifty smart lens itself gets all the glamour photos, but patients are also required to wear an antenna around the orbit *and* a data recording device around the neck. One can argue that clinical value trumps convenience and aesthetics—rightly so—but wearables need better consumer appeal if patients are going to let them into their lives routinely.

Apple understands this and works hard to position its watch as a fashionable (or at least inoffensive) accessory. And its recent launch of a platform called CareKit seeks to further integrate tech and health by letting developers write software so that patients can record symptoms and medication effects in real time. Imagine an Apple Watch app that dry eye patients tap each time they feel burning or stinging, or another that lets a contact lens wearer grade comfort throughout the day.

For now, smart contact lenses hold much promise. Alcon continues to work with Google on a lens to monitor glucose levels in diabetes patients and an accommodating lens for presbyopes. Human trials are set to begin this year on the latter. We wish them luck. And foresight.

Gotta go—just felt another tap on the wrist. Maybe Oculus Rift pre-orders are now open. ■


Vision is the art of seeing what is invisible.
With outstanding support and unforgettable dedication, Marchon does more than just sell frames, they build relationships. Marchon me with customer service.
– Sol Regwan
Optometrist
Tarzana, California
Marchon me.
MARCHON
FOCUSED ON YOU
Marchon is a registered trademark of Marchon Eyewear Inc. Marchon.com

On Next: Optometry Live

Today's gadgets have some doctors worried about constant surveillance. But if you embrace your own antics, you've got nuthin' to worry about. **By Montgomery Vickers, OD**

These days, I am constantly reminded that we may all, sooner or later, be the star of someone's viral video. Does this make you paranoid? Not me. It makes me grateful that I accomplished 99% of my craziness while big ol' rotary telephones stalked the Earth. I can look anyone in the eye and confidently proclaim, "No! I never climbed onto Lincoln's lap in D.C. in 1974!" No one can dispute that and, Gumper, if you do, I will hunt you down.

So, does everything that happens in your office stay in your office? Is that lady in the chair recording your every word and deed for posterity? I would just live my life as if the answer is "certainly." Maybe your phone should be tuned in too.

Maybe we should use body cameras to film everything that happens in our lives! Imagine the drama as four million people tune in to hear you expertly explain astigmatism or watch you eat that bucket of fried chicken during your 10-minute lunch "hour." (Note to my wife: I know about my cholesterol, so I never did that! Expertly explain astigmatism, that is.)

I am *so* glad my life was not on video back in the day:

• In optometry school, I wore big thick ST-25 bifocals because some resident in the vision therapy program diagnosed me with accommodative infacility as the root of my lazy study habits—and I could more easily sell that to my dad.

• I caught German measles my second year and spent a week in the shower to keep from itching, which was a marvelous excuse to miss 10 fascinating lab days learning how to make a hard contact lens from a lump of blue plastic. This would have been amazing on YouTube.

• I have had at least 17 days in the past 6,000 during which I examined a patient with my zipper down.

• My wife and I won a dirty dancing contest back when optometry meetings were more like breakfast with Caligula. I would actually like that to be online!

• After weeks of dealing with an annoying patient dissatisfied with the cheap glasses he bought elsewhere, I may have accidently stomped them into little pieces while adjusting them for the 67th time. This was absolutely worth the remake and could easily have been one of the finest unrecorded moments in my illustrious career.

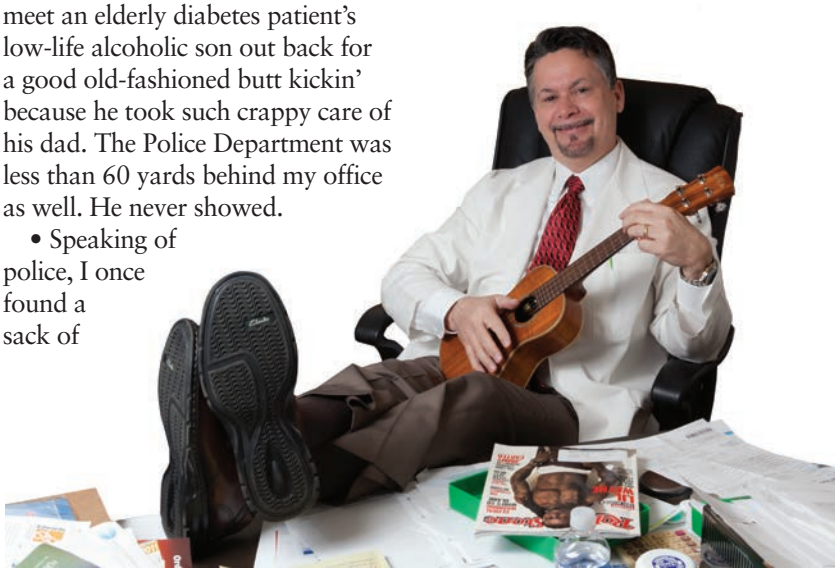
• Rumor has it I once offered to meet an elderly diabetes patient's low-life alcoholic son out back for a good old-fashioned butt kickin' because he took such crappy care of his dad. The Police Department was less than 60 yards behind my office as well. He never showed.

• Speaking of police, I once found a sack of marijuana at that same back door. I wish I could prove by video that I immediately called Rodney, my patient and chief of police. Rodney, you know I did—and you never did develop glaucoma, did you?

• I invented the term "desk adjustment." Some folks just cannot adapt to their new glasses, but if you leave them on your desk for a week and then dispense them, they are "much, much better." Sorry, you'll never prove that with a video.

Even today, we sometimes get lucky when someone can't get their phone ready in time. I grandly, but humbly, visited a nursing home social worker yesterday to apologize for a communication SNAFU during our mobile optometry day. My head was awash with satisfaction for my honest admission, right up until one of my assistants informed me that my zipper was down.

Film at 11. ■




Life is too short to wear boring glasses.
A variety of brands, colors, and styles that leave my customers satisfied. Marchon has it all and they do it right. Marchon me with design.
– Esther Zuniga
Optician
Napa, California
Marchon me.
MARCHON
FOCUSED ON YOU
Marchon is a registered trademark of Marchon Eyewear Inc. Marchon.com

An Evil Clinical Twin

Two conditions present with similar clinical findings; but imaging reveals they don't exist on the same family tree, explaining divergent responses. **Edited by Paul C. Ajamian, OD**

Q I have a few patients whom I thought had an atypical form of wet AMD, but the retinal specialist treated them with intravitreal anti-VEGF to no avail. Is there something else I should be looking for?

A The anti-VEGF revolution has allowed us to inhibit AMD progressionm and in some cases actually recover visual function, according to Jay Haynie, OD, of Retina and Macula Specialists in Tacoma, WA. "However, some patients fail to respond to this staple treatment modality." Given the standard-bearing nature of anti-VEGF, a lack of response is enough to raise eyebrows. "Several reasons exist as to why; however, one thing to be critical of is whether you have the correct diagnosis," says Dr. Haynie.

Macular telangiectasia (MT) often presents with visual symptoms and retinal findings resembling AMD, leading to misdiagnosis. "Patients with MT tend to have similar visual symptoms as sufferers of AMD: distortion, missing letters and trouble reading fine print," says Dr. Haynie. The symptoms of MT also tend to develop in the fourth to sixth decades of life, similar to AMD, he adds.

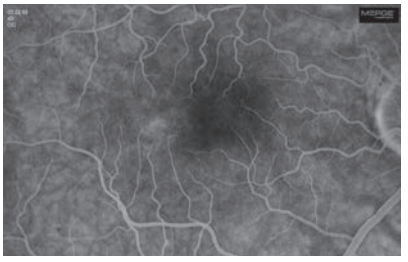
OCT Reveals the Culprit

While AMD and macular telangiectasia present with similar clinical findings, they show quite differently on OCT, revealing the disparate nature of each condition. Indeed, the etiopathogeneses of the two conditions do not overlap, and this is reflected in their differential responses to anti-VEGF treatment. Careful examination of the OCT—in particular, looking at the RPE complex and inner retinal layers—can reveal the culprit, says Dr. Haynie. "AMD is a disease of the choroid and ultimately alters the contour of the RPE while sparing the inner retinal layers. In contrast, macular telangiectasia initially causes an alteration of the inner retina. In the late phases it disrupts the outer retinal layers; however, the RPE layer remains intact in most cases," he says.

On SD-OCT, Dr. Haynie says one can differentiate AMD from MT easily if you understand the diseases. "In MT, you will initially see inner retinal changes that are described as 'schisis-like' changes as opposed to cystoid spaces, *per se*," he says. As the condition progresses—over decades for most—he outer retina begins to thin along with an alteration of the ellipsoid and PIL structures seen on the OCT, he explains.

Clues in the Fundus

Fundus findings in both conditions also have their share of similarities and key differences. "Macular telangiectasia is not associated with hallmarks of AMD (i.e., drusen and subretinal hemorrhage). However, they both show macular pigment mottling and, given the ages of the patients—generally the fourth to sixth decade of life—the diagnosis of AMD is made," says Dr. Haynie. Yet, there are findings to look out for in the fundus in order to differentiate the two conditions. "In the posterior segment, the retinal surface



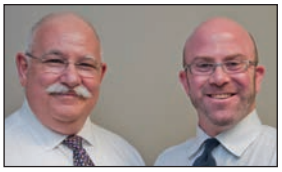
Fluorescein angiogram reveals late leakage in the temporal fovea of the right eye. Note the "right angle" appearance of the vasculature.

appears crystal-like in appearance; the parafoveal area appears gray and thick and small, irregular capillaries can be seen, generally temporal to the fovea," says Dr. Haynie. "These telangiectatic vessels are best seen with red-free photography or fluorescein angiography and are pathognomonic for the disease," he explains. Importantly, Dr. Haynie says that the clinical fundus characteristics in MT vary from that of AMD in that no drusen hemorrhage or lipid is seen upon your clinical examination.

The Takeaway

MT is not well understood. "Unless the disease has progressed to the fifth stage—characterized by the development of CNV and subretinal fibrosis—it does not respond to anti-VEGF compounds." And in Dr. Haynie's experience, very few cases progress to stage five over patients' lifetimes. So, keep in mind that a lack of response to VEGF blockade may be a signal of a disease not associated with AMD, such as macular telangiectasia. ■


Give a girl the right glasses and she can conquer the world.
My business is successful because of the relationship with my sales reps. Marchon hooks me up with the latest fashion trends in the industry. Marchon me with partnership.
– Ebony Thomas
Optician
Austin, Texas
Marchon me.
MARCHON
FOCUSED ON YOU
Marchon is a registered trademark of Marchon Eyewear Inc. Marchon.com



When Astigmatism Goes Off-Key

Professions and hobbies can expose patients to environmental influences on refractive error that alter astigmatism over time. **By Marc B. Taub, OD, MS, and Paul Harris, OD**

Nearly all of us were taught to view astigmatism as the result of some accidental, idiopathic misshaping of the cornea, and that two types of astigmatism exist: with- and against-the-rule. In the old days, we measured the corneal curvatures with keratometers and applied Javal's rule to predict the amount of astigmatism present in the eye. If the astigmatic portion of the refraction was close to the Javal's rule prediction, we knew that the astigmatism was due to the corneal curvature. If the astigmatic portion of the refraction didn't match our Javal's rule prediction, we knew the lens was the cause of the refractive error. Regardless, we knew that it should not change significantly over a person's lifetime.

Overture

Then, along Elliott Forrest, OD, a professor at the State University of New York, College of Optometry with a model about eye scan, head scan, and posture and astigmatism. Dr. Harris first heard of Dr. Forrest's model of astigmatism in the early 1980s and the significance of the information hit home almost immediately. Dr. Harris, a classically trained bass trombonist, came upon a way to test the theory. He knew first-hand that musicians must remain in constrained postures for extended periods of time to play their instruments. For example, we are all familiar with the head tilt left of the violinist or the head tilt right for those who play the flute. A trombone, particularly a bass trombone, blocks left visual space and all trombone players around the world must look at their music to their right.

Fig. 1. A trombone player with the music placed asymmetrically to his right. Here, he is practicing a concerto with the orchestra, standing to play.

So without getting much into the specifics of Dr. Forrest's theory, let's take this month's column to look at some evidence that supports it. In a future article, we can look at the clinical prescribing insights that emerge from this model.

Fig. 2. A cello player with her music well off to her right. She shares the music stand with another player on her right and is in this posture chronically as she sits in the front row of players closest to the conductor.

Dissonance

The model predicts that in the case of a person with a chronic asymmetric posture where they have to look to their right more, that the left eye should have more astigmatism. This is just what we expect to see with a trombone player as well as a string player, who shares a stand and is seated on its left side, and has to look back to their right.

The theory predicts that the trombonist *(Figure 1)* should have more astigmatism in the left eye. Let's see if this holds. The prescription worn by the trombone player is:

- OD -1.00 -1.75 x 15
- OS -3.00 -2.25 x 160

This is just what we expect. Why, you might ask, isn't the difference even greater? The answer: trombonists rarely get to play concertos—a solo performance requiring the musician to stand up. When they do give such performances, they are maximally off-center as seen in Figure 1. Most of the time, their role as a trombonist dictates simply a need to sit directly behind the stand, which is only slightly more rightward than centered.

The theory also predicts that the cellist *(Figure 2)* should have more astigmatism in her left eye. Let's see if this holds. The prescription worn by our cello

player is:

- OD +0.75 -0.75 x 100
- OS +0.75 -1.50 x 90

This is just what we expect, more astigmatism in the left eye.

Let's look at one more example, violin players. A refraction from a violinist in the Baltimore Symphony is:

Fig. 3. The famous violinist Joshua Bell, with the classic head tilt left while performing.

- OD -5.25 -1.50 x 175
- OS -4.75 -1.50 x 175

Again, just as Dr. Forrest predicted.

Magnum Opus

"Okay," you say, "seems like just few cases here, which could be carefully chosen to make a point. Seriously, this couldn't really hold for so many musicians, could it?"

In 1996, four Norwegian authors went to six different Norwegian symphony orchestras, and after performing refractions found 212 musicians with astigmatism. Their results were published in a paper entitled, "Synssituasjonen blant profesjonelle orkestermusikere" a strict translation of which is "Visual conditions of professional orchestra musicians." Their data showed a nearly 100% correlation between the instruments played, the corresponding posture necessary to play the instruments and the predicted astigmatism.

Coda

Dr. Forrest's insights have proven invaluable in prescribing. In particular, with some patients we find a change in their refraction, specifically a change in either the axis of the cylinder or the amount of the astigmatism. This information helps us know to look for a chronic change in posture that may explain the development of asymmetric astigmatism. In future articles, we will explore some of those cases. ■

1. Harris P. Visual conditions of symphony musicians. JAOA. 1988;59(12):952-9.
2. Forrest EB. A new model of functional astigmatism. JAOA 1981;52(11):889-97.
3. Stensland M, Myklebust E, Faaberg T, Jonassen H. Synssituasjonen blant profesjonelle orkestermusikere. Thesis for graduation from Hogskolen I Buskerud, Kongsberg, Norway,

Urgent Flashes and Floaters

These pesky symptoms can have dire consequences. **By Richard Mangan, OD**

On a recent Saturday night, the answering service called and relayed a message from a patient complaining of flashes and floaters. The patient, a 50-year-old high myope who had an onset of flashes and floaters 10 days earlier, was seen by an optometrist that day and was diagnosed with an uncomplicated posterior vitreous detachment (PVD). At that visit, she was educated on the warning signs of retinal detachment and instructed to call the office immediately should there be any worsening or change in her symptoms. When she noticed an increase in floaters and felt that the lower segment of her vision had become affected, she called. Based on her symptoms, we asked her to meet us in the office that night. Surprisingly, she asked if this could wait until tomorrow. Because she lives by herself, in a rural town approximately 45 minutes away, and it was snowing, she was not comfortable driving herself. When I explained that she may have a retinal detachment at risk of involving her central vision, she said she would try and find a ride and would get back to me.

This column will review the risks of waiting eight to 12 hours to make this diagnosis and determine whether it is reasonable for the patient to simply prepare for possible surgery in the morning.

Full-Thickness Tear Risk

PVD is largely regarded as a degenerative process of the vitreous resulting in the separation of the vitreous gel from the internal limiting membrane of the retina. In most cases, the posterior hyaloid separation occurs without complication, resulting in a complete or incomplete Weiss ring "floater" that casts a vacillating shadow of varying darkness, depending on its proximity to the retina. However, in a minority of cases, tractional forces can lead to a full-thickness tear that, if not addressed in a timely fashion, can lead to rhegmatogenous retinal detachment (RRD).

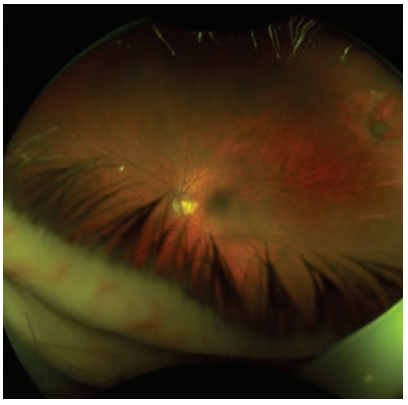


Fig. 1. An 82-year-old asymptomatic male with an old self-sealing horseshoe retinal tear.

PVD is largely an age-related event.[1] Patients in their 50s have an expected prevalence of only 25%, while almost 90% of patients in their 80s will have already had a PVD.[1] With that said, investigators report PVD occurs a full decade earlier in highly myopic patients (>6.00D). In fact, the higher the myopia, the earlier the onset.[1]

Tear or Detachment Risk

An evidence-based review and meta-analysis sought to find the percentage of patients with symptoms of flashes or floaters, or both, who are likely to present with a retinal tear or detachment.[2] It found that, in all PVD cases, when patients reported the acute onset of flashes or floaters, or both, the prevalence of a retinal break or tear was 14%.[2] Interestingly, the incidence was almost identical in cases of just flashes without floaters (13.7%) to those reporting just floaters without flashes (13.5%).[2] The study also found that, in patients with additional subjective complaints of vision reduction, the risk of complicated PVD increased to 45%.[2]

It also found that patients previously diagnosed with an uncomplicated PVD have an approximate incidence of 3.4% of developing a retinal tear within six weeks.[2] Predictive symptoms for retinal tear in this subset of patients include a sudden increase in floaters (less than 10 floaters) or subjective vision loss, or both.[2]

Not all retinal tears lead to detachment. Studies show approximately one-third to nearly half of retinal tears actually result in retinal detachment (*Figure 1*).[3,4]

The mechanism of RRD or extension is largely dependent on such factors as size and location of the retinal break, residual vitreous traction and the degree of vitreal syneresis (liquefied vitreous).[5,6] Superior breaks in the retina present a greater risk for detachment, especially if there is persistent vitreoretinal traction. The vitreous has a higher specific gravity than

Besivance®
besifloxacin ophthalmic suspension, 0.6%

When treating your patients with bacterial conjunctivitis –

Unleash power against pathogens of concern.

- The first and only topical ophthalmic chlorofluoroquinolone[1]
- Provides long-lasting tear concentrations[2]
- Proven efficacy against a broad spectrum of pathogens including[1,3]:
  - *S. aureus, S. epidermidis, S. pneumoniae,* and *H. influenzae*
  - *Pseudomonas aeruginosa*

Indication

BESIVANCE® (besifloxacin ophthalmic suspension) 0.6% is a quinolone antimicrobial indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following bacteria: *Aerococcus viridans**, CDC coryneform group G, *Corynebacterium pseudodiphtheriticum**, *Corynebacterium striatum**, *Haemophilus influenzae*, *Moraxella catarrhalis**, *Moraxella lacunata**, *Pseudomonas aeruginosa**, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis**, *Staphylococcus lugdunensis**, *Staphylococcus warneri**, *Streptococcus mitis* group, *Streptococcus oralis*, *Streptococcus pneumoniae*, *Streptococcus salivarius**

*Efficacy for this organism was studied in fewer than 10 infections.

Important Safety Information about BESIVANCE®

- BESIVANCE® is for topical ophthalmic use only, and should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.
- As with other anti-infectives, prolonged use of BESIVANCE® may result in overgrowth of non-susceptible organisms, including fungi. If super-infection occurs, discontinue use and institute alternative therapy.
- Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with BESIVANCE®.
- The most common adverse event reported in 2% of patients treated with BESIVANCE® was conjunctival redness. Other adverse events reported in patients receiving BESIVANCE® occurring in approximately 1-2% of patients included: blurred vision, eye pain, eye irritation, eye pruritus and headache.
- BESIVANCE® is not intended to be administered systemically. Quinolones administered systemically have been associated with hypersensitivity reactions, even following a single dose. Patients should be advised to discontinue use immediately and contact their physician at the first sign of a rash or allergic reaction.
- Safety and effectiveness in infants below one year of age have not been established.

Please see brief summary of Prescribing Information on adjacent page.

To learn more about BESIVANCE® call your Bausch + Lomb sales representative today.

References: 1. BESIVANCE® Prescribing Information, September 2012. **2.** At 12 hours, the concentration of besifloxacin in tears was >10 µg/mL. Proksch JW, Granvil CP, Siou-Mermet R, Comstock TL, Paterno MR, Ward KW. Ocular pharmacokinetics of besifloxacin following topical administration to rabbits, monkeys, and humans. *J Ocul Pharm Ther.* 2009;25(4):335-344. **3.** Comstock TL, Paterno MR, Usner DW, Pichichero ME. Efficacy and safety of besifloxacin ophthalmic suspension 0.6% in children and adolescents with bacterial conjunctivitis: a post hoc, subgroup analysis of three randomized, double-masked, parallel-group, multicenter clinical trials. *Paediatr Drugs.* 2010;12(2):105-112.

BAUSCH + LOMB

Besivance®
besifloxacin ophthalmic suspension, 0.6%

BRIEF SUMMARY OF PRESCRIBING INFORMATION
This Brief Summary does not include all the information needed to use Besivance safely and effectively. See full prescribing information for Besivance.

Besivance (besifloxacin ophthalmic suspension) 0.6%

Sterile topical ophthalmic drops
Initial U.S. Approval: 2009

1 INDICATIONS AND USAGE

Besivance® (besifloxacin ophthalmic suspension) 0.6%, is indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following bacteria:

*Aerococcus viridans**, CDC coryneform group G, *Corynebacterium pseudodiphtheriticum**, *Corynebacterium striatum**, *Haemophilus influenzae, Moraxella catarrhalis**, *Moraxella lacunata**, *Pseudomonas aeruginosa**, *Staphylococcus aureus, Staphylococcus epidermidis, Staphylococcus hominis**, *Staphylococcus lugdunensis**, *Staphylococcus warneri**, *Streptococcus mitis* group, *Streptococcus oralis, Streptococcus pneumoniae, Streptococcus salivarius**

*Efficacy for this organism was studied in fewer than 10 infections.

2 DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once before use.

Instill one drop in the affected eye(s) 3 times a day, four to twelve hours apart for 7 days.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Topical Ophthalmic Use Only NOT FOR INJECTION INTO THE EYE.

Besivance is for topical ophthalmic use only, and should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.

5.2 Growth of Resistant Organisms with Prolonged Use As with other anti-infectives, prolonged use of Besivance (besifloxacin ophthalmic suspension) 0.6% may result in overgrowth of non-susceptible organisms, including fungi. If super-infection occurs, discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and, where appropriate, fluorescein staining.

5.3 Avoidance of Contact Lenses Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with Besivance.

6 ADVERSE REACTIONS

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in one clinical trial of a drug cannot be directly compared with the rates in the clinical trials of the same or another drug and may not reflect the rates observed in practice.

The data described below reflect exposure to Besivance in approximately 1,000 patients between 1 and 98 years old with clinical signs and symptoms of bacterial conjunctivitis.

The most frequently reported ocular adverse reaction was conjunctival redness, reported in approximately 2% of patients.

Other adverse reactions reported in patients receiving Besivance occuring in approximately 1-2% of patients included: blurred vision, eye pain, eye irritation, eye pruritus and headache.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Pregnancy Category C. Oral doses of besifloxacin up to 1000 mg/kg/day were not associated with visceral or skeletal malformations in rat pups in a study of embryo-fetal development, although this dose was associated with maternal toxicity (reduced body weight gain and food consumption) and maternal mortality. Increased post-implantation loss, decreased fetal body weights, and decreased fetal ossification were also observed. At this dose, the mean C_{max} in the rat dams was approximately 20 mcg/mL, >45,000 times the mean plasma concentrations measured in humans.

The No Observed Adverse Effect Level (NOAEL) for this embryo-fetal development study was 100 mg/kg/day (C_{max}, 5 mcg/mL, >11,000 times the mean plasma concentrations measured in humans).

In a prenatal and postnatal development study in rats, the NOAELs for both fetal and maternal toxicity were also 100 mg/kg/day. At 1000 mg/kg/day, the pups weighed significantly less than controls and had a reduced neonatal survival rate. Attainment of developmental landmarks and sexual maturation were delayed, although surviving pups from this dose group that were reared to maturity did not demonstrate deficits in behavior, including activity, learning and memory, and their reproductive capacity appeared normal.

Since there are no adequate and well-controlled studies in pregnant women, Besivance should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers Besifloxacin has not been measured in human milk, although it can be presumed to be excreted in human milk. Caution should be exercised when Besivance is administered to a nursing mother.

8.4 Pediatric Use The safety and effectiveness of Besivance® in infants below one year of age have not been established. The efficacy of Besivance in treating bacterial conjunctivitis in pediatric patients one year or older has been demonstrated in controlled clinical trials *[see CLINICAL STUDIES (14)]*.

There is no evidence that the ophthalmic administration of quinolones has any effect on weight bearing joints, even though systemic administration of some quinolones has been shown to cause arthropathy in immature animals.

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

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action Besifloxacin is a fluoroquinolone antibacterial *[see CLINICAL PHARMACOLOGY (12.4)]*.

12.3 Pharmacokinetics Plasma concentrations of besifloxacin were measured in adult patients with suspected bacterial conjunctivitis who received Besivance bilaterally three times a day (16 doses total). Following the first and last dose, the maximum plasma besifloxacin concentration in each patient was less than 1.3 ng/mL. The mean besifloxacin C_{max} was 0.37 ng/mL on day 1 and 0.43 ng/mL on day 6. The average elimination half-life of besifloxacin in plasma following multiple dosing was estimated to be 7 hours.

12. Microbiology

Besifloxacin is an 8-chloro fluoroquinolone with a N-1 cyclopropyl group. The compound has activity against Gram-positive and Gram-negative bacteria due to the inhibition of both bacterial DNA gyrase and topoisomerase IV. DNA gyrase is an essential enzyme required for replication, transcription and repair of bacterial DNA. Topoisomerase IV is an essential enzyme required for partitioning of the chromosomal DNA during bacterial cell division. Besifloxacin is bactericidal with minimum bactericidal concentrations (MBCs) generally within one dilution of the minimum inhibitory concentrations (MICs).

The mechanism of action of fluoroquinolones, including besifloxacin, is different from that of aminoglycoside, macrolide, and β-lactam antibiotics. Therefore, besifloxacin may be active against pathogens that are resistant to these antibiotics and these antibiotics may be active against pathogens that are resistant to besifloxacin. *In vitro* studies demonstrated cross-resistance between besifloxacin and some fluoroquinolones.

In vitro resistance to besifloxacin develops via multiple-step mutations and occurs at a general frequency of $< 3.3 \times 10^{-10}$ for *Staphylococcus aureus* and $< 7 \times 10^{-10}$ for *Streptococcus pneumoniae*.

Besifloxacin has been shown to be active against most isolates of the following bacteria both *in vitro* and in conjunctival infections treated in clinical trials as described in the INDICATIONS AND USAGE section:

*Aerococcus viridans**, CDC coryneform group G,

*Corynebacterium pseudodiphtheriticum**, *C. striatum**, *Haemophilus influenzae, Moraxella catarrhalis**, *M. lacunata**, *Pseudomonas aeruginosa**, *Staphylococcus aureus, S. epidermidis, S. hominis**, *S. lugdunensis**, *S. warneri**, *Streptococcus mitis* group, *S. oralis, S. pneumoniae, S. salivarius**

*Efficacy for this organism was studied in fewer than 10 infections.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility Long-term studies in animals to determine the carcinogenic potential of besifloxacin have not been performed.

No *in vitro* mutagenic activity of besifloxacin was observed in an Ames test (up to 3.33 mcg/plate) on bacterial tester strains *Salmonella typhimurium* TA98, TA100, TA1535, TA1537 and *Escherichia coli* WP2uvrA. However, it was mutagenic in *S. typhimurium* strain TA102 and *E. coli* strain WP2(pKM101). Positive responses in these strains have been observed with other quinolones and are likely related to topoisomerase inhibition.

Besifloxacin induced chromosomal aberrations in CHO cells *in vitro* and it was positive in an *in vivo* mouse micronucleus assay at oral doses × 1500 mg/kg. Besifloxacin did not induce unscheduled DNA synthesis in hepatocytes cultured from rats given the test compound up to 2,000 mg/kg by the oral route. In a fertility and early embryonic development study in rats, besifloxacin did not impair the fertility of male or female rats at oral doses of up to 500 mg/kg/day. This is over 10,000 times higher than the recommended total daily human ophthalmic dose.

14 CLINICAL STUDIES

In a randomized, double-masked, vehicle controlled, multicenter clinical trial, in which patients 1-98 years of age were dosed 3 times a day for 5 days, Besivance was superior to its vehicle in patients with bacterial conjunctivitis. Clinical resolution was achieved in 45% (90/198) for the Besivance treated group versus 33% (63/191) for the vehicle treated group (difference 12%, 95% CI 3% - 22%). Microbiological outcomes demonstrated a statistically significant eradication rate for causative pathogens of 91% (181/198) for the Besivance treated group versus 60% (114/191) for the vehicle treated group (difference 31%, 95% CI 23% - 40%). Microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

17 PATIENT COUNSELING INFORMATION

Patients should be advised to avoid contaminating the applicator tip with material from the eye, fingers or other source.

Although Besivance is not intended to be administered systemically, quinolones administered systemically have been associated with hypersensitivity reactions, even following a single dose. Patients should be advised to discontinue use immediately and contact their physician at the first sign of a rash or allergic reaction.

Patients should be told that although it is common to feel better early in the course of the therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Besivance or other antibacterial drugs in the future.

Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with Besivance.

Patients should be advised to thoroughly wash hands prior to using Besivance.

Patients should be instructed to invert closed bottle (upside down) and shake once before each use. Remove cap with bottle still in the inverted position. Tilt head back, and with bottle inverted, gently squeeze bottle to instill one drop into the affected eye(s).

Manufactured by: Bausch & Lomb Incorporated
Tampa, Florida 33637

US/BES/15/0019
Based on 9142605(flat)-9142705(folded)

aqueous. When the adhesion between the vitreous and retina is strong, a small break can turn into a large retinal tear in short order. The longer the break goes undiagnosed, the greater the risk of RRD secondary to fluid migration into the subretinal space. Conversely, gravitational forces of the vitreous can provide some tamponade effect on inferior retinal breaks.[7,8]

Clinical Findings of Concern

In the same meta-analysis, investigators reviewed 12 studies looking at predictive factors for retinal tear based on direct clinical examination. They found two significant findings that should raise concern of a possible retinal tear:[2]

1. Vitreous hemorrhage (62% chance of retinal tear or detachment).
2. Pigment dusting of the vitreous (88% probability of the same).

Retinal detachment occurs with an estimated incidence of 12 per 100,000 persons per year and with a prevalence of 0.3%.[9,10] Risk factors for retinal detachment include, among others, age, aphakia, myopia, pseudophakia, recent eye surgery and trauma. While retinal detachments involving the macula are considered less urgent, "macula-on" detachments are usually considered an ocular urgency.[10]

What the Studies Say

The timing of surgical repair for macula or foveal-sparing RRDs has been a source of debate recently among retinal specialists. While most surgeons attempt to evaluate and repair macula-on detachments in a timely fashion, sometimes there are medical (i.e., comprehensive medical clearance for comorbid conditions) or logistical barriers (i.e., operating room, anesthesia, and caregiver availability) preclude timely surgery. A number of studies have reviewed the importance of timing for surgery in this subset of patients, and their conclusions might surprise you.

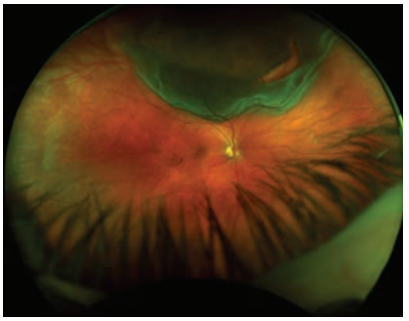


Fig. 2. This widefield image displays a patient's superiorly located retinal break with a secondary macula-on RRD, which we discovered using indirect ophthalmoscopy.

One retrospective analysis studied 199 patients who underwent scleral buckling surgery for macula-on detachments. While the majority of patients had the surgery within the first 24 hours (52%), 27% were addressed within one to three days, 10% between three to seven days and the rest longer than one week. The authors did not find a relationship between the timing of surgery and postoperative acuity at any time interval.[11]

Because this and other studies suggest that the rate of RRD progression is likely slower than intuitively expected, in some cases, it may be beneficial to delay surgery 24 to 48 hours.

Recognize an Emergency

While the data suggests we can be flexible concerning the timing of surgical repair for macula-on detachments, those involving giant retinal tears that are superiorly located and encroaching on the macula should be treated as an ocular emergency. When barriers exist to timely surgery, however, limited activity and bed rest should be considered. Some advocate occluding both eyes to limit saccadic eye movements, which can increase fluid dynamics and migration into the subretinal space.

Our patient called back within 20 minutes indicating she had found a ride. I instructed her to pack a bag of clothes and not to eat anything before her visit. Upon examining her, it was determined that she had preserved central vision (BCVA 20/20- each eye), but had reduced confrontation fields inferiorly in her left eye and slight asymmetry in her intraocular pressures (16mm Hg OD, 12mm Hg OS). Prior to and after dilation, slit-lamp exam of the vitreous increases revealed mild pigmentary "dusting" of the anterior vitreous. Indirect ophthalmoscopy revealed a large, superiorly located retinal break with a secondary "macula-on" rhegmatogenous retinal detachment (*Figure 2*). In six hours she was undergoing surgical intervention. ■

1. Hikichi T, Hirokawa H, Kado M, et al. Comparison of the prevalence of posterior vitreous detachment in whites and Japanese. Ophthalmic Surg. 1995;26(1):39-43.
2. Hollands H, Johnson D, Brox A, et al. Acute-onset floaters and flashes: is this patient at risk for retinal detachment? JAMA. 2009 Nov 25;302(20):2243-9.
3. Davis M. Natural history of retinal breaks without detachment. Arch Ophthalmol. 1974;92(3):183-94.
4. Shea M, Davis MD, Kamel I. Retinal breaks without detachment, treated and untreated. Mod Probl Ophthalmol. 1974;12(0):97-102.
5. Lincoff H, Gieser R. Finding the retinal hole. Arch Ophthalmol. 1971;85(5):565–9.
6. Machemer R. The importance of fluid absorption, traction, intraocular currents, and chorioretinal scars in the therapy of rhegmatogenous retinal detachments. XLI Edward Jackson Memorial Lecture. Am J Ophthalmol 1984;98(6):681–93.
7. Pederson J, MacLellan H. Experimental retinal detachment. I. Effect of subretinal fluid composition on reabsorption rate and intraocular pressure. Arch Ophthalmol. 1982;100(7):1150 –4.
8. Wilkinson C, Rice T. Michels retinal detachment. 2nd ed. St. Louis: Mosby;1997:471–81.
9. Sodhi A, Leung LS, Do DV, et al. Recent trends in the management of rhegmatogenous retinal detachment. Surv Ophthalmol. 2008;53:50-67.
10. Haimann MH, Burton TC, Brown CK. Epidemiology of retinal detachment. Arch Ophthalmol. 1982; 100(2):289-92.
11. Wykoff C, Smiddy W, Mathen T, et al. Fovea-sparing retinal detachments: time to surgery and visual outcomes. Am J Ophthalmol. 2010;150:205-10.

Sun Ophthalmics is a subsidiary of Sun Pharmaceutical Industries Ltd.

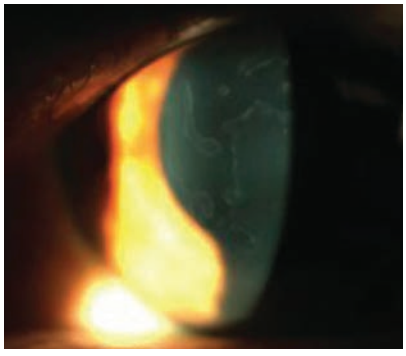

A dedicated team focused solely on eye care professionals.
An innovative pipeline designed to improve the way you treat.
A shared passion for advancing the field of ophthalmics.
With our unique approach and concierge customer care, **Sun Ophthalmics** offers the promise of new beginnings in the ophthalmic landscape.
Discover a brighter eye care community at SunIsOnTheRise.com.
Brightening the future of eye care
SUN
OPHTHALMICS

DIGGING DEEPER INTO SUPERFICIAL CORNEAL DYSTROPHIES

New discoveries in genetic mutations can help you diagnose and manage these conditions. **By Sherry Bass, OD**

There may be times a clinician sees a pattern of dots, spots, lines or a combination of all three on both corneas and wonders if the patient has a corneal dystrophy or a corneal degeneration. Corneal dystrophies are inherited conditions—usually passed on as autosomal dominant traits—characterized by a specific bilateral, often symmetric pattern of opacities. These opacities are initially found in the central cornea of younger individuals, and over time become denser and spread to the periphery. Some opacities are small and do not affect vision early on but coalesce as time progresses, resulting in reduced visual function. Most are slowly progressive, leaving the patient asymptomatic for years.

Dystrophies are rarely associated with systemic disease and are not the result of inflammation. Therefore, any unusual pattern of corneal opacities associated with corneal neovascularization is not a dystrophy and clinicians should investigate other etiologies. Most dystrophies do not require any surgical intervention until later in life, and advances in surgical procedures have resulted in faster recovery of visual function.



Map-type changes in epithelial basement membrane dystrophy.

Since corneal dystrophies are most often autosomal dominant in inheritance, clinicians should examine family members, given as many as 50% can be affected as well. Corneal dystrophies should not be confused with corneal degenerations, which tend to be asymmetric opacities in the periphery and are the result of aging and metabolic changes—as is the case with crocodile shagreen, Vogt's girdle and arcus senilis—and inflammation, as seen in band keratopathy and Salzmann's nodular degeneration.

Categorizing Corneal Dystrophies

Corneal dystrophies are categorized by the layers in which the opacities are found. However, new discoveries in the mutations that lead to the corneal dystrophies have increased our knowledge of their pathophysiology and may one day result in reclassification. Currently there are a number of dystrophies that have different phenotypic variations but are the result of mutations that occur in the same gene. Knowing the mutations that cause the dystrophies we see clinically will increase our understanding of the pathophysiological pathways that result in the deposition of the abnormal proteins interfering with corneal function and vision. This will someday lead to the development of medications that can interfere with these pathways to reduce deposition and the subsequent need for treatment.

Superficial corneal dystrophies affect the corneal epithelium, Bowman's layer and, initially, the anterior portion of the stroma. Some will also result in changes that affect the epithelial layers of the cornea.

These more superficial dystrophies are amenable to treatment with less invasive surgical procedures than a full penetrating keratoplasty (PK) or deep anterior lamellar keratoplasty (DALK). Recognizing a corneal dystrophy is important for prognosis of vision loss and early treatment to help avoid future vision loss.

The goal of the International Committee for Classification of the Corneal Dystrophies, formed in 2005, was to devise a new classification system for the corneal dystrophies. The committee divided the dystrophies into four categories, published in 2008, depending upon the phenotypic presentation that defined the condition and the genetics, such as whether the identification of the mutation was known, it was mapped to a specific location on a gene or the gene was not yet identified:[1]

- ***Category 1:*** A well-defined corneal dystrophy in which the gene is mapped and the mutation that causes the dystrophy is known.
- ***Category 2:*** A well-defined corneal dystrophy that is mapped to one or more specific chromosomal loci but the causative gene or genes are not known.
- ***Category 3:*** A well-defined corneal dystrophy that has not been mapped to any specific chromosomal locus.
- ***Category 4:*** A suspected or new corneal dystrophy that has not been well-defined as a corneal dystrophy.

As more genetic information is acquired, category 2, 3 and 4 dystrophies will ultimately become category 1 dystrophies.

Detecting Opacities: Biomicroscopy and OCT

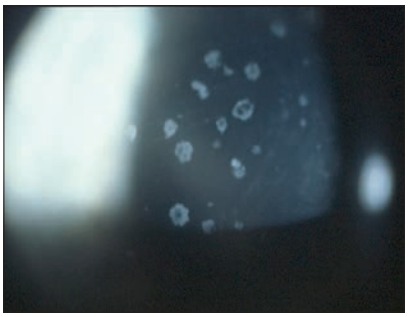
The ability to detect corneal dystrophies is dependent on good biomicroscopic technique and various methods of illumination, as some of the early changes may be subtle. Direct illumination using a broad, oblique beam allows clinicians to identify the number, types and location (central/peripheral) of the opacities. Narrowing the beam to an optic section will reveal the corneal layer that is affected. Indirect illumination using sclerotic scatter and retroillumination through a dilated pupil will uncover more opacities that may not be evident with direct illumination. Newer technologies such as anterior segment optical coherence tomography (OCT) allow for more precise identification of the affected layers than biomicroscopy.

Treatment

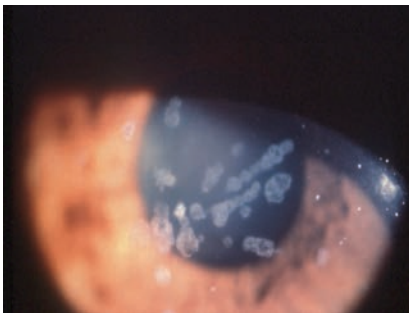
Many superficial corneal dystrophies affect the integrity of the corneal epithelium, resulting in recurrent corneal erosions (RCEs). Over time, the RCEs as well as the dystrophy itself result in an irregular epithelial surface, which can affect vision. In addition, the RCEs themselves cause pain and photophobia. Treatment is always case specific, but it is initially aimed at treating the RCEs to reduce the pain and photophobia. Eventually other treatment modalities will be needed, such as specialty fit contact lenses for the irregular astigmatism caused by the RCEs and surgical procedures such as superficial keratectomy (SK), lamellar keratectomy (LK) and phototherapeutic keratectomy (PTK).

These procedures are minimally invasive compared to PK, which results in longer recovery times. PTK uses an excimer laser (193nm) to remove the affected superficial layers of the cornea by photoablation.[2] One pulse of laser can remove 0.25µm of corneal tissue, so it is quite precise and results in a smooth and regular corneal surface, which improves visual outcomes.[2] It is used regularly to treat superficial corneal dystrophies affecting the epithelial and stromal layers for relief of symptoms secondary to RCEs and for visual improvement by removing or reducing the superficial corneal deposits associated with the corneal dystrophy. PTK should not be confused with photorefractive keratectomy (PRK), which is used to reduce refractive error. But because corneal dystrophies affect the central cornea, the ablation procedure mimics that of myopia correction. The result is an induced hyperopia, the amount of which is dependent on the ablation depth. This may be countered to some degree by simultaneously performing an anti-hyperopia treatment with the laser. Although PTK may induce refractive error, the patient's best-corrected visual acuity and comfort may improve.

If clinicians suspect a corneal dystrophy, they should initially try to examine family members and, if in doubt, refer to a corneal specialist for confirmation based on the phenotypic presentation. Since many dystrophies progress slowly, the patient can be monitored. Anterior segment photo documentation with OCT is important when the patient is being followed. Genetic confirmation is indicated if a family member is interested or if the clinical picture is not diagnostic. Testing for the transforming growth factor beta-induced (TGFBI) gene—a common gene that has mutations causing some of the corneal dystrophies—is available commercially, and insurance may or may not reimburse the patient. Clinicians should educate patients about what to expect regarding deterioration of vision with increasing opacification, symptoms of RCEs, if that is a part of the dystrophy, and potential treatment options if and when necessary.



Granular dystrophy in a 22-year-old asymptomatic female with 20/20 visual acuity in both eyes.



Granular dystrophy in the patient's 45-year-old mother with 20/40 visual acuity.

Epithelial Dystrophies

A number of corneal dystrophies affect the cornea's epithelial layer:

• ***Epithelial basement membrane dystrophy (EBMD).*** The most common epithelial dystrophy is EBMD, previously referred to as map-dot-fingerprint dystrophy. As its name suggests, this dystrophy is characterized by patterns that look like small continents on a map, fingerprint swirls, small dot opacities and bleb or milky-white opacities. These patterns are created by the opacities composed of abnormal basement membrane material. The deposits can occur within the epithelial layers (maps), between the epithelial cells (fingerprint swirls) or within the epithelial cells (dots). Some of these changes can best be appreciated after instillation of fluorescein dye, since wetting is irregular over the maps and fingerprint opacities.

RCEs can occur after the third decade of life. Patients presenting with RCE with no prior history of corneal trauma, surgery or contact lens wear should be suspect for an epithelial dystrophy, although corneal dystrophies affecting other layers may also result in RCEs as well.

EBMD is not always a true dystrophy, however, in the sense that some of these changes can also appear following corneal trauma or surgery. Some forms of EBMD have been noted to be of autosomal dominant inheritance. Mutations are localized to the TGFBI gene on chromosome 5, making some forms of EBMD a category 1 dystrophy.[3] The TGFBI gene, also known as the keratoepithelin gene, interacts with collagen and is responsible for corneal development and healing. Mutations in TGFBI actually cause seven corneal dystrophies in total, with varying phenotypic expression, affecting the epithelium, Bowman's membrane as well as the stroma.

The RCEs can be treated with antibiotics, artificial tear solutions and bandage contact lenses. Repeated RCEs that cause corneal irregularity and reduced vision can be successfully treated with anterior stromal puncture, epithelial debridement and polishing as well as PTK.[4]

• ***Meesmann dystrophy.*** This dystrophy is characterized by diffuse, tiny, gray-white vesicles that extend to the limbus.[5] Unlike most other corneal dystrophies, Meesmann dystrophy is often first apparent on exam at quite an early age. It progresses slowly until such time as there are RCEs, which occur when the vesicles burst. Meesmann dystrophy usually causes no effects on vision until middle age.

The mutation that causes Meesmann dystrophy has been localized to two keratin-specific genes, KRT3 on chromosome 12q12 and KRT12 on chromosome 17q12, making Meesmann dystrophy a category 1 corneal dystrophy.[6] Treatment is initially targeted to treat the pain and photosensitivity of RCEs. Eventually PTK and LK may be needed to treat the irregularity of the corneal surface due to repeated RCEs.[7]

• ***Lisch corneal dystrophy.*** Originally named whirled, band-shaped, microcystic dystrophy after the patterns of interesting opacities, this dystrophy has since been shortened to Lisch corneal dystrophy after the ophthalmologist Karl Lisch who first described it.[8] It is a rare dystrophy inherited as a sex-linked trait and is characterized by interesting, almost artistic patterns of whirls, feathery-shaped and linear opacities, all consisting of small deposits in the epithelial cells. On histologic exam, these deposits are due to the vacuolization of the epithelial cell cytoplasm and disappear when patients wear gas permeable contact lenses.

Because the clinical appearance of tiny vacuoles is similar to Meesmann corneal dystrophy, the question arose whether Lisch dystrophy was a variant of Meesmann dystrophy. However, the gene that causes Lisch dystrophy has been mapped to the X chromosome, Xp22.3, unlike Meesmann dystrophy, but the mutation has not yet been identified, making it a category 2 dystrophy.[9] This is a perfect example of how genetics has helped differentiate a dystrophy that is phenotypically similar to another.

• ***Epithelial recurrent corneal erosion dystrophy (ERED).*** Perhaps one of the worst of the epithelial dystrophies is ERED, as it results in RCEs by age five.[10] Patients are besieged by repeated attacks of RCEs that can be triggered by smoke, dry air, upper respiratory infection and minimal trauma. Treatment is problematic,


Phoroptor® VRx
DIGITAL REFRACTION SYSTEM
Reichert
AMETEK
SHIFT YOUR EHR INTO GEAR
DRIVE PRACTICE EFFICIENCY WITH PHOROPTOR® VRx
Subjective
Sphere Adjust
Clear
In
Fog
Near
XCyl
BB
Cyl +/-
Out
VD
x1000 EHR
You've spent time and money implementing your practice's EHR system. Now take it out of neutral. Let the all-new Reichert® Phoroptor® VRx Digital Refraction System accelerate your exam time and drive practice efficiency.
Effortless EHR and prescreen device integration. Thinnest and most compact design. Incredibly fast. Ultra-quiet. Made in the USA.
www.reichert.com/vrx
Limited time offer: Free ClearChart® 2
Take a test drive with an authorized Reichert® distributor or at Vision Expo East - Booth MS 6810.
Reichert TECHNOLOGIES
AMETEK
© 2015 AMETEK, Inc. & Reichert, Inc. (2-2016) · Phoroptor is a registered trademark of Reichert, Inc. · Made in USA · www.reichert.com

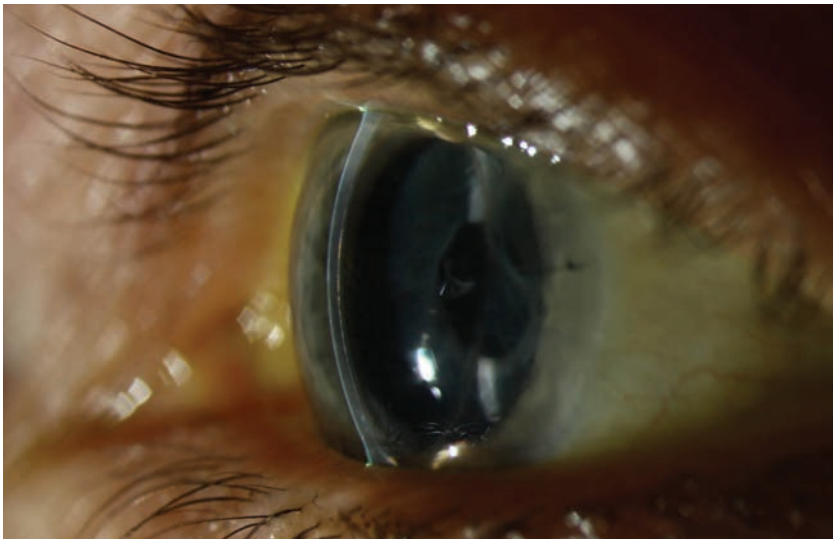


Photo: Christine W. Sindt, OD.

Posterior corneal changes in a patient with EBMD and Fuch's dystrophy.

and attacks can last weeks. Eventually, the cornea scars from repeated RCEs and small keloids form, resulting in irregular corneas and vision loss. While PTK has been attempted, this dystrophy is difficult to treat. By the third to fourth decade of life, patients' RCEs subside, but the corneal damage has already occurred. A corneal graft may be needed in about 25% of cases.[10]

Bowman's Layer Dystrophies

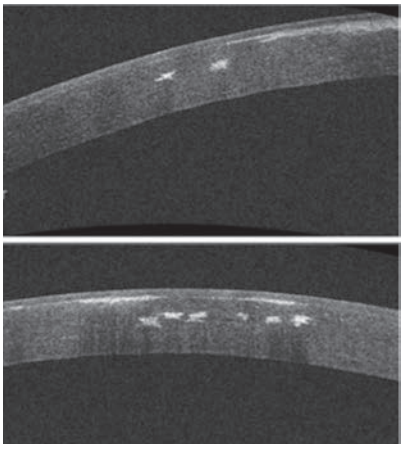
There are a few dystrophies of Bowman's layer, but the most common is Reis-Buckler corneal dystrophy (RBCD). This dystrophy is characterized by ring-shaped opacities that result from localized areas of Bowman's membrane thickening.[11] It results in epithelial irregularity that causes irregular astigmatism and RCEs. Visual acuity is usually good until the later decades when the ring-shaped opacities become more pronounced, spreading to the periphery.

Treatment for the RCEs and corneal irregularity by therapeutic contact lenses, superficial keratectomy (SK), PTK and PK have all been used to treat RBCD; however, the dystrophy recurs within a few years. Investigators report that mitomycin C can help prevent recurrences.[12] The mutation that causes RBCD has been identified in the TGFBI gene on chromosome 5q31, making it a category 1 dystrophy.[13]

As RBCD progresses, the ring-shaped opacities spread to the corneal periphery. In addition, the RCEs eventually cause scarring.

Thiel-Benkhe dystrophy (TBCD), which also affects Bowman's layer, is less progressive than Reis-Buckler dystrophy, but has the same opacities. Some consider TBCD to be a variant of RBCD. Research also describes another similar dystrophy in only one family, which may also simply be a variant of RBCD.[14]

Above, advanced granular dystrophy in a 79-year-old male with 20/200 visual acuity. At right, OCT of the patient's cornea demonstrates the anterior and mid-stromal nature of these deposits.



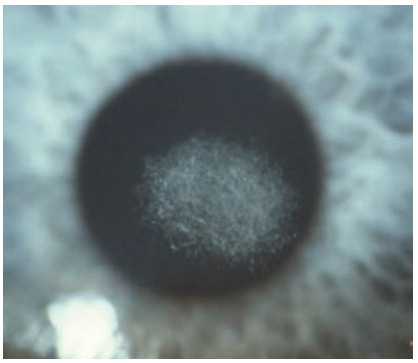
Anterior Stromal Dystrophies

There are myriad corneal dystrophies that affect the stroma, since the stroma is the thickest layer of the cornea. But only stromal dystrophies that affect the anterior stroma are most amenable to treatment with PTK. Many of these dystrophies also cause RCEs and have an effect on epithelial function and structure. Although PTK has been attempted in some of the other corneal dystrophies that affect the deeper stroma, PTK has not been successful.

• *Granular dystrophy.* One of the most common of the anterior stromal dystrophies is granular dystrophy. As its name suggests, granular dystrophy is characterized by powdery and granular or crumb-like opacities in the central cornea that are composed of hyaline.[15] The stroma between these opacities is clear, and vision is normal for most of the patient's life. Vision slowly deteriorates, but treatment is not usually necessary until the seventh or eighth decade of life.

The mutation that causes granular dystrophy is on the TGFBI gene on chromosome 5q31, one of the seven corneal dystrophies resulting from TGFBI mutations. The mutation


RED ROSE
Red Rose, an Ogi Eyewear Brand
www.redroseglasses.com | 1.888.560.1060



Schnyder corneal dystrophy reveals central crystalline changes made of cholesterol deposits.

results in accumulation of hyaline, causing the types of deposits seen, which can be treated with PTK.[16]

• *Lattice dystrophy.* Another common stromal dystrophy which may be treated with PTK is lattice dystrophy. Lattice dystrophy gets it name from the lattice-like network of refractile lines that lie in the anterior stroma. There are several types of lattice dystrophy, all of which are characterized by the same refractile lattice-type lines. In all types, the lattice lines are made up of amyloid.[17] Type 1 lattice dystrophy is a typical dystrophy, inherited as an autosomal dominant trait. The lines start in the central cornea and spread to the periphery in the later years. Because the stroma between is relatively clear early on, vision is fairly good until later in life when the lattice lines spread to the periphery of the cornea and amyloid plaques form. Lattice dystrophy may also cause RCEs, which may be treated by PTK. Such treatment may be effective early on, but some experts feel that the UV light in PTK may increase formation of the deposits. The mutations that cause type 1 lattice dystrophy are also in TGFBI in chromosome 5q31.

Type 2 lattice dystrophy manifests the same refractile lattice lines as type 1, but is one of the rare dystrophies associated with a systemic disorder, namely systemic amyloidosis—a disorder of amyloid metabolism caused by mutations on the gelsolin gene on chromosome 6.[18] Amyloid will deposit in the skin, sclera and peripheral nerves as well as the cornea. The lattice deposits seen in type 2 develop later in life than in type 1 and are thicker and more peripheral. This type does not cause RCEs.

A number of other types of lattice dystrophy have been reported in the literature depending on the pedigree, mode of inheritance and phenotypic expression. These are typically later-onset dystrophies with deeper stromal opacities with various forms of amyloid deposition.[19,20]

• *Combined granular-lattice dystrophy (Avellino corneal dystrophy).* A pedigree was reported in the small town of Avellino, Italy, that appeared to have corneal deposits described as being both granular and lattice-like refractile lines. The granular opacities predominated in the younger individuals, while the lattice lines appeared in the older individuals as the granular opacities coalesced and thickened.[21] Histology demonstrated that in this combined granular-lattice dystrophy, the granular opacities are composed of hyaline, and the lattice lines are composed of amyloid. Since it was first described, the name has been changed from Avellino corneal dystrophy to combined granular-lattice dystrophy. Since both dystrophies are the result of mutations in the TGFBI gene, it is possible that the mutations segregate together.

Advanced lesions have been treated with PTK in combined dystrophy, but research shows PTK can result in more rapid and advanced recurrence of the opacities, presumably due to the ultraviolet light.[22]

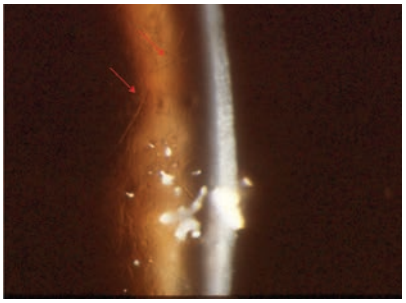
• *Crystalline dystrophy of Schnyder.* Crystalline dystrophy, as its name suggests, is a stromal dystrophy characterized by crystalline, refractile deposits in the stroma. These deposits are composed of cholesterol and phospholipids.[23] Early cases present with central crystalline deposits with minimal effect on visual acuity. With time, some patients may also have an associated arcus composed of cholesterol.

Although corneal dystrophies are rarely associated with a systemic disorder, a young patient presenting with crystalline deposits should be worked up for systemic dyslipidemia. Mutations in the UBIAD1 gene, which may regulate or play a role in cholesterol biochemistry, transport or storage, have been reported in some pedigrees.[24]

Corneal Dystrophy Discoveries

Recently, the corneal dystrophies have undergone an evolution of categorization and genetic discovery. Many patients suffer from pain and photophobia secondary to the RCEs that are associated with many of the superficial corneal dystrophies, as well as visual compromise due to the increased density of the opacities with age and the corneal irregularity that results from repeated RCEs.

When specialty contact lenses and topical drops are no longer effective, PTK is the most commonly used treatment for smoothing the



The cornea of a 35-year-old patient with early lattice dystrophy. The refractile lines are best appreciated in indirect illumination (red arrows).

irregular corneal surface and removing or reducing the density of the opacities associated with the superficial corneal dystrophies; however, success varies and recurrences are common.

The identification of the mutation responsible for the corneal dystrophy is a critical step toward understanding the pathophysiology of the formation of the deposits. Once the pathways that form the abnormal proteins associated with the corneal dystrophies are identified, other treatments may be developed to interfere with the production of these abnormal proteins. This ultimately results in less deposition of opacities, less symptoms and less need for surgical intervention.

Early diagnosis will be even more important for timely intervention once new treatment becomes available. In the meantime, patients have access to therapeutic options that offer better comfort and vision. ■

Dr. Bass is a distinguished Ttaching professor at the SUNY State College of Optometry. She lectures on hereditary diseases of the eye.

1. Weiss J, Maler H, Lisch W, et al. The IC3D classification of the corneal dystrophies. Cornea. 2008; 27(Suppl 2):S1–83.
2. Starr M, Donnenfeld E, Newton M, et al. Excimer laser phototherapeutic keratectomy. Cornea. 1996;15:557-65.
3. Boutboul S, Black G, Morre J, et al. A subset of patients with epithelial basement membrane corneal dystrophy have mutations in TGFBI/BIGH3. Human Mutation. 2006;27(6):553-7.
4. Pogoulov P, Langenboucher A, Kruse A, et al. Long-term results of PTK for corneal map-dot-fingerprint dystrophy (Cogan-Guerry). Cornea. 2006;25(7):774-7.
5. Fine P, Yanoff M, Pitts E, et al. Meesman's epithelial dystrophy of the cornea. Am J Ophthalmol. 1977;83:633-42.
6. Swensson O, Swensson B, Nolle B, et al. Mutations in the keratin gene as a cause of Meesmann-Wilke corneal dystrophy and autosomal skin cornification disorders. Klin Monatsbl Augenkunde. 2000;217(1):43-51.
7. Jabert I, Stapleton F. Management of symptomatic Meesmann dystrophy. Optom Vis Sci. 2009;86(10):1202-6.
8. Lisch W, Steuhl K, Lisch C, et al. A new, band-shaped and whorled microcystic dystrophy of the corneal epithelium. Am J Ophthalmol. 1992;114(1):35-44.
9. Lisch W, Buttner A, Oeffner F, et al. Lisch corneal dystrophy is genetically distinct from Meesmann's corneal dystrophy and maps to Xp22.3. Am J Ophthalmol. 2000;130(4):461-8.
10. Hammer B, Bjorck E, Langenstedt K, et al. A new corneal disease with recurrent erosive episodes and autosomal dominant inheritance. Acta Ophthalmol. 2008;86(7):758-63.
11. Bucklers M. Uber eine wekere familiar Hornhaut-dystrophie. Klin Monatsbl Augenkunde. 1949;114:386-97.
12. Omdahl M, Fagerholm R. Treatment of corneal dystrophies with phototherapeutic keratectomy. J Refract Surg. 1998;14(2):129-35.
13. Miller A, Solomon R, Bloom A, et al. Prevention of recurrent Reis-Bucklers dystrophy following excimer laser phototherapeutic keratectomy with topical mitomycin C. Cornea. 2004;23(7):732-5.
14. Grayson M, Willebrandt H. Dystrophy of the anterior limiting membrane of the cornea (Reis-Buckler's type). Am J Ophthalmol. 1966;61:345-9.
15. Groenouw A. Knotcchenformige Hornhauttrubungen. Arch Augenheld. 1890;21:281-89.
16. Vyas S, Rathi V. Phototherapeutic keratectomy for granular dystrophy. Asian J Ophthalmol. 2008;10:123-5.
17. Klintworth GK. Lattice corneal dystrophy. An inherited variety of amyloidosis restricted to the cornea. Am J Pathol. 1967;50(3):371-99.
18. Gorevic PD, Munoz PC, Gorgone G, et al. Amyloidosis due to a mutation of the gelsolin gene in an American family with lattice corneal dystrophy type II. N Engl J Med. 1991 Dec 19;325(25):1780-5.
19. Stock EL, Feder RS, O'Grady RB, et al. Lattice corneal dystrophy type IIIA. Clinical and histopathological correlations. Arch Ophthalmol. 1991;109(3):354-8.
20. Fujiki K, Hotta Y, Nakayasu K, et al. A new L527R mutation of the beta GH3 gene in patients with lattice corneal dystrophy with deep stromal opacities. Hum Genet. 1998;103:286-9.
21. Kennedy SM, McNamara M, Hillery M, et al. Combined granular lattice dystrophy (Avellino corneal dystrophy). Br J Ophthalmol. 1996;80(5):489-90.
22. Lee JH, Stulting R, Lee D, et al. Exacerbation of granular dystrophy type II (Avellino corneal dystrophy) after LASEK. J Refract Surg 2008;24(1):39-45.
23. Garner A, Tripathi PC. Hereditary crystalline corneal dystrophy of Schnyder II. Histopathology and ultrastructure. Br J Ophthalmol 1972;56(5):400-8.
24. Orr A, Dubé M-P, Marcadier J, Jiang H, Federico A, George S, et al. (2007) Mutations in the UBIAD1 Gene, Encoding a Potential Prenyltransferase, Are Causal for Schnyder Crystalline Corneal Dystrophy. PLoS ONE 2(8): e685.

PEER • REVIEWED • PRA • ARTICLE

The Ins and Outs of Corneal Wound Healing

Learn the science and key clinical points of corneal wound healing and adjunct modalities such as amniotic membranes. **By Tarah N. Lee, OD**

As the anterior-most structure of the eye, the cornea plays an important role in vision, the mechanical integrity of the eye and immunological defense. It is highly structured—a trait critical to its abilities to refract light and prevent infection. However, the cornea's position leaves it susceptible to a variety of injuries and insults. Proper function of the tear film, lids and conjunctiva are all essential in maintenance of the cornea, which leaves corneal function vulnerable to disruption from all corners of the globe—and beyond. Corneal healing mechanisms are in place to aid in proper repair and preservation of corneal structure after injury. And, when these fail, therapeutic advances are available that aim to minimize long term complications.

Corneal A&P

A typical episode of corneal wound healing consists of a complex sequence of events that involves numerous cell types within the appropriate biochemical environment. Maintaining an understanding of the anatomical and physiological characteristics of the cornea—from its multilayer structure down to its cellular junctions—can help practitioners better understand the clinical key points in this process.

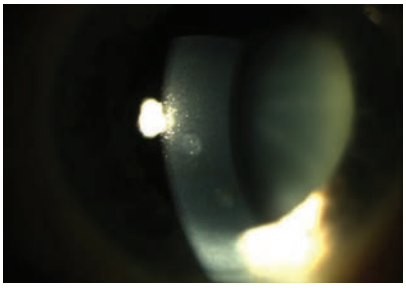


Fig. 1. Two anterior stromal scars.

From anterior to posterior, five familiar layers comprise the cornea: epithelium, Bowman's layer, stroma, Descemet's membrane and the endothelium. A sixth corneal layer, the so-called Dua's layer or pre-Descemet's layer, has been proposed as a necessary addition to the list, but its disputed nature means it remains a separate classification for now.[1]

• ***Corneal epithelium.*** Composed of five to seven layers of cells, and approximately 50µm thick, the epithelium contains several cell types oriented in layers from anterior to posterior, paralleling the larger corneal structure itself. Specific cell junctions are responsible for maintaining the relatively dehydrated state of the cornea, for cellular communication and exchange of materials, and for the cornea's selective permeability. The epithelial cells aid in maintaining a stable tear film, and for secreting the epithelial basement membrane—critical in corneal healing. Corneal epithelial cells are constantly turned over as the outermost cells are shed into the tear film. The entire epithelium is turned over in approximately seven to 10 days. This process is accelerated during wound healing and generally leads to rapid healing for corneal injuries that only involve the epithelial cells.[8] (See, *"A Closer Look: The Corneal Epithelium,"* p. 46).

• ***Bowman's layer.*** This acellular layer, approximately 8µm to 14µm thick, is composed primarily of collagen and organized as randomly arranged fibrils 20nm to 25nm in diameter. This fibril arrangement evens out towards the posterior as it intermingles with the underlying stroma. Bowman's layer is highly

E N H A N C I N G L I F E T H R O U G H B I R T H®

BioDOptix®
Amniotic Extracellular Matrix

You are focused on healing. We are focused on improving your clinical experience.

BioDOptix is a dehydrated, extracellular membrane allograft derived from human amniotic tissue that is intended for use as a scaffold for ocular tissue repair and regeneration.

CONVENIENT
For use in the inpatient, outpatient, and clinical setting. No refrigeration required.

PERFORMANCE
Adheres without sutures or glue to sclera and conjunctiva when applied to ocular surface.

AVAILABLE
In multiple sizes to fit your needs.

Visit us at biodlogics.com for more information.

Vision Expo East
April 14 – 17, 2016
New York City
Booth #MS6662

BioD, LLC

1715 Aaron Brenner Drive
Suite 204
Memphis, TN 38120

Toll Free - 1-877-675-4149
contact@biodllc.com
www.biodlogics.com

resistant to penetration or damage; however, if it does become injured, it cannot regenerate, leading to its necessary replacement by epithelial tissue or stromal scar tissue.

• ***Stroma.*** The thickness of the cornea is largely due to the presence of the stroma, which measures approximately 500µm thick. This medial layer is composed of an organized network of collagen fibrils and extracellular ground substance, a porous, hydrated gel composed primarily of proteoglycan aggregates. Keratocytes—specialized fibroblasts—is the primary cell type within the stroma and help maintain its integrity. They also produce collagen, glycosaminoglycans (GAGs) and matrix metalloproteinases (MMPs). As such, the precise organization of collagen fibrils within the corneal stroma is imperative to maintaining corneal clarity and appropriate stromal hydration.

• ***Descemet's membrane.*** Measuring just 3µm to 5µm thick, Descemet's lies between the corneal stroma and the endothelium, essentially functioning as the basement membrane of the corneal endothelium. Descemet's membrane is separated into the anterior lamina, which is composed of the collagen that gives the layer its elastic properties, and a posterior lamina, which is secreted by the endothelium. The posterior lamina is constantly produced by the endothelium, thickening throughout life. Like Bowman's layer, Descemet's membrane is highly resistant to trauma but can regenerate if damaged.

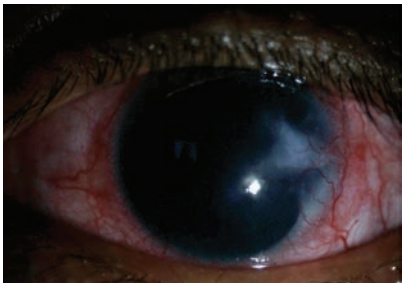


Fig. 2. This patient presented with a vascularized corneal scar.

• ***The corneal endothelium.*** The posterior-most corneal layer consists of a single polyhedral cell layer that maintains the cornea's deturgescence via ionic pumps. The cells' basal surface lies against Descemet's membrane, while their apical surface lines the anterior chamber. Though the corneal endothelial cells are joined by gap junctions and tight junctions, the barrier formed by the two is more penetrable than the cornea's anterior surface, thus allowing for corneal uptake of nutrients from the aqueous humor. These cells cannot divide or replicate, so when they are lost, those that remain employ changes in shape or size to fill the spaces in the endothelium.

A Closer Look: The Corneal Epithelium

The superficial layer of cells comprising the epithelium is approximately two cell layers thick and composed of non-keratinized squamous cells.[2] These cells are fairly flat with numerous microvilli and microplicae, which increase their total surface area to help stabilize the overlying tear film. The epithelial glycocalyx helps adhere the tears to the corneal surface cells, thereby preventing the binding of pathogens.[3] These surface cells are joined together by desmosomes as well as tight junctions, which are primarily composed of zonula occludens. The tight junctions help provide a highly selective barrier to substances in the tear film.[4] Intercellular junctions help prevent unwanted substances from entering the cornea and aids in maintaining the deturgesence of the cornea.

The second layer of the epithelium is composed of two to three layers of wing cells joined together by desmosomes and adherens junctions. They are attached anteriorly to the surface cells and posteriorly to basal cells by desmosomes and also joined together by gap junctions, allowing molecules to be exchanged directly between individual cells

The basal cell layer consists of a single layer of columnar cells that form the posterior-most layer of the corneal epithelium. These cells are attached to each other via gap junctions—which play a role in mediating and differentiating intercellular communication—and desmosomes. These basal cells secrete a basement membrane, which is divided into an anterior lamina lucida and a more posterior lamina densa.[5] The corneal epithelial basement membrane is composed primarily of collagens, laminins, proteoglycans and nidogens.[6]

The basement membrane plays an important role in cellular functions, including those involved in healing, by controlling the binding of growth factors and their local concentrations between cell layers. The basement membrane of the basal cells attaches via hemidesmosomes to the underlying Bowman's layer, while anchoring fibrils pass through the hemidesmosomes to the Bowman's layer and down into the underlying stroma, where they attach to anchoring plaques of the extracellular matrix, forming an anchoring complex.[7]

Epithelial Wound Healing

The process of corneal epithelial wound healing can be divided into phases that occur in sequence, but may overlap in time. They are the latent or lag phase, migration, proliferation and epithelial reattachment.

• ***The latent phase.*** The first phase of the corneal wound healing process is characterized by cellular remodeling and changes to tear composition in preparation for healing.[12] This phase results in an increased production of enzymes (including MMP-9s), which degrade the damaged epithelial basement membrane.[4] Matrix metalloproteinases decrease cellular adhesion and help enhance cellular migration; they are also important in the degradation and remodeling of normal extracellular matrix (ECM) maintenance. However,

See us at VEE Booth# MS6803

Your Exam... Only Better!

- Increased efficiency
- Combat reductions in reimbursements
- Enhanced practice image
- EMR integration
- Eliminate back and shoulder pain
- Patient referrals

VEATCH
OPHTHALMIC INSTRUMENTS

WWW.VOI2020.COM

800.447.7511

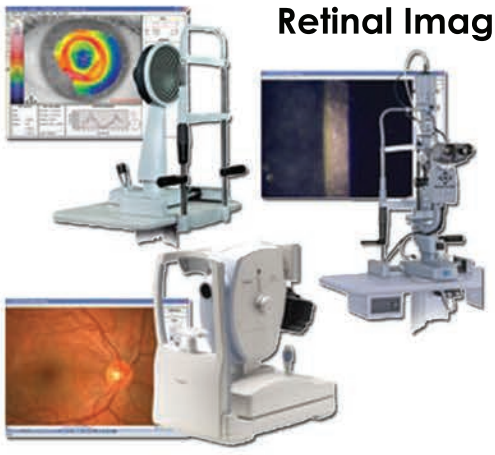
A Company with an Eye for Good Service

ReSeeVit

Anterior Segment Imaging

Corneal Wavefront Topography

Retinal Imaging



Additional Offers From Veatch

Exam Lane Packages Starting at $12,995

excessive levels of these enzymes can hinder healing.[13]

The latent phase involves several distinct steps and takes place over several hours: first, epithelial cells damaged during injury undergo apoptosis and are shed into the tear film. Next, adherens junctions and gap junctions in cells near the border of the defect are lost and the attachments of basal cells to the basement membrane near the wound edges are broken down. These basal cells then change shape and lose their microvilli, before they form cellular extensions known as filopodia and lamellipodia.[9] The epithelial defect is then coated with fibronectin, which serves as a foundation for the adjacent epithelial cells to migrate over.

• ***Migration.*** The next phase occurs as cells near the wound edge flatten and spread. The filopodia and lamellipodia are sent out and form temporary attachments to the substrate; contractile elements then pull the cell forward toward the defect.[4] Adjacent cells remain attached by desmosomes and maintain their position relative to each other as they slide across the denuded area. The aforementioned temporary attachments are then cleaved, and the filopodia and lamellipodia are again sent forward to repeat the process. This cycle continues until the defect is completely sealed by a single layer of cells. The process typically takes place over 24 to 36 hours, though time can vary depending on the defect's location and size.

• ***Proliferation.*** After migration is complete, the monolayer of cells covering the defect proliferates to restore the normal thickness of the epithelium and fill in the defect. The transient amplifying basal cells reproduce via mitosis and the new cells move inwards toward the center of the defect, then upwards to fill it.[9] Cells convert from basal cells to wing cells, then finally squamous surface cells as they move. Tight junctions form to re-establish the cornea's barrier function, and gap junctions, adherens junctions and desmosomes reform between cells.

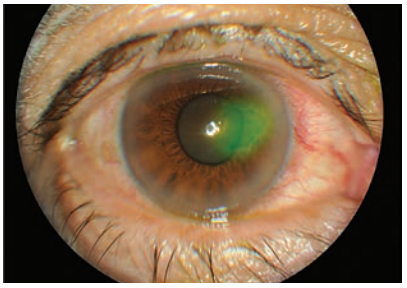


Fig. 3. Traumatic cornea abrasion stained with sodium fluorescein.

• ***Epithelial reattachment.*** During the final phase, hemidesmosomes reassemble to firmly attach the epithelial layer to the substrate as anchoring fibrils reattach to anchoring plaques in the stroma. As long as the basement membrane did not receive any damage, this process occurs in a matter of days; if damage did occur however, final formation of attachments and re-anchoring of cells can take months or longer.[8]

Stromal Healing

The process of stromal remodeling break down resynthesizes and reorganizes the corneal stroma following stromal and epithelial injury. This process, which involves the differentiation and actions taken by keratocytes, is typically lengthy and crucial for restoring corneal transparency.

The first stromal event following epithelial injury is keratocyte apoptosis. In this stage, soluble mediators from the corneal epithelium cause cell death via apoptosis of the underlying stromal keratocytes, while other keratocytes undergo transformation into fibroblasts and myofibroblasts. Keratocytes also increase production of the chemokines that attract other inflammatory cells to the corneal stroma from the limbal blood supply and tear film. These inflammatory cells scavenge the remains of apoptotic cells and debris; keratocytes may also eventually become fibroblasts and participate in wound closure as well as play a role in nerve regeneration.[13]

Myofibroblasts within the corneal stroma are thought to derive from keratocytes via influence from transforming growth factor beta (TGF-β) and platelet-derived growth factor (PDGF). The myofibroblasts lay down a provisional ECM and generate contractile forces in an attempt to close the wound; as such, they are important in collagen and ECM remodeling, as well as in corneal haze formation and regression.[14] A delay in regeneration of the epithelial basement membrane (EBM), due to damage, dystrophy or elevated levels of MMP-2 and MMP-9 can allow TGF-β and PDGF to continue entering the corneal stroma from the epithelium, which perpetuates the generation of myofibroblasts.

Ongoing myofibroblast presence can lead to an abundantly disorganized ECM, which contributes to corneal opacity and scarring. Myofibroblasts can also hinder the appropriate restoration of the anterior stromal keratocyte population, which is critical to full recovery of the EBM.[6] Only when the EBM is appropriately re-established do proper stromal levels of TGF-β and PDGF settle, causing myofibroblast apoptosis, keratocyte repopulation, clearing of abnormal ECM and the restoration of corneal transparency.

Inhibition of Proper Healing

The corneal epithelium is maintained in a complex balance that can be easily disrupted. Abnormalities in the lids or tear film, damage to corneal nerves, injuries and infections can all compromise corneal integrity.

Coding Connection

By John Rumpakis, OD, MBA, Clinical Coding Editor

Amniotic Membranes: The Perfect Cover

Success with amniotic membranes depends on establishing medical necessity, having a meticulous medical record and following the ICD-10 rules.

Only five years ago, a small company in southern Florida, Bio-Tissue, pursued getting a CPT code for the placement of an amniotic membrane on the eye. In 2011, Bio-Tissue achieved its goal and the American Medical Association created CPT code 65778 (currently defined as: "Placement of amniotic membrane on the ocular surface; without sutures,") in recognition of the importance of delivering the wound healing properties of cryopreserved amniotic membrane to the ocular surface without the use of sutures.

The use of amniotic membranes on the ocular surface is now a well-established therapy that can speed healing, particularly for severe inflammatory conditions. It may become even more important as we move to an outcomes-based payment system, considering it could provide significant cost savings. However, not all amniotic membranes are created equal, which CMS noted in a recent Local Coverage Determination:[1]

"Amnion [Bio-Tissue] 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."

So while it may be tempting to use less effective technology to increase profitability, it may not be the wisest choice in the era of outcomes-based care.

Surgical Coding

Clinical application of an amniotic membrane is virtually identical to the insertion of a bandage contact lens; however, CPT references it as a surgical procedure, and clinicians must remember to follow surgical coding rules.

Coding for a minor surgical procedure is not difficult. In accordance with minor surgical rules, an office visit (either 920XX or 992XX) is generally not separately billable when performed on the same date of service as CPT code 65778. Reimbursement for the 65778 code already includes compensation for the office visit related to the decision to perform this procedure. It would be rare to append modifier -25 to an E/M office visit performed on the same day as the application of an amniotic membrane.

As of January 1, 2016, the global period was reduced from 10 days to zero, meaning there is no longer a period of time following the application of an amniotic membrane incorporated into the payment. Each follow up after the application, other than on the day of the procedure, is now billable. This does not mean you can bill simply for the removal of the membrane. You have to meet the requirements and definitions for an office visit just as you would for any follow-up visit, whether it be a 9921X or 9201X.

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 itself, so clinicians cannot bill for V2790 with 65778. Rarely, commercial carriers may have policies that allow for reimbursement of the procedure and the materials, and if so, the appropriate HCPCS Level II code is V2790 ("Amniotic membrane for surgical reconstruction, per procedure"). My advice—don't bill for it as a separate item.

OSD Particulars

With respect to ocular surface disease (OSD), amniotic membranes are generally reserved for more advanced disease, as you are not treating the "dry eye," but the corneal sequelae of the OSD, so medical necessity for this procedure would generally be established after the failure of other management strategies.

Success in the Future

The growing popularity of amniotic membranes reminds us how far we have come in being able to provide emerging technology in caring for our patients—providing outcomes we could only dream of a few years ago. Your long-term success will always depend on your ability to properly establish medical necessity, having a meticulous medical record and following the detailed documentation rules the ICD-10 requires. ■

1. Centers for Medicare and Medicaid Services. Local Coverage Determination (LCD): Amniotic Membrane- Sutureless Placement on the Ocular Surface (L36237). www.cms.gov/medicare-coverage-database/indexes/lcd-list.aspx?Cntrctr=369&ContrVer=1&CntrctrSelected=369*1&s=All&DocType=Active%7CFuture&bc. Accessed March 8, 2016.

Epithelial defects are deemed persistent (PEDs) when they remain unresponsive to treatment two weeks after therapeutic initiation. PEDs may result in disassembly of hemidesmosomes and the degradation of Bowman's layer and the corneal stroma. When corneal healing is impaired, the cornea becomes especially vulnerable to repeated epithelial defects or recurrent erosions, neovascularization or chronic stromal inflammation and scarring *(Figure 2)*.

Recurrent corneal erosions (RCE) may occur following trauma or in certain corneal dystrophies *(Figures 3 and 4)*. They wear away the corneal epithelium due to defective epithelial cell anchoring, which can occur from the improper formation of the anchoring complex, or as a result of abnormalities of the EBM.

Abnormalities in composition and formation of the basement membrane appear to be associated with epithelial basement membrane dystrophy (EBMD) as well as RCE. Corneas displaying EBMD produce redundant layers of basement membrane that can extend into the corneal epithelium instead of lying beneath it.[15] These additional layers of basement membrane, seen as lines or fingerprints within the cornea, may prevent the normal movement of cells from the basal layer through to the wing and surface cell layers of the epithelium. Additionally, cells can become trapped with cellular debris in the basement membrane to form cysts. Abnormal cell layering and inadequate adhesion of cells to the underlying stroma may lead to disruptions in corneal clarity as well as painful RCEs. Disruptions in the corneal basement membrane can also lead to increased levels of TGF-β1 and PDGF in the corneal stroma, leading to decreased transparency.[16]

Inadequate adhesion of the epithelium to the stroma or injuries that damage the basement membrane and disrupt hemidesmosome formation can lead to RCE, as the poorly adhered epithelium is easily removed via mechanical disruption by the eyelids. Increased levels of MMP-2 and MMP-9 have been found in the tear fluid of patients with RCE.[17,18] An increase in MMPs may result in abnormal or excessive degradation of the ECM, hindering proper corneal wound healing and leading to RCEs. Other conditions and lifestyle factors associated with improper corneal healing include diabetes, neurotrophic disease, ocular surface disease and smoking. A study shows that altered cell migration and proliferation signaling pathways, as well as impaired corneal nerve function, is associated with delayed wound healing in diabetic corneas.[13]

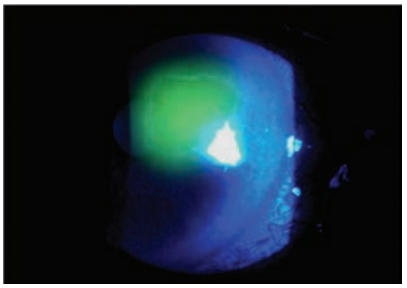


Fig. 4. Traumatic cornea abrasion stained with sodium fluorescein.

Treatment Advances

Traditional treatment goals for corneal epithelial defects are to minimize pain, decrease the likelihood of infection and expedite healing. A recent increase in understanding of RCE and PED pathophysiology has led to new treatment modalities such as oral tetracyclines, topical steroids, autologous serum eye drops and amniotic membrane (AM) patching or grafting. These treatments aim to decrease inflammation and optimize the environment for healing.

Documented medical use of amniotic membranes (AM) has existed since the early 1900s. The material was used in 1940 by researchers as a biological dressing for the ocular surface and was then rarely mentioned in connection with ophthalmic use again until 1995, when researchers first used it as a surgical graft for ocular surface reconstruction in rabbit corneas. That same year, they used cryopreservation to commercially prepare AM as a graft.[11] AM has since experienced a resurgence as an ophthalmic healing modality and is believed to inhibit inflammation, fibrosis and angiogenesis, as well as support wound healing by aiding in cell migration and differentiation. Research also suggests its use as an antimicrobial, antiviral and analgesic agent.

Due to this wide range of reported actions that influence wound healing, AM has been used for the treatment of persistent corneal defects and ulcerations, RCEs, acute chemical or thermal burns, bullous keratopathy, partial limbal stem cell deficiency and in surface reconstruction of the conjunctival tissue.

The amnion, the innermost layer of the fetal placenta, varies in thickness from 0.02 to 0.5mm.[20] AM is composed of three basic layers: a single layer of cuboidal epithelial cells; a thick basement membrane layer; and a collagen-rich, nearly avascular mesenchymal layer or stroma. The stroma contains an inner compact layer, middle fibroblast layer and outer spongy layer.[21]

AM epithelial cells have numerous microvilli and produce cytokines and other factors involved in cell proliferation and differentiation.[22-25] They also produce antimicrobial peptides that may decrease the risk of infection.[20] The basement membrane (BM) of the AM contains proteoglycans and other molecules that maintain membrane integrity

and include various collagens, fibronectin, laminin, fibroblasts and growth factors.[11] The BM is used to promote epithelial cell migration, adhesion and differentiation.[26]

The AM stroma is a collagen rich layer that provides tensile strength and contains abundant proteoglycans, glycoproteins and hyaluronic acid (a glycosaminoglycan). Research demonstrates that the AM stroma suppresses TGF-β signaling, myofibroblast proliferation and differentiation.[14] Myofibroblast suppression may help reduce scarring, fibrovascular ingrowth and corneal haze. As such, in this manner AM may modulate healing by promoting tissue reconstruction rather than scar formation.[20] The AM stroma also suppresses inflammatory cytokines and sequesters infiltrating inflammatory cells.[25,27]

Research suggests AM may also help maintain nerve growth factor signaling, which is thought to promote nerve regeneration.[19,22,25] Additionally, AM may not express most of the major histocompatibility antigens that could result in transplant rejection.[19,21,27] More recent studies have found that AM may only produce these antigens in small quantities, which is supported by the lack of significant immune response associated with AM use. This positive property of AM may be related to an immunosuppressive effect exerted by apoptotic AM cells, allowing AM to be used without the need for immunosuppression.[11,20,21,23,28]

Fresh amnion is a good source of biologically active factors that encourage growth and wound healing, proliferation and migration of epithelial cells as well as ECM remodeling. The tissue can either be heated or air-dried, though doing so may result in loss of some of the tissue's biological properties. AM may also be lyophilized or freeze-dried, then sterilized by gamma radiation and stored at room temperature. Freeze-dried AM was shown to retain most of its physical, biologic and morphologic characteristics.[26] It may also be stored on nitrocellulose paper and preserved in glycerol for cryopreservation. Cryopreserved AM may be stored between 12 to 24 months and may retain more of the membrane's initial structural, physiological, and biochemical properties.

Research suggests that AM epithelial cells are non-viable in either fresh or preserved preparations, as substances are either released from the devitalized cells or the supporting basement membrane and stroma.[3,23,29] Despite this, though some of the biological properties of the preserved AM are retained, they are likely only viable for a limited time.[24] Both cryopreserved and dehydrated AM appear to demonstrate comparable clinical efficacy. [26]

Amniotic Membrane Grafting

Clinically, AM can be used to treat corneal wounds of a wide range of size and severity. AM may be incorporated as a graft (in the inlay technique), as a bandage (in the onlay technique), or in combination.

During the inlay procedure, the wound is debrided and the AM is applied with its epithelium facing upward, then sutured into place. The AM serves as a permanent substitute for the basement membrane; as such, neighboring recipient epithelial cells eventually migrate onto the AM and integrate it into the host cornea.[23] AM can be used as an inlay for patients with PEDs or corneal ulcerations, or after removal of conjunctival lesions.

PEDs or RCEs that are unresponsive to conservative treatments with artificial tears, autologous serum and bandage contact lenses may particularly benefit from an AM, with complete healing generally observed within one to two weeks of its application.[31] Research using confocal microscopy to investigate amniotic membrane transplantation (AMT) found that the epithelial layer progressively dissolves over a period of two weeks, though the basement membrane and stroma of the graft were detectable for months.[29] In fact, traces of an AM graft can remain for months or years.

As part of the onlay technique, a large amniotic membrane covers the epithelial defect as well as part of the surrounding ocular surface in a fashion similar to a bandage contact lens. It protects the delicate epithelium from the mechanical shearing action of the lids, acts as a barrier to inflammatory cells and substances from the tear film, and aids in hydration of the epithelium. AM orientation may not be particularly important, though placement of the AM stroma-side up may allow for greater contact with the precorneal tear film.[19] The AM is sutured to the ocular surface, but detaches in

A Closer Look: Limbal Epithelial Stem Cells

New corneal epithelial cells are formed in the basal layer, the only mitotically active layer of the cornea.[8] Limbal epithelial stem cells (LESC) are located near the limbus and provide a supply of basal cells that later convert into wing and surface cells as they migrate anteriorly.

LESCs provide epithelial cells throughout their lifetime and produce transient amplifying cells, which populate the basal epithelium in the peripheral cornea and limbus.[10] The cells then migrate centrally, proliferate, and terminally differentiate as central epithelial cells. If the LESC are damaged, corneal epithelial cells may be replaced with conjunctival cells, resulting in opacification of the cornea.[11] LESCs generally proliferate slowly but this process is accelerated in response to corneal injury to repopulate the corneal epithelium.

The next generation of autorefraction is here. Fast, portable, and scary accurate, SVOne Pro is the go-to choice for the modern professional.

Learn more at
www.smartvisionlabs.com/autorefractors

Visit us at Vision Expo East Booth MS6614

SMART VISION LABS

US Patent 09066683 | U.S. Application No. 14/991,055 (pending)

one to two weeks: a fresh AM can be applied if healing is not complete by this point.[23] The AM should be changed weekly, If it does remain, it may dissolve over weeks to months, losing efficacy.

AM can be used as an onlay for conditions characterized by a large amount of inflammation (e.g., following burns or in the case of Stevens-Johnson syndrome), given its anti-inflammatory, anti-angiogenic, anti-scarring and analgesic properties. In these cases, it may be wise to use AM early following disease onset to suppress inflammation and prevent cicatricial complications.

The inlay-onlay technique is used for extensive ulcerations and perforations of the ocular surface. Numerous smaller pieces of AM are used to fill the defect while a larger piece is used as an onlay overtop. The onlay portions protect the inlay pieces and promote epithelialization.

AM may also be used in sutureless techniques along with fibrin glue and either a therapeutic contact lens or a scleral ring conformer *(Figure 5)*.[3] Dehydrated AM is available as a sutureless graft, and cryopreserved AM is commercially available in a sutureless form clipped between two polycarbonate carrier rings.

In cases where the LESC population is damaged or deficient, corneal PEDs can occur, or the corneal surface can become populated by the conjunctival epithelium, leading to chronic inflammation, scarring, neovascularization or ulceration of the corneal surface. This leaves the eye vulnerable to perforation or intraocular infection.[19] Patients with total LESC deficiency may undergo LESC transplantation using an autograft from the fellow eye if it's viable, or an allograft from another donor.[3,22] AM has also been used as a biological substrate and carrier for culturing of *ex vivo* limbal epithelial sheets

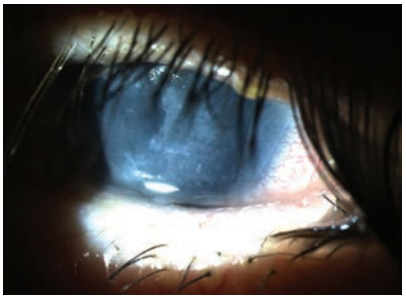


Fig. 5. Sutureless amniotic membrane graft under a bandage soft contact lens for treatment of a neurotrophic ulcer.

presumably containing LESCs, which research suggests may allow for use of smaller LESC grafts to decrease the likelihood of LESC deficiency for the donor eye.[19,23] (See, *"A Closer Look: Limbal Epithelial Stem Cells,"* page 52.)

AM grafts are in use for an ever-expanding list of indications. Their positive healing properties, low immunogenicity and biocompatibility make them ideal adjuncts to traditional treatment modalities.

Though AM is anatomically similar to the ocular surface and its physical characteristics as a pliable biological membrane are directly observable, its clinical efficacy is still speculative.[31] Widespread anecdotal reports of clinical success suggest that AM shows great potential as an adjunctive modality to the therapeutic armamentarium available to eye care providers to aid in ocular surface healing. However, additional research is needed confirm its efficacy as a first-line modality. ■

Dr. Tarah Lee is a fellow of the American Academy of Optometry and an adjunct clinical faculty member for the UC Berkeley School of Optometry.

1. Dua HS, Faraj LA, Said DG, et al. Human corneal anatomy redefined: a novel pre-Descemet's layer (Dua's layer). Ophthalmology. 2013 Sep;120(9):1778-85.
2. Remington L. 2004. Clinical anatomy of the visual system, 2nd edition. Butterworth-Heinemann, St. Louis, MO, 304 pps.
3. Rauz S, Saw VP. Serum eye drops, amniotic membrane and limbal epithelial stem cells--tools in the treatment of ocular surface disease. Cell Tissue Bank. 2010 Feb;11(1):13-27.
4. Lu L, Reinach PS, Kao WW. Corneal epithelial wound healing. Exp Biol Med (Maywood). 2001 Jul;226(7):653-64.
5. Eghrari AO, Riazuddin SA, Gottsch JD. Overview of the Cornea: Structure, Function, and Development. Prog Mol Biol Transl Sci. 2015;134:7-23.
6. Torricelli AA, Singh V, Santhiago MR, et al. The corneal epithelial basement membrane: structure, function, and disease. Invest Ophthalmol Vis Sci. 2013 Sep 27;54(9):6390-400.
7. Mantelli F, Mauris J, Argüeso P. The ocular surface epithelial barrier and other mechanisms of mucosal protection: from allergy to infectious diseases. Curr Opin Allergy Clin Immunol. 2013 Oct;13(5):563-8.
8. Ashby BD, Garrett Q, Wilcox MDP. Corneal injuries and wound healing – review of processes and therapies. Austin J Clin Ophthalmol. 2014 March; 1(4):1-25.
9. Steele C. Corneal wound healing: a review. Optometry Today. 1999 Sept; 28-32.
10. Castro-Muñozledo F. Review: corneal epithelial stem cells, their niche and wound healing. Mol Vis. 2013;19:1600-13.
11. Alió JL, Abad M, Scorsetti DH. Preparation, indications and results of human amniotic membrane transplantation for ocular surface disorders. Expert Rev Med Devices. 2005;2(2):153-60.
12. Liu CY, Kao WW. Corneal Epithelial Wound Healing. Prog Mol Biol Transl Sci. 2015;134:61-71.
13. Ljubimov AV, Saghizadeh M. Progress in corneal wound healing. Prog Retin Eye Res. 2015 Nov;49:17-45.
14. Eraslan M, Toker E. Mechanisms of corneal would healing and its modulation following refractive surgery. Marmara Medical Journal. 2009; 22(2); 169-178.
15. Sacchetti M, Macchi I, Tiezzi A, et al. Pathophysiology of Corneal Dystrophies: From Cellular Genetic Alteration to Clinical Findings. J Cell Physiol. 2016 Feb;231(2):261-9.
16. Torricelli AA, Santhanam A, Wu J, et al. The corneal fibrosis response to epithelial-stromal injury. Exp Eye Res. 2016 Jan;142:110-8.
17. Sakimoto T, Sawa M. Metalloproteinases in corneal diseases: degradation and processing. Cornea. 2012;31 Suppl 1:S50-6.
18. Ramamurthi S, Rahman MQ, Dutton GN, et al. Pathogenesis ,clinical features and management of recurrent corneal erosions. Eye (Lond). 2006 Jun;20(6):635-44.
19. Sippel KC, Ma JJ, Foster CS. Amniotic membrane surgery. Curr Opin Ophthalmol. 2001 Aug;12(4):269-81.
20. Mamede AC, Carvalho MJ, Abrantes AM, et al. Amniotic membrane: from structure and functions to clinical applications. Cell Tissue Res. 2012 Aug;349(2):447-58.
21. Malhotra C, Jain AK. Human amniotic membrane transplantation: Different modalities of its use in ophthalmology. World J Transplant. 2014 Jun 24;4(2):111-21.
22. Tseng SC, Espana EM, Kawakita T, et al. How does amniotic membrane work? Ocul Surf. 2004 Jul;2(3):177-87.
23. Meller D, Pauklin M, Thomasen H, et al. Amniotic membrane transplantation in the human eye. DtschArztebl Int. 2011 Apr;108(14):243-8.
24. Litwiniuk M, Grzela T. Amniotic membrane: new concepts for an old dressing. Wound Repair Regen. 2014 Jul-Aug;22(4):451-6.
25. Dekaris I, Mravici I, Barisi A, et al. Amniotic membrane transplantation in the treatment of persistent epithelial defect on the corneal graft. CollAntropol. 2010 Apr;34Suppl 2:15-9.
26. Sangwan VS, Burman S, Tejwani S, et al. Amniotic membrane transplantation: a review of current indications in the management of ophthalmic disorders. Indian J Ophthalmol. 2007 Jul-Aug;55(4):251-60.
27. Shimmura S, Shimazaki J, Ohashi Y, et al. Antiinflammatory effects of amniotic membrane transplantation in ocular surface disorders. Cornea. 2001 May;20(4):408-13.
28. Thatte S. Amniotic membrane transplantation: An option for ocular surface disorders. Oman J Ophthalmol. 2011;:4(2):67-72.
29. Nubile M, Dua HS, Lanzini TE, et al. Amniotic membrane transplantation for the management of corneal epithelial defects: an in vivo confocal microscopic study.Br J Ophthalmol. 2008 Jan;92(1):54-60.
30. Clare G, Suleman H, Bunce C, et al. Amniotic membrane transplantation for acute ocular burns. Cochrane Database Syst Rev. 2012 Sep 12;9:CD009379.
31. Liu J, Sheha H, Fu Y, et al. Update on amniotic membrane transplantation. Expert Rev Ophthalmol. 2010 Oct;5(5):645-661.

NEW Biofinity® XR toric lenses

For astigmatic patients with high refractive errors

The most advanced lenses are now in reach

COMING SOON!

National Availability: **June 2016**

CooperVision®
Live Brightly®

No Insult To Injury: Treating Corneal Trauma

Learn to treat corneal injuries—from abrasions to burns—and help patients on the road to recovery. **By Lori Vollmer, OD**

Corneal injuries are often intensely painful and present the potential for ocular morbidity with vision loss. While the causes of abrasions and foreign bodies—and their effects on the eyes—are seemingly unlimited, the overall treatment goal is similar: minimize pain, maintain integrity of the globe, prevent corneal scarring and infection, and preserve visual acuity.

Patients with corneal trauma report redness, photophobia, decreased acuity (when the injury involves the visual axis) and varying degrees of pain. Because patients have different thresholds for pain, its presence or absence is not always helpful from a diagnostic perspective. However, management is often dictated by this factor.

Clinicians should always take a detailed history and document a patient's visual acuity, which may have to be obtained while triaging them. Though the use of anesthetic drops may be necessary due to patient discomfort, clinicians should quickly assess the scope of the injury and attempt to check visual acuity, including pinhole, prior to the instillation of any medications.

Corneal Healing

When managing a corneal injury, it is helpful to remember these key points of the healing process:

- The cornea repairs by cell migration, proliferation and differentiation, followed by extracellular matrix remodeling.[1]
- Corneal epithelial healing relies on limbal stem cells and remodeling of the basement membrane.
- The corneal regenerative response to an abrasion is related to the size and depth of the wound. Small epithelial defects typically heal in 24 to 48 hours, whereas large defects may take significantly longer, particularly if the stroma is involved. Corneal edema may remain after the epithelium heals and may continue to cause a decrease in visual acuity until its resolution.
- For deeper injuries, the corneal stroma heals via the transformation of keratocytes to fibroblasts and myofibroblasts, which may result in opacification and scarring.[1]
- In the initial phase of healing, epithelial cells flatten, spread and move. Cellular and subcellular reorganization and migration of the epithelial cells also occurs at the wound edge.[2]
- Cell proliferation, necessary to heal large abrasions, begins approximately 24 hours after injury. Stem cells from the limbus give rise to transient amplifying cells (TAC), which migrate to heal the corneal defect and replenish the wounded area.[3] The majority of the defect is covered by a single layer of epithelium that "slides" over the wound, with a normal thickness restored by proliferation and upward movement of cells from the basal layer.[2] The wound healing is not complete until the newly regenerated epithelium has anchored firmly to the underlying connective tissue, which does

not occur until the defect is completely covered. Although transient attachments are regularly formed and released during the cell migration process, formation of normal adhesions takes approximately six weeks.[2]

Management of Corneal Epithelial Defects

Corneal abrasions make up the majority of corneal injuries, and many treatment methods exist to resolve them without visual complications. Topical management typically involves:

- ***Antibiotics.*** This is administered as a prophylactic measure, and several options can achieve similar efficacies. Ultimately, antibiotic choice is often based upon physician preference. Fourth-generation fluoroquinolones have a wide spectrum of coverage, are less toxic than some traditionally used medications and are used regularly for prophylaxis in surgical patients.[4-7] Other acceptable medications include Polytrim (trimethoprim/polymyxin B ophthalmic solution, Allergan), aminoglycosides (e.g., gentamycin or tobramycin) or less desirable early-generation fluoroquinolones such as ciprofloxacin and ofloxacin.
- ***Artificial tears.*** These are used to flush away antigenic material, promote epithelial repair and provide relief from discomfort.
- ***A cycloplegic agent.*** This will reduce secondary inflammation and uncomfortable ciliary spasm. It may be necessary to remove any retained foreign material or debride the loose epithelial edges to improve the healing process.

Small Abrasions

Lesions without significant loss of epithelial tissue generally heal well and quite quickly in the absence of treatment. If a patient has minimal to no pain, an artificial tear with a prophylactic antibiotic is typically adequate. Advise patients to rest and reassure them that they will likely feel significantly better in the morning, given the minor nature of their injuries.

Case 1: The Exploding Egg

A 57-year-old black female presented urgently with eye swelling and facial burns from an "egg exploding in her face" after reheating it in the microwave, while in the shell. The patient reported initially to the emergency room and was diagnosed with facial and ocular burns and placed on erythromycin ointment for the eyes and Neosporin (neomycin/polymyxin B/bacitracin, Johnson & Johnson) ointment for her facial burns.

Fig. 1. Thermal burns to face and cornea.

The following day, the patient reported to the clinic due to increasing lid edema and consistent ocular pain that was greater in the right eye than in the left. She was an established patient with a history of systemic lupus erythematosus and associated keratitis sicca. She was using Restasis (cyclosporine ophthalmic emulsion 0.05%, Allergan) OU BID and artificial tears for her dry eye condition. Systemically, she was taking Plaquenil (hydroxychloroquine, Sanofi-Aventis) 200mg BID, pantoprazole, omega-3 fatty acids, metoprolol, meloxicam, Imuran (azathioprine, Prometheus Laboratories), folic acid, aspirin, Rocaltrol (calcitriol, Roche) and Advair diskus by inhalation (fluticasone propionate and salmeterol inhalation powder, GlaxoSmithKline).

The patient's uncorrected visual acuity on initial examination was 20/100 OD and 20/80 OS. Clinical examination revealed blistering of the skin on the face as well as 4+ lid edema in both eyes (Figure 1). Her right cornea had a 6mm-by-5mm abrasion. In addition, there was 4+ SPK on both corneas. The anterior chamber was clear and well formed in both eyes. There was no evidence of foreign bodies or penetrating injuries.

A bandage lens was placed on the patient's right eye with some difficulty due to lid edema, and the patient noted immediate relief. She was instructed to discontinue the erythromycin ointment and was prescribed prophylactic moxifloxacin OD TID and artificial tears every hour in both eyes.

The patient returned the following day and reported feeling significantly better. The bandage lens was moisturized with artificial tears and carefully removed. The corneal epithelial defect was significantly improved with a 1mm by 0.5mm defect remaining. A bandage lens was no longer needed, and the patient was advised to continue with her topical drops.

The patient returned two days later, and her uncorrected visual acuity was 20/20 OD and 20/25+ OS. Her eyes were white and the edema had nearly resolved. The abrasion was healed, though there was still a 3+ SPK in both eyes secondary to her keratitis sicca. The patient was instructed to discontinue her moxifloxacin, continue artificial tears and resume her Restasis OU BID. The patient was seen one week later and her facial burns had nearly healed with some pigment abnormalities remaining and her keratitis sicca persists.

Large Corneal Abrasions

For patients with an abrasion affecting 25% to 50% of the cornea, prophylactic antibiotic, preservative-free artificial tears every hour and in-office cycloplegia (e.g., homatropine 5%) are generally adequate. Often it is difficult for the patient

Case 2: Would You Like Bacon With that Egg?

A 35-year-old black female presented emergently with severe pain in the right eye. She reported feeling intense pain that started suddenly while cooking breakfast. She believed she was splashed with hot oil. The patient's visual acuity was 20/200 OD. Clinical examination revealed a corneal abrasion as well as foreign body particles that appeared to be small pieces of bacon (Figure 2). The anterior chamber was clear and well formed. The eye was irrigated, the foreign bodies removed with forceps and the loose corneal epithelium debrided. The patient was treated with a bandage contact lens, a prophylactic antibiotic and artificial tears every 30 minutes to an hour.

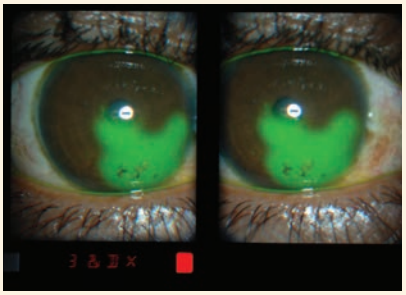


Fig. 2. Thermal burn with foreign body of bacon.

The patient returned the following day feeling significantly better, with the abrasion approximately 75% resolved. The bandage lens was replaced and her topical medications continued. When the patient returned 48 hours following the accident, her cornea was completely healed. Topical antibiotics were discontinued and she continued with artificial tears for comfort as needed.

to obtain the cycloplegic medication at a pharmacy. However, since the majority of the wound will be repaired within 24 to 48 hours, in-office administration is often sufficient, especially if the patient is seen on a daily basis.

The largest corneal abrasions—affecting greater than 50% of the cornea—may take longer to heal and cause the patient significant pain. Over-the-counter analgesics or prescription medication, such as acetaminophen with codeine or hydrocodone, may be necessary for a short period of time.

These abrasions are often associated with stromal folds from edema. Once the epithelium is eroded, fluid will readily migrate into the cornea. The edema, once accumulated, will not clear until the epithelium completely regenerates, which may take as long or longer to resolve than the epithelial defect—the defect may take two weeks to re-epithelialize, while the edema may last for up to six weeks.[8] Large abrasions are treated with prophylactic antibiotics, copious artificial tears every hour and a cycloplegic agent. A slightly stronger cycloplegic such as atropine 1% may be necessary. If the patient is in significant pain, an NSAID or prescription oral analgesic may be used. Topical hyperosmotics may be helpful for resolving corneal edema and promoting tighter attachments of the epithelial cells to the basement membrane.

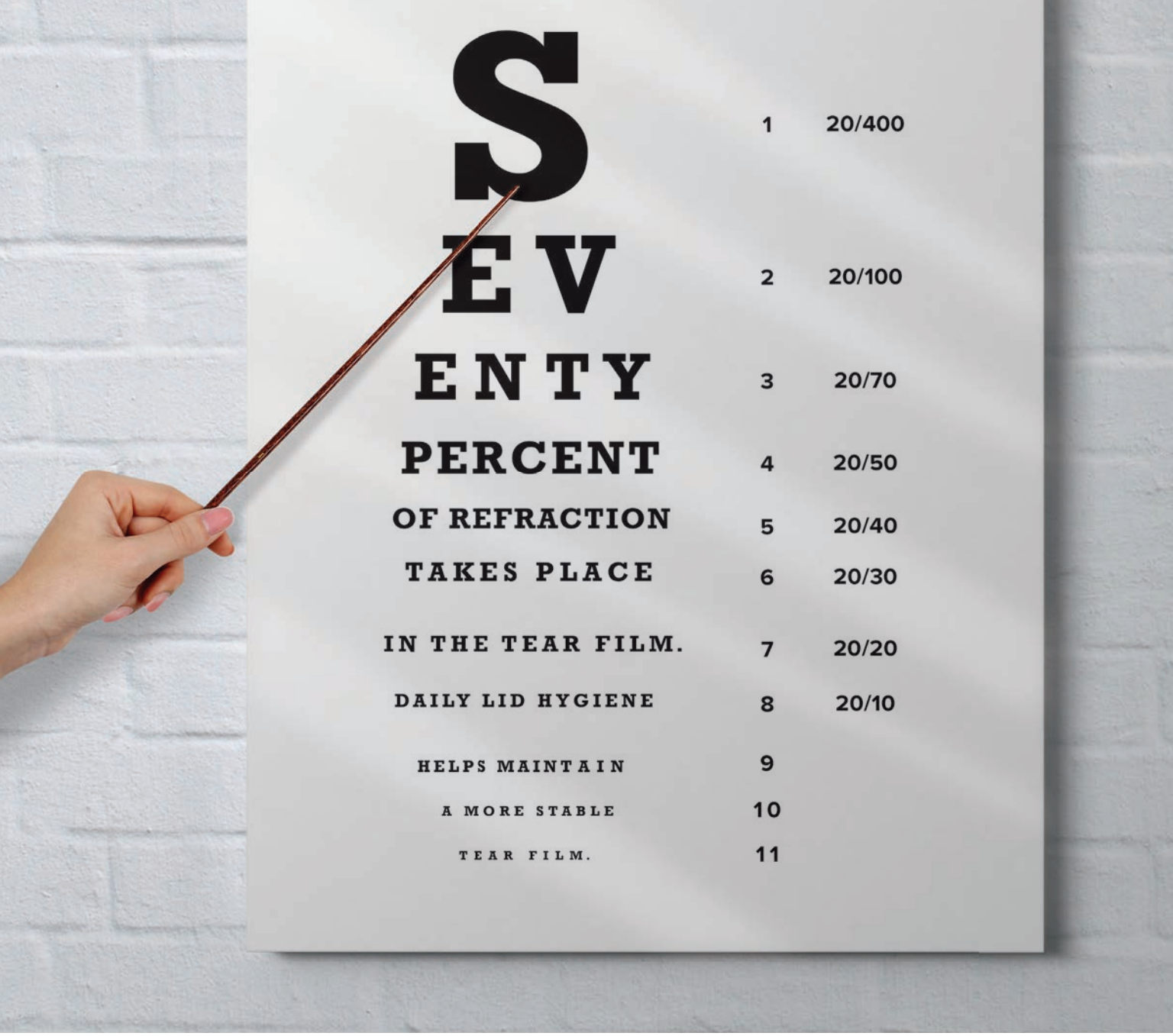
Bandage contact lenses can be very helpful for patients with significant pain from large abrasions. However, tight bandage lenses or materials with low oxygen permeability may worsen corneal edema. For this reason, only high Dk lenses should be used for this purpose.[9] The newly formed epithelial attachments are very weak and may be pulled off easily when removing the bandage lens. To avoid this, float the contact lens in solution or artificial tears first to be certain it is loose before removing. Bandage contact lenses should be replaced at each follow up as necessary for pain management, as the cornea will need to be assessed and the patient will be using antibiotic drops over the lens. It is important to differentiate an epithelial defect from a contact lens-related corneal infiltrate. Bandage contact lenses should not be used to treat epithelial defects associated with contact lens wear.

Topical ointments are commonly used to treat epithelial injuries. However, ointments are not sustained-release medications and thus provide little benefit. Further, while topical ointments may provide some lubrication, they may blur vision.

Any drug placed on the surface of the eye is in some way toxic and may interfere with re-epithelialization. Therefore, the "less is more" philosophy is a prudent choice when treating corneal abrasions.

A secondary infection from an abrasion is rare today due to the routine use of prophylactic topical antibiotics. Though studies on the conversion of corneal trauma to infectious keratitis or abscess are scant, ocular trauma is considered one of the most common causes of secondary infections following contact lens wear.[10-12] One study revealed that as much as 15% of the bacterial keratitis in younger patients resulted from trauma, with even higher rates in rural areas, and is the number one cause in developing countries.[12] When it does occur, an infectious ulcer or abscess on the cornea can have devastating consequences to the patient, potentially leading to perforation and vision loss. Therefore, topical antibiotics should always be used if possible.

Recurrent corneal erosion (RCE) may occur following a re-epithelialized abrasion—within days after the



Visit NovaBay at Vision Expo East, booth MS6760!

Add Avenova® with Neutrox® (Pure Hypochlorous Acid 0.01% as a preservative), the only Rx lid hygiene product with pure hypochlorous acid, to the lid & lash hygiene regimen for all your patients.

NovaBay®

Avenova®

Daily lid and lash hygiene.

AVENOVA.COM | 1-800-890-0329 | RX ONLY

initial injury, or potentially months to years later in chronic cases due to poor anchoring of the epithelial cells to the basement membrane. The dry state of the eye's surface when sleeping, combined with the weak attachments to the basement membrane, cause the epithelial tissue to lift off with the lids. RCEs are more common following injury in patients with basement membrane dystrophy.[13] Typically, patients experience pain upon wakening similar to that of a small abrasion. RCEs are initially treated the same as a small abrasion, though repeat episodes may require additional procedures such as anterior stromal puncture, diamond burr debridement or laser resurfacing. There is also anecdotal evidence supporting the use of amniotic membrane tissue as a new treatment method for severe RCE.[14-17]

A mild to moderate anterior chamber reaction may be associated with corneal injury. This inflammation generally resolves as the abrasion heals, but can respond well to a cycloplegic agent alone.

Thermal Burn Abrasions

Ocular thermal burns can occur upon exposure to flame, scalding liquid, blast injury or handheld objects such as curling irons and cigarettes. Injury associated with thermal burns is estimated to be between 7.5% and 27% of ocular trauma cases, with periocular damage more common than ocular surface damage due to the blink reflex and Bell's phenomenon.[18-20]

In cases of severe burns, diagnosis and management may be delayed due to the critical nature of the condition. However, patients with superficial and partial thickness injuries may present to the optometric practice acutely for initial care.

Management of a thermal corneal defect is similar to that of an abrasion. Many traumatic epithelial defects require debridement to promote quicker healing, and often the necrotic white epithelium can simply be wiped off with a swab or Weck-Cel (Beaver Visitec). Prophylactic antibiotics are indicated at the minimum therapeutic dose to prevent bacterial colonization. Cycloplegics may be used if the patient is in pain or an inflammatory reaction has started, and may be instilled in-office since thermal corneal thermal defects are likely to heal quickly. Homatropine 2% or 5% as well as scopolamine 0.25% are appropriate. Preservative-free artificial tears help to aid in the re-epithelialization process and should be used frequently—as often as every 30 to 60 minutes. Topical steroids may be used on follow-up if secondary inflammation persists. Oral analgesics may also be used as needed for patients experiencing severe pain from large thermal abrasions. Bandage lenses are helpful; carefully remove and replace them on every follow-up.

Severe corneal and conjunctival thermal damage may cause symblepharon, corneal ulceration, perforation, scarring, neovascularization or limbal stem cell damage. These patients require amniotic membrane placement or surgical consultation for tarsorrhaphy, symblepharon ring and/or limbal stem cell transplantation.[20-21] In some cases, oral doxycycline or ascorbic acid can be used for collagen synthesis.[19] Scleral lens vaulting for corneal coverage is also used while awaiting surgical repair for severe thermal injuries.[19]

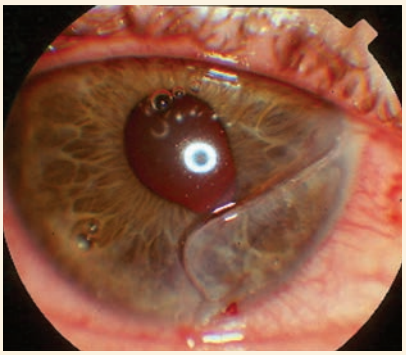
Chemical Burn Abrasions

Acids with pHs less than four and bases with pHs greater than 10 induce burns. Acidic compounds bind with tissue proteins and create their own barrier, whereas alkaline compounds saponify and "melt" fatty tissues, causing further penetration, leading to injuries more severe than acids.

The diagnostic signs of burns are redness or blanching of the conjunctiva, edema and burns to the skin or lids, anterior segment inflammation and corneal staining or haze. Corneal haze is correlated with the

Case 3: Home Repair Nightmare

A 21-year-old plumber came in for an emergency visit after hitting himself with the blunt end of a screwdriver. He noted fluid running down his cheek and blurry vision. He also noted a "loose piece of skin" on his eye, which he attempted to remove. He was taking acetaminophen for discomfort. Upon examination the patient was in extreme pain and had reduced visual acuity. A linear corneal defect was noted as well as an irregular pupil and bubbles in the anterior chamber. Additional testing revealed a positive Seidel's test. (Figure 3). The patient was diagnosed with a corneal laceration, and a shield was placed over the eye. He was referred for immediate surgical repair.



Courtesy: Joseph Sowka, OD

Fig. 3. Corneal lacerations can occur due to blunt force trauma.

Service in a Second

Smart System 20/20 USA All-in-One with 22" monitor

MANUFACTURED IN THE **USA**

When your practice has a need – it's immediate. Not tomorrow, not through a call center off-shore, not via an online request form. And, you're not wanting half answers, or to be transferred around or put on hold forever. We understand.

M&S Technologies has the right team standing by, ready to meet your every service need. Whether it's an urgent order, a technical support question, or a feature inquiry, we'll have you back on track in no time!

See us at Vision Expo East, Booth MS6718!

M&S TECHNOLOGIES 25 YEARS

M&S holds US Patents 7,354,155; 7,926,948; 8,425,040; 8,167,429; 8,419,184 & 8,550,631. Other Patents Pending.

M&S® TECHNOLOGIES

The First Choice in Vision Testing Systems

www.mstech-eyes.com
1-877-225-6101

severity of the burn and the prognosis, according to the Roper-Hall (Ballen) classification: [22]

- ***Grade I:*** no corneal haze and a good prognosis
- ***Grade II:*** some corneal haze but iris details are visible with a good prognosis
- ***Grade III:*** total epithelial loss with stromal haze obscuring iris details and a guarded prognosis
- ***Grade IV:*** an opaque cornea and no iris or pupil details visible and a poor prognosis

A white, blanched eye indicates destruction of the vessels and eventual tissue necrosis. Chemical insult may also damage the epithelial stem cells located at the limbus, resulting in delayed healing, conjunctivalization, corneal vascularization, conjunctival epithelial in-growth and opacification.[8] It may also result in secondary glaucoma and requires careful monitoring of IOP.

Severe burns may require penetrating keratoplasty (PKP) with limbal stem cell transplant, amniotic membrane transplant or oral mucosal cell sheet transplant.[23-26] Indications for surgical intervention involve chronic pain, severe ischemia, destruction of limbal stem cells and corneal destruction.

The initial management of any chemical burn is the same: copious irrigation. Patients calling to report chemical trauma should be advised to irrigate their eyes for 30 minutes prior to presenting to the office. When the patient arrives, use a litmus test to determine if the substance was acidic or alkaline. All patients should be irrigated upon arrival, including sweeping of the fornices for any particulate material. The severity of acid burns is typically clinically observable the day of the exam. In the case of alkaline burns, a patient's presentation may worsen over a 24-hour period; they should be monitored very closely.

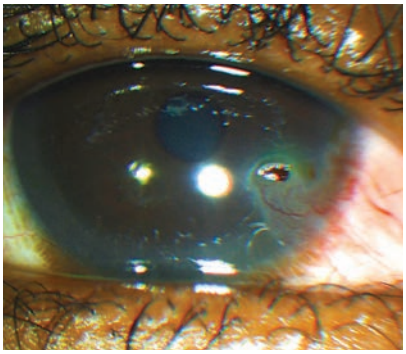


Fig. 4. Foreign body of a portion of a bug.

The goal of treating chemical burns is to control the inflammation of the underlying corneal stroma, preserve the limbal vasculature and restore the limbal stem cells. Managing chemical burns involves topical antibiotics, topical steroids with careful monitoring, artificial tears and oral analgesics as necessary. Take care when using bandage contact lenses with chemical burns, as any residual chemical remaining in the eye may impregnate the lens material and lengthen the contact with the eye.

Patients with mild acidic chemical burns generally respond well to preservative-free artificial tears every hour, prophylactic antibiotic drops and possibly in-office cycloplegia if the patient is in discomfort. Moderate to severe acid burns may require the addition of a mild to moderate strength topical steroid, such as fluorometholone or Lotemax (loteprednol, Bausch + Lomb) QID, or possibly prednisolone acetate 1.0%.

Topical steroids play an important role in managing alkaline burns in particular. These injuries have a biphasic pattern: the initial burn, then the secondary endothelial breakdown. Steroids are helpful in preventing the secondary breakdown and promoting endothelial repair.[27] In addition, topical steroids prevent goblet cell loss and improve ocular surface health.[28] Alkaline burns result in the release of collagenases and proteases, leading to corneoscleral melting.[29] Topical steroids are useful for managing inflammation, but should be monitored very carefully. Collagenase inhibitors may be used in patients with severe corneal thinning who are at risk of perforation. Monitor these patients closely.

Ascorbate and citrate may be useful in severe alkaline burns. Researchers evaluated patients using topical prednisolone 0.5% along with topical ascorbate 10% and found no association with increase corneal melt if topical steroids were used until re-epithelialization.[29]

Foreign Body Removal

Any type of material can lodge in the eye, from bug wings to metal to superglue *(Figure 4)*. Removal of any foreign body involves a thorough examination, assessment of the foreign body's depth and location, and then the plan for its complete removal. Instruments that may be helpful include a spud, which may be used to remove the object and scrape adjacent tissue, and jeweler's forceps. If the object is metallic, rust may form, necessitating the use of an Alger brush. Following removal of the foreign body, the patient will be left with an abrasion, which should then be managed accordingly.

Corneal Lacerations

Fortunately, full-thickness corneal lacerations are not as common as abrasions. However, when they occur, they can be associated with tremendous ocular morbidity. The classic sign of a corneal perforation is a positive Siedel test demonstrating leaking of the aqueous from the anterior chamber. Additional signs include bubbles in the anterior chamber, pupil irregularity, corectopia, iris prolapse, shallow or flat

anterior chamber, hypotony and extrusion of ocular contents.

When treating a patient you suspect has suffered a perforation, remember that topical medications are not formulated for intraocular use and their effects cannot be predicted if they enter the globe, and placing them in an open globe may place the patient at risk for infection.[31] If you suspect the cornea has been perforated, use only sterile products, such as saline and a fluorescein strip.

If an antibiotic is deemed necessary due to a delay in repair, though not sterile, moxifloxacin is not preserved and is often used directly in the anterior chamber during cataract surgery. Rather than coating the laceration with the strip, apply it in small amounts along the laceration to better control the response and distinguish how much of the laceration is a full-thickness penetration. If you are certain the cornea is perforated, place nothing in the eye. Anything placed in the eye in an attempt to help the pain or prevent infection may further contaminate the eye and encourage the patient to rub or wipe the eye, increasing the likelihood of uveal extrusion. Simply apply a rigid shield over the eye to prevent the patient from touching the eye and send them immediately to a specialist for repair. Educate the patient to avoid food and water, as they will likely require anesthesia.

Surgical repair may include tissue glue for partial-thickness lacerations or small perforations of 2mm or less.[32-33] Bandage lenses may be used over the tissue glue for an additional barricade. Amniotic membranes are typically used more often in nontraumatic corneal defects, but may have a role in lacerations and used in conjunction with tissue glue.[34] Sutures are most often used for full-thickness perforations. Often this may be accompanied with an air or gas (e.g., perfluoropropane) tamponade to prevent aqueous leakage.[35] Following repair of the laceration and successful preservation of the integrity of the globe, grafting may be necessary for improvement in visual acuity. Corneal grafting is typically delayed for three months to improve primary repair success.[36]

In cases of open globe injury, be vigilant for increased inflammation and visual degradation, which may indicate endophthalmitis requiring referral to a retinal specialist.

Conclusion

Corneal injuries are common, painful clinical encounters in optometric practice that require quick, accurate decisions. When evaluating patients with corneal injuries, the first step is to determine the nature and mechanism of the injury—only then can we formulate proper management strategies. Patients with any corneal injury need to be closely monitored until the injury resolves or you have made an appropriate referral. Patients will be grateful for your assurance, care and confidence. ■

Dr. Vollmer is associate professor of optometry and director of residency programs for Nova Southeastern University. Her interests lie in primary care and ocular disease.

1. Ljubimov A, Saghizadeh M. Progress in corneal wound healing. Progress Ret and Eye Res. 2015;49:17-45.
2. Dua HS, Gomes JA, Singh A. Corneal epithelial wound healing. Br J Ophthal. 1994;78(5):401-8.
3. O'Sullivan F, Clynes M. Limbal stem cells, a review of their identification and culture for clinical use. Cytotech. 2007;53:101-6.
4. Alfonso E, Crider J. Ophthalmic infections and their anti-infective challenges. Surv of Ophthal. 2005;50(Suppl. 1):S1-6.
5. Burke JM, Bower KS, Vanroekel RC, et al. The effect of fourth generation fluoroquinolones gatifloxacin and moxifloxacin on epithelial healing following photorefractive keratectomy. Amer J Ophthal. 2005;140(1):83-7.
6. Schlech BA, Alfonso E. Overview of the potency of moxifloxacin ophthalmic solution 0.5% (Vigamox). Surv of Ophthal. 2005 Nov;50(Suppl. 1):S7-15.
7. Sclech BA, Blondeau J. Future of ophthalmic anti-infective therapy and the role of moxifloxacin ophthalmic solution 0.5% (Vigamox). Surv Ophthal. 2005 Nov;50(Suppl 1):S64-7.
8. Carlson EC, Wang IJ, Liu CY, et al. Altered KSPG expression by keratocytes following corneal injury. Molecular Vision 2003;9:615-23.
9. Foulks GN, Harvey T, Raj CV. Therapeutic contact lenses: the role of high Dk lenses. Ophthalmol Clin North Am. 2003 Sept;16(3):455-61.
10. Baklouti K, Ayachi M, Mhiri N, et al. Corneal abscess presumed to be of bacterial origin. Bull Soc Belge Ophtalmol. 2007;305:39-44.
11. Stefan C, Nenciu A. Post-traumatic bacterial keratitis- a microbiological prospective clinical study. Oftalmologia. 2006;50(3):118-22.
12. Bourcier T, Thomas F, Borderie V, et al. Bacterial keratitis: predisposing factors, clinical and microbiological review of 300 cases. Br J Ophthalmol. 2003;87(7):834-8.
13. Diez-Feijoo E, Duran, J. Optical coherence tomography findings in recurrent corneal erosion syndrome. Cornea. 2015 March;34(3):290-5.
14. Kordi R, Sui SP, Jandrokovi S, et al. Application of the amniotic membrane extract (AMX) for the persistent epithelial defect (PED) of the cornea. Coll Antropol. 2013;37(1):161-4.
15. Suri K, Kosker M, Raber I, et al. Sutureless Amniotic Membrane ProKera for Ocular Surface Disorders: Short-Term Results. Eye & Contact Lens: Science & Clinical Practice. 2013;39(5):341–7.
16. Yildiz E, Nurozler A, Ozkan A, et al. Amniotic membrane transplantation: indications and results. Eur J Ophthalmol. 2008;18(5):685-90.
17. Prabhasawat P, Tesavibul N, Komolsuradej W. Single and multilayer amniotic membrane transplantation for persistent corneal epithelial defect with and without stromal thinning and perforation. Br J Ophthalmol. 2001;85:1455-63.
18. Lin A, Petel N, Yoo D, et al. Management of ocular conditions in the burn unit: thermal and chemical burns and Stevens-Johnson Syndrome/Toxic Epidermal Necrolysis. J Burn Care & Res. 2011;32(5):547-60.
19. Czyz C, Kalwerisky K, Stacey A, et al. Initial treatment of ocular exposure and associated complication in severe periorbital thermal injuries. J Trauma Injury, Infection, and Critical Care. 2011;71:1455-59.
20. Bouchard C, Morno K, Perkins J, et al. Ocular complications of thermal injury: A 3-year retrospective. J Trauma Injury, Infection, and Critical Care. 2001;50:79-82.
21. Liang X, Zhiping L, Lin Y, et al. A modified symblepharon ring for sutureless amniotic membrane patch to treat acute ocular surface burns. J Burn Care & Research. 2012;33:32-8.
22. Roper-Hall MJ. Thermal and chemical burns. Trans Ophthalmol. Soc UK. 1965;85: 631-53.
23. Frucht-Pery J, Siganos CS, Solomon A, et al. Limbal cell autograft transplantation for severe ocular surface disorders. Graefes Arch Clin Exp Ophth. 1998 Aug;236(8):582-7.
24. Kruse FE. Stem cells and corneal epithelial regeneration. Eye. 1994;8(Pt 2):170-83.
25. Singh P, Tyagi M, Kumar Y, et al. Ocular chemical injuries and their management. Oman J Ophthalmol. 2013;6(2);83-6.
26. Fish R, Davidson R. Management of ocular thermal and chemical injuries, including amniotic membrane therapy. Curr Opin Ophthalmol. 2010(21);317-21.
27. Gomes JA, Romano A, Santos MS, Dua HS. Amniotic membrane use in ophthalmology. Curr Opin Ophthalmol. 2005 Aug;16(4):233-40.
28. Brent BD, Karcioglu ZA. Effect of topical corticosteroids on goblet cell density in an alkali burn model. Ann Ophthal. 1991 June; 23(6):221-3.
29. Davis AR, Ali QK, Aclimandos WA, Hunter PA. Topical steroid use in the treatment of ocular alkali burns. Br J Ophthalmol. 1997 Sep;81(9):732-4.
30. Kabat A, Sowka J. Cornea Atlas: Part III: From abrasions to burns. How to manage corneal injuries. Review of Optometry. Oct 1999.
31. Chung JH, Paek SM, Choi JJ, et al. Effect of topically applied 0.1% dexamethasone on endothelial healing and aqueous composition during the repair process of rabbit corneal alkali wound. Curr Eye Res. 1999;18(2):110-6.
32. Siatiri H, Moghimi S, Malihi M, Khodabande A. Use of sealant (HFG) in corneal perforations. Cornea. 2008;27(9):988-91.
33. Hick S, Demers P, Brunette I, et al. Amniotic Membrane Transplantation and Fibrin Glue in the Management of Corneal Ulcers and Perforations: A Review of 33 Cases. Cornea. 2005 May;24(4):369-77.
34. Duchesne B, Tahi H, Galand A. Use of human fibrin glue and amniotic membrane transplant in corneal perforation. Cornea. 2001;20(2):230-2.
35. Hussin HM, Biswas S, Majid M, et al. A novel technique to treat traumatic corneal perforation in a case of presumed brittle cornea syndrome. Br J Ophthalmol. 2007 Mar;91(3):399.
36. Nobe JR, Moura BT, Robin JB, Smith RE. Results of penetrating keratoplasty for the treatment of corneal perforations. Arch Ophthalmol. 1990;108(7):939-41.

Corneal Disease Report

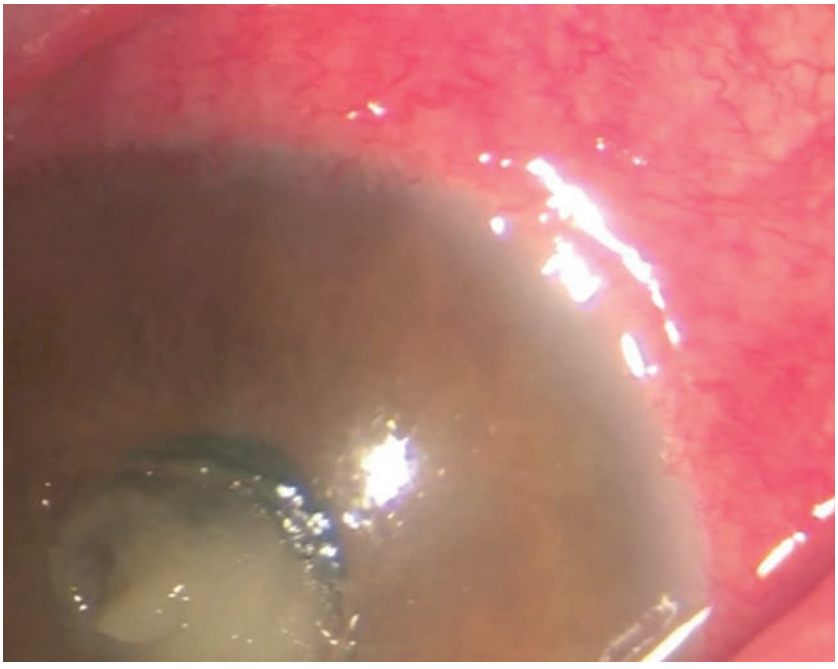
Collecting a Corneal Culture

When guesses and hunches won't do, get the facts.

By Jessica Robinson, OD, Jason Ellen, OD, Brandon Hadel, OD, and Nathan Lighthizer, OD

When sight-threatening conditions strike, they can swiftly cause our patients great detriment. Among these threats, a relatively common occurrence is the corneal ulcer—of which there are several types. Clinicians can evaluate them based on clinical characteristics and patient history, but several of these infections have a similar appearance during various stages of ulceration and can't be easily distinguished.

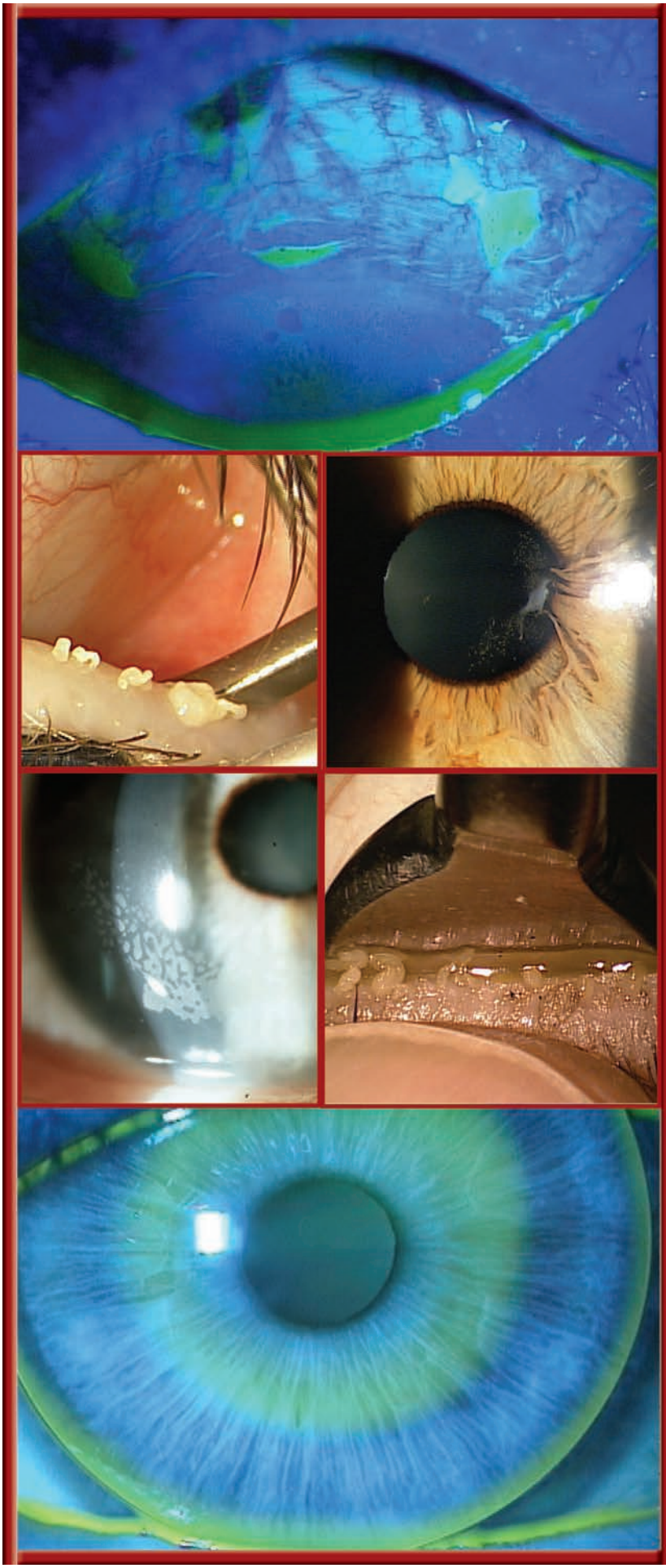
The bottom line is, while clinical characteristics and patient history can guide you, they will not always provide the final diagnosis. To reach this, optometrists need a more concrete, objective test. Corneal cultures can help identify the specific type of corneal ulcer you're dealing with in each case and help you tailor treatment accordingly.



This patient's corneal ulcer could have any of a number of causes. Culturing the ulcer can provide the materials to identify the etiology and help target treatment.

This article provides an overview of how to obtain a corneal culture in your own office as well as how to use it in your management of corneal ulcers.

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



EyeRes™

Digital Imaging Systems

for slit lamps.

"Educate Patients, Inspire Positive Behaviors!"

TelScreen

email: DryEye@TelScreen.com
www.TelScreen.com

When to Culture

Consider a variety of factors when deciding if an ulcer needs to be cultured. Small, peripherally-located lesions, or lesions that have no epithelial defect, may be best treated empirically without a culture.[1-3] Culturing may be indicated if the ulcer is large, central, not responding to current treatment or if an atypical infectious organism is suspected.[1,4] Because the stakes are higher, consider if the patient is post-surgical, monocular or immunocompromised.[2]

In our clinic, we often refer to the "3-2-1 guideline" when determining when we should culture. This recommends a culture be performed prior to starting treatment if:

(3) the ulcer is *3mm* or greater in size at its widest diameter,

(2) there are *two* or more ulcers,

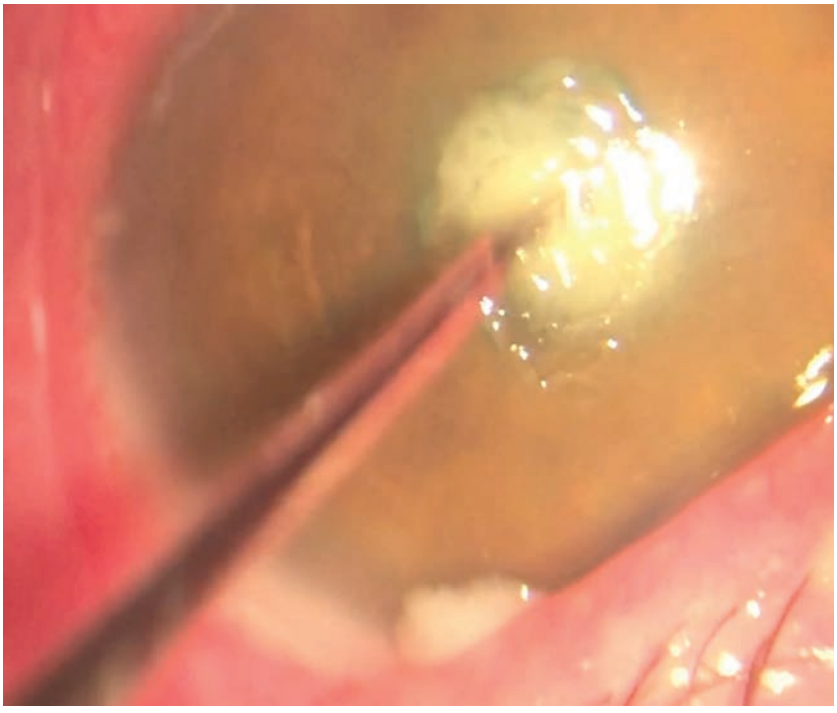
(1) or the ulcer is within *1mm* of the visual axis.

Of course, any guideline has exceptions. For instance, it may be advisable to culture an ulcer that is smaller and peripheral if it has suspicious characteristics. If there is any initial concern for a fungal infection, perform cultures early in the presentation, as it can take up to two weeks for fungus to grow on agar.

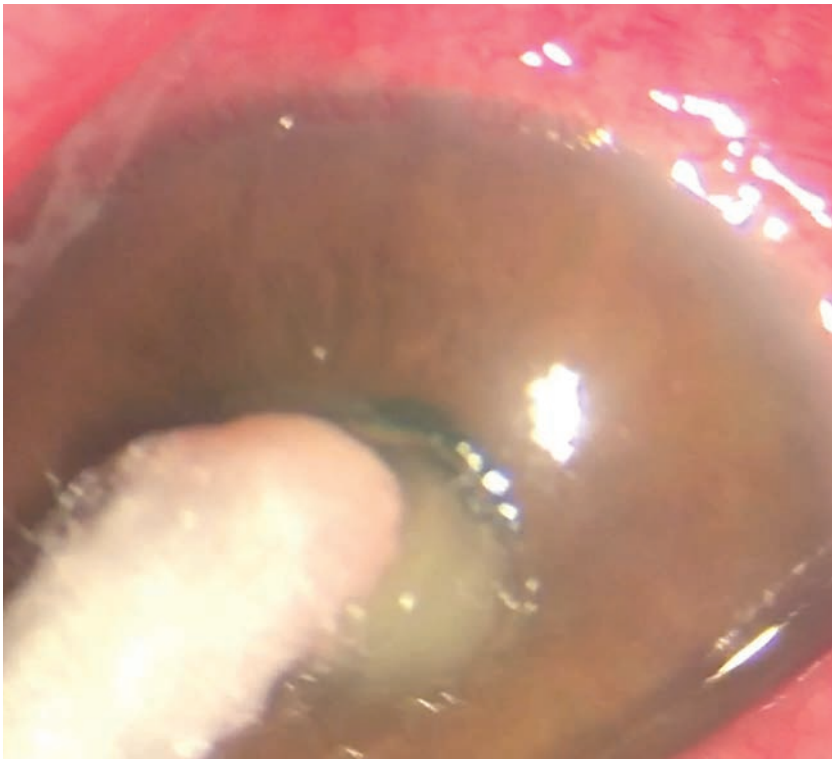
It is best to perform cultures before initiating any treatment, as topical medications will decrease the likelihood of obtaining a positive culture result. If you are not comfortable performing the culture in your office, it may be best to refer for this service prior to starting treatment.

Culture Options

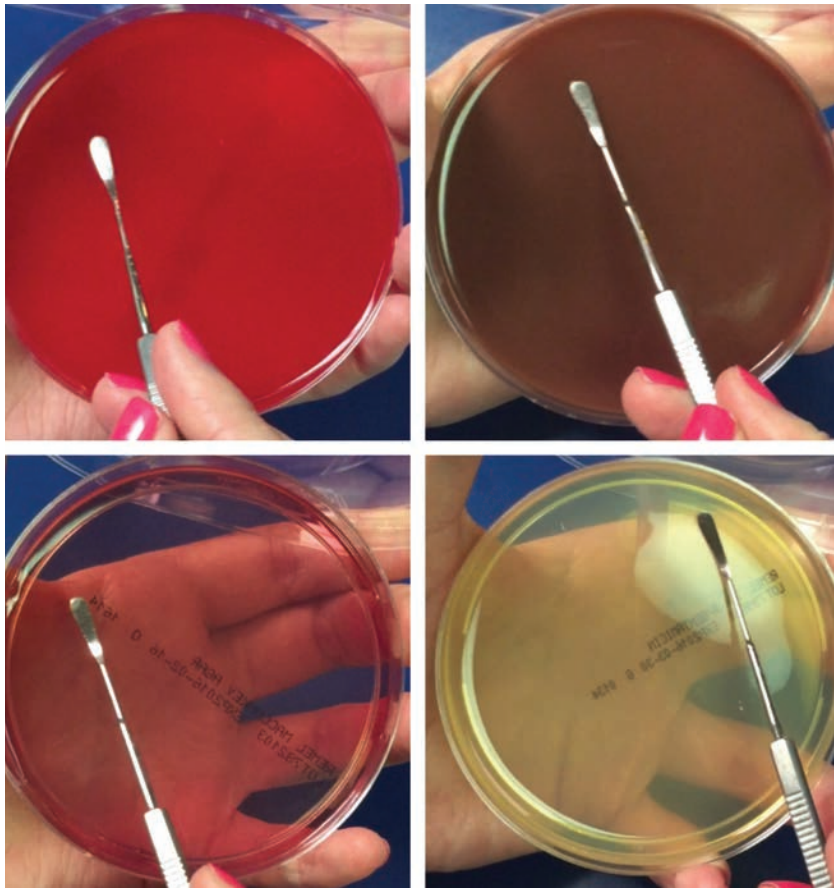
A culture on the eye can be performed several ways. The simplest option is called a "quick culture." This involves collecting a small sample with a sterile swab, often



Collect a small amount of specimen at the ulcer base and at the leading edge of the ulcer. You can use a spatula, spud or swab to achieve this. Here, we are using a spud.



We typically use a sterile, cotton-tipped swab for thioglycollate broth and for a quick culture. After collecting this material, it is placed directly into a vial with broth.



These various agars (clockwise from the top: blood, chocolate, IMA with gentamicin and MacConkey) are routinely used to cover a wide variety of organisms.

Table 1. Nutrient Agar Plates

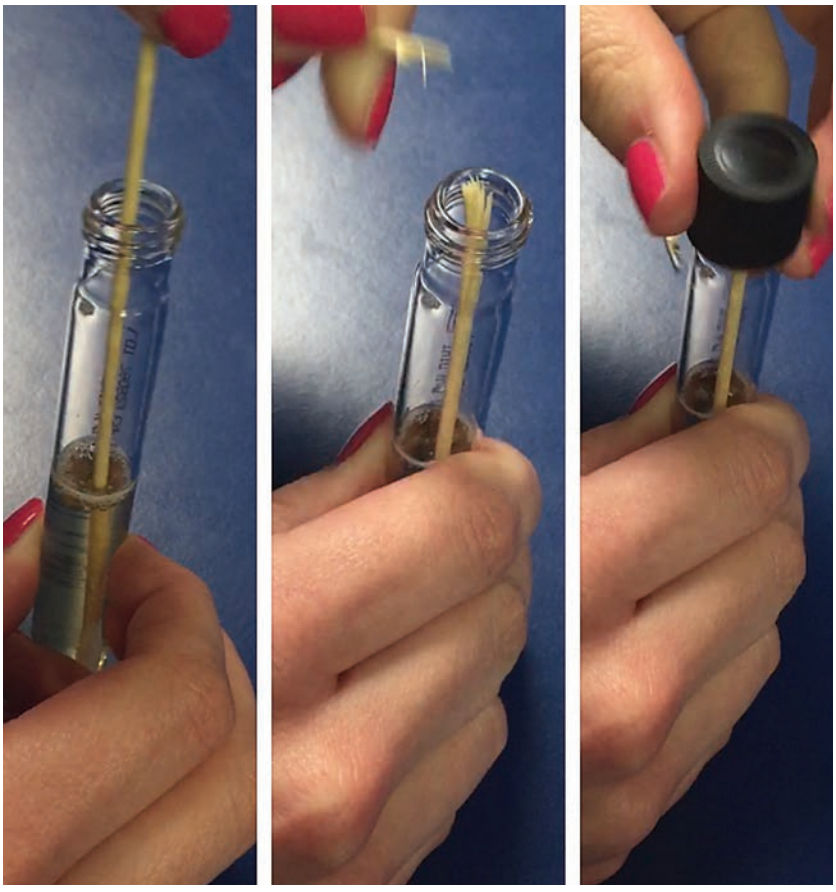
Media	Growth Supported
Blood agar	Most bacteria and fungi, except *Neisseria*, *Haemophilus*, and *Moraxella*
Chocolate agar	*Haemophilus*, *Moraxella* and *Neisseria*
Sabouraud dextrose agar	Fungi
MacConkey	Gram negative bacteria only, differentiate lactose positive and negative, which is helpful in identifying *Pseudomonas*
IMA with gentamicin	Fungi
Thioglycollate broth	Wide range of bacteria, including anaerobic, and fungi
Löwenstein-Jensen medium	Mycobacteria and *Nocardia*
Non-nutrient agar with *Escherichia coli*	*Acanthamoeba*
Brain heart infusion	*Streptococci*, *meningococci*, yeast and fungi
Cooked meat broth	Anaerobic and fastidious bacteria

included in the culturing kit. The swab is then placed into the prepared broth and sent directly to the lab, where it will be placed on nutrient plates for identification. A quick culture can be performed on the cornea or on the conjunctiva. There is also an option for transferring the specimen directly to the necessary plates in-office (*Table 1*). This procedure is described in-depth below.

Microscopy staining on slides, which can either be interpreted in-office or performed at a laboratory, is another diagnostic test option to consider (*Table 2*).

In combination, these two tests can differentiate bacteria, fungi, *Acanthamoeba* and other atypical organisms.

Directly transferring the specimen to the nutrient plates can improve the likelihood of culture growth, but performing a quick culture with the use of transport media allows the lab to prepare its own plates and employ additional agars that you may not have in your office.[1] In our clinical experience, performing both types of cultures has increased our overall likelihood for positive growth.



When using a thioglycollate broth, be sure to only hold the handle toward its end—and then to break that end off—so the portion you touch does not contaminate the broth. You may consider wearing sterile gloves for this.

Corneal Scrape and Culturing Procedure

In our clinic, we use the following procedure to perform a corneal culture:

1. Inform the patient about the procedure's risks and benefits, and obtain proper consent before proceeding.

2. Instill topical anesthetic. Proparacaine is preferred over other anesthetics, as it is less bactericidal.[4] A nonpreserved anesthetic should provide the best results.[3]

3. Align the patient in the slit lamp, as the magnification will be beneficial for the procedure.

4. Using a spatula, spud or swab, scrape the ulcer at its base and at the leading edge of the infiltrate, as the greatest microbial yield will be at these locations. Use enough pressure to indent the cornea slightly. If there is concern for a fungal infection, the scrape needs to be performed deep into the ulcer base to obtain the specimen. If there is significant thinning at the site of the ulcer, it may be best to avoid the base and apply less pressure, so as to decrease the likelihood of a perforation. It is also best to avoid obtaining only purulent material, as it is unlikely to yield a positive result.[1,3]

5. Transfer the specimen to the plate, spreading the material throughout the agar. If you are also preparing slides, place the specimen on the slide first and then the plate.

When preparing plates, avoid breaking the surface of the solid agars. It is convention that a corneal specimen be drawn on the plate in the shape of a "C," however this is not necessary as long as the plate is clearly labeled as a corneal culture. The specific patterns on the plates become more important if you are also collecting cultures from the lids or conjunctiva.

6. Rescrape the ulcer for each different plate or agar, using a sterilized tool each time. A platinum spatula can be beneficial, as it can

You can also provide a slide for the lab to perform microscopy stains, such as the Gram stain. Here, the specimen is mixed with a sterile solution and covered. Table 2 below indicates which slides can identify which type of organisms.

Table 2. Slides for Microscopy Stains

Slides	Organism Identified
Gram stain	Bacteria, fungi and *Microsporidia*
Giemsa stain	Fungi, *Acanthamoeba* and *Microsporidia*
Calcofluor white	Bacteria, fungi, *Microsporidia* and *Acanthamoeba*
Acid-fast stain	*Mycobacterium* and *Nocardia*
Grocott-Gömöri mehenamine-silver	Fungi, *Acanthamoeba* and *Microsporidia*
Periodic acid-Schiff (PAS)	Fungi and *Acanthamoeba*

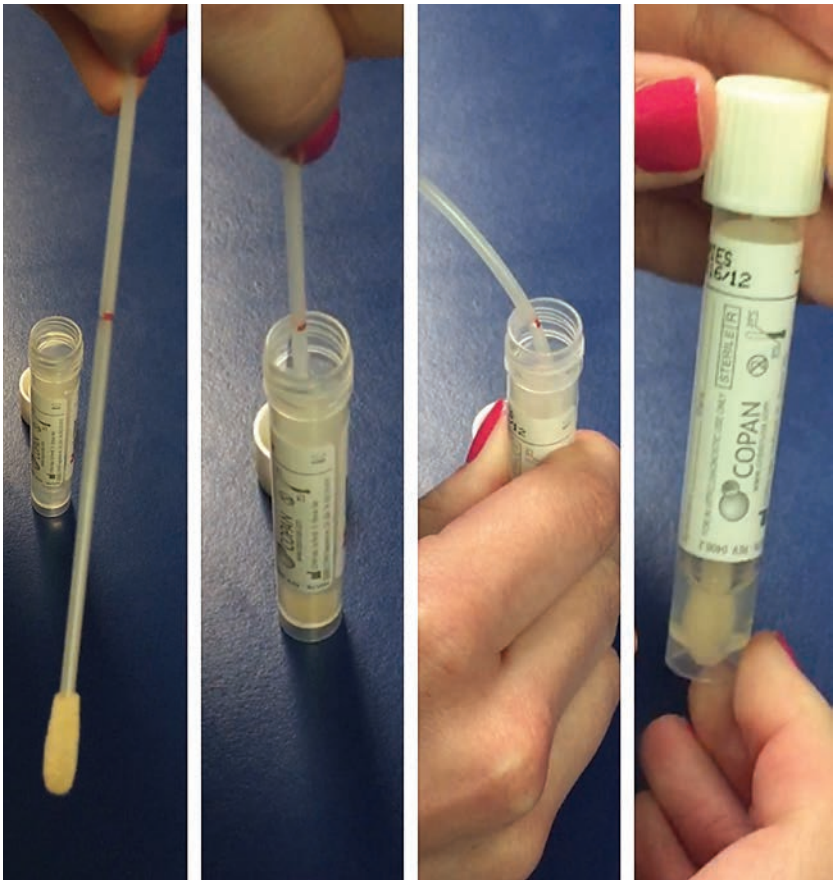
be heat-sterilized between specimens, and cools quickly.

If you prefer not to sterilize your tools between scrapes, plate any agars with antibiotic infusion last, such as inhibitory mold agar (IMA) with gentamicin, to prevent the antibiotic in the agar from affecting your results on other plates. If using thioglyocollate broth or a quick culture as part of your testing, use a sterile cotton swab on the ulcer and then place it directly in the broth, breaking the applicator off below the area that you were holding. Do not touch any part of the handle that will be placed into the vial. Wearing sterile gloves can help reduce contamination.

7. Measure the defect after culturing, as there will be greater epithelial disruption following the procedure.

8. Label the plates, vials and slides with information identifying the patient and locations cultured. Fill out the laboratory request form, including information about the site of the ulcer, what plates you are sending for testing and the tests you wish to have performed. You will also want to request sensitivities for medications, including the specific medications that the patient is using or will be starting.

9. Immediately start the patient on empirical-based treatment, if not already begun.



This quick culture kit includes a stale swab along with a prepared broth. Note the red line on the swab's handle. It's there to indicate where to hold the handle to prevent contamination. The swab snaps apart at this red line when bent.

Lab Reports

The lab will communicate to you any positive growth from the cultures. Results may be obtained within a few hours for stains or one to two days for bacterial growth. Slow growing fungal infections can take up to two weeks to show positive growth on plates. Therefore, it may be necessary to begin antifungal treatment prior to receiving the culture results if there is a high suspicion for fungal infection.

The lab can also provide sensitivity reports, which will inform you about the effectiveness of various antimicrobials against the isolated organism. These reports are typically sent out at one or two days, seven days or two weeks.[3]

The medication in question may be described as susceptible, intermediate or resistant.

- *Susceptible* indicates the infectious organism is sensitive to a normal dose of the medication.
- *Intermediate* means the organism is sensitive to the medication, but only at high dosages.
- *Resistant* means the organism won't respond to the antimicrobial.

Antimicrobials classified as susceptible will be the most effective against the infection.

Additional Notes

Culturing may yield a positive result in only 50% to 60% of cases.[2] If the patient presents to your office currently on a topical antibiotic, the likelihood of a positive result decreases. It is best to perform a culture before instilling any antibiotic. In some cases, if an ulcer is not responding well to treatment, the provider may discontinue topical medications for a period (usually no longer than 12 to 24 hours) to repeat a corneal culture.[1]

Proper technique can also help improve test results. If conventional cultures have failed, a corneal specialist may chose to perform a corneal biopsy on the affected tissue. Additionally, a confocal microscope can be a useful, noninvasive tool for ruling out fungi or *Acanthamoeba*.

Communication with your lab is key. Plates should be labeled with essential patient identification information. Be sure to specify if you cultured the cornea, conjunctiva or lid. If you want specific agars plated or specific stains performed at the lab, you can make that request. Furthermore, most labs will provide many of the culturing materials to you at no cost, including agars, broths and quick culture kits. If you are interested in culturing in your office, contacting your local lab is the best first step.

For some cases of corneal ulcers, empirical treatment alone is sufficient. However, in cases that do warrant a culture, the procedure must be performed correctly and early. If this is not something you wish to do in-office, learn to recognize which cases should be quickly referred to a provider that will perform the procedure, as an early culture can have a great impact on the outcome for these patients. ■

Dr. Robinson is from Morehead, KY and graduated from the University of Houston College of Optometry in May 2015. She is the current ocular disease and ocular and refractive surgery resident at the Oklahoma Medical Eye Group and nJoy Vision in Tulsa, OK.

Dr. Ellen graduated from Northeastern State University Oklahoma College of Optometry in 1999 and completed an ocular disease and refractive surgery residency through BVA Advanced Eyecare and TLC Laser Eye Center in Oklahoma City. He serves as the co-coordinator for the Oklahoma Medical Eye Group/nJoy-Tulsa residency in ocular surgery/disease and refractive surgery.

Dr. Hadel is a graduate of the Southern College of Optometry and completed a residency at the VA Medical Center in Kansas City, MO, where he trained in ocular disease and low vision rehabilitation. He practices at the Oklahoma Medical Eye Group where he specializes in the diagnosis and management of ocular disease.

Dr. Lighthizer is the assistant dean for clinical care services, director of continuing education, and chief of both the specialty care clinic and the electrodiagnostics clinic at NSU Oklahoma College of Optometry.

Resistance Warning

In the management of bacterial keratitis, the introduction of fluoroquinolones made it more feasible to treat suspected bacterial ulcers empirically, as they could be used to treat a wide variety of common infections. However, the prevalence of antibiotic resistance has been increasing, and even topical fluoroquinolones are affected.[1] In fact, approximately 80% of all strains of MRSA are now resistant to fluoroquinolones.[2] Also, consider the possibility of fungal, herpetic, atypical bacteria or *acanthamoeba*—none of which can be treated by a broad-spectrum antibiotic.

1. American Academy of Ophthalmology Cornea/External Disease Panel. Preferred Practice Pattern Guidelines. Bacterial Keratitis. San Francisco, CA: American Academy of Ophthalmology; 2013. Available at: www.aao.org/preferred-practice-pattern/bacterial-keratitis-ppp--2013.
2. Onofrey, B, Skorin L, Holdeman N. Bacterial Keratitis. Ocular Therapeutics Handbook: A Clinical Manual. 3rd ed. Philadelphia: Lippincott Williams & Wilkins; 2011:165-73.
3. Kanski J, Bowling B. Bacterial Keratitis. Clinical Ophthalmology: A Systematic Approach. 7th ed. Edinburgh: Butterworth-Heinemann/Elsevier, 2011:173-80.
4. Gerstenblith A, Rabinowitz M. Bacterial keratitis and corneal culture procedure. The Wills Eye Manual: Office and Emergency Room Diagnosis and Treatment of Eye Disease. 6th ed. Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins;2012:69-73, 435-437.

The Art of Conversation:

Talking With Patients About the *True* Value of **DAILIES TOTAL1®** Contact Lenses

Eye care professionals (ECPs) have been recommending DAILIES TOTAL1® daily disposable contact lenses to their patients since the moment these lenses became available because they know DAILIES TOTAL1® lenses represent a significant advance in contact lens technology.[1] Having the discussion with patients about DAILIES TOTAL1® means talking with them about the unique Water Gradient Technology behind the lenses and how DAILIES TOTAL1® lenses bring value in terms of comfort, wettability, and convenience.[2-4] Here are some communication strategies that many ECPs have successfully used when discussing the benefits and value of DAILIES TOTAL1® with their patients:

Emphasize the advanced technology behind DAILIES TOTAL1® contact lenses. Explain to patients how DAILIES TOTAL1® lenses are the *first and only* contact lenses with Water Gradient Technology, creating a lens with water content approaching 100% at the outermost surface* that provides a cushion of moisture.[2-5] DAILIES TOTAL1® represents a leap forward in technology compared with traditional soft contact lenses, providing long-lasting lubricity[6,7] and exceptional all-day comfort.[1,8]

Make sure to understand your patients' needs. Ask every patient about his or her current lens-wearing experience. By asking patients a few simple questions (such as "Over the past 2 weeks, how often did your lenses feel uncomfortable?" or "If there was anything you could change about your contact lenses, what would it be?"), potential problems are identified and you can provide a solution by explaining how DAILIES TOTAL1® contact lenses, with its Water Gradient Technology, can help address problems with discomfort.[8]

Present the cost of the lens in terms of overall value. When discussing the price of DAILIES TOTAL1® contact lenses, explain to patients that, because DAILIES TOTAL1® lenses represent the latest technology, they are a bit more expensive than

other daily disposable lenses. For many patients, however, the increased price is far outweighed by the value of the lens in terms of outstanding end-of-day comfort.[9] Patients benefit from this technology for about $2 a day—often no more than the price of their daily cup of coffee or a daily bus trip to work. By recommending DAILIES TOTAL1® to all patients who could benefit from its technology, you give your patients the opportunity to wear lenses that are more breathable,** highly wettable, and more comfortable than the lenses they are currently wearing.[1-4]

Give them a try! No amount of discussion can substitute for patients actually experiencing DAILIES TOTAL1® contact lenses for themselves. For the majority of patients, *trying is believing*. Research shows that more than 80% of DAILIES TOTAL1® contact lens wearers are "extremely" or "very likely" to recommend them to friends or family, which can lead to patient referrals.[9]

New lens wearers, patients who complain of discomfort, and "silent sufferers"—those who have come to believe that discomfort is a normal part of contact lens wear[10]—may all benefit from DAILIES TOTAL1® contact lenses with Water Gradient Technology. By starting the conversation about DAILIES TOTAL1® during every lens fitting and making a strong recommendation, you can start your patients down the road to an unsurpassed lens-wearing experience.

By recommending DAILIES TOTAL1® to all patients who could benefit from its technology, you give your patients the opportunity to wear lenses that are more breathable, highly wettable, and more comfortable than the lenses they are currently wearing.

**Based on laboratory measurement of unworn lenses.*
***High oxygen transmissible lenses: DAILIES TOTAL1 (delefilcon A) contact lenses: Dk/t = 156 @ -3.00D.*

1. Perez-Gomez I and Giles T. European survey of contact lens wearers and eye care professionals on satisfaction with a new water gradient daily disposable contact lens. *Clinical Optometry*. 2014;6:17- 23.
2. Thekveli S, Qui Y, Kapoor Y, et al. Structure-property relationship of delefilcon A lenses. *Contact Lens Anterior Eye*. 2012;35(suppl1):e14.
3. Based on laboratory measurement of unworn lenses; Alcon data on file, 2011.
4. Based on the ratio of lens oxygen transmissibilities, among daily disposable lenses; Alcon data on file, 2010.
5. Angelini TE, Nixon RM, Dunn AC, et al. Viscoelasticity and mesh-size at the surface of hydrogels characterized with microrheology. *Invest Ophthalmol Vis Sci*. 2013;54:E-Abstract 500.
6. Based on critical coefficient of friction measured by inclined plate method; significance demonstrated at the 0.05 level; Alcon data on file, 2011, 2013.
7. Alcon data on file, 2011.
8. Alcon data on file, 2014.
9. Based on a survey of 1,339 participants through October 2014. Alcon data on file, 2014.
10. Alcon data on file, 2008.

See product instructions for complete wear, care, and safety information.

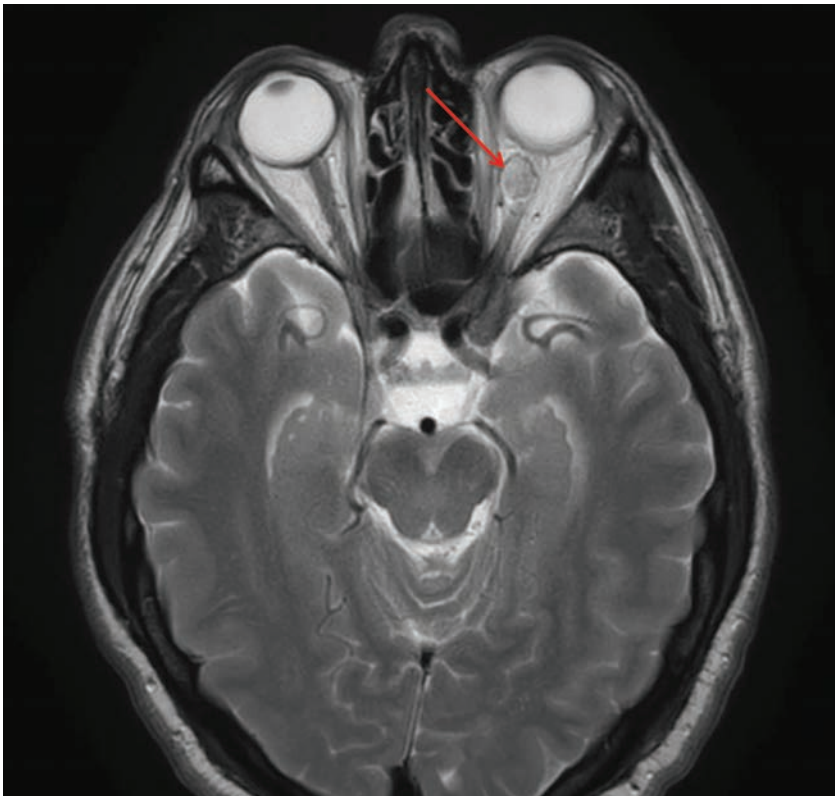
Glaucoma: Hone Your Differential Diagnosis

Discovering the true diagnosis can be challenging when patients present with glaucoma-like findings. Here are some differentials to look out for.

By Justin Cole, OD, and Jarett Mazzarella, OD

Glaucoma is a pressing public health concern, specifically due to the asymptomatic nature of the disease, the increasing prevalence and the risk for blindness. Researchers estimate that approximately 2% of the US population aged 40 to 80 years have a diagnosis of glaucoma, with another 2% undiagnosed.[1] Furthermore, studies estimate that the number of people with glaucoma in the United States is expected to increase to 6.3 million by 2050 and to 112 million worldwide by 2040.[2,3]

With glaucoma on the rise, clinicians need to be prepared to diagnose these patients early and choose the best treatment plan. But making a diagnosis of glaucoma can be challenging—not only because glaucoma itself is complex and involves many variables, but also because many other pathologies can masquerade as glaucoma. This article discusses the various



This patient's axial MRI shows a left intraconal lesion of orbit compressing the optic nerve.

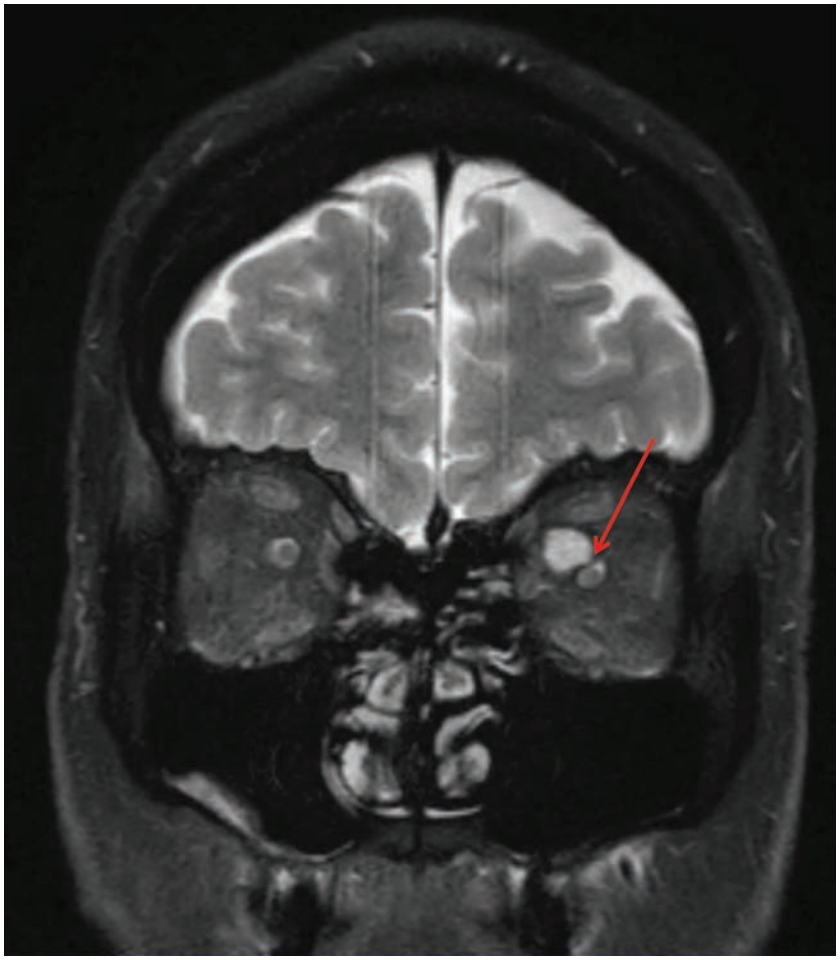
differential diagnoses to help clinicians properly identify the true disease process in play and plan a management strategy accordingly.

POAG vs. Secondary

First and foremost, practitioners must differentiate primary open angle glaucoma (POAG) from secondary glaucoma, as the different pathophysiology of the glaucomatous damage will dictate the first line of treatment.

Patient demographics are also important, as POAG is found more frequently in the older population. If a patient presents with signs consistent with glaucoma, is below the age of 40 and shows no signs of a secondary glaucomatous process, other diagnoses should be considered. In a review study that looked at primary open angle glaucoma prevalence across different ethnicities, researchers found that, most often, glaucoma prevalence was low below the age of 40, at about 2% to 3% across all ethnicities. The same study found that Americans of African decent had the highest prevalence, about 5%, at 60 years of age. The greatest increase of prevalence with age was in Hispanics and Caucasians.[2] Therefore, it is vital for clinicians to be cognizant of the red flags that may elicit an alternative diagnosis.

Once clinicians have differentiated primary from secondary glaucoma, we must gain a firm understanding of the patient's systemic health through a thorough examination, rule out therapeutic contraindications and tailor the topical therapy to best suit the initial target range. Clinicians must take into consideration ease of use, possible side effects, cost and the medication's mechanism of action to determine the best topical management for each patient.



The same patient's coronal MRI shows the compression of the ONH by orbital lesion.

Glaucoma Masqueraders

Common masqueraders of glaucomatous optic neuropathy are usually ocular conditions or manifestations of ocular disease that can change the appearance of the optic nerve. Studies have shown that particular exam testing—specifically, visual acuity, visual field testing and serial retinal photography—can help differentiate between nonglaucomatous optic nerves and glaucomatous ones. As a primary eye care provider, recognizing a variance in the disease course is essential in properly taking care of patients. Clinicians should be on the lookout for these other differential diagnoses when a patient presents with findings consistent with glaucoma:

• ***Vascular Differentials.*** Often, patients with a history of ischemic optic neuropathy in one eye can be labeled glaucoma suspects based on what may be perceived as glaucomatous cupping. The visual field defect that classically accompanies an ischemic optic neuropathy is an inferior or superior altitudinal defect, which may be incomplete and can extend into the arcades or may be located within the central 10 degrees of the macula. However, variable visual field defects are possible and the disease process can be differentiated by the lack of optic nerve cupping or notching and,

Primary Open Angle Glaucoma

POAG is a chronic, progressive optic neuropathy with pathognomonic visual field loss and corresponding optic nerve neuroretinal rim changes. By definition, the irido-corneal angle is open on gonioscopic examination. The typical damage that ensues produces gradual excavation of the optic nerve, which can be defined by thinning, notching or cupping of the neuroretinal rim. It is not uncommon for open angle glaucoma to be asymmetric on presentation. Increased IOP is not required for the diagnosis, but it is—along with thin central corneal thickness (CCT)—a risk factor for the development of glaucoma.

Making the Diagnosis

The diagnosis of POAG is complex and involves many variables. Classically, signs noted on clinical exam include increased cup-to-disc ratio, which may or may not be accompanied by increased IOP. An asymmetry between the optic nerve cupping should also raise suspicion. Thinning or notching of the superior or inferior neuroretinal rim is indicative of loss of retinal nerve fiber layer (RNFL) and ganglion cell death. The resulting manifestations of the disease process include peripheral field loss, which may progress to central vision loss and legal blindness without intervention in the advanced disease state. The standard in glaucoma evaluation is visual field testing, which looks for characteristic early glaucomatous visual field patterns such as nasal step, arcuate (Bjerrum) scotomas and paracentral scotomas. All glaucomatous visual field defects should respect the horizontal raphe. This is the rationale for the glaucoma hemifield analysis software algorithms included on automated perimetry devices.[4]

The advent of spectral domain optical coherence tomography (SD-OCT) has given optometrists another means to assist in the diagnosis and management of glaucoma. Most models feature segmentation software to assess retinal layers and include a ganglion cell complex platform. Current SD-OCT systems also possess recognition software and progression or change functions to accurately track and monitor progression of RNFL loss over time. In assessing the validity of OCT test results, every clinician should understand the standardized normative database of their OCT model when evaluating OCT RNFL in glaucoma management.[5] The wide variance in normal optic nerve anatomy and the different optic neuropathies mimicking glaucomatous RNFL thinning on the OCT can give the examiner a false sense of security, so it is imperative that the clinician correlate exam findings and visual field testing to help determine if nerve fiber loss on OCT is a glaucomatous process or a masquerader.

The Influence of Eye Pressure

Ocular hypertension (OHTN) can be defined as IOP that routinely is above the normative range of 10mm Hg to 21mm Hg, but does not show the progressive optic nerve damage or visual field defects indicative of glaucoma. The Ocular Hypertension Treatment Study (OHTS) has demonstrated that treating patients with OHTN reduced the cumulative probability of developing glaucoma by 60% in the group treated with topical medication. At five years the probability of developing POAG in the treated groups was 4.4% and in the untreated group it was 9.5%.[6] This represented only a 5% relative risk reduction in conversion to glaucoma, so determining which ocular hypertensive patients will develop glaucoma still depends on identifying a patient's risk factors.

The Role of Central Corneal Thickness and Corneal Hysteresis

The OHTS revealed that thin CCT is a risk factor for the development of glaucoma.[6] Generally, a thick CCT leads to artificially high IOP measurements and a thin CCT leads to artificially low IOP measurements. The cornea has viscoelastic characteristics that will respond to a force differently depending on its rigidity and biomechanical properties. Corneal hysteresis is defined as the biomechanical properties of the cornea when a force is exerted on it and how the cornea exerts a force back.[7] These biomechanical properties of the cornea have been postulated to play a role in glaucoma and the way IOP is interpreted. Studies show that low corneal hysteresis is common in eyes with glaucoma regardless of the glaucoma subtype.[8] Studies show that CCT of different ethnicities can be variable, with people of African decent having the thinnest CCT on average, followed by those of Japanese descent, while Caucasians, Hispanics, Chinese and Filipinos having approximately equal CCT.[9]

Studies have tried to link corneal hysteresis and anatomical disc changes associated with glaucomatous cupping, but these findings have shown no significant correlation.[10,11] Although corneal hysteresis has yet to become a mainstream measurement in clinical practice, knowing that the cornea is a dynamic tissue that can have varying rigidity, understanding the implications of CCT and applying what is known about ethnicity and glaucoma will allow clinicians to optimally manage patients suspected of glaucoma.

instead, the presence of pallor as the manifestation of the ischemic event.

• ***Retinal vascular occlusions.*** These can also complicate the clinician's ability to diagnose a glaucomatous optic disc. Branch retinal artery occlusions can result in visual field defects that correspond to the damaged retinal tissue and can appear arcuate-like due to having the same vascular supply. Retinal emboli or atrophic sclerotic vessels may or may not accompany a past arterial occlusion; however, the optic nerve should reveal more pallor than cupping in the affected neuro retinal rim sector.

icare
tonometer

NO CALIBRATION
NO DROPS, NO AIR

REBOUND TONOMETER

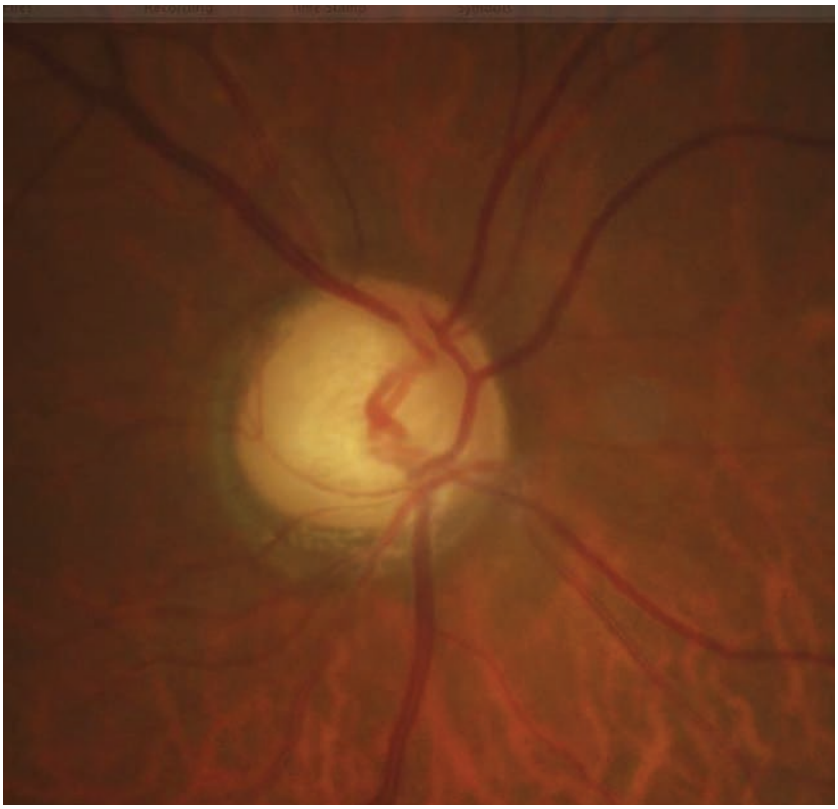
MORE EFFECTIVE

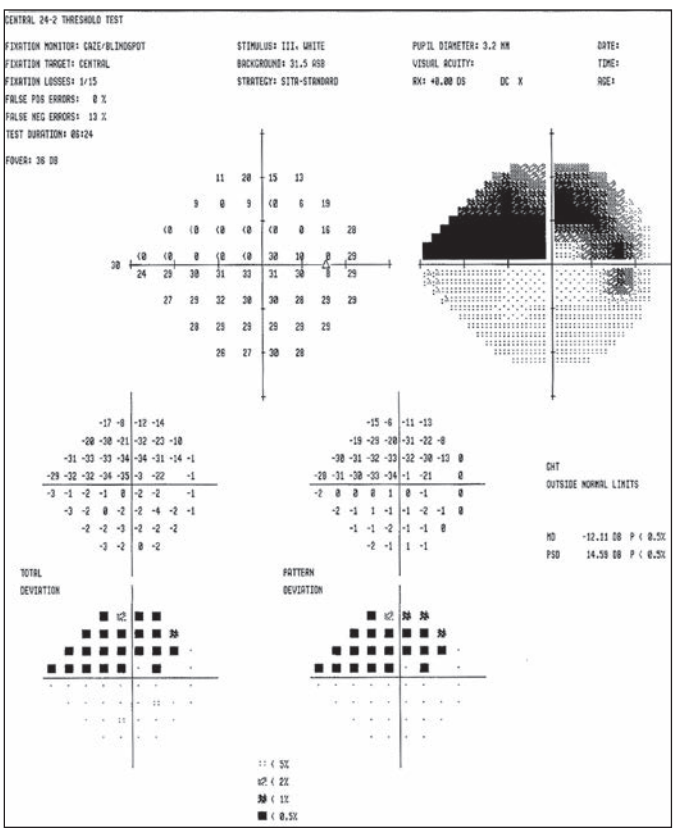
MORE **EFFICIENT**, MORE **RELIABLE**

VISIT US AT VISION EXPO EAST BOOTH MS7014.
YOUR PATIENTS WILL THANK YOU FOR IT!

LEARN MORE:

847.533.5939 | info@icare-usa.com | www.icare-usa.com





At right, the visual field shows a dense glaucomatous arcuate scotoma in the right eye. Above, the fundus image shows glaucomatous thinning corresponding to the visual field.

Branch retinal vein occlusions, however, would have additional retinal findings such as collateral retinal vessels bridging arteries and veins, which can cross the horizontal raphe. Residual retinal hemorrhages along the distribution of the occlusion may also be present, which helps confirm the diagnosis.

Knowing what to look for and understanding that glaucoma can arise in the presence of concurrent ocular vascular conditions ensure clinicians are prepared to monitor those patients who present with multiple comorbidities.

• ***Compressive nonglaucomatous optic neuropathy.*** A compressive lesion can be mistaken for glaucoma, especially when the field loss and glaucomatous damage is slow and insidious. Compressive optic neuropathy can mimic glaucomatous optic nerve changes early in the disease process. The unilateral nature of the optic nerve findings and the worsening visual field defects in the presence of controlled and often normal intraocular pressure (IOP) should increase suspicion of a masquerader. A study from a tertiary referral center evaluated patients with normal tension glaucoma and found that the two most common intracranial tumors noted to cause optic nerve changes were pituitary tumors and meningiomas.[12]

However, several studies show that the visual field defects associated with compressive optic neuopathy most often exhibit patterns not clinically consistent with glaucomatous field loss, and the degree of optic nerve cupping can be disproportionate to the visual field defects. Researchers also discovered that, in forms of compressive optic neuropathy, nonglaucomatous optic nerve cupping and visual field loss was usually accompanied by

Comfortear® Lacrisolve™ 180

ABSORBABLE PUNCTUM PLUG

*"The Comfortear® Lacrisolve™ 180 Absorbable Punctum Plugs are **great for my patients who have difficulty instilling drops multiple times throughout the day**. We know these plugs will dissolve within 180 days and they **offer increased comfort for our patients with dry eye and surface disease."***

A.J. Contento, OD, FAAO
Eye Care Unlimited
Bronx, NY

DEFEAT DRY EYES with the Comfortear® Family of Punctum Plugs

TO PLACE YOUR ORDER, CALL

(888) 424-1192

Visit punctumplug.com for more information. From outside the U.S., call +1 (503) 206-5733.

M063-0316-01

Paragon BioTeck, Inc. | 4640 SW Macadam Ave, Ste 80 Portland, OR 97239 | (888) 424-1192 | www.paragonbioteck.com

Comfortear is a U.S. Registered Trademark of Delta Life Science, Inc. Lacrisolve is a Trademark of Paragon BioTeck, Inc.

Paragon BioTeck, Inc.

Nonglaucomatous Optic Neuropathies

Clinical signs and symptoms will help differentiate between suspected glaucoma and other etiologies of optic disc changes.

Glaucoma Masquerader	Key Differentiating Characteristics
Optic nerve pit	• Congenital rather than acquired. Congenital pits may raise concern for macular schisis/detachment, while acquired pits can be signs of progressive nerve fiber loss from glaucomatous damage[18]
Ischemic optic neuropathy	• Pallor more than cupping • Usually altitudinal visual field defect
Traumatic optic neuropathy	• Pallor outweighing optic nerve cupping/excavation • Deep visual defects
Optic atrophy (unilateral)	• Pallor outweighing optic nerve cupping/excavation • Healthy optic nerve of fellow eye
Foster Kennedy syndrome	• Unilateral optic disc swelling, with contralateral optic atrophy • Likely other neurological signs/symptoms, ipsilateral anosmia, frontal lobe mass on imaging
Pseudo Foster Kennedy syndrome	• Unilateral optic disc swelling, with contralateral optic atrophy • No neurological signs noted as in above condition, without frontal lobe mass
Pituitary adenoma/apoplexy	• Compression of optic chiasm • Possible bitemporal hemianopsia visual field defect • Bow tie optic nerve pallor
Meningiomas of: suprasellar, cavernous sinus, optic nerve, sphenoid wing of the bony orbit	• Asymmetric optic disc appearance with pallor • +RAPD without asymmetrical visual field loss • Involvement of any cranial nerves • Variable visual field defects which do not respect horizontal raphe
Cavernous sinus: fistula, carotid artery aneurysm	• Involvement of other cranial nerves, anterior segment signs, abnormal conjunctival vessels, proptosis, decreased acuity
Leber's hereditary optic neuropathy	• Slow central visual loss secondary to bilateral optic degeneration • Early in life, less than 50 years old
Dominant optic atrophy	• Insidious symmetrical vision loss that is mild to moderate • Onset in the first or second decade of life • Temporal optic disc pallor
Morning glory syndrome/optic disc coloboma/tilted optic disc/optic nerve hypoplasia	• Variable visual field defects, but defects should not be progressive • Presence noted at early age with history of longstanding nature

decreased visual acuity and optic nerve head pallor.[12-14]

• ***Traumatic optic neuropathy.*** A history of ocular or head trauma should be considered in the differential diagnosis in any case of asymmetric optic disc cupping or suspected optic nerve pallor. Traumatic optic neuropathy can be longstanding, and patients may recall an associated event with vision loss. These patients' visual acuity would often, but not always, be reduced, and variable visual field defects are likely. In the case of unilateral trauma, an afferent pupillary defect may be present, which would likely be accompanied by optic nerve pallor and not cupping.[15] The visual field exam would also produce variable visual field defects inconsistent with the early glaucomatous visual field loss.

• ***Optic disc swelling.*** Previous optic nerve swelling with resultant optic atrophy also needs to be considered when evaluating a patient who presents with findings consistent with glaucoma. An active inflammatory or swollen optic disc will intuitively lead to another diagnosis; however, optic atrophy from past events without active inflammation or disc swelling can be challenging to differentiate, even for the most seasoned clinician. Systemic diagnoses of diabetes mellitus, hypertension, anemia, a history of lymphoma or leukemia, multiple sclerosis, neuromyelitis optica, or pseudotumor cerebri can help in the differential diagnosis, as past optic nerve swelling or inflammation can change the anatomic structure and appearance of the optic nerve.

Hints It May NOT Be Glaucoma

Acuity, pupillary function, optic nerve appearance, visual field and OCT of the retinal nerve fiber layer (RNFL) and ganglion cell complex are tests that assist in the

Visit us at
Vision
Expo East
Booth MS6934

FAMOUS FOR SEEING WHAT OTHERS CAN'T.

Innovation and craftsmanship that helps you rise above.

Haag-Streit vision spans more than 150 years. Our goal is simple: to develop ever more useful tools for the precise understanding of the human eye. At Haag-Streit, you will see the future clearly.

Haag-Streit
BQ 900 LED

Octopus 600

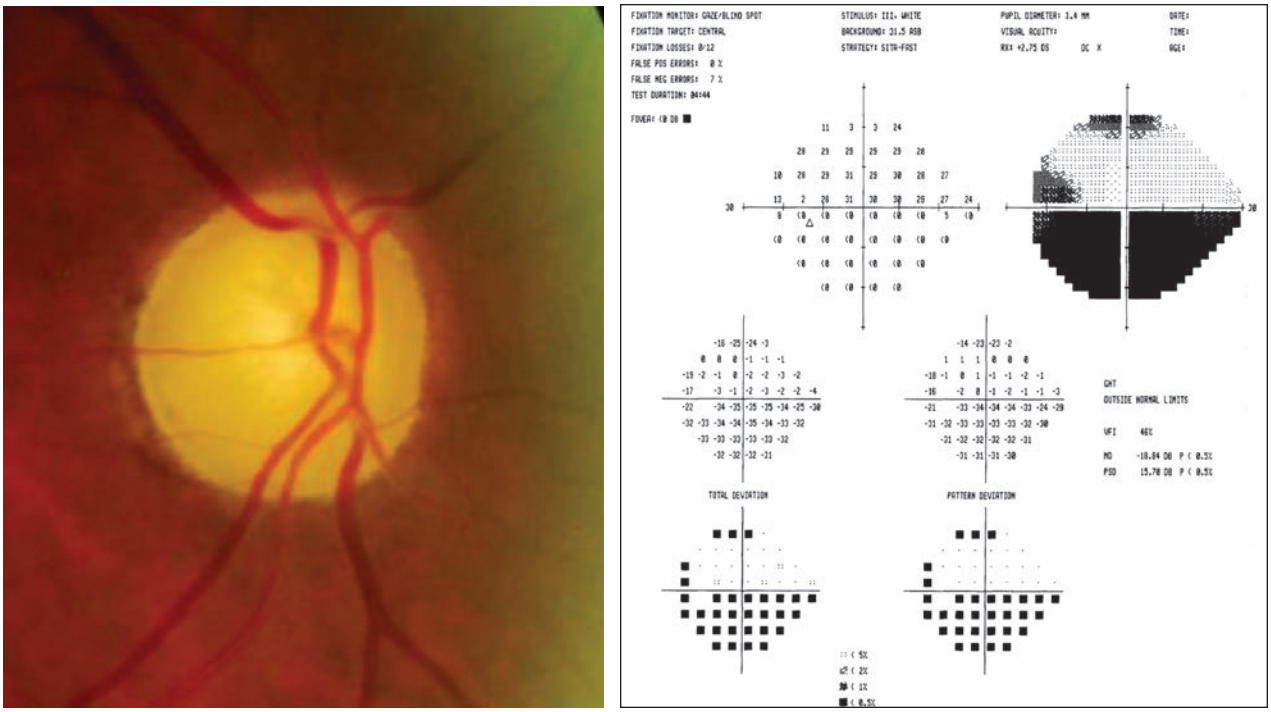
Octopus 900

Reliance
FX920

Reliance
520

800.787.5426
haag-streit-usa.com

HAAG-STREIT
USA



This visual field depicts an ischemic optic neuropathy of the left eye. The fundus image shows pallor from ischemic optic neuropathy.

differential between glaucoma and other masqueraders. Visual acuity is generally unaffected until late in the disease process in patients with POAG. The presence or absence of an RAPD is not necessarily pathognomonic for other optic neuropathies over a glaucomatous optic neuropathy, as studies have shown 25% to 30% of POAG patients have an +RAPD.[19] However, the presence of an +RAPD can sometimes be attributed to the asymmetric presentation of POAG. Therefore, the presence of an +RAPD, outside the setting of asymmetrical visual field loss, asymmetrical cup-to-disc ratio and RNFL loss could potentially suggest a nonglaucomatous disease process.[20]

It is essential to differentiate between optic nerve cupping and optic nerve pallor, as pallor is generally not present in early glaucomatous optic neuropathy. A more difficult task is recognizing a patient with large physiological optic nerve cupping in the presence of pallor from a nonglaucomatous optic neuropathy. Clinicians should compare the anatomy of one eye to that of the other to better evaluate any subtle anatomical changes; it is also important to take serial optic nerve head photos to assess change over time.

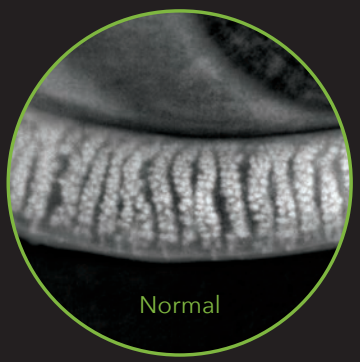
In a study from a tertiary referral center in which POAG patients showed progression on visual field exam, with otherwise controlled IOP, researchers noted patients with glaucomatous optic neuropathy had these common variables compared with patients with nonglaucomatous optic neuropathy: better visual acuity, history of an optic nerve hemorrhage, vertical elongation of the optic disc and visual field defects that

Meningiomas

The most common adult tumors of the optic nerve are optic nerve sheath meningiomas. They account for an estimated 2% of orbital tumors.[16] Optic nerve sheath meningiomas tend to be present in younger patients, on average from 40 to 45 years old with a female preponderance, while intracranial meningiomas (which can affect the anterior and posterior visual pathway) tend to occur in patients between 45 and 55 years old.[17] Orbital meningiomas can occur in close proximity to the optic nerve, within the optic nerve sheath, foramen of the optic canal, the chiasm and in the bony structure of the orbit, specifically the sphenoid wing. This can cause variable ocular signs and symptoms such as proptosis, conjunctival chemosis, decreased vision, afferent pupillary defects, color vision deficits and visual field loss. These meningiomas, in general, tend to be compressive, so depending on the location, the anterior visual pathway, optic chiasm, cavernous sinus and orbital contents can be affected.

MGD Now in Plain Sight

Dry Eye from previously hidden Meibomian Gland Disease impacts quality of vision and ocular comfort.



Dynamic Meibomian Imaging (DMI™)

LipiFlow® BY TEARSCIENCE

Now affordable for your patients.

Start treating for as low as $484/mo, full system as low as $1,275/mo

Based on Mar. 2016 financing estimate with approved credit. Tax not included. Restrictions may apply.

LipiFlow Activator with Vectored Thermal Pulse (VTP™)

LipiFlow inner-lid technology has been rigorously studied.*

* 31 peer reviewed reports, including 5 large multi-centered, randomized, controlled studies.

919-459-4880 | tearscience.com | info@tearscience.com

Typical Signs in the Differential Diagnosis of Glaucoma vs. Nonglaucomatous Optic Neuropathy

A summary of important exam findings when glaucoma does NOT seem to be the diagnosis.

	Glaucoma	Nonglaucomatous Optic Neuropathy
Acuity	Normal, usually unaffected until advanced disease state	Decreased early in disease state, can lose vision at variable rates depending on etiology, often worse than 20/40
Age	50 years or older for POAG	Patients less than 50 years
Neuroretinal rim appearance	Inferior and superior arcuate bundle loss, vertical notching or rim thinning, generally sparing temporal rim	Pallor more often than cupping; rim can appear cupped due to loss of color
Presence of optic disc hemorrhage	Yes	No
RNFL loss by OCT imaging	Most often superior and inferior	Can be sectoral or diffuse loss, often temporal loss corresponding to the papillomacular bundle
Visual field defects	Most often inferior or superior arcuate/nasal step, can be paracentral or cecocentral	More often paracentral or cecocentral defects; defects crossing horizontal raphe; defects which respect vertical meridian
(+RAPD)	Absent in symmetrical disease states; However, can be present in 25% to 30% of cases with asymmetry of visual field and retinal nerve fiber layer thinning which coincide with neuroretinal glaucomatous damage	Can present with an +RAPD early in the disease state which does not correlate to visual field loss or nerve fiber layer/neuroretinal rim thinning
IOP	Can be increased, normal, or low	Often normotensive, without history of spikes or ocular hypertension

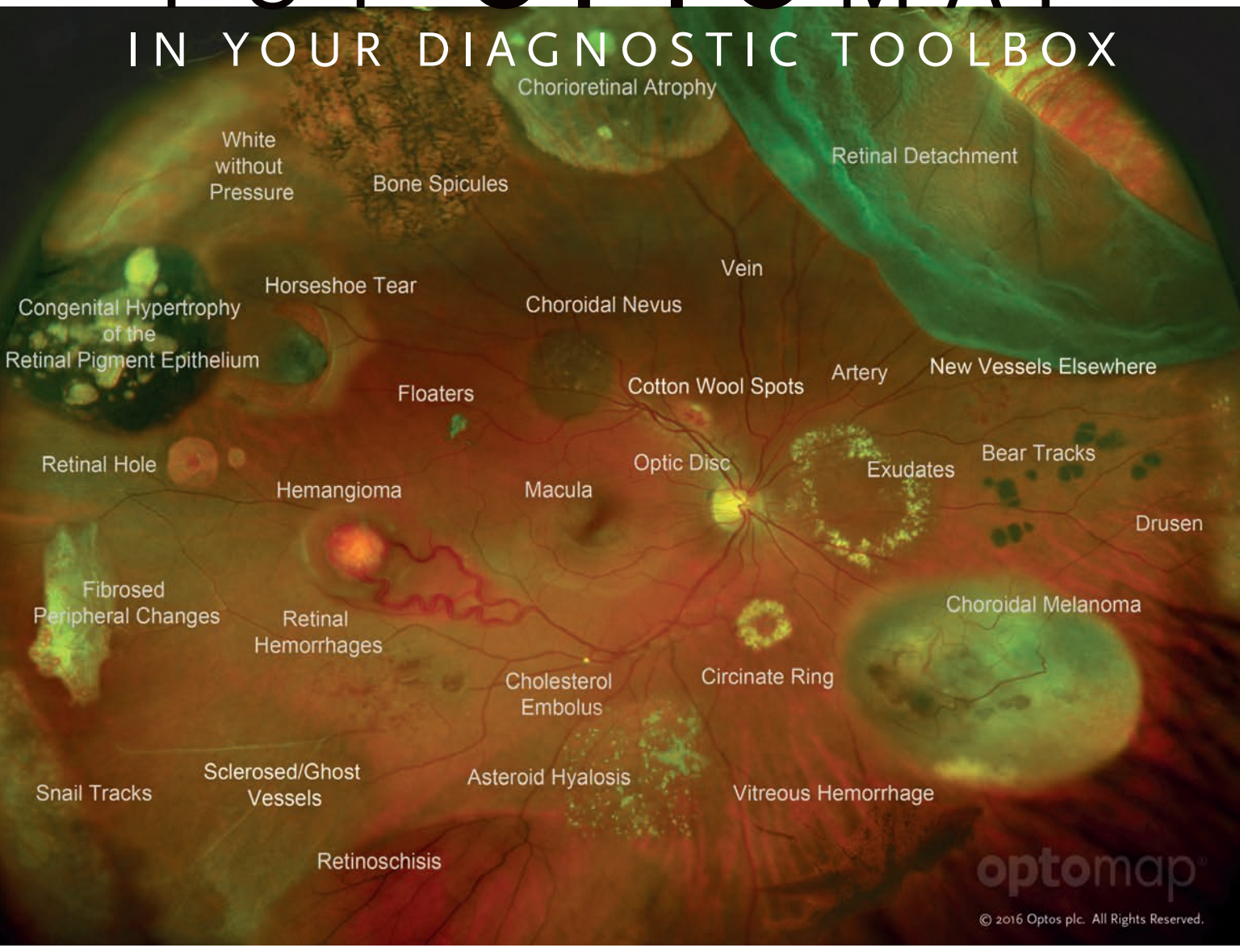
respected the horizontal raphe of the RNFL.[21] Clinicians should keep these variables in mind in cases where glaucoma patients continue to have progressive field loss in the presence of controlled IOP. Consider neuroimaging of the head and orbits to rule out other nonglaucomatous etiologies, especially in patients with normal tension and progressive visual field loss.

Visual field defects associated with glaucoma are known to respect the horizontal raphe of the retina, which is due to the anatomic distribution of the RNFL and is a reflection of how nerve fiber is lost in glaucoma. Nonglaucomatous optic neuropathies, however, can have a variety of visual field defects. Most importantly, they can cross the horizontal raphe and in some cases respect the vertical midline, which is not typical of glaucomatous field loss.[22,23] Nonglaucomatous optic neuropathies often affect the papillomacular bundle, which will often give the funduscopic appearance of temporal optic nerve pallor and present as paracentral or cecocentral visual field defects early in the disease course.[24]

The OCT RNFL findings of glaucoma vs. nonglaucomatous cupping can elicit overlap, making it difficult to distinguish one from the other. Glaucomatous damage noted on OCT RNFL is similar to quiescent forms of optic atrophy from past optic neuritis, ischemic optic neuropathy, optic disc drusen and loss from neurodegenerative diseases such as Parkinson's and Alzheimer's.[25,26] Nonglaucomatous optic neuropathies will also have thinning of the RNFL; however, it is usually located temporally at the disc and should correspond to pallor of the optic nerve on exam.

In conclusion, differentiating glaucoma from other nonglaucomatous masqueraders can be difficult, but the astute optometrist should be able to recognize the red flags that could alter or change the diagnosis. Understanding the glaucomatous disease process, the pathophysiology of visual loss from glaucoma and distinguishing cases that fall outside of the predicted disease course is essential. Using imaging modalities such as optic nerve photos to look for subtle optic disc neuroretinal rim and

PUT OPTOMAP
IN YOUR DIAGNOSTIC TOOLBOX



See More. Discover More.™

- **Only optomap®** provides up to a 200° view of the retina in a single capture
- **The only** ultra-widefield, ultra-high definition color, autofluorescence, red-free, retinal imaging device
- Simultaneous evaluation of the peripheral and central retina
- Clinically supported by 300+ peer reviewed studies

Contact us today **800-854-3039**
or email **BDS@optos.com**

Interested in adding ultra-widefield and ultra-widefield *af* capabilities to your practice?

Connect with us at Vision Expo East!

- **Visit our Booth # MS6848**
- **Attend Course MS33:**
  EMERGING UTILITY OF ULTRA-WIDEFIELD IMAGING IN CLINICAL PRACTICE
  Rishi Singh, MD - Staff Physician, Cole Eye Institute
  April 16, 2016 1:00 - 2:00 pm
  Medical and Scientific Theater

optos®
Building *The* Retina Company
optos.com

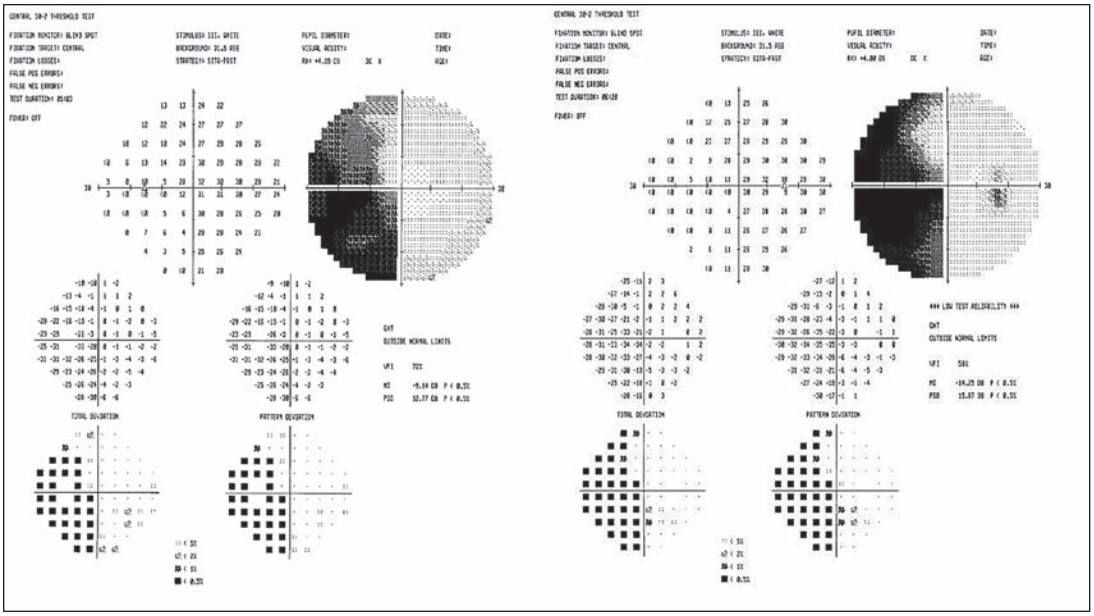
color changes, OCT retinal nerve fiber layer, ganglion cell analyses and reviewing visual field data will help to distinguish those cases of nonglaucomatous cupping. The aforementioned variables should increase awareness of the accuracy of the diagnosis so that glaucomatous masqueraders are recognized early and alternative management is instituted, avoiding potential adverse patient outcomes. ■

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

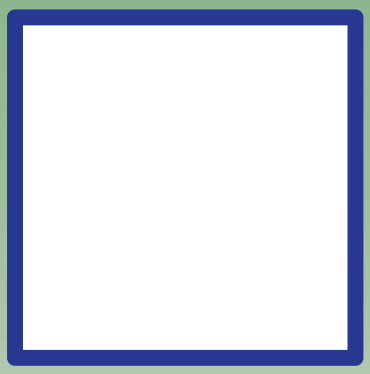
Metastatic Lesions

These lesions to the orbit always have to be considered in patients with a history of cancer, even those in remission. The most common metastases to the orbit that can cause compression are breast, lung, renal, gastrointestinal and prostate tumors.[12] Not only can these lesions invade the orbit, they can also spread to the brain where they can affect the posterior visual pathway, simulating neurological or stroke-like visual field defects. These metastatic lesions can also invade the orbit and regions of the anterior visual pathway, causing compression of the optic nerve or optic chiasm and producing visual field defects, which may mimic early glaucomatous loss.

1. National Eye Institute. Open-angle Glaucoma Defined. Accessed March 14, 2016. www.nei.nih.gov/eyedata/glaucoma.
2. Kapetanakis VV, Chan MPY, Foster PJ, et al. Global variations and time trends in prevalence of primary open angle glaucoma (POAG): a systematic review and meta-analysis. Br J Ophthalmol. 2016;100:86-93.
3. Tham Y, Li X, Wong TY, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040. A systemic review and meta-analysis. Ophthalmol. 2014;121:2081-2090.
4. Ritch R, Shields BM, Krupin T. The Glaucomas. Vol I, II, III. St. Louis, MO: Mosby; 1996.
5. Mansoori T, Balakrishna N, Viswanath K. Influence of disc area on retinal nerve fiber layer thickness measurement by spectral domain optical coherence tomography. Indian Journal of Ophthalmology. 2014;62(5):615-8.
6. Kass MA, Heuer DK, Higginbotham EJ, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open angle glaucoma. Arch Ophthalmol. 2002;120:701-713.
7. Deol M, Taylor DA, Radcliffe NM. Corneal hysteresis and its relevance to glaucoma. Curr Opin Ophthalmol. 2015;26:96-102.
8. Mangouritsas G, Morphis G, Mourtzoukos S, Feretis E. Association between corneal hysteresis and central corneal thickness in glaucomatous and non-glaucomatous eyes. Acta Ophthalmol. 2009;87:901-905.
9. Aghaian E, Choe JE, Lin S, Stamper RL. Central corneal thickness of Caucasians, Hispanics, Filipinos, African Americans, and Japanese in a glaucoma clinic. Ophthalmol. 2004;111:2211-9.
10. Doughty MJ, Zaman ML. Human corneal thickness and its impact on intraocular pressure measures: A review and meta-analysis approach. Surv Ophthalmol. 2000;44:367-408.
11. Mansouri K, Leite MT, Weinreb RN, et al. Association between corneal biomechanical properties and glaucoma severity. Am J Ophthamol. 2012;153:419-27.
12. Kupersmith MJ, Krohn D. Cupping of the optic disc with compressive lesions of the anterior pathway. Ann Ophthalmol. 1984;16:948-953.
13. Kalenak JW, Kosmorsky GS, Hassenbusch SJ. Compression of the intracranial optic nerve mimicking unilateral normal pressure glaucoma. J Clin Neuro-Ophthalmol. 1992;12:230-235.
14. Jackson A, Patankar T, Laitt RD. Intracanalicular optic nerve meningioma: A serious diagnostic pitfall. Amer J Neuroradiology. 2003;24:1167-1170.
15. Chaon BC, Lee MS. Is there a treatment for traumatic optic neuropathy? Current Opinion Ophthalmol. 2015 Nov;26(6):445-9.
16. Char DH. Clinical Ocular Oncology. 2nd ed. Philadelphia: Lippincott-Raven; 1997.
17. Saeed P, et al. Optic nerve sheath meningiomas. Ophthalmology. 2003 Oct;110(10):2019-2030.
18. Lee SH, Lee EJ, Kim T. Structural characteristics of the acquired optic disc pit and the rate of progressive retinal nerve fiber layer thinning in primary open angle glaucoma. JAMA Ophthalmol. 2015 Oct;133(10):1151-8.
19. Schiefer U, Dietzsch J, Dietz K, et al. Associating the magnitude of relative afferent pupillary defect (RAPD) with visual field indices in glaucoma patients. Br J Ophthalmol. 2012;96:629-633.
20. Chew SSL, et al. Retinal nerve fiber layer loss in glaucoma patients with a relative afferent pupillary defect. Invest Ophthalmol Vis Sci. 2010 Oct;51:5049-53.
21. Greenfield DS, Siatkowski RM, Glaser JS, et al. The cupped disc. Who needs neuroimaging? Ophthalmology. 1998;105:1866-74.
22. Fraser CL, White AJ, Plant GT, Martin KR. Optic nerve cupping and the neuro-ophthalmologist. J Neuro Ophthalmol. 2013;33:377-89.
23. Greenfield, DS. Glaucomatous versus nonglaucomatous optic disc cupping: clinical differentiation. Semin Ophthalmol. 1999;14(2):95-108.
24. Pasol J. Neuro-ophthalmic disease and optical coherence tomography: glaucoma look-alikes. Curr Opin Ophthalmol. 2011;22:124-132.
25. 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.
26. 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.



Example of left hemianopsia due to stroke.



Built in purifying filter

Preservative free multi-dose bottle

Over 240 drops

Now there's a clear choice for **preservative free dry eye relief.**

Introducing Clear Eyes® Pure Relief™, a revolutionary first line therapy for your patients:

- Unique glycerin formula with **hyaluronic acid** for advanced comfort
- Low actuation force with 1 drop control
- 90 day open bottle stability
- Up to 12 hours of soothing comfort
- Available over-the-counter

For more information visit www.cleareyes.com/professionals.

Seeing Blue: The Impact of Excessive Blue Light Exposure

Learn the science and key clinical points to help educate—and ultimately protect—your patients. **By Heather Flint Ford, OD**

The steep rise in personal electronics use and the transition from traditional incandescent lighting sources to compact fluorescent lights (CFL) and light-emitting diodes (LED) is dramatically increasing our exposure to blue light, raising new concerns about ocular health risks.

Blue light plays an important role in the body: it maintains circadian rhythms, improves alertness and can even be used in conjunction with photodynamic therapy to treat cancerous lesions; however, various types of blue light also pose hazards to our eyes and bodies.

As optometrists, we know that blue light is part of the visible spectrum of electromagnetic radiation. Visible light covers a range of electromagnetic wavelengths from approximately 380nm to 780nm. The blue-colored bands of light—known also as high-energy visible (HEV) light—are much more energetic than their longer wavelength counterparts.[1] Blue light has been found to penetrate deeper into the eye than other wavelengths of light, and thus has the potential to cause changes in retinal tissues, including the macula.

The prevailing wisdom concerning how light can impact human health has matured in recent decades, and continues to evolve as new technologies and research techniques are developed. Early research centered on the hormone melatonin, which is produced by the pineal gland from the amino acid tryptophan, and from the tryptophan-based neurotransmitter serotonin. Melatonin was first isolated from the bovine pineal gland in 1958, confirming the pineal gland as one of the regulatory centers for circadian rhythms in humans. Melatonin is secreted by the pineal gland in the presence of darkness with peak levels during the hours of 3am to 4am. It is at this time that the human body is most likely to sleep.[2,3]

Sleep Cycle Disruption

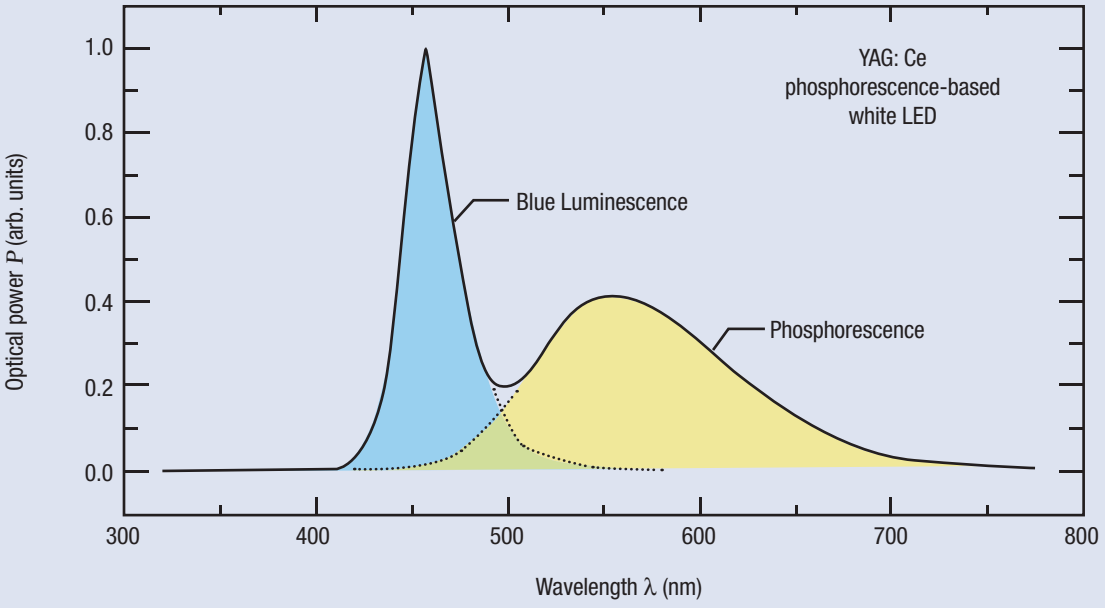
Blue light exposure at night has been shown to affect the quality of sleep. Researchers recently tested the effects of using e-readers prior to sleep for four hours vs. reading from a traditional book for four hours before sleep each night. The study found three notable results:

- Exposure to e-readers caused a 10-minute delay in sleep onset vs. the control group.
- The experimental group spent less time in rapid eye movement (REM) sleep (109.04 ± 26.25 min vs. 120.86 ± 25.32 min in the print-book condition).
- There was a significant difference between groups in subjective feelings of tiredness and alertness the following morning.[4]

The researchers attribute the difference to decreased time spent in REM sleep, given its importance in learning and storing memories.[5]

These findings are concerning, given the behavior of our teenag-

Optical Power Across the Blue Light Spectrum



ers and young adults, who tend to spend their leisure time using digital devices in the evening prior to bedtime (and indeed all throughout the day). Concerns already exist that we have a sleep epidemic in the United States—people receive fewer hours of sleep at night than in the past and significantly less than the recommended amounts. Couple this with reduced sleep from electronic use prior to bedtime, and its resulting next-morning lethargy and lack of alertness, and we are at risk for having an underproductive, fatigued population prone to motor vehicle accidents and errors on the job and in school.

Impact on Refraction

With the push for higher energy efficiency and cost savings in our schools, many school districts are now switching their lighting to LED-based lighting systems. While this may be good for school budgets, it is a detriment to children's vision. LED-based lighting, even the LED lights that emit a whiter rather than blue light, emit a significantly greater amount of blue light than traditional fluorescent lights used in classrooms. The change to LED-based lighting, coupled with the frequent use of computers by our students in the classroom, is cause for significant concern. Blue light has been shown to cause significant overaccommodation in students. Researchers found that when exposed to wavelengths below 430nm, rather than having the typical 0.3D lag of accommodation when focusing on a near target, students experience 1.0D of overaccommodation on average, or 1.3D sum total accommodative change from the normal posture for focusing at near. Additionally, this overaccomodation can cause distance blur as well.[6] These accommodative changes are constant even in decreased luminance. The overaccommodation, mediated by the parafovea, appears to be caused by the absence of short-wavelength sensitive cones in the central fovea.[6] This mechanism is also thought to trigger night myopia and is a potential driver of the myopic shift seen in our population in recent years.

While some lighting specialists are promoting the use of LED lights in the classroom to help reset student circadian rhythms for early start times and to improve student alertness, only lighting in the 444nm to 486nm wavelengths has been shown to impact the circadian rhythm, with peak sensitivity at 459nm to 464nm.[7] By switching school lighting systems to LED lights, students are being exposed to all of the blue wavelengths of light for the entire school day, including the problematic wavelengths below 455nm. If schools wish to improve student alertness with lighting, research needs to be conducted to determine the appropriate duration and time of day students should be exposed to the 455nm to 486nm bandwidth,

before such measures are put into place. A better idea: resolve to set later start times for middle and high schools to naturally align with student circadian rhythms—as the American Academy of Pediatrics has recently proposed.[14]

For our students, this classroom LED lighting change is being found to cause asthenopia and distance blur. As standardized testing and student performance is of major concern in our schools, this gives us as optometrists the potential to intervene with this lighting change by proactively meeting with school superintendents to recommend retaining traditional fluorescent lights in the classrooms until blue-light filtered LED systems are developed, reserving the installation of LED lights for areas only where student focusing needs are not required, such as in the hallways and cafeteria.

The Role of the Pineal Gland

For many years, researchers suspected that the suprachiasmic nucleus (SCN) of the hypothalamus was a primary regulatory center for the circadian rhythm after discovering that its removal led to a total disruption of the cycle.[8] With the development of new gene analysis techniques in the early 2000s, a large number of receptors for melatonin were located in the SCN, confirming the SCN's role in the circadian rhythm cycle.[9] However, it wasn't until 2002 that a new type of retinal photoreceptor—the intrinsically photosensitive retinal ganglion cell (ipRGC)—was identified as the primary mediator of the circadian rhythm pathway within the SCN of the hypothalamus.[10,11] Researchers discovered that a photopigment called melanophore in the ipRGCs is involved in the neuronal relay process to the hypothalamus. These melanophores provided a concrete link between the circadian rhythm system of the hypothalamus and the retinal ganglion cells—identified as early as 1923.[12]

More recently, scientists have come to view the pineal gland, via its secretion of melatonin, as the primary source of antioxidant activity. In 1993 melatonin was first identified as a free radical scavenger using the modern, oxygen-radical absorbance capacity assay technique.[13] Evidence shows that melatonin directly scavenges free radicals (OH, H_2O and single-oxygen molecules) in vitro and inhibits lipid peroxidation. Melatonin also stimulates a number of antioxidative enzymes.[9] Melatonin has been shown to increase the efficiency of the electron transport chain and, as a consequence, to reduce electron leakage and the generation of free radicals, as well as to stabilize microsomal membranes, thus resisting oxidative damage.[14,15]

The pineal gland has also been shown to have an anti-oncogenic, tumor-suppressing role in the body. A link exists between the pineal gland and cancer, a mutual and dynamic interaction between the secretion of melatonin and malignant growth.[16] A fresh tumor is 'sensed' by the pineal gland via neuroimmunoendocrine changes, leading to a stimulation of melatonin secretion, which in turn activates endogenous defense processes. At this stage of cancer development, melatonin can exert a direct tumor-inhibitory activity.[17] While melatonin has not been found to suppress advanced tumor growth (its tumor suppressing effects are seen primarily with early tumor growth), even in more advanced stages of cancer, melatonin has been found to improve quality of life with longer survival times.[14] "The research suggests the effect of melatonin is due to its ability to induce sleep as well as positively affecting pain by interacting with the endorphin system.[17]

Most optometrists are already aware of the impact of blue light on the different tissues and structures in the eye. In 2004, researchers found evidence suggesting the impact of blue light exposure on the risk of macular degeneration in the retina.[18] This led to subsequent studies on the long-term effects of visible light on the eye. In 2013, researchers identified the most damaging visible wavelengths to be in the blue-violet range of 415nm to 455nm. These wavelengths were found to be the most harmful to cells in the eye, as they can penetrate deeper into the eye and harm the retina, particularly the retinal pigment epithelium, causing the development of a toxic, apoptosis-causing molecule called N-retinlyidene-N-retinylethanolamine (A2E) to be produced within the RPE cells, causing cell viability loss.[19,20]

Does Blue Light Complicate Cancer Therapy?

One of the newest studies supporting the theory of blue light impacting human health builds upon and synthesizes the research regarding the anti-oncogenic properties of melatonin with the impact of blue light on circadian rhythms and tissues in the human body. In 2014, researchers found that light exposure at night (LEN) suppresses melatonin production, and that altering light/dark cycles with dim LEN speeds the development of breast tumors and leads to tamoxifen resistance.[21] They concluded that dim light exposure at night disturbs melatonin production and can render tumors insensitive to tamoxifen.[21]

As optometrists routinely follow patients being treated with tamoxifen on a semi-annual or annual basis because of the potential for tamoxifen retinopathy, we are in a unique position to discuss the health risks of nighttime light exposure with these patients. I contacted the researchers of the study to see if they had looked at the impact of blue light at night

For allergic conjunctivitis[1]

THE POWER TO CALM THE ITCH

BEPREVE®—FIRST-LINE, YEAR-ROUND, WITH BROAD-SPECTRUM ALLERGEN COVERAGE

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.

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

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

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

BAUSCH + LOMB

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

BEPREVE®
(bepotastine besilate ophthalmic solution) 1.5%

BEPREVE® (bepotastine besilate ophthalmic solution) 1.5%

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

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

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

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

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

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

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

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

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

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

Revised: 10/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

1 INDICATIONS AND USAGE
2 DOSAGE AND ADMINISTRATION
3 DOSAGE FORMS AND STRENGTHS
4 CONTRAINDICATIONS
5 WARNINGS AND PRECAUTIONS
5.1 Contamination of Tip and Solution
5.2 Contact Lens Use
5.3 Topical Ophthalmic Use Only
6 ADVERSE REACTIONS
6.1 Clinical Trial Experience
6.2 Post-Marketing Experience
8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
8.3 Nursing Mothers
8.4 Pediatric Use
8.5 Geriatric Use
11 DESCRIPTION
12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
12.3 Pharmacokinetics
13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis and Impairment of Fertility
14 CLINICAL STUDIES
16 HOW SUPPLIED/STORAGE AND HANDLING
17 PATIENT COUNSELING INFORMATION
17.1 Topical Ophthalmic Use Only
17.2 Sterility of Dropper Tip
17.3 Concomitant Use of Contact Lenses

*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.

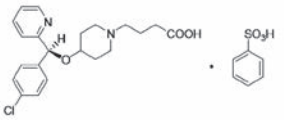
8.3 Nursing Mothers
Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 mcg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection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

Manufactured by: Bausch & Lomb Incorporated
Tampa, FL 33637
Under license from:
Senju Pharmaceutical Co., Ltd.
Osaka, Japan 541-0046

vs. other wavelengths, to which Dr. Steven Hill, one of the researchers, replied that they are in the process of conducting such a study right now and that he will keep me apprised of their results. "Although we have not yet published work regarding blue and green wavelength light, we are well aware of their potent melatonin suppressive actions," Dr. Hill stated. "Thus, we believe those using computers, cell phones, and televisions at night will have a 1.5 to 2-hour delay in their nighttime rise in melatonin after going to bed in the dark, and this will have an important negative impact on their breast cancer or other malignancies."[22]

While the blue wavelengths of 415nm to 455nm were found to be damaging to the retina, the wavelengths between 450nm to 550nm provide the strongest stimulation of circadian and neuroendocrine responses.[1,23] As practitioners, we need to keep up to date on the latest studies reflecting the effects of light on our patients' health, and we need to educate our patients on the risks of not only the blue light in the 415nm to 455nm band, but also those wavelengths in the 450nm to 550nm band as well.

Breast cancer is a major public health concern worldwide, and identifying an easily modifiable contributor to its development and successful treatment is of enormous consequence. What is remarkable about this study is that it runs counter to the prevailing assumption that a little bit of light at night is fine. How many of us grew up with a nightlight in our bedroom? Most of the public has heard bits and pieces about how being on the computer late at night disrupts our sleep cycle, but not much attention has been given to the risks of any light at all during nighttime. We need to take particular care to address this issue with our patients actively undergoing cancer treatment as well as those patients that are in remission, particularly with patients on tamoxifen adjuvant therapy.

We should specifically point out to patients unrecognized sources of blue light. We need to educate all our patients regarding the risks of blue light from electronics as well as light exposure at night. As our patients (particularly our school-age and young adult patients) become more and more dependent on their use of computers in all walks of life, they are exposed to more blue light than any generation before. It is vital to consider the potential hazards of such exposure and to educate our patients about its risks, including the loss of antioxidant and anticancer functioning, disruption to the circadian rhythm and sleep cycle, and potential vision loss from AMD.

Researchers will continue refining the blue light theory and developing ways to protect the eyes through optical lenses, changes to the lighting sources for computer monitors, software that reduces blue light emissions from computer screens and through general public health education. As new hazards emerge and evolve, it is our responsibility to update our education and interventional efforts. ■

Dr. Heather Flint Ford works in private practice at Clear Choice EyeCare, in Pottstown, Pa. She is a recipient of the Future Stem Teachers of America Scholarship, a scholarship designed to bring industry professionals into the classroom. She is currently completing a program through Western Governors University to receive her teaching certification in Middle School Science.

1. Smick K et al. Blue light hazard: new knowledge, new approaches to maintaining ocular health. Report of roundtable sponsored by Essilor of America in NYC, NY. 2013, March 16.
2. Lerner A, Case J, Takahashi Y et al. Isolation of melatonin, the pineal gland factor that lightens melanocytes. J Amer Chem Soc. 1958;80:2587-92.
3. Khullar A. The role of melatonin in the circadian rhythm sleep-wake cycle. Psychiatric Times online. http://www.psychiatrictimes.com/sleep-disorders/role-melatonin-circadian-rhythm-sleep-wake-cycle. 2012, July 9.
4. Lissoni P, Barni S, Ardizzoia A et al. A randomized study with the pineal hormone melatonin versus supportive care alone in patients with brain metastases due to solid neoplasms. Cancer. 1994;(73):699–701.
5. Chang A, Aeschbach D, Duffy J, Czeisler C. Evening use of light-emitting eReaders negatively affects sleep, circadian timing, and next-morning alertness. Proceedings of the National Academy of Sciences, 2015 Jan 27;112(4):1232-37.
6. Graef K and Schaeffel, F. Control of accommodation by longitudinal chromatic aberration and blue cones. J of Vis. 2012;12(1):14.
7. Hanifin J, Brainard G. Photoreception for circadian, neuroendocrine, and neurobehavioral regulation. J Phys Anthro. 2007;26(2):87-94.
8. Abe K, Kroning J, Greer M, Critchlow V. Effects of destruction of the suprachiasmatic nuclei on the circadian rhythms in plasma corticosterone, body temperature, feeding and plasma thyrotropin. Neuroendocrinology. 1979;29(2):119-31.
9. Anisimov V, Popovich I, Zabezhinski M, et al. Melatonin as antioxidant, geroprotector and anticarcinogen. Biochimica et Biophysica Acta. 2006;1757:573–89.
10. Hattar S, Liao H, Takao M, et al. Melanopsin containing retinal ganglion cells: architecture, projections, and intrinsic photosensitivity. Science. 2002 Feb 8; 295(5557):1065-70.
11. Wong K, Dunn F, Berson D. Photoreceptor adaptation in intrinsically photosensitive retinal ganglion cells. Neuron. 2005 Dec 22;48(6):1001-10.
12. Zimmer C. Our strange, important, subconscious light detectors. Discover Magazine. 2012 Feb. Retrieved online: discovermagazine.com/2012/jan-feb/12-the-brain-our-strange-light-detector.
13. Hanifin J, Brainard G. Photoreception for circadian, neuroendocrine, and neurobehavioral regulation. J Phys Anthro. 2007;26(2);87-94.
14. American Academy of Pediatrics. Policy statement: school start times for adolescents. Pediatrics. Sept 2014;134(3).
15. Tan D, Chen L, Poeggeler B, et al. Melatonin: a potent, endogenous hydroxyl radical scavenger. Endocr. J. 1993;1:57–60.
16. Bartsch C, Bartsch H. Pineal gland and cancer—an epigenetic approach to the control of malignancy: evaluation of the role of melatonin. Madame Curie Bioscience Database [Internet]. 2000; Austin, TX: Landes Bioscience. Available from: hwww.ncbi.nlm.nih.gov/books/NBK6233
17. Qi W, Reiter R, Tan D, et al. Increased level of oxidatively damaged DNA induced by chromium (III) and H2O2: protection by melatonin and related molecules. J Pineal Res 2001;29:54–61.
18. Karbownik M, Garcia J, Lewinski A, Reiter R. Carcinogen-induced, free radical-mediated reduction in microsomal membrane fluidity: reversal by indole-3-propionic acid. J. Bioenerg. Biomembr. 2001;33:73–8.
19. Dillon J, Zheng L, Merriam JC, Gaillard ER. Transmission of light to the aging human retina: possible implications for age related macular degeneration. Exp Eye Res. 2004 Dec;79(6):753-9.
20. Arnault E, Barrau C, Nanteau C, et al. Phototoxic action spectrum on a retinal pigment epithelium model of age-related macular degeneration exposed to sunlight normalized conditions. PLoS ONE. 2013;8(8):1-12.
21. Dauchy R, Xiang S, Mao L, et al. Circadian and melatonin disruption by exposure to light at night drives intrinsic resistance to tamoxifen therapy in breast cancer. Cancer Research. 2014 Aug 1;74(15). Retrieved from cancerres.aacrjournals.org on April 19, 2015.
22. Hill, Steven and Ford, Heather – direct e-mail correspondence 3/24/15 - 3/26/15.
23.Hanifin J, Brainard G. Photoreception for circadian, neuroendocrine, and neurobehavioral regulation. J Phys Anthro. 2007 26(2):87-94.

Current and Emerging Therapies for Allergic Conjunctivitis

With so many tools at your disposal, knowing the right treatment strategy can be challenging. **By Stephanie Fromstein, OD**

The classic symptoms of ocular allergy—itching, redness and chemosis—can be a trifecta of trouble for eye care practitioners (ECPs). Although we can help our patients when the condition is appropriately identified, there continues to be no uniform management protocol to address this atopic population's signs and symptoms.[1,2]

This is also a growing problem, with incidence increasing worldwide; ocular allergy now represents a full one-third of referrals and is one of the most commonly encountered conditions for ECPs.[2,3] The underlying mechanism for this increase has yet to be fully understood, but researchers suspect it is multifactorial, including genetics, air pollution in urban areas, pets and early childhood exposure.[4] Prescribing for the condition has also surged by 20%, inflating what was already a six billion dollar industry.[5,6]

In the context of these increases, failure to appropriately manage these patients is a mounting problem, which may ultimately lead to decreased quality of life. Studies indicate that more than 50% of patients reported an inability to comfortably go outdoors, difficulty driving or trouble sleeping.[7] This article summarizes the landscape of allergy treatment, while emphasizing novel approaches to an age-old problem.

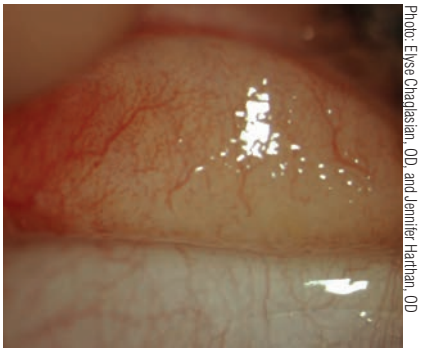


Photo: Elyse Chadjasian, OD, and Jennifer Harthan, OD

With seasonal and perennial allergic conjunctivitis, superior involvement may indicate a more chronic or severe form of allergy.

Classification

Ocular allergic disease is an umbrella term which encompasses myriad hypersensitivity disorders of the ocular surface; affected structures include the eyelids, cornea and, most frequently, the conjunctiva.[8,9] Seasonal allergic conjunctivitis (SAC) and perennial allergic conjunctivitis (PAC) together comprise about 95% of clinical presentations, with atopic keratoconjunctivitis (AKC), vernal keratoconjunctivitis (VKC), giant papillary conjunctivitis (GPC) and other contact-lens related allergic conjunctivitis comprising the balance of cases.[1,10] SAC and PAC are similar in their clinical presentation but vary in their inciting agents: SAC is mediated by grass and pollen allergens and tends to peak seasonally, whereas PAC is rooted in allergies to commonly encountered allergens year-round, including dust mites and feather and animal dander, which tends to make PAC chronic.[9,10] Chronic forms of the disease are more likely to involve the lid and cornea and may require comanagement with other specialists such as allergists, dermatologists and pediatricians. The remainder of the conditions—AKC, VKC, GPC and contact conjunctivitis—have some common markers of allergy, but differ from SAC/PAC in clinical features and presentations. Vernal and atopic disease need to be aggressively managed to prevent complications such as corneal scarring and consequent vision loss.[3]

Pathophysiology

All ocular allergies represent a localized type 1 hypersensitivity reaction, wherein an antigen binds to immunoglobulin E, crosslinking the molecules on the mast cell surface and causing degranulation of inflammatory mediators from the mast cell. Histamine—long-established as a

principal harbinger of ocular allergy symptoms—is among these mediators and is released from the mast cells, causing vasodilation and fluid transudation. This results in redness, swelling and itching, as fluid in the perivascular area stimulates adjacent nerve endings.[11]

Histamine exerts these effects via a number of distinct histamine receptors: stimulation of the H1 receptor causes itching, while stimulation of the H2 receptor causes vasodilation of conjunctival vessels.[9,11] Researchers suspect H3 and H4 receptors are expressed on the ocular surface as well.[11] This immediate histamine response lasts 20 to 30 minutes and is amplified by a late-phase response through a different set of mediators and cascades.[3]

Clinical Examination

History is a critical part of the examination. Itching is the cardinal symptom of ocular allergy, and practitioners should seek alternative differentials for patients who do not exhibit this complaint. Itching at the nasal aspect of the eye near the caruncle, which may be worse because it is a lymphoid tissue, should confirm your suspicion of allergy.[12] It may also be accompanied by other symptoms such as redness, inflammation, stinging, tearing and burning. Watery or mucoid discharge may be present as well.[3,13] Because patients with seasonal allergies may not present at the time of peak symptomology, clinicians should probe regarding symptoms during other times of the year and initiate treatment prophylactically.

A search for signs of allergy should include a thorough slit lamp examination, paying special attention to the conjunctiva, as it is the principal ocular immunologic tissue that responds to allergens. In the case of SAC or PAC, there may be a papillary response, which is more likely to present inferiorly than superiorly.[13,14] Papillae are nonspecific and may also be noted in healthy children and teenagers and should not be considered a pathognomonic sign.[11] Conjunctival injection, conjunctival chemosis and inflammation of surrounding structures (including the lids) may be present.

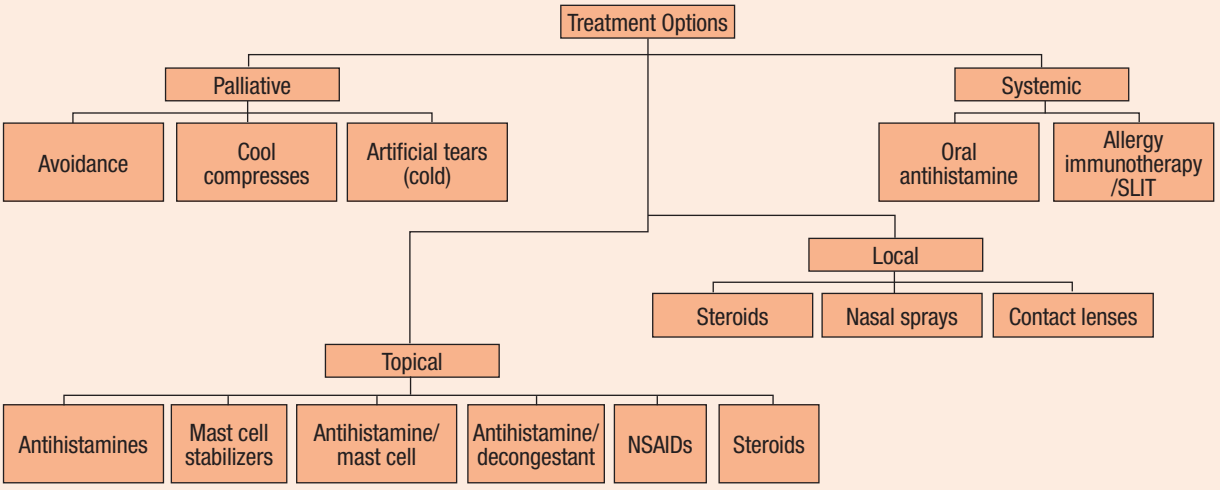
Comorbidities

Because a number of allergic conjunctivitis symptoms are relatively nonspecific, comorbidities such as dry eye disease or blepharitis should be ruled out. Clinically, it is not uncommon for a patient to present with both allergic disease and a secondary condition, which may exacerbate the former.[15]

The tear film is an important innate defense against allergens, and a dry eye (whether evaporative or aqueous deficient) has less of this important defense. As a result, more allergens come in contact with the ocular surface at higher concentrations for longer amounts of time. This relationship becomes increasingly important, as treatment for one condition can deteriorate another if not appropriately identified.

For example, punctal plugs for dry eye hold allergens on the ocular surface, and oral antihistamines have a well-established history of worsening ocular dryness. The association of the conditions necessitates a thorough ocular surface examination—including vital dyes, tear break-up time and examination of the tear meniscus and lid margins—as well as a management plan that treats each condition independently while being mindful of the overall impact. A good rule is to treat the prevailing symptomology first, whether dryness or allergy, with the understanding that failure

Choosing the Right Ocular Allergy Treatment



to manage associated conditions will lead to difficulty in achieving full symptomatic relief. Crossover therapies—including artificial tears and avoidance of inciting agents—may be of particular utility. Emerging wisdom indicates that failure to address comorbidities may be what underlies much of the therapeutic failure of allergy treatment.

In addition to a thorough ocular examination, new point-of-care testing is available for allergy sufferers in the form of an in-office skin test known as Doctor's Allergy Formula (Bausch + Lomb).[1,16] ECPs have started performing this test—typically the realm of allergists—to corroborate their diagnosis and comanage with other specialties.

It serves to identify sensitivities to specific allergens and can be customized to include allergens specific to your geographic location. It may be performed by a nurse or technician, but is currently only billable for ODs practicing in a multidisciplinary setting associated with an MD or DO. Hopefully the test will become available for more widespread use in the optometric community. Along with other point-of-care diagnostic testing, it will allow practitioners to make more objective and informed decisions about the etiology of symptoms and formulate comprehensive management strategies.

Treatment

Treatment options for ocular allergy vary widely, from non-pharmaceutical to systemic therapeutics, and should be initiated using a stepwise approach. Many agents used over the years continue to be effective at managing allergic disease, and a better understanding of the underlying disease has fine-tuned these agents.

• ***Palliative Therapy.*** The most elementary and effective management plan for ocular allergy is avoidance of inciting allergens. Functionally, it may also be the most challenging for patients. The conjunctiva is, relatively speaking, a vast surface area for allergens, and minimizing contact is paramount.[3] Staying indoors when the allergen count is high, keeping windows closed, wearing wrap-around sunglasses, cleaning filters and ducts, replacing allergen-harboring items such as pillows or carpet and even washing one's hair before going to sleep can all be effective at reducing exposure.[1,7,13] Cool compresses also provide palliative relief and should be recommended along with artificial tears to minimize eye rubbing, which leads to further histamine release and worsening symptoms.[7,15]

Artificial tears on their own are not only palliative but can also be therapeutic, helping to diffuse ocular allergens and preventing them from interacting with the ocular surface.[1] Many practitioners recommend patients refrigerate the artificial tears to provide more immediate relief of symptoms. Preservative-free artificial tears should be the product of choice, as they avoid the complication of a preservative in a patient already predisposed toward atopy.[1]

• ***Topical Therapeutics.*** A multitude of topical therapeutic options are on the market for the management of ocular allergy. They can be used as monotherapy or in combination, though simpler dosing generally correlates with increased compliance. Each of the agents remain effective at targeting allergy in some capacity—the real skill, as always, is in the art of prescribing.

Many antihistamine (e.g., emedastine, levocabastine) and mast cell stabilizer (e.g., pemirolast, neocromil, lodoxamide, cromolyn)

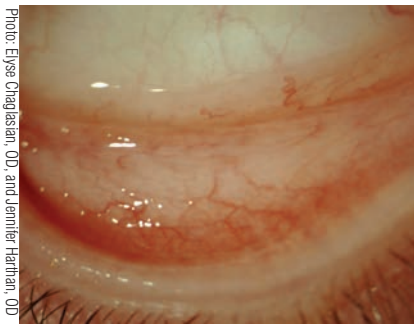


Photo: Elyse Chaglasian, OD, and Jennifer Hartman, OD

Papillae on lower lid eversion in a patient with moderate allergy symptoms.

monotherapy mainstays are on the market. These drops are most effective for acute and preventative treatment, respectively. Antihistamines reversibly block the histamine receptor and provide rapid relief of redness and itching. They suffer from a more limited duration of action (dosed at four times per day, same as mast cell stabilizers) and do not prevent the action of other pro-inflammatory mediators, including prostaglandins and leukotrienes.[3] Although antihistamines are effective at acute relief, they have less ability to prevent allergies in a prophylactic capacity by targeting the mast cells.

Mast cell stabilizers, on the other hand, are especially effective at decreasing or eliminating symptoms of an attack when taken in advance.[1] Using a mast cell stabilizer after the patient is exhibiting symptoms is like repairing the hole in the bucket after the water has drained—the damage (and degranulation) is already done. Eye care practitioners can prescribe a mast cell stabilizer weeks or months in advance of a patient's peak symptoms to target and mitigate impending histamine release.[1] For acute attacks, an antihistamine or combination agent should be considered instead.

Topical combination antihistamine/mast cell stabilizers (e.g., alcaftadine, azelastine, bepotastine, epinastine, ketotifen, olopatadine) are key agents in the management of allergic conjunctivitis, and there have been a number of recent changes in this market segment. These agents have the combined benefit of immediate relief—owing to the antihistamine properties—as well as the long-term benefit of mast cell stabilization. An added advantage is the once-daily dosage a number of medications offer.

The newest combination therapy drug is a higher concentration of olopatadine (0.7% vs. 0.2%), and research shows it improves relief compared with previous iterations.[19]

Bepotastine is a prescription-only twice-daily drop that is unique in its high specificity for the histamine 1 receptor, meaning that it is particularly effective at preventing ocular itch.[1] Furthermore, one study shows it reduces nasal congestion, rhinorrhea, ear/palate itching and nasal itching.[17] This top-down, gravity-driven influence of ocular agents on the nasal mucosa is an area of significant research and will likely be exploited to improve cardinal symptoms of allergy without initiating oral or systemic treatment.[18]

A number of ketotifen-based drops are now available over-the-counter (OTC) for use twice a day, such as Zaditor (Alcon), Alaway (Bausch + Lomb), Refresh Eye Itch Relief (Allergan) and TheraTears Eye Itch Relief (Akorn). The release of these OTC options allow us to provide a safe and effective long-term therapy for allergy sufferers, with low risk for harm and abuse.[20] The once-daily dosage of the prescription-only agents, however, continues to be an advantage to prescription medications over the twice-daily dosing of OTC products.

Although decongestants (e.g., oxymetazoline, tetrahydrozoline and naphazoline) compounded

with antihistamines have traditionally been a cornerstone of allergy therapy, they are decreasing in popularity due to their adverse effects—mydriasis, rebound hyperemia and a contraindication in patients with narrow angle glaucoma—and the advent of newer agents with better safety profiles and efficacy.[11] They remain effective at decreasing redness and itch, but because their use should be limited to a maximum of 10 to 14 days, their utility in chronic allergic conditions is limited.[20]

Topical nonsteroidal anti-inflammatory drugs (NSAIDs) are another allergy treatment option whose usage is less prevalent than in the past. While effective at decreasing the irritation associated with ocular allergy, they do not address other symptoms and have complications with long-term use, including risk for corneal melt. In addition, they have the potential to incite a leukotriene-mediated enhancement of the inflammatory response, which runs counter to the goal of effective allergy management.[12]

Topical steroids used for allergy relief typically include loteprednol, fluorometholone or prednisolone acetate 0.125% because of their propensity for effective control of inflammation and low side effect profile. Steroids exert their action early and often in the inflammatory cascade and are the single most effective agent at combating the inflammation associated with ocular allergy.[12] They are typically reserved for cases nonresponsive to conventional therapy, or in cases of acute, pronounced allergic response. Be aware of the side effects, including the chance of IOP elevation and cataracts; these agents should not be used for long-term therapy.[3] More potent steroids such as Pred Forte and difluprednate may be used in advanced and nonresponsive cases.

There are numerous areas of research in topical therapy for allergy. Building on our current arsenal of topical agents, research on the off-label use of topical cyclosporine has shown its promise as an alternative to steroids for patients with severe or chronic forms of the disease.[11] Also, research shows MMP-9 activity is elevated in patients with allergic conjunctivitis and dry eye, indicating promise for a novel topical agent targeting this activity.[11] Investigation into the use of conjunctival injections into the upper tarsal area as a means for managing more serious, chronic cases of allergy such as VKC has shown promise, as have glucocorticoid receptor agonists, an investigative class of drugs that target inflammatory disease.[11] Finally, researchers are also investigating vaccinations (peptide and cDNA), adjuvants, anti-IgE antibodies and intracanalicular dexamethasone depots, which may represent the future of allergy treatment.

• ***Local Therapeutics.*** Inflammation is often concentrated in, but not limited to, the conjunctival surface in ocular allergy. Research shows that allergic inflammation of the eyelid skin in conditions such atopic dermatitis or eczema is unresponsive to topical antihistamines and mast-cell stabilizers.[15] Instead, the practitioner should consider a topical steroid, keeping in mind the possible side effects of skin-thinning and discoloration. In an effort to decrease these side effects, investigators are looking into the use of pimecrolimus or tacrolimus off-label as a safe, nonsteroidal alternative for long-term therapy.[15]

A secondary area of frequent inflammation is the nasal mucosa, where reports indicate that roughly 14.5 million Americans have a combined rhinoconjunctivitis.[21] Nasal and ocular mucosa show similar characteristics and symptoms, and research has discussed the crossover effect of some topical ocular therapeutics on the nasal mucosa.[13,15] What is perhaps more surprising is that steroidal and nonsteroidal nasal sprays also show a beneficial impact on reducing symptoms at the ocular mucosa.[18] To this end, triamcinolone and fluticasone nasal sprays have recently become available OTC, making treatment more accessible for comprehensive management of the various aspects of allergic symptoms. Most patients require dual therapy (ocular and nasal) for full symptomatic relief.

• ***Prophylactic measures.*** Contact lenses have emerged as a possible treatment modality for ocular allergy. The lenses provide protection against allergens, and symptoms of itching, burning, stinging, dryness and discomfort were all shown to be reduced in patients wearing "enhanced moisturizing" daily disposable lenses.[22] This was attributed to a barrier effect, similar to the effect on tearing for the wearer when cutting onions.[22] Drug-infused contact lenses would combine this protection with an additive therapeutic effect. There are no such lenses currently on the market; however, with the continued investigation into infusing contact lens materials with medicinal agents, it is easy to imagine great potential for an allergy-targeted therapeutic lens moving forward. We strongly emphasize frequent replacement (ideally daily disposable) and good lens hygiene for all of our contact lens-wearing patients with allergy.[23] If treating with drops, patients should instill them at least 10 minutes before inserting their contact lenses to prevent accumulation of the active ingredients—as well as the attendant preservatives—in the material of the lens.[7]

• ***Systemic Therapeutics.*** Oral antihistamines remain a pillar of allergy treatment and generally provide moderate relief of ocular symptoms. While the newer second- and third-generation formulations are less sedating that older formulations, they can still contribute to dryness of the ocular surface, with some studies showing tear flow reduction of up to 30%.[15,24] Furthermore, oral agents may be unsuccessful at relieving the itch associated with ocular allergy.[15] Depending on the predominant symptomology, if the patient is getting minimal relief of ocular symptoms with an oral agent, it might be prudent to discontinue the oral agent and replace it with a more targeted topical or local therapy.[18] One exception would be a patient suffering from allergic sinusitis, who likely needs an oral agent containing a decongenstant.[7]

Allergy immunotherapy is another treatment modality with proven systemic relief.[11] It consists of giving the patient injections of increasing quantities of allergens in order to decrease the patient's own allergic response to that allergen. It has shown variable success in managing a patient's ocular symptoms.[11]

More recently, however, a new alternative to subcutaneous injections has emerged. Sublingual immunotherapy is gaining popularity and shows effectiveness against allergic rhinitis and, to a lesser extent, allergic conjunctivitis.[13,25] Oralair (Greer) is the first approved sublingual allergy extract for patients sensitive to grass pollens.[1] While its impact on allergic conjunctivitis is inconsistent, further forays into this research may prove promising in successfully managing both systemic and ocular symptoms.[9]

Ocular allergy is a clinical problem with a many solutions. For now, proper understanding of the pathophysiology and the available agents are critical to tackling a patient's symptomology. Updated treatments and wider availability of current therapeutics should make solving the problem easier than ever. ■

Dr. Fromstein is an assistant professor at the Illinois College of Optometry, where she splits her time between didactic education and clinical teaching in the Cornea and Contact Lens, Urgent Care and Primary Care Services.

1. Trubo R. Seasonal ocular allergy: new options for a recurring problem. Cornea. 2015 Mar:31-3.
2. Wong AH, Barg SS, Leung AK. Seasonal and perennial conjunctivitis. Recent Pat Inflamm Allergy Drug Discov. 2009;3:118-27.
3. La rosa M, Lionetti E, Reibaldi M, et al. Allergic conjunctivitis: a comprehensive review of the literature. Italian Journal of Pediatrics. 2013;39:18.
4. Leonardi S, del Giudice Miraglia M, La Rosa M, et al. Atopic disease, immune system, and the environment. Allergy Asthma Proc. 2007;28(4):410-17.
5. Origliery C, Bielory L. Emerging drugs for conjunctivitis. Expert Opin Emerg Drugs. 2009;14(2):523-36.
6. Bielory L. Update on ocular allergy treatment. Expert Opin Pharmacother. 2002;3(5):541-53.
7. Karpecki P. Contact lens wear and ocular allergy. Contact Lens Spectrum. 2012;27: 26-32.
8. Abelson MB, Smith L, Chapin M, et al. Ocular allergic disease: mechanisms, disease sub-types, treatment. The Ocular Surface. 2003;1(3):127-49.
9. Berdy GJ. New strategies in the diagnosis and management of ocular allergy. Cataract & Refractive Surgery Today. 2012.
10. Slonim CB, Boone R. The ocular allergic response: a pharmacotherapeutic review. Formulary. 2004;39:213-22.
11. Raizman MB, Luchs JI, Shovlin J, Wolf RL. Ocular allergy: a scientific review. Review of Opthalmology. 2012 May.
12. Thoughts on the management of ocular allergy. Ocular Surgery News. 2009.
13. Bowling E. What's trending in ocular allergy treatment. Optometry Times. 2015.
14. Bielory L, Friedlaender MH. Allergic conjunctivitis. Immunol Allergy Clin North Am. 2008;28:43-58.
15. Raizman MB. Ocular allergy, nasal allergy, and dry eye disease. Advanced Ocular Care. 2010 Mar:48-9.
16. Cooper MS. A new player in point-of-care allergy testing. Optometry Times. 2015.
17. Macejko TT, Meier EJ, Bergmann MT, et al. Bepotastine besilate ophthalmic solution 1.5% for up to 8 hours following dosing reduces total non-ocular symptoms, rhinorrhea, and tearing in a multi-site clinical model of allergic conjunctivitis. Poster presented at 2009 American Academy of Allergy Asthma and Immunology Annual Meeting, March 3-17, 2009; Washington, DC
18. Karpecki PM. Anti-allergy eye drops can effectively treat non-ocular symptoms. Primary Care Optometry News. 2011.
19. Alcon. Pazeo Package Insert. Fort Worth, TX, 2015.
20. Mandese MJ, McCann W, Croteau V. When to 'prescribe' an OTC allergy drop. Review of Optometry. 2010;147(8):31-6.
21. Bousqet J, Khaltaev N, Cruz AA, et al. Allergic rhinitis and its impact on asthma (ARIA) 2008 update. Allergy. 2008;63(8)160.
22. Wolffsohn JS, Emberlin JC. Role of contact lenses in relieving ocular allergy. Contact Lens & Anterior Eye. 2011;34:169-72.
23. Byrne J. Help allergy sufferers wear contact lenses more comfortable. Primary Care Optometry News. 2005.
24. Welch D, Ousler G, Nally L, et al. Ocular drying associated with oral antihistamines (loratidine) in the normal population - an evaluation of exaggerated dose effect. Adv Exp Med Biol. 2002;506:1051-5.
25. Vitaliti G, Leonardi S, Miraglia Del Giudici M, et al. Mucosal immunity and sublingual immunotherapy in respiratory disorders. J Biol Regul Homeost Agents. 2012;26:S85-S93.

2 CE Credits
(COPE approval pending)

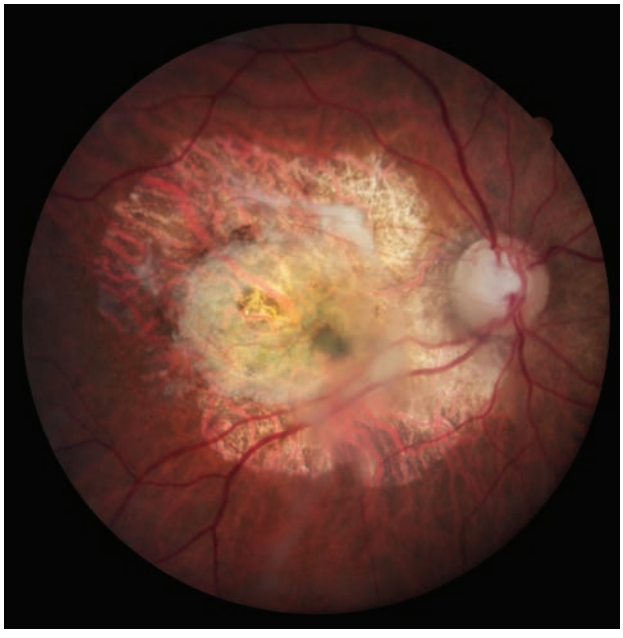
PEER • REVIEWED • PRA • ARTICLE

Are You Clear on Your Macular Function Screening Responsibilities?

How the latest technologies can change how you practice. By Sherrol A. Reynolds, OD

Macular disease is on the rise in the United States. For example, advanced sight-threatening neovascular or "wet" age-related macular degeneration (AMD) is projected to increase to three million by 2020.[1] Likewise, the spike in systemic conditions such as diabetes has led to a dramatic rise in diabetic retinopathy and maculopathy, which is projected to climb to 11 million by 2030, according the National Eye Institute.[2]

Clinicians must provide patients timely detection, prompt management and, just as importantly, patient education to prevent vision loss. Macular function screening technologies are vital tools you'll

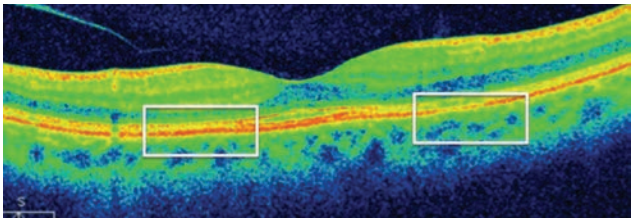


Fundus photography is essential to documenting disease. For instance, this 85-year-old female patient's advanced AMD is clearly visible. However, we now have a host of additional imaging capabilities that may enable earlier detection and intervention.

Release Date: April 2016
Expiration Date: April 1, 2019
Goal Statement: With the prevalence of macular disease rising, optometrists are more likely than ever to encounter damage to this structure. The many new imaging devices and functional tests available to evaluate the macula should be used in concert with each other by a skilled clinician. This article reviews the available tests, when—and for which patients—their use is appropriate and how their use has improved diagnostic capabilities for conditions such as vitreomacular adhesion, vitreomacular traction, hydroxychloroquine toxicity and others.
Faculty/Editorial Board: Sherrol Reynolds, OD
Credit Statement: COPE approval for 2 hours of CE credit is pending for this course. Check with your local state licensing board to see if this counts toward your CE requirement for relicensure.
Joint-Sponsorship Statement: This continuing education course is joint-sponsored by the Pennsylvania College of Optometry.
Disclosure Statement: Dr. Reynolds has no financial relationships to disclose.

need to accomplish that.

This article provides an overview of those tools, what they can accomplish, the methods and techniques for evaluating macular function and guidelines for when to employ which technique.



This SD-OCT image of a patient on Plaquenil (hydroxychloroquine-HCQ, Sanofi Aventis) for 15 years shows loss in photoreceptor inner/outer segment (IS/OS) junction and thinning of the outer retina in the parafoveal region.

Standard Macular Screening Procedures

In addition to visual acuity and color vision testing, basic procedures may be considered adjunctive screening techniques for the evaluation of macular function and disease. For example, the Watzke-Allen slit beam test provides subjective assessment in testing for a full-thickness macular hole defect. The central lens of the Goldmann three-mirror provides excellent stereoscopic views of subtle macular pathologies (i.e., cystoid macular edema, central serous chorioretinopathy). Amsler grid is beneficial in detecting metamorphopsia, central scotoma or micropsia. Although these procedures are subjective, they are noninvasive, readily accessible and provide early hints of macular abnormalities. Today, many optometrists have access to the following testing technologies as well:

• ***Fundus photography*** is essential in documenting and monitoring macular disease. It permits serial comparison of structural and functional changes as well as disease progression. High-quality fundus images can capture subtle early defects, such as exudates or microaneurysms, which can be missed during the clinical evaluation. It also has value as an educational tool for patients to learn about their condition—knowledge that may ultimately lead to better adherence. It also gives you exam findings in digital form to share with colleagues and other health providers.

Every practitioner should have access to a fundus camera. Combining that technology with other imaging modalities, such as spectral-domain optical coherence tomography (SD-OCT), is not only practical, but a sound return on the investment. Newer fundus cameras have the ability to adapt to smartphones, while others are available in combination with fundus autofluorescence (FAF) or optical coherence tomography (OCT) systems, allowing for multimodal imaging.

• ***SD-OCT*** provides high-resolution, volumetric and cross-sectional functional assessment and structural imaging of macular pathology. SD-OCT in particular is a must-have technology in the understanding, care and management of macular pathologies. Prior to SD-OCT, it would have been impossible to make an accurate diagnosis of vitreomacular adhesion (VMA) and vitreomacular traction (VMT). These devices enable early diagnosis and detection of an impending macular hole (MH). SD-OCT has greatly improved the potential for early detection of choroidal neovascular membrane in AMD, which has led to improved visual outcomes for many. In some cases, SD-OCT may be equal or superior to angiography in making the initial diagnosis (e.g., DME and CSCR).

OCT imaging has progressed to include newer imaging technology. For example, en face OCT imaging combines SD-OCT with transverse (C-scans) images of the macula.[3] This allows for imaging individual retinal layers, especially in diseases that focally affect a specific retinal sublayer, such as AMD.

Newer enhanced-depth imaging (EDI) OCT provides improved visualization of the choroid, which allows for the assessment of choroidal changes in maculopathies such as AMD and polypoidal choroidal vasculopathies (PCV). While these imaging techniques may not be readily available in most optometric practices, patients who may benefit from the additional visualization could be comanaged with a retina specialist with access to EDI-OCT. In time, software upgrades to existing SD-OCT technology could make routine use of this modality possible.

Recently, the FDA approved optical coherence tomography angiography (OCTA), a noninvasive test that allows for the assessment of retinal and choroidal vasculature. Although fluorescein angiography (FA) and indocyanine green angiography (ICGA) remain commonly used for directing treatment of choroidal neovascularization (CNV) and retinal neovascularization, both are invasive tests with drawbacks, such as the potential for anaphylactic response.[4-5] OCTA uses motion contrast—a 3D scanning technique—instead of intravenous dye to provide high-resolution images in seconds, which is an advantage over FA and ICGA, which take longer.[6]

Using OCTA, you can pinpoint the precise size and localization of lesions, visualize both the retinal and choroidal vasculature pattern and show structural and blood flow information. However, its disadvantages include a limited field of view and an inability to capture leakage.[6]

OCTA may not be readily available in most optometric practices; nevertheless, as the technology becomes available it has the potential to allow ODs enhanced evaluation of vascular changes like CNV in AMD and diabetic retinopathy.

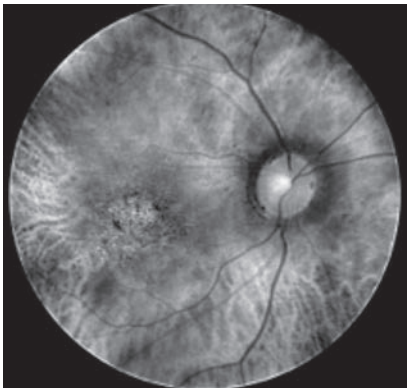
• ***FAF imaging*** detects lipofuscin, a metabolic biomarker of the photoreceptor/retinal pigment epithelium (RPE) complex that indicates AMD, hereditary retinal disorders, toxic maculopathy and other macular diseases.[7] FAF reveals RPE defects with reduced fluorescence and can show areas of photoreceptor damage—which appear as increased fluorescence from an accumulation of lipofuscin.[8-9]

• ***Automated 10-2 visual field testing*** is a valuable tool for functional assessment of macular damage. As the macula comprises ±8 degrees of the retina, using other tests, such as the 24-2 visual field, misses damage to this area. In some cases, AMD patients may retain good visual acuity, but experience distortion and other qualitative visual changes. Visual field assessment can detect the size and depth of the defects, leading to early detection and intervention of AMD. Likewise, a new Plaquenil (hydroxychloroquine-HCQ, Sanofi Aventis) screening guideline mandates a 10-2 white-stimulus visual field be performed on all patients taking this medication.

Additional Testing Options

Not all tests of macular function are readily available in the average OD's office. Accessing many of these tests require connections with local retina specialists, eye hospitals or co-management with fellow ODs who have access to these technologies. Here are some of the less common, but still beneficial, technologies:

• ***Macular pigment optical density (MPOD)*** testing measures macular pigments lutein and zeaxanthin, which help protect the photoreceptors from oxidative stress caused by ultraviolet and blue light damage.[10] Low MPOD has been associated with potential progression of AMD.[11]



This multispectral image reveals neovascular AMD with pigment epithelial detachments.

MPOD is a simple noninvasive test that uses heterochromatic flicker photometry technology to measure and gauge the effects of dietary change and supplementation of macular pigment; scores range from 0 to 1. Patients with low (0 to 0.21) or moderate (0.21 to 0.44) MPOD scores benefit from dietary changes and vitamin supplementation that increase their intake of the carotenoids lutein and zeaxanthin.[12]

The Age-Related Eye Disease Study (AREDS) showed a 25% beneficial effect of nutritional supplementation reducing the risk of progression to advanced AMD—at five years—in patients with intermediate AMD or with advanced AMD in one eye.[13] Furthermore, AREDS2 demonstrated an 18% reduction in progression to advanced AMD with a recommended dose of 10mg lutein and 2mg of zeaxanthin for patients older than 50 years and with high risk for AMD progression.[14]

MPOD should be retested in three to six months, until the MPOD score registers 0.45 or above.

• ***Multispectral imaging (MSI)*** allows visualization of the retina in spectral slices, from the internal limiting membrane (ILM) to the choroid. MSI employs discrete, light-emitting wavelengths ranging from 520nm (green) to 940nm (infrared), which penetrate the choroidal layer.[15]

MSI technology provides a means to monitor RPE for changes or disease progression. Using MSI, you can detect various macular changes and conditions that "masquerade" as AMD, such as PCV. MSI is also available with FAF capability.

• ***Multifocal electroretinography (mfERG)*** creates a map of retinal function that reflects cone-mediated responses from the photoreceptor and bipolar cells.[16] Eyes with macular disease, such as AMD and hereditary macular conditions, have reduced mfERG findings.[17] This test is recommended for patients on Plaquenil therapy, as it can detect subtle changes in the early stages of toxicity. The most specific waveform pattern observed with Plaquenil toxicity is paracentral amplitude loss, indicative of decreased retinal function in the susceptible perifovea.[18-19]

• ***Dark adaptation*** provides automated functional assessment of dark adaptation time (AdaptDx, Maculogix). This automated test exposes a patient to bright light and plots a visual recovery curve. Dark adaptation has been shown to decrease in patients with early to late AMD and other conditions such as retinitis pigmentosa or inherited macular conditions.[20]

• ***Macular microperimetry*** allows for specific testing of macular function. It maps the pattern of a patient's retinal sensitivity onto an image of that individual's fundus. The advantage of microperimetry testing over a 10-2 visual field test is that it allows for the detection of small and discrete macular lesions and to retest these areas accurately

over time.[21] For example, in AMD, microperimetry can detect early functional changes for atrophy or neovascularization as well as monitor progression of the disease.

For Baby Boomers

In addition to the aforementioned technologies, additional measures can be employed as part of your macular screening responsibilities, leading to early detection or delayed progression for some common macular conditions.

AMD is on the rise, primarily among the rapidly aging Baby Boomer generation.[22] Nearly 90% of patients have the "dry" or atrophic type of AMD, while 10% develop choroidal neovascularization (CNV), or "wet" AMD.[23] Vision loss can occur if AMD is undetected, untreated, unsuccessfully treated or inappropriately treated.[23]

Assessing AMD risks is an important component in macular function and structural evaluation. For example, large drusen and retinal pigmentary abnormalities are established risks of AMD progression and functional loss. However, a recently published study found that patients are four times more likely to develop sight-threatening AMD if they show signs of medium drusen (63µm to 124µm) plus RPE abnormalities.[24] Consequently, AMD patients with these findings require close monitoring for the early detection of a CNV, which requires prompt treatment with anti-VEGF.

Some AMD risks, such as smoking, obesity (BMI greater than 30) and cardiovascular risk (hypercholesterolemia and hypertension) can be changed.[25] Light-induced (sunlight and blue light) oxidative damage can lead to the development of AMD and should be addressed with lenses designed to selectively filter or block UV or blue-violet light.[26]

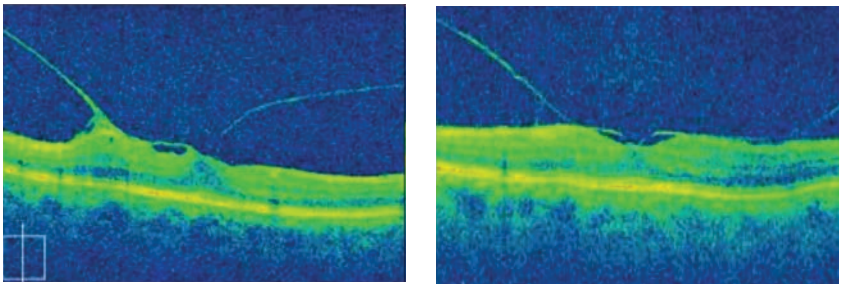
Fixed factors such as race, gender (postmenopausal women are at greater risk), family history and genetics should be identified.[27] The understanding of the role multiple genetic variants, specifically the complement factor H (CFH) and age-related maculopathy susceptibility 2 (ARMS2) alleles, play in the development and progression of AMD has evolved. For example, complement factor genes CFH and C3, ARMS2 genes and other mitochondrial genes strongly suggest that inflammation contributes to the pathogenesis of AMD, so it may be worthwhile to assess genetic types using commercially available screening tools.[28-29]

VMA, VMT and MH together form a spectrum of disorders related to persistent vitreous adhesion at the vitreoretinal interface and anomalous or incomplete posterior vitreous detachment, common with aging.[30] The adherent posterior vitreous cortex or posterior hyaloid membrane can exert tractional pull on the internal limiting membrane of the macula, resulting in the aforementioned conditions and potential visual loss.

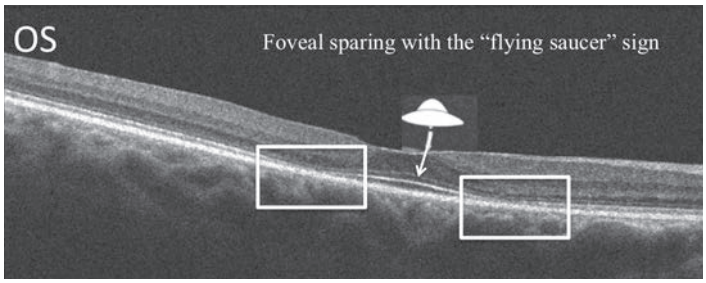
OCT imaging is essential in understanding, visualizing and managing these conditions. VMA results from vitreous attachment to the macula, which can be focal (less than 1500µm) or broad (greater than or equal to 1500 µm) with no structural changes. VMT, either focal or broad, does result in structural changes—including distortion of the foveal surface, intraretinal pseudocyst and cystoid macular edema (CME). Now, our understanding of VMT has evolved

Table 1. Differentiating VMT From VMA

IVTS Classification[33]	MH classification	Management
VMA	Stage 0	Observation
VMT with foveal detachment	Stage 1: macular cyst	Observation *3 months follow-up *Prompt RTC if new symptoms develop
A Stage 2 hole (<400µm) with 20/70 vision	FTMH with VMT	*Vitreoretinal surgery *Ocriplasmin
A Stage 3 hole (≥400µm) cuff of subretinal fluid VA 20/100 to 20/400	FTMH with VMT	Vitreoretinal surgery
Stage 4 holes ((≥400µm) complete PVD 20/100 to 20/400	FTMH without VMT	Vitreoretinal surgery



At left, VMT and, at right, VMA, are both conditions that would have been impossible to diagnosis without the advent of OCT imaging.



Macular damage from Plaquenil toxicity can be imaged using SD-OCT to look for the "flying saucer" sign.

to include an impending (stage 1) macular hole.[31-33]

These disorders may progress, remain stable or resolve spontaneously; therefore, it is imperative to re-examine patients using SD-OCT for persistent traction changes, including CME or a stage 1 MH (impeding MH), every six to 12 weeks, followed by every three months. Although some stage 1 macular holes may resolve spontaneously and completely, 50% may progress to a full-thickness macular hole (FTMH).[34, 35] It's important to assess the other eye as well, as 10% to 20% of patients develop a MH in the fellow eye, especially in the presence of VMA, within five years.[36]

For Arthritis Patients

Plaquenil or the less frequently used Aralen (chloroquine-CQ, Sanofi Aventis) are anti-malarial medications prescribed for rheumatological disease such as systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). HCQ causes RPE degeneration with sparing of the foveal center, leading to bull's eye maculopathy, due to its appearance.[37] Anterior segment changes (such as corneal verticillata) should prompt careful structural and functional evaluation of the macula.

Risk for toxicity includes a dosage greater than 400mg/day, which is the commonly prescribed two 200mg pills per day. The patient's height is also a risk, as those who are shorter than 5'7" in stature should take less than 400mg of Plaquenil per day.[38]

Because HCQ is not retained in fatty tissues, there is increased risk for obese patients (BMI greater than 30). Patients who are obese should be dosed on the basis of "ideal" body weight, which depends on the patient's height, and not body weight. If this is not done, patients are at risk of being overdosed, thus increasing their risk of maculopathy. An optometrist's vigilant watch over these patients and their dosing could help reduce their maculopathy risk.

In addition to a standard dilated examination, the American Academy of Ophthalmology screening guideline recommends a white-stimuli 10-2 visual fields—which can detect subtle paracentral visual field defects, indicative of early toxic maculopathy—using either SD-OCT, FAF or mfERG to help monitor these patients.[38]

SD-OCT may detect significant structural alterations prior to the development of visible HCQ retinopathy, such as the loss of the external limiting membrane, disruption of the outer ellipsoid zone, parafoveal thinning of the outer nuclear layer and RPE damage.[39] One notable finding is foveal sparing, sometimes referred to as the "flying saucer" sign of HCQ retinopathy.[40] This ovoid appearance is created by the intact central foveal outer retinal structures contrasting to the adjacent perifoveal loss of the photoreceptor ellipsoid band and outer nuclear layer atrophy.[40]

Since the RPE is damaged in HCQ maculopathy, FAF intensity in the pericentral macula changes to a speckled or mottled appearance, which eventually merges into dark areas of absence of FAF signal.[9]

In using the functional mfERG test for HCQ toxicity suspects, look for paracentral amplitude loss, which is indicative of decreased retinal function in the susceptible perifoveal area.[19]

There is no consensus on which testing device is the best for detecting early HCQ toxicity. The take-away message is to not rely on any single procedure. The combined knowledge we can gather from not only structural but functional changes—via a combination of FAF, mfERG or SD-OCT—for concomitant abnormalities is imperative for comprehensive patient evaluation. Low-risk patients may be followed at five years, while those that are high risk should be evaluated annually.[38]

If probable or definite toxicity is detected, HCQ should be stopped immediately in consultation with the patient's rheumatologist. Even then, those patients will continue to require close monitoring since progression of toxicity can endure for up to three years after discontinuing the medication.[41,42]

For Diabetes Patients

As diabetes has increased in prevalence over the last few decades, we have seen a corresponding dramatic rise in macular conditions such as diabetic macular edema (DME). Diabetic maculopathy is one of the main causes of poor visual functioning in patients with diabetes.[43] The ETDRS deemed clinically significant DME—based on stereoscopic slit-lamp biomicroscopy and stereo color fundus photography—to include the following:[44]

1. Retinal thickening within 500µm of the macular center.

2. Hard exudates with thickening within 500µm of the macular center.

3. One or more disc diameters of retinal thickening, part of which is within one disc diameter of the macular center.

However, the EDTRS classification methods are subjective and may be unable to identify or localize small changes in retinal thickness, which can be observed on SD-OCT.[45] OCT retinal thickness measurement is essential in monitoring progression and assessing treatment outcomes after laser photocoagulation, anti-VEGF and steroids or vitrectomy.[46]

Two major risk factors—disease duration and poor glycemic control—contribute considerably to the onset, severity and progression of complications. Other modifiable risk factors, including hypertension, dyslipidemia and obesity, should be assessed as well.[47] Consequently, knowing the "ABCs" of diabetes—glycosylated hemoglobin (HbA1c), blood pressure (≤140/90) and cholesterol is key to DME assessment.

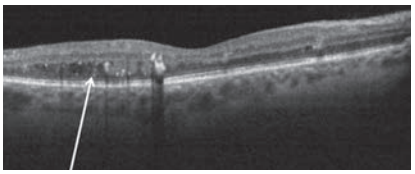
Some medications—for example Avandia (rosiglitazone, Glaxo SmithKline) and Actos (pioglitazone, Takeda Pharmaceuticals)—reportedly increase the risk of DME.[48] So, you may have to be more vigilant in evaluating for DME among those patients taking these medications.

When patients experience visual symptoms—even if they're aware of a systemic disease—they may assume such changes stem simply from a refractive error. It is imperative to consider the possibility of macular disease. With the expanding base of both functional testing and structural imaging tools, optometrists are better equipped than ever to make the diagnosis and begin treatment of these potentially sight-threatening conditions. ■

Dr. Reynolds is an associate professor of optometry and Nova Southeastern University College of Optometry. She is currently the instructor for the clinical medicine course and lectures on a variety of topics in ocular disease, She is a member of the Optometric Retina Society.

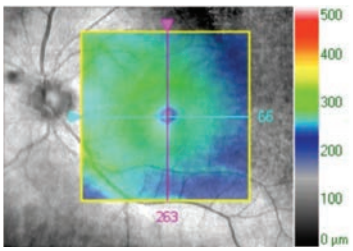
Table 2. HCQ Risk Factors

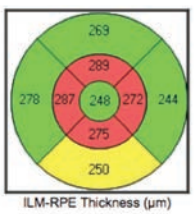
Duration of Use	>5 years
Cumulative Dose	>1000g HCQ (7 years)
Daily Dose	> 400mg (6.5mg/kg/day) HCQ
BMI (>30) Height (short)	HCQ is not retained in fat (adipose) tissue
Age	> 60 years of age
Systemic Disease	Kidney or liver disease
Ocular Disease	Retinal or macular disease



OCT image shows sponge-like swelling of the retina accompanied by intraretinal cystoid diabetic macular edema.

1. Friedman D, O'Colmain B, Muñoz B, et al. Prevalence of age-related macular degeneration in the United States: Arch of Ophthal. 2004;122(4):564–72.
2. National Eye Institute. Eye Disease Factsheet. Available at: https://nei.nih.gov/sites/default/files/neipdfs/NEI_Eye_Disease_Statistics_Factsheet_2014_V10.pdf. Accessed January, 2016
3. Rosen RB, Hathaway M, Rogers J, et al. Multidimensional en-face OCT imaging of the retina. Opt Express. 2009;17:4112-4133.
4. Do D, Gower E, Cassard S, et al. Detection of new-onset choroidal neovascularization using optical coherence tomography: the AMD DOC study. Ophthalmology. 2012;119:771–8.
5. Kotsolis A, Killian F, Ladas I, Yannuzzi L. Fluorescein angiography and optical coherence tomography concordance for choroidal neovascularization in multifocal choroiditis. Br J Ophthalmol. 2010;94:1506–8.
6. de Carlo T, Romano A, Waheed N, Duker J. A review of optical coherence tomography angiography (OCTA). International Journal of Retina and Vitreous. 2015;(1)5:1-15.
7. Schmitz-Valckenberg S, Holz F, Bird A, Spaide R. Fundus autofluorescence imaging: review and perspectives. Retina. 2008;28:385-409.
8. Von Rückmann A, Fitzke F, Bird A. Distribution of fundus autofluorescence with a scanning laser ophthalmoscope. Br J Ophthalmol. 1995 May;79(5):407-12.
9. Kellner U, Renner A, Tillack H. Fundus autofluorescence and mfERG for early detection of retinal alterations in patients using chloroquine/hydroxychloroquine. Invest Ophthalmol Vis Sci. 2006;47(8):3531-8.
10. Bian Q, Gao S, Zhou J, et al. Lutein and zeaxanthin supplementation reduces photo-oxidative damage and modulates the expression of inflammation-related genes in retinal pigment epithelial cells. Free Radical Biology & Medicine. 2012;53:1298–307.
11. Bernstein P, Delori F, Richer S, et al. The value of measurement of macular carotenoid pigment optical densities and distribution in age-related macular degeneration and other retinal disorders. Vision Research. 2010;50(7):716-28.
12. Ma L, Yan S, Huang Y, et al. Effect of lutein and zeaxanthin on macular pigment and visual function in patients with early age-related macular degeneration. Ophthalmology. 2012;19(11):2290–7.
13. The Age-Related Eye Disease Study Research Group. A randomized, placebo-controlled, clinical trial of high-dose supplementation with vitamins C and E, beta carotene, and zinc for age-related macular degeneration and vision loss. Arch Ophthalmol. 2001;119:1417–36.
14. The Age-Related Eye Disease Study 2 (AREDS2) Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. JAMA Ophthamol. 2013;09:2005-15.
15. Everdell N, Styles I, Calcagni A, et al. Multispectral imaging of the ocular fundus using light emitting diode illumination. ReSciInstrum. 2010;81(9):093706.
16. Hood D, Frishman L, Saszik S, Viswanathan S. Retinal origins of the primate multifocal ERG: implications for the human response. Invest Ophthalmol Vis Sci. 2002;43:1673–85.
17. Jurklies B, Weismann M, Husing J. Monitoring retinal function in neovascular maculopathy using multifocal electroretinography: early and long-term correlation with clinical findings. Graefes Arch Clin Exp Ophthalmol. 2002;240:244–64.
18. Lyons J, Severns M. Detection of early hydroxychloroquine retinal toxicity enhanced by ring ratio analysis of multifocal electroretinography. Am J Ophthalmol. 2007;143:801-9.
19. Maturi R, Yu M, Weleber R. Multifocal electroretinographic evaluation of long-term hydroxychloroquine users. Arch Ophthalmol. 2004;122:973-81.
20. Jackson G, Scott I, Kim I, et al. Diagnostic sensitivity and specificity of dark adaptometry for detection of age-related macular degeneration. Invest Ophthalmol Vis Sci. 2014 Mar 10;55(3):1427-31.
21. Fujii G, De Juan E, Humayun M, et al. Characteristics of visual loss by scanning laser ophthalmoscope microperimetry in eyes with subfoveal choroidal neovascularisation secondary to age related macular degeneration. Am J Ophthamol. 2003;136:1067-78.
22. Colby S, Ortman J. Projections of the size and composition of the US Population: 2014 to 2060 (US Census Bureau, March 2015). P.5.
23. AMD Alliance International. Basic facts about AMD. Available at: http://www.amdalliance.org/information_overview_basic_facts.html. Accessed March 2016
24. Joachim N, Mitchell P, Kifley A, Wang J. Incidence, progression, and associated risk factors of medium drusen in age-related macular degeneration: Findings from the 15-year follow-up of an australian cohort. JAMA Ophthalmol. 2015 Jun;133(6):698-705.
25. Seddon J, Reynolds R, Yu Y, et al. Risk models for progression to advanced age-related macular degeneration using demographic, environ-





OCT reveals bilateral perifoveal thinning with preservation of the central macula representing bull's eye maculopathy.

mental, genetic, and ocular factors. Ophthalmology. 2011;118:2203–11.
26. Sui G, Liu G, Liu G. Is sunlight exposure a risk factor for age-related macular degeneration? A systematic review and meta-analysis. Br J Ophthalmol. 2013;97:389–394.
27. Haan M, Klein R, Klein B, et al. Hormone therapy and age-related macular degeneration: the Women's Health Initiative Sight Exam Study. Arch Ophthalmol. 2006;124(7):988- 92.
28. Klein R, Zeiss C, Chew E. Complement factor H polymorphism in age-related macular degeneration. Science. 2005;308:385–9.
29. Jakobsdottir J, Conley Y, Weeks D, et al. Susceptibility genes for age-related maculopathy on chromosome 10q26. Am J Hum Genet. 2005;77:389–40.
30. Sebag J. Anomalous posterior vitreous detachment: a unifying concept in vitreo-retinal disease. Graefes Arch Clin Exp Ophthalmol. 2004 Aug;242(8):690-8.
31. Steel D, Lotery A. Idiopathic vitreomacular traction and macular hole: a comprehensive review of pathophysiology, diagnosis, and treatment. Eye. 2013;27:1–21.
32. Gass J. Reappraisal of biomicroscopic classification of stages of development of a macular hole. Am J Ophthalmol. 1995;119:752-9.
33. Duker J, Kaiser P, Binder S. The international vitreomacular traction study group classification of vitreomacular adhesion, traction, and macular hole. Ophthalmology. 2013 Dec;120(12):2611-9.
34. de Bustros S, Vitrectomy for Prevention of Macular Hole Study Group. Vitrectomy for prevention of macular holes. Results of a randomized multicenter clinical trial. Ophthalmology. 1994;101:1055-9.
35. Hikichi T, Yoshida A, Akiba J, Trempe C. Natural outcomes of stage 1, 2, 3, and 4 idiopathic macular holes. Br J Ophthalmol. 1995;79:517-20.
36. Niwa H, Terasaki H, Ito Y, Miyake Y. Macular hole development in fellow eyes of patients with unilateral macular hole. Am J Ophthalmol. 2005;140:370-5.
37. Michaelides M, Stover N, Francis P, Weleber R. Retinal toxicity associated with hydroxychloroquine and chloroquine. Arch Ophthalmic. 2011 Jan;129(1):30-9.
38. Marmor M, Carr R, Easterbrook M, et al. American Academy of Ophthalmology recommendations on screening for chloroquine and hydroxychloroquine retinopathy: a report by the American Academy of Ophthalmology. Ophthalmology. 2002 Jul;109(7):1377-82.
39. Kellner S, Weinitz S, Kellner U. Spectral domain optical coherence tomography detects early stages of chloroquine retinopathy similar to multifocal electroretinography, fundus autofluorescence and near-infrared autofluorescence. Br J Ophthalmol. 2009;93(11):1444-7.
40. Chen E, Brown D, Benz M, et al. Spectral domain optical coherence tomography as an effective screening test for hydroxychloroquine retinopathy (the "flying saucer" sign). Clin Ophthalmol. 2010;4:1151-8.
41. Mititelu M, Wong B, Brenner M, et al. Progression of hydroxychloroquine toxic effects after drug therapy cessation: New evidence from multimodal imaging. JAMA Ophthalmol. 2013;131:1187-97.
42. Marmor M, Hu J. Effect of disease stage on progression of hydroxychloroquine retinopathy. JAMA Ophthalmol. 2014;132(9):1105-12.
43. Garweg J, Wenzel A. Diabetic maculopathy and retinopathy. Functional and sociomedical significance. Ophthalmologe. 2010;107:628–35.
44. Early Treatment Diabetic Retinopathy Study Research Group. Grading diabetic retinopathy from stereoscopic color fundus photographs: An extension of the modified Airlie House classification. ETDRS Report Number 10. Ophthalmology. 1991;98:786-806.
45. Hee M, Puliafito C, Wong C, et al. Quantitative assessment of macular edema with optical coherence tomography. Archives of Ophthalmology. 1995;113(8):1019–29.
46. Helmy Y, Allah H. Optical coherence tomography classification of diabetic cystoid macular edema. Clin Ophthalmol. 2013;7:1731–7.
47. Cheung N, Mitchell P, Wong T. Diabetic retinopathy. Lancet. 2010;376:124–36.
48. Idris I, Warren G, Donnelly R. Association between thiazolidinedione treatment and risk of macular edema among patients with type 2 diabetes. Arch Intern Med. 2012 Jun;11:1-7.

OSC QUIZ

You can obtain transcript-quality continuing education credit through the Optometric Study Center. Complete the test form *(page 107)*, and return it with the $35 fee to: Optometric CE, P.O. Box 488, Canal Street Station, New York, NY 10013. To be eligible, please return the card within one year of publication. You can also access the test form and submit your answers and payment via credit card at *Review of Optometry* online, www.reviewofoptometry.com.

You must achieve a score of 70 or higher to receive credit. Allow eight to 10 weeks for processing. For each Optometric Study Center course you pass, you earn 2 hours of transcript-quality credit from Pennsylvania College of Optometry and double credit toward the AOA Optometric Recognition Award—Category 1. Please check with your state licensing board to see if this approval counts toward your CE requirement for relicensure.

1. Which of the following procedures can detect a full-thickness macular hole?
a. Amsler grid.
b. Macular pigment optical density.
c. Central 10-2 visual field.
d. Slit beam test.

2. Which of the following is preferred for the detection of an occult CNV?
a. Fundus photography.
b. Multispectral imaging.
c. Indocyanine green angiography.
d. Fundus autofluorescence.

3. The recently approved optical coherence tomography angiography has all the following features, except:
a. It is an invasive procedure.
b. Uses motion contrast, not intravenous dye.
c. Provides angiographic imaging of blood flow.
d. Has a limited field of view.

4. Fundus autofluorescence imaging detects _____, a metabolic biomarker of the photoreceptor/RPE complex.
a. Drusen.
b. Macular pigment.
c. Lipofuscin.
d. Exudates.

5. What percentage of patients with AMD will likely progress to the advanced, sight-threatening neovascular form?
a. 5%.
b. 10%.
c. 50%.
d. 25%.

6. Which of the following is not a modifiable risk factor for AMD?
a. Smoking.
b. BMI greater than or equal to 30.
c. Age.
d. Hypertension.

7. Which of the following treatment options is preferred contemporarily for AMD patients?
a. Anti-VEGF.
b. Photodynamic therapy.
c. Laser photocoagulation.
d. Intravitreal kenalog.

8. The AREDS2 study demonstrated a ___% reduction in progression to advanced AMD with 10mg lutein and 2mg of zeaxanthin.
a. 25%.
b. 5%.
c. 18%.
d. 30%.

9. All of the following are associated with vitreomacular traction, except:
a. Distortion of the foveal surface.
b. CNV.
c. Intraretinal pseudocyst.
d. Cystoid macular edema.

10. A stage 1 (impending) macular hole is classified by the International Vitreomacular Traction Study Group as:
a. Vitreomacular adhesion.
b. Vitreomacular traction with foveal detachment.
c. Full-thickness macular hole with vitreomacular traction.
d. Pseudohole.

11. Which of the following is a treatment option for stage 2 macular holes?
a. Anti-VEGF.
b. Photodynamic therapy.
c. Ocriplasmin.
d. Intravitreal kenalog.

12. A stage 4 macular hole is characterized by:
a. Vitreomacular adhesion.
b. Complete posterior vitreous detachment.
c. Less than 400µm diameter.
d. Macular cyst.

13. What percentage of stage 1 macular holes may progress to a full-thickness macular hole?
a. 50%.
b. 20%.
c. 5%.
d. 80%.

14. The presence of a _____ increases the risk of developing a full-thickness macular hole in the fellow eye.
a. Complete posterior vitreous detachment.
b. Vitreomacular adhesion.
c. Epiretinal membrane.
d. choroidal neovascularization.

OSC QUIZ

15. Obese patients are at an increased risk for hydroxychloroquine toxicity because:
a. The medication is not retained in fatty tissues.
b. Dosing is based on their actual weight.
c. Medication is retained in adipose tissue.
d. None of the above.

16. The ovoid appearance created by intact central foveal outer retinal structures contrasting to the adjacent perifoveal loss of the photoreceptor observed on OCT of a hydroxychloroquine patient is called a(n) _____:
a. Intraretinal cyst.
b. Flying saucer sign.
c. Internal limiting membrane draping.
d. Speckled or mottled appearance.

17. A 53-year-old black female presents with systemic lupus erythematosus. She reports taking Plaquenil (hydroxychloroquine) 200mg BID for three years. Which statement regarding screening is correct?
a. A central 10-2 visual field with a red stimulus should be performed.
b. Color vision should be performed.
c. Concomitant retinal disease is not a risk.
d. Perifoveal thinning is observed on OCT.

18. Which of the following is the best management for patients with bull's eye maculopathy?
a. Consult with prescribing physician.
b. Laser photocoagulation.
c. Intravitreal kenalog.
d. Anti-VEGF.

19. Progression of Plaquenil toxicity can endure for up to _____ after discontinuing the medication.
a. 5 years.
b. 3 years.
c. 15 years.
d. Stops once medication is discontinued.

20. Which of the following diabetic medication can increase the risk of diabetic macular edema?
a. Insulin.
b. Metformin.
c. Actos.
d. None of the above.

TAKE THE TEST ONLINE TODAY!
www.reviewofoptometry.com/continuing_education

Examination Answer Sheet

Valid for credit through April 1, 2019

This exam can be taken online at www.revoptom.com/continuing_education. Upon passing the exam, you can view your results immediately and download a real-time CE certificate. You can also view your test history at any time from the website.

Are You Clear on Your Macular Function Screening Responsibilities?

Directions: Select one answer for each question in the exam and completely darken the appropriate circle. A minimum score of 70% is required to earn credit.

Mail to: Jobson - Optometric CE, PO Box 488, Canal Street Station, New York, NY 10013

Payment: Remit $35 with this exam. Make check payable to Jobson Medical Information LLC.

COPE approval for 2 hours of CE credit is pending for this course.

This course is joint-sponsored by the Pennsylvania College of Optometry

There is an eight-to-ten week processing time for this exam.

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

1 = Excellent 2 = Very Good 3 = Good 4 = Fair 5 = Poor

Rate the effectiveness of how well the activity:

21. Met the goal statement: ① ② ③ ④ ⑤
22. Related to your practice needs: ① ② ③ ④ ⑤
23. Will help you improve patient care: ① ② ③ ④ ⑤
24. Avoided commercial bias/influence: ① ② ③ ④ ⑤
25. How would you rate the overall quality of the material presented? ① ② ③ ④ ⑤
26. Your knowledge of the subject was increased:
◯ Greatly ◯ Somewhat ◯ Little
27. The difficulty of the course was:
◯ Complex ◯ Appropriate ◯ Basic

How long did it take to complete this course? _____

Comments on this course:

Suggested topics for future CE articles:

Please retain a copy for your records. Please print clearly.

First Name
Last Name
E-Mail

The following is your: ☐ Home Address ☐ Business Address

Business Name
Address
City State
ZIP
Telephone # - -
Fax # - -

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

Signature _____ Date _____

Lesson 112519 RO-OSC-0416

San Antonio

Up to 19 CE Credits
(COPE approval pending)

REVIEW OF OPTOMETRY®
EDUCATIONAL MEETINGS OF CLINICAL EXCELLENCE

New Technologies and Treatments N T & T IN VISION CARE 2016

May 20-22, 2016

Superior Education with 3 Interactive Workshops

San Antonio Marriott Riverwalk

In the Heart of Downtown San Antonio

889 East Market Street | San Antonio, Texas 78205 | 210-224-4555

Discounted room rate $189/NIGHT

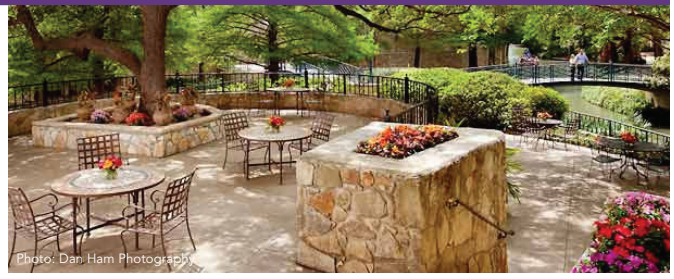
Program Chair: **Paul Karpecki, OD**

REGISTER NOW!

www.ReviewofOptometry.com/SanAntonio2016

Or Email **Lois DiDomenico**: **ReviewMeetings@Jobson.com** | Call: **866-658-1772**

REGISTRATION: **3 DAYS - 19 CE CREDITS* - $495**



Please see registration website for a list of sponsors and meeting agenda.

Administered by
Review of Optometry®

cope®
*Approval pending

May 20-22, 2016

For hotel reservations call 800-648-4462
Discounted room rates limited.
Identify yourself as a participant of
"*Review of Optometry*" for group rate.

Registration Information

NAME | NPI # (NPI numbers will only be used for Sunshine reporting purposes) | OE TRACKER #

PRACTICE AFFILIATION

MAILING ADDRESS | CITY | STATE | ZIP CODE

TELEPHONE | FAX | E-MAIL

Name Badge Information (please print clearly)

MY NAME | MY GUEST | ADDITIONAL GUESTS

Payment Information

	RATE PER PERSON	NO. IN PARTY	SUBTOTAL
OD Registration - $495 (includes up to 19 hours of CE, breakfasts, reception) Call or visit registration website for daily and student rates.	$495	x _____	= $_____
Additional Guest(s) - $45 (12 years and older, includes reception)	$45	x _____	= $_____
Concurrent Optional Workshop Sessions (Saturday, May 21st - Earn 2 additional CE credits) Select **only one** if interested in additional session and credits.			Complimentary

- ❑ Retina Workshop (2:00pm-3:40pm)
- ❑ Glaucoma Workshop (2:00pm-3:40pm)
- ❑ Ocular Surface Disease Workshop (4:00pm - 5:40pm)

❑ Check enclosed (make checks payable to *Review of Optometry*)

Charge my: ❑ American Express ❑ Mastercard ❑ Visa

CREDIT CARD NUMBER | EXP DATE

CARDHOLDER (PRINT NAME)

SIGNATURE

CONFERENCE CANCELLATION POLICY
Full refund on registration fee until April 2, 2016
50% Refund of registration fee until April 21, 2016
No refund past April 21, 2016

For more information or to register,
contact Lois DiDomenico at 866-658-1772
or at ReviewMeetings@Jobson.com.

MAIL FORM:
Review Group Meetings c/o Jobson
11 Campus Blvd, Ste. 100
Newtown Square, PA 19073

FAX FORM:
Review Meetings Group
610-492-1039

Administered by
Review of Optometry®

cope®
Approval pending

What's That Gut to Do With It?

When treating a patient with ocular rosacea, consider this unusual connection.

Edited by Joseph P. Shovlin, OD

Q Several patients presented to my clinic with severe rosacea and marked corneal opacity. I know of reports of gastrointestinal-associated bacterial overgrowth. Is there sufficient evidence that eradicating this overgrowth helps with the corneal response?

A "The question of treating gastrointestinal-associated bacterial overgrowth to improve ocular rosacea is an interesting one," says Andrea Murphy, OD, and Richard Frick, OD, of the White River Junction VAMC in Vermont, who manage patients with severe ocular rosacea leading to corneal ulcer formation. "In short, small intestinal bacterial overgrowth (SIBO) is defined as an unexpected microbial concentration (>10^5 colony-forming units/mL) in the jejunal aspirate culture, and is caused by numerous predisposing disorders, including the reduction of gastric acid secretion, intestinal motor and anatomic abnormalities, and immune function impairment."[1] Though the amount of literature connecting rosacea and SIBO is limited, research suggests that patients with rosacea are 13 times more likely to have SIBO compared with healthy controls, they add.[2]

Other gastrointestinal diseases associated with rosacea formation include *Helicobacter pylori* gastritis, ulcerative colitis, Crohn's disease, inflammatory bowel disease and hypochlorhydria, says Sara Weidmayer, OD, of the VA Ann Arbor Healthcare System. "The proposed mechanism of these GI diseases ultimately leading to rosacea is increased intestinal permeability, which transmits pro-inflammatory cytokines and bacterial products into the blood, leading to inflammation elsewhere in the body. Rosacea—a chronic inflammatory condition—is a manifestation of that inflammation," she says. Regarding the ocular subtype of rosacea, she notes that a study does exist that links it with *H. pylori*, but adds that the study was small with no controls.

Photo: Sara Weidmayer, OD

Typical eyelid findings with ocular rosacea.

"There is a rapidly growing interest in examining the relationship of the human microbiome, particularly the portion that resides in the gut, and immune system development and activity," says Jonathan Greene, MD, a corneal, cataract and refractive surgery specialist at the University of Michigan's Kellogg Eye Center. "It is not a stretch to consider that rosacea, a disease characterized by inflammation, may be similarly affected by microbes residing in the gut."

Regardless, consider coordinating with the patient's primary care doctor if traditional topical or oral therapies for ocular rosacea fail, Drs. Murphy and Frick suggest. Diagnosis methods for SIBO other than the jejunal aspirate culture include lactulose and glucose H2/CH4 breath tests.[1] Additionally, use of rifaximin may be beneficial.[1-3] They also note that patients with a *Demodex* infestation and SIBO exhibited more severe rosacea, so a slit lamp evaluation to look for these mites may be warranted.[2] Many of these patients are on long-term doxycycline or minocycline, and reports suggest chronic use of these drugs instigating a breach in immunologic tolerance to certain autoimmune syndromes.[4] ■

1. Parodi A, Paolino S, Greco A, et al. Small intestinal bacterial overgrowth in rosacea: clinical effectiveness of its eradication. Clin Gastroenterol Hepatol. 2008 Jul:6(7):759-64.
2. Agnoletti AF, DE Col E, Parodi A, et al. Etiopathogenesis of rosacea: a prospective study with a three-year follow-up. G Ital Dermatol Venereol. 2006 Feb 18. [Epub ahead of print.]
3. Micromedix Solutions [online database]. Available at: www.micromedexsolutions.com/home/dispatch.
4. Lawson TM, Bulgen NA, Williams BD. Minocycline-induced lupus: clinical features and response to rechallenge. Rheumatology. 2001;40(3):329-35.

New: Corneal Hysteresis (CH) **CPT® Code 92145**

TAKE THE UNCERTAINTY OUT OF PREDICTING GLAUCOMA RISK WITH

CORNEAL HYSTERESIS.

You shouldn't have to be a fortune teller to predict glaucoma progression.

Only **Ocular Response Analyzer®** measures **Corneal Hysteresis**, a superior predictor of glaucoma progression, providing you with a more confident glaucoma risk assessment.

Introducing the all-new **Ocular Response Analyzer® G3**.
Learn more at **www.reichert.com/ora**

Register to **WIN** Ocular Response Analyzer® G3 at **Vision Expo East 2016 - Booth MS 6810!**

Reichert® TECHNOLOGIES

Advancing Eye Care. American Innovation.

AMETEK®

Ocular Response Analyzer® G3 is made in USA · CPT is registered trademark of the American Medical Association.

Doctor, I Can See These Halos

Try to discern what's causing this patient's flashes, floaters and other visual pests.

By Mark T. Dunbar, OD, and Nabila Gomez, OD

A 61-year-old female was referred for neurological evaluation because she reported seeing constant textured spots surrounded by a white halo in her vision. She had floaters in the past, but felt this was different. She also noted flashes of light for the past two years that were more prominent in the superior nasal field of both eyes. She denied a history of headaches, seizures or trauma.

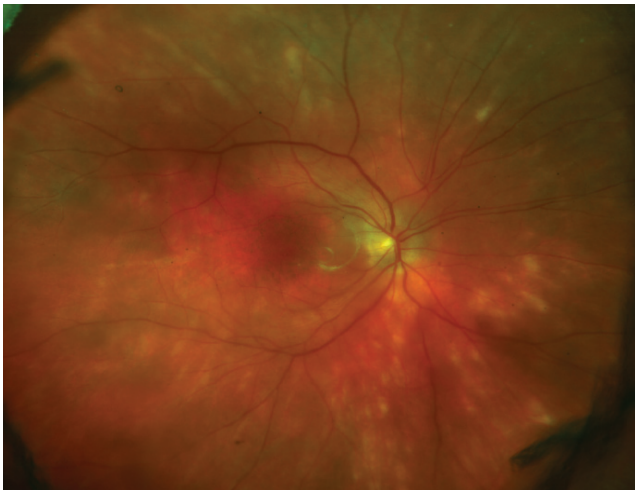
Her past ocular history was significant for macular edema following cataract surgery in both eyes and a retinal tear in the left eye treated with laser retinopexy.

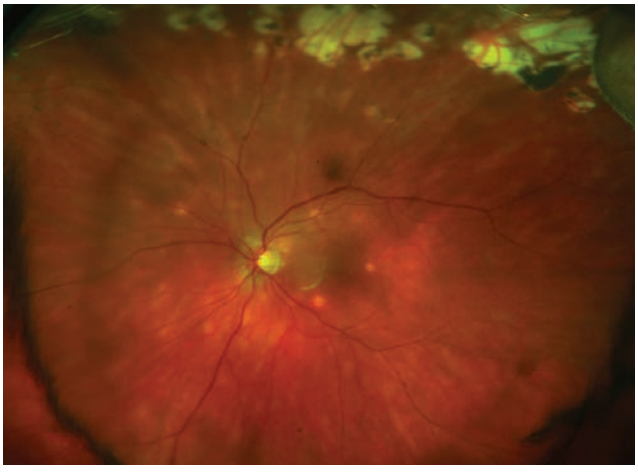
Upon examination, her best corrected vision was 20/40 OD and 20/60 OS. She had full fields to confrontation with finger counting and full motilities. Her pupils were equally round and reactive to light with no afferent pupillary defect. Intraocular pressure (IOP) was 19mm Hg OD and 20mm Hg OS.

A slit lamp examination of the right eye was remarkable for a few fine keratic precipitates inferiorly and trace cell in the anterior chamber. The left eye also had trace cell in the anterior chamber.

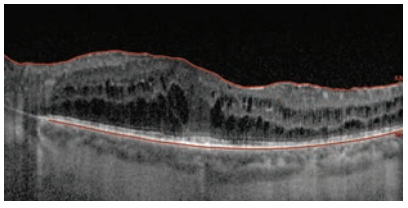
On dilated fundus exam, both eyes were positive for +1 cell in the vitreous, grade 1 optic nerve edema, retinal pigment epithelium (RPE) changes in the macula and extensive streaks and punctate depigmentation in the periphery (*Figures 1 and 2*).

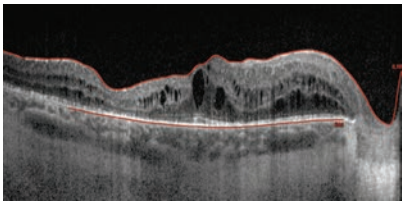
OCT images of both eyes were also taken (*Figures 3 and 4*). Finally, fluorescein angiography (FA) was ordered at the visit (*Figure 5*). Our patient's lab test results appeared to be normal.





Figs. 1 and 2. At left, these fundus images show a variety of signs including; optic nerve edema, changes to the RPE and extensive streaks and punctate depigmentation in the periphery. Figs. 3 and 4. Below, do the patient's OCT images help identify a diagnosis?





Take the Retina Quiz

1. What is the late-stage FA finding seen on both eyes?

a. Staining from vasculitis.

b. Leakage from vasculitis.
c. Staining from optic nerve swelling.
d. Hypofluorescence from macular edema.

2. The patient is HLA-A29 (+); what is the most likely diagnosis?
a. Multiple evanescent white dot syndrome.
b. Serpiginous choroiditis.
c. Birdshot chorioretinitis.
d. Multifocal choroiditis.

3. What does the OCT reveal?
a. Outer retinal tubules.
b. Macular schisis.
c. Cystoid macular edema.
d. Choroidal neovascularization.

4. How should this patient be treated?
a. Anti-VEGF.
b. Antivirals.
c. Laser photocoagulation.
d. Steroid and immunosuppressives.

Diagnosis

Our patient had a history of chronic treatment with topical steroids and nonsteroidal anti-inflammatory drops for the past three years for presumably cystoid macular edema that developed as a complication of her cataract surgery. However, based on demographics, history, symptoms, clinical findings, imaging, normal blood lab results and HLA-A29 positivity, our patient actually has birdshot chorioretinitis (BSCR).

BSCR is among a group of idiopathic multifocal inflammatory conditions involving the retina and the choroid that are known as the "white dot syndromes," characterized by white dots in the fundus. These include acute posterior multifocal placoid pigment epitheliopathy, serpiginous choroiditis, multiple evanescent white dot syndrome, multifocal choroiditis and panuveitis, punctate inner choroidopathy and diffuse subretinal fibrosis.

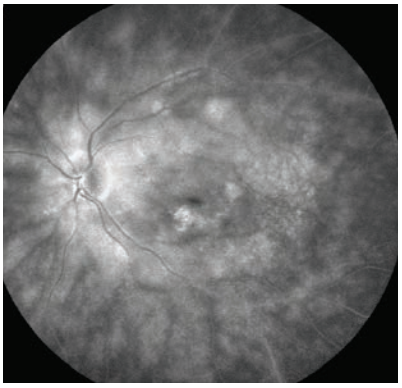


Fig. 5. What can this fluorescein angiography image, combined with our patient's medical history, tell you?

The spectrum of conditions responsible for the "white dot syndromes" is broad; however, a careful history and detailed clinical examination can help narrow the differential diagnosis.

Our patient was in her sixth decade of life when the symptoms began (two years before being referred to us) and had developed a bilateral and chronic process where inflammation is mostly limited to the posterior segment. In addition, she had negative lab results, which helped rule out infectious, autoimmune and neoplastic etiologies. She did have a positive HLA-A29, a haplotype that 85% to 95% of affected BSCR patients carry.[1]

Discussion

The hallmark of the disease is the presence of multiple hypopigmented, cream-colored, irregularly shaped choroidal lesions, often clustered around the optic disc; optic nerve edema; retinal vasculitis; and vitritis with no snow banking.[1] A mild anterior uveitis may be present with minimal to no keratic precipitates. It is usually seen in middle-aged Caucasian females 30 to 70 years old. It is bilateral, idiopathic and has an insidious onset. BSCR represents 6% to 8% of all posterior uveitis.[2]

The pathogenesis of inflammation occurs independently but simultaneously in the choroid and the retina. The pathophysiology is poorly understood. Only two histological reports have been published indicating that the hypopigmented choroidal lesions represent nodules of lymphocyte aggregation and that retinal involvement is characterized by an exudative vasculopathy involving both small capillaries and large retinal vessels.[3]

Symptoms of floaters and flashes were consistent with birdshot lesions located, primarily, in the nasal peripapillary choroid, but also beyond the vascular arcades up to the midperiphery. Early-stage birdshot chorioretinitis (when "birdshot" lesions are not yet present) can only be diagnosed or confirmed by using indocyanine green angiography (ICG), which reveals evenly distributed occult choroidal hypofluorescent dark dots.[4] Decreased visual acuity in these patients is attributed to macular edema. However, nyctalopia and color vision deficiencies may precede decreased visual acuity and the onset of classic depigmented spots in the fundus by several years.

Management and Treatment

The creamy-light colored lesions will fade over time and be replaced by diffuse pigmentary loss. FA can provide panoramic information on retinal inflammation and is useful to assess complications and treatment response of cystoid macular edema, retinal vasculitis and optic nerve edema.

ICGA is more sensitive than FA and detects choroidal inflammation in early stages of the disease.[4] OCT helps to monitor macular edema, retinal thickness and atrophy. Visual outcome is dependent on visual acuity at the onset of the treatment; early intervention and targeted treatment may improve a patient's outcome.[5]

Because of the chronic nature of this disease, patients with BSCR are usually treated with a combination of oral steroids (prednisone 40mg to 60mg) and a second-line immunosuppressive agent.[1] These include T-cell inhibitors, antimetabolites and biologics (anti-TNF). Once the disease is under control, the steroid may be stopped. However, most patients will need to maintain use of one of the second-line immunosuppressive agents indefinitely. There's no accepted optimal treatment protocol, and switching between agents can be useful. Planned therapy is at least four to five years.

Localized ocular immunosuppressive therapy in the form of a steroid implant may also control inflammation. Examples of these medications include Ozurdex (dexamethasone, Allergan) and Retisert (fluocinolone acetonide, Bausch + Lomb).[6]

Our patient was first treated with oral prednisone 40mg, then started on CellCept (mycophenolic acid, Genentech) 1g twice daily with oral prednisone taper. Given the unsuccessful resolution of her macular edema, the patient was started on tacrolimus 1mg twice daily and given Ozurdex injection in both eyes, which helped stabilize edema for only a month. The patient was then switched from tacrolimus to cyclosporine 150mg a day, but continued having persistent macular edema with further vision loss. She was then treated with Retisert in both eyes, which resolved her macular edema for the past six months. Unfortunately, she developed steroid-induced glaucoma and will likely need a glaucoma drainage device. ■

Dr. Gomez is an optometric resident at the Bascom Palmer Eye Institute in Miami.

1. Shah K, Levinson R, Yu F, et al. Birdshot chorioretinopathy. Surv Ophthalmol. 2005;50:519-41.
2. Levinson R, Brezin A, Rothova A, et al. Research criteria for the diagnosis of birdshot chorioretinopathy: results of an international consensus conference. Am J Ophthalmic. 2006;141:185-7.
3. Shao E, Menezo V, Taylor S. Birdshot chorioretinopathy. Curr Opin Ophthalmol. 2014;25:488-94.
4. Papadia M, Herbort C. Indocyanine green angiography (ICGA) is essential for the early diagnosis of birdshot chorioretinopathy. Klin Monbl Augenheilkd. 2012;229(4):348-52
5. Rothova A, Berendschott T, Probst K, et al. Birdshot chorioretinopathy: long term manifestation and visual prognosis. Ophthalmology. 2004;111:954-9.

LOMBART CS-5 CHAIR & STAND

Quality, Style & Value

Package includes:

- The ***Lombart CS-5*** Chair & Stand
- ***Topcon VT-10*** Refractor
- ***Topcon SL-2G*** Slit Lamp

- ***Lombart CVS Essential Visual Acuity System*** with RF Remote Control
- Additional upgrades & configurations available.

$13,995

Or lease for $277/mo. for 60 months*

*Lease rate subject to credit approval, 1st payment is due at signing with 59 remaining rental payments of $265 and a $1.00 purchase option. Taxes, freight and installation additional. Hand Instruments optional. Subject to change without notice.

1-800-566-2278

Call 1-800-Lombart

Or Your Local Lombart Representative

Corporate Office - 5358 Robin Hood Road, Norfolk, VA 23513-2430
757-853-8888 | FAX 757-855-1232 | 800-566-2278
www.lombartinstrument.com
lombart@lombartinstrument.com

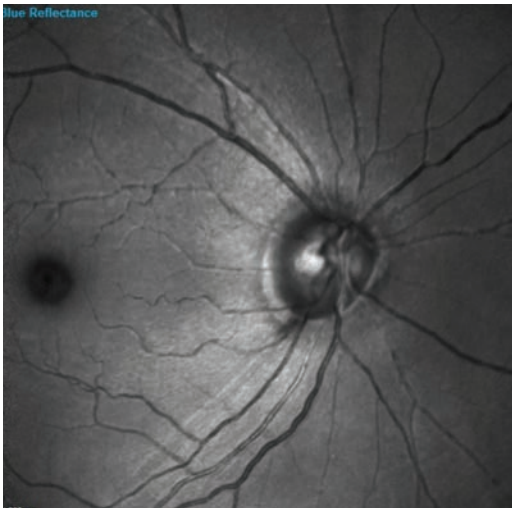
Sales and Service Centers Coast to Coast

ATLANTA • BALTIMORE/WASHINGTON D.C. • BOSTON • BOYNTON BEACH/MIAMI • BRADENTON • CHARLOTTE • CHICAGO • CINCINNATI • DALLAS • DENVER • DETROIT • GREENSBORO • HOUSTON
JACKSON • KANSAS CITY • KNOXVILLE • LOS ANGELES • MILWAUKEE • MINNEAPOLIS • NEW JERSEY/NEW YORK/PENNSYLVANIA • NORFOLK • PORTLAND • SAN ANTONIO • SAN DIEGO • SAN FRANCISCO

It Happens… Conversion, That Is

A 71-year-old long-standing glaucoma suspect converts at a particularly inopportune time. **By James L. Fanelli, OD**

After an 18-month absence, a 71-year-old female patient presented back to the office for a progress examination related to her "glaucoma suspect" status. Since last being seen, she had lost her husband to cardiovascular issues and had been spending time with her family out of the area. She has been a patient of mine for approximately 10 years and was followed regularly as a glaucoma suspect, due to family history and disc cupping asymmetry. She was always diligent in her care, and I was surprised it had been 18 months since she was last seen. Given the specifics of her case, she had been seen once every six months.



Blue laser image of the right optic disc and perioptic region. Note the disc hemorrhage between 6 o'clock and 7 o'clock as well as the RNFL wedge defect in the adjacent tissue.

History

When initially seen, and through subsequent follow up visits, her Intraocular pressure averaged approximately 18mm Hg to 19mm Hg OD and OS. Pachymetry readings were 536µm OD and 544µm OS. The optic discs were of average size, but the asymmetry in the cupping was pronounced. She had optic nerves characterized by cupping judged to be 0.6 x 0.65 OD and 0.3 x 0.4 OS, and these estimates were supported by HRT 3 imaging. Her overall systemic health was reasonably good, and she was currently medicated with Cymbalta (duloxetine, Eli Lilly) 60mg QD, Zyrtec (cetirizine, Johnson & Johnson) QD, Ditropan (oxybutynin, Janseen) 10mg HS and had recently discontinued Prozac (fluoxetine, Eli Lilly) QD. She reported allergies to sulfa-based medications.

Best-corrected visual acuities when initially seen were 20/20 OD, OS, OU through hyperopic astigmatic and presbyopic correction. Visual acuities have gradually declined over the period in which she was seen, primarily due to the development of age-consistent nuclear and cortical cataracts. Pupils were equal, round and reactive to light and accommodation with no afferent pupillary defect.

Examination

After the 18-month hiatus, a slit lamp examination of the anterior segments was entirely unremarkable. IOPs were 20mm Hg OD and 19mm Hg OS at 11:15am. Her anterior chamber angles were well formed and deep, as estimated by von Herrick angle estimation and confirmed on gonioscopy. There was normal trabecular pigmentation and no angle abnormalities visible on gonioscopy OU over the entire period she was seen. Her crystalline lenses were characterized by nuclear and cortical cataracts consistent with her best-corrected visual acuity of 20/30+ OD and 20/30- OS.

Through dilated pupils, there were bilateral PVDs noted. Stereoscopic evaluation of the optic nerves demonstrated similar neuroretinal rim appearances as described above, along with the new finding of a small disc hemorrhage in the right eye at 6:30. There appeared to be a small RNFL wedge defect in the area contiguous with the disc hemorrhage, which was not noted previously. Both maculae were characterized only by fine RPE granulation, consistent with her age.

The retinal vascular examination was characterized by mild arteriosclerotic retinopathy, with no crossing changes noted. Her peripheral retinal examination was unremarkable in both eyes.

The patient underwent HRT 3 imaging of the optic nerves, as well as OCT imaging of the perioptic RNFL and macular regions. There was demonstrable change

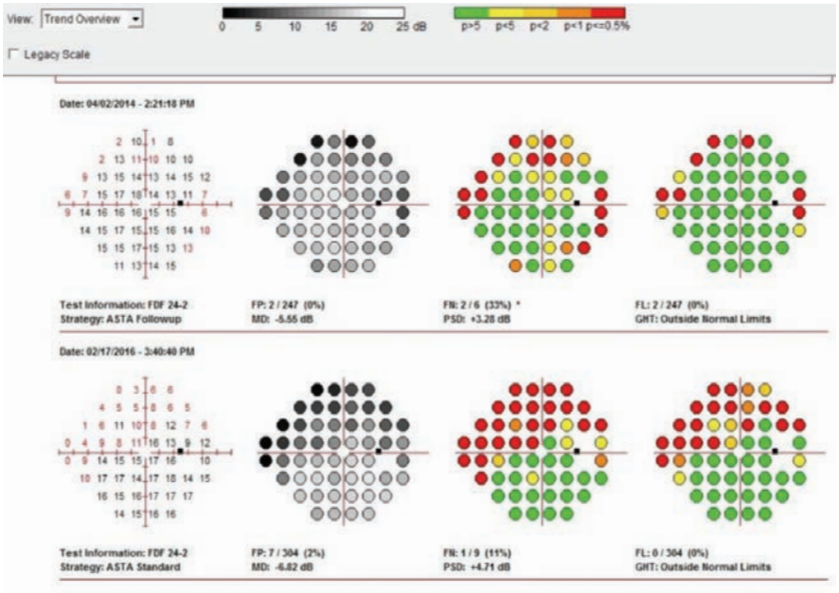
in the inferotemporal segment of the right eye in the HRT 3 scan compared with previous visits and her baselines, which were obtained 10 years earlier. There was similar RNFL loss inferotemporally to the right eye on the OCT study, compared with baseline images obtained five years earlier that was also not noted in previous scans.

Diagnosis

Given the noted changes to the structure of the right neuroretinal rim—tissue loss, disc hemorrhage and RNFL loss in the same area—it was evident that the patient had converted from a glaucoma suspect in the right eye to a patient with structural damage consistent with glaucomatous optic neuropathy. The left eye did not show any changes on the HRT3 or OCT studies and was currently deemed stable. As such, the patient was asked to return for threshold visual field testing, stereo optic nerve imaging and anterior segment angle OCT.

The patient returned for follow up as directed. At this visit, applanation tensions were 18mm Hg OD and OS at 10:00am. Threshold visual fields employing the Flicker Defined Form strategy demonstrated a pronounced arcuate defect superiorly to the right eye, which was significantly different (progressed) compared with earlier visual field studies. The field in the left eye was unremarkable, and both fields were obtained with good reliability indices. Multimodal disc and macular images were obtained using the Spectralis Multi Color Image Acquisition system, which clearly showed the RNFL wedge defect inferotemporally in the right eye.

Anterior segment OCT imaging of the anterior chamber angles demonstrated normal iris approach to the angle with no subtle plateau iris configuration.



Threshold HEP (Heidelberg Edge Perimeter) FDF field studies demonstrating the development of a superior arcuate defect in the right eye as compared with the previous study.

Discussion

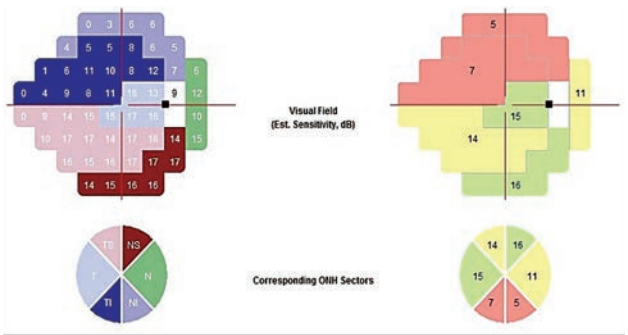
While the evidence in this case strongly suggests that the patient converted from a glaucoma suspect in the right eye to a patient with both structural and functional defects consistent with glaucoma in the right eye, it is striking that this conversion occurred during the time the patient was unable to obtain her maintenance care. There were no significant medication changes in her history and no personal health changes that could have reasonably played a role in the conversion to glaucoma—other than the possible effects from personal life stressors.

There was no previous trauma or angle abnormalities that would precipitate an abrupt conversion. It simply just happened.

Conversion Happens

When it happens can depend on several things: IOP, the patient's overall cardiovascular health, angle abnormalities, nocturnal hypotension and fragility of the neuroretinal rims, to name a few. In some individuals—for example those with narrow angles that occlude—the conversion can be abrupt and, frankly, expected. But in the majority of open angle glaucoma cases, the conversion occurs gradually and, most importantly, can happen at any time.

And therein lies the difficult position in which we find ourselves—walking that fine line in determining the frequency of follow up visits for the patient who we determine is a patient at risk for developing glaucoma. How much is too much? How little is too infrequent? Neither too much nor too little is desired. But the frequency of care and follow up is based on our clinical judgment. In



Corresponding ONH Sector	Mean Sensitivity (dB)	Mean Deviation (dB)	Classification
Temporal	15.40	-3.01	Within Normal Limits
Temporal Superior	13.93	-4.45	Borderline
Temporal Inferior	7.00 p<=0.5%	-10.82 p<=0.5%	Outside Normal Limits
Nasal	10.75	-6.32	Borderline
Nasal Superior	15.57	-2.74	Within Normal Limits
Nasal Inferior	4.63 p<=0.5%	-11.81 p<=0.5%	Outside Normal Limits

Visual field and corresponding optic nerve sector representation of the structure and function deficits found in this patient.

general, in those patients where we consider the risk of conversion to be great, we see them more frequently than those patients that we've determined have a low risk to convert. Fortunately, we have a plethora of studies that help guide us in shedding light on who is more likely to convert and what factors are involved in their conversion. And we have some tremendous technology available to help us determine subtle changes in both structure and function that shed light on conversion. But, at the end of the day, we really don't know when conversion will occur. So we see the patient every year and torture them with visual field studies, bright lights and drops.

Naturally, patients can become disaffected with the follow up visits, and some may ask why they should continue since "nothing has happened so far." It then becomes a challenge for us to relay the importance of continuing care to the patient.

But what happens when the doctor begins to doubt the necessity of the follow up care and stretches the time between visits? While on one hand that may be prudent (only if a thorough evaluation has been made of the patient's risk and it was deemed to be low), this case highlights what happens all the time in glaucoma management: there is never any convenient time for patients to convert.

Like in mutual fund investing, the caveat "past performance is no guarantee of future results" applies. Just because the patient hasn't converted in 10 years doesn't mean it won't happen. It can and does. That's why we need to be continually vigilant in our management of the patient. ■

VISION FOR TOMORROW BECOMES REALITY – **TODAY!**

For a quarter of a century Vision Source® has been committed to enriching the lives of independent optometrists by enabling them to reach their full potential. This commitment remains stronger than ever as evidenced by our latest introduction – **The Vision Source® Practice of the Future.**

The Vision Source® Practice of the Future — Created By Optometrists, For Optometrists

This state-of-the-art model will change how independent optometrists engage with their patient universe. A seamless 360° solution delivers a world-class patient experience that will be in sync with consumer expectations for years to come.

Vision Source® Signature Eye Care™ 25th Anniversary

Today, 25 years and 4,000+ members since our inception, we train our vision on forging an even brighter future for our network members that promises:

MORE **PATIENTS** MORE **PROFITS** MORE **TIME**

For more information on joining Vision Source®, go to **www.VisionSourcePlan.com**

Vision Source® Signature Eye Care™


Irresponsible Education

Be ready to answer patients' questions based upon misleading information.

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

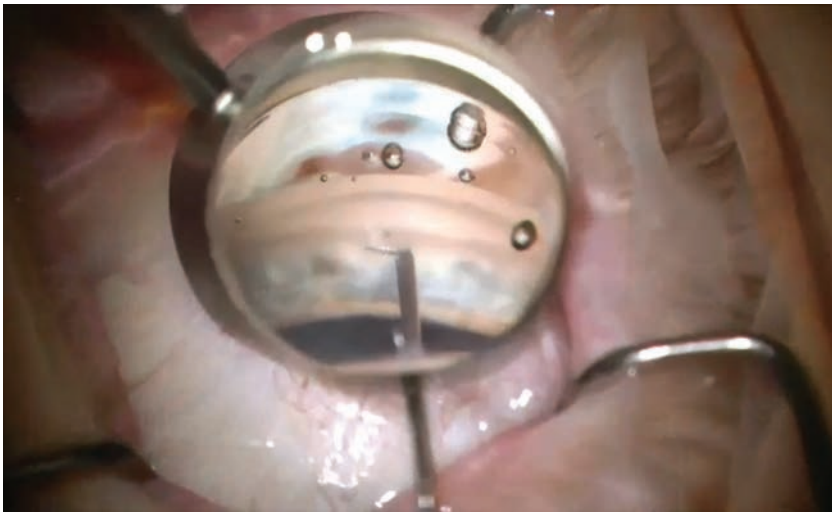
Recently, two patients presented requesting more information about some "educational" materials they received. In both instances, the literature was cringe-inducing and underscored the probably vast amounts of misinformation to which patients are exposed.

Stents

The first patient was a 56-year-old woman with primary open angle glaucoma (POAG). She was being treated medically and had to try several medications before finding one without intolerable side effects. The patient, British by birth, brought in a United Kingdom newspaper and shared an article that she wanted to discuss entitled, "The Simple Jab in the Eye that Could Cure Glaucoma." She questioned why she had to tolerate the adverse effects of chronic topical therapy when there was a simple procedure that could cure her once and for all. The article discussed the Xen Gel Stent (Allergan). The first paragraph began: "Glaucoma can now be cured with a simple injection, according to eye surgeons."

The article went on to discuss the procedure, in lay terms, and reported that, while it's still 'not perfect,' it's much faster than traditional trabeculectomy without the discomfort or complications— though it doesn't control intraocular pressure (IOP) and costs more than current procedures.

However, most readers with glaucoma aren't going to venture much further than that resonating first sentence about an easy cure. Not a treatment, mind you, but a "cure."



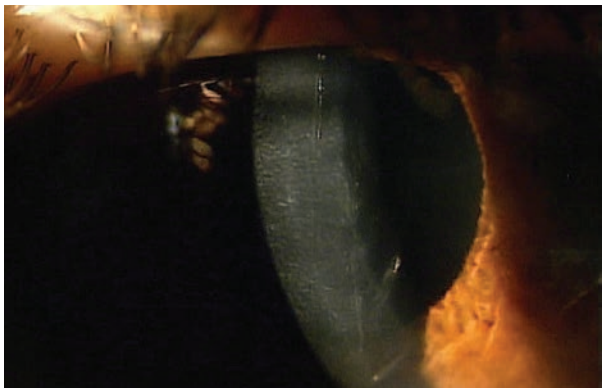
Stents and shunts, as seen here being implanted, can help glaucoma patients, but they are, by no means, a "cure," as some news sources have billed them.

In the United States, the Xen Gel Stent is currently an investigational device. It is made of a permanent, soft, collagen-derived gel. It is 6mm long and is injected through a small self-sealing corneal incision using a preloaded injector. Like all glaucoma filtration surgeries, it provides drainage from the anterior chamber, through the trabecular meshwork, into the subconjunctival space. It functions similar to conventional drainage implants, albeit with a smaller footprint. Preclinical and human testing shows the implant does not seem to occlude inside the lumen and the implant material does not appear to cause tissue reaction in the eye.[1] The placement of this stent offers a minimally invasive IOP-lowering procedure, with minimum conjunctival tissue disruption, and restricted flow to avoid hypotony.[1] As the implant is not yet available in the United States outside of clinical trials, there is little scientific information available about its effectiveness or complications.

The information in the patient's UK newspaper consisted of anecdotal quotes from surgeons beginning to use the procedure. They agreed that it was quicker to perform than trabeculectomy. One surgeon was quoted saying that it probably wasn't as effective at lowering IOP as trabeculectomy, while another stated that it was as effective without the traditional complications or discomfort.

A sole report published late last year detailed a patient with a previously uncomplicated Xen Gel Stent implant who developed a hypertrophic bleb and mechanical ectropion. The treatment consisted of draining the hypertrophic bleb following blockage with viscoelastic material of the stent and bleb sealing with a tissue adhesive.[2]

In our case, the patient was guided through the article to point out the language stating that the procedure reduced IOP, may not be as effective as conventional treatments, and was not available in the United States. She was further educated that, despite the headline, it was not a cure, but merely another IOP reducing therapy. Moreover, she was reminded that POAG cannot be cured; it can be merely controlled by lowering IOP. She seemed satisfied with the explanation.



SLT is a relatively safe procedure. However, the claim that it has "no side effects," as one patient's literature stated, is innaccurate as clinical studies show several potential—albeit rare—side effects, such as corneal edema, seen at right.

Selective Laser Trabeculoplasty

The second patient was a 52-year-old woman who recently had been diagnosed with ocular hypertension and sought a second opinion. She was concerned that the previous doctor had spent minimal time with her, didn't perform a thorough enough evaluation (according to her) to make an accurate diagnosis, and seemed aggressive about performing laser treatment on her as soon as possible.

The patient had no family history of glaucoma that she could recall. She was 20/20 in each eye. Her IOP was 23mm Hg OD and 25mm Hg OS. Her optic discs had robust rim tissue and a C/D ratio of 0.4/0.4 in each eye. There was a healthy appearing retinal nerve

fiber layer (RNFL) in each eye. Ultrasound pachymetry revealed a central corneal thickness of 580µm in the right eye and 592µm in the left. Optical coherence tomography showed a normal RNFL and ganglion cell complex in each eye, and threshold perimetry revealed visual fields that were full in each eye.

The previous diagnosis of ocular hypertension was confirmed and she felt that we had spent enough time and diagnostic testing for her satisfaction. Treatment options were discussed, including observation vs. therapeutic pressure reduction. It was mutually agreed that her risk of conversion to glaucoma was low and she would be followed without treatment.

She asked if laser treatment would be a viable option should her IOP need to be lowered and was informed that trabeculoplasty would be a suitable alternative to medications. She then proffered an educational brochure on selective laser trabeculoplasty (SLT) that had been given to her at her previous office. The brochure, entitled, "SLT: The Gentle Alternative for Glaucoma Therapy," was prepared not by the previous doctor's office, but by a medical information company. The majority of the information was accurate and easy for patients to understand. However, there was one statement that was even more cringe-worthy than the previous example. It stated, "SLT is painless and there are no side effects to worry about." A claim of no side effects is tempting to patients, but all physicians know that there is no therapy that is entirely devoid of adverse events.

SLT results in selective absorption of energy by trabecular pigmented cells, enhancing aqueous outflow. In contrast to argon laser trabeculoplasty, there is no thermal damage imparted to the trabecular meshwork. Clinical studies suggest that SLT is efficacious in lowering IOP, as the initial treatment option or when medical therapy is insufficient, with response rates after one year ranging from 59% to 96%.[3] Indeed, SLT is a current and effective treatment for lowering IOP; adverse effects are uncommon, mild and transient in nature in most cases. The most common post-procedure adverse effects are inflammation and subsequent IOP rise, both of which are typically self-limiting or easily managed with topical medications.[3]

However, there are well-known severe complications that can occur as a result of SLT. Macular edema has been reported to occur following SLT.[4-6] The genesis of the macular edema is unknown, but may be related to prostaglandin induction in the inflammatory cascade initiated by SLT. While treatment is usually quite effective in resolving macular edema, the condition can persist for months.[5]

Other reported side effects potentially occurring from SLT are corneal edema, haze and thinning. In the majority of cases, topical steroid treatment resolved the edema within several weeks, but in several cases patients were left with mildly reduced visual acuity due to stromal haze.[7-9] It is not known what factors predispose patients to these corneal changes following SLT. Commensurate with these corneal changes, several patients had hyperopic refractive shifts. One report noted shifts of nearly 2.0 to greater than 6.0 diopters in eyes that were moderately to highly myopic prior to SLT.[9]

We have personally witnessed a patient develop severe corneal edema with folds in Descemet's membrane following SLT. This individual required a protracted course of topical steroids with a subsequent elevation in IOP, placing him at risk for further glaucomatous damage.

Other rare complications from SLT have been documented. In one case, a patient developed a significant anterior chamber reaction, shallow anterior chamber and choroidal effusion.[10] In another, the patient developed hyphema after the procedure.[11] While SLT has been shown to be a safe and effective pressure-lowering treatment overall, it would be irresponsible for any physician or educational piece to suggest that, "there are no side effects to worry about."

Mythbusting

Education about diseases and therapeutic options are a paramount part of the doctor-patient relationship. However, it can become an uphill struggle when patients are exposed to false and misleading statements about their treatments. ■

1. Lewis RA. Ab interno approach to the subconjunctival space using a collagen glaucoma stent. J Cataract Refract Surg. 2014;40(8):1301-6.
2. Fernández-García A, Romero C, Garzón N. "Dry Lake" technique for the treatment of hypertrophic bleb following XEN Gel Stent placement. Arch Soc Esp Oftalmol. 2015;90(11):536-8.
3. Barkana Y, Belkin M. Selective laser trabeculoplasty. Surv Ophthalmol. 2007;52(6):634-54.
4. Ha J, Bowling B, Chen S. Cystoid macular oedema following selective laser trabeculoplasty in a diabetic patient. Clin Experiment Ophthalmol. 2014;42(2):200-1.
5. Wu Z, Huang J, Sadda S. Selective laser trabeculoplasty complicated by cystoid macular edema: report of two cases. Eye Sci. 2012;27(4):193-7.
6. Wechsler D, Wechsler IB. Cystoid macular oedema after selective laser trabeculoplasty. Eye (Lond). 2010;24(6):1113.
7. Moubayed SP, Hamid M, Choremis J, Li G. An unusual finding of corneal edema complicating selective laser trabeculoplasty. Can J Ophthalmol. 2009;44(3):337-8.
8. Regina M, Bunya VY, Orlin SE, Ansari H. Corneal edema and haze after selective laser trabeculoplasty. J Glaucoma. 2011;20(5):327-9.
9. Knickelbein JE, Singh A, Flowers BE, et al. Acute corneal edema with subsequent thinning and hyperopic shift following selective laser trabeculoplasty. J Cataract Refract Surg. 2014;40(10):1731-5.
10. Kim DY, Singh A. Severe iritis and choroidal effusion following selective laser trabeculoplasty. Ophthalmic Surg Lasers Imaging. 2008;39(5):409-11.
11. Shihadeh WA, Ritch R, Liebmann JM. Hyphema occurring during selective laser trabeculoplasty. Ophthalmic Surg Lasers Imaging. 2006;37(5):432-3.

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

Contact Lenses

New Wearer Starter Kits

For a limited time, optometrists can offer starter kits to their new contact lens wearers. Alcon has announced the upcoming release of a limited supply of kits for new wearers of its Dailies AquaComfort Plus lines, created to help transition new wearers into contact lenses, according to the company.

The kits include:

- Lens insertion and removal instructions.
- Annual supply value pack with a rebate and coupons for OTC products.
- Dailies family consumer brochure.
- Carrying case with a mirror to help with insertion.
- Dailies AquaComfort Plus trial contact lenses with optometrist office inserts.

A limited number of kits are available from sales representatives in the United States.

Visit www.dailies.com/products.

Three Diameter Contact Lens Option

X-Cel Specialty Contacts now offers a new, three-diameter daily disposable lens option. The Extreme H2O Daily comes in 13.6, 14.2 and 14.8 diameters, enabling practitioners to get a precise fit on all their patients, according to the company.

The company provides a slide ruler for quick and efficient HVID measurement by a technician. Patients with an HVID larger than 12.3 should be fit in the larger 14.8 diameter lens, and patients with an HVID less than 11.4 should be fit in the smaller 13.6 diameter lens, according to the company.

Available parameters in all diameters are: +0.50 to +6.00 and -0.50 to -10.00 (0.50D steps after -6.00).

Visit www.xcelspecialtycontacts.com.

Practice Management

EHR System

Compulink Business Systems will unveil new EHR systems the manufacturer claims will streamline documentation while maximizing efficiency and ease of use. OneTab will allow providers to view and document entire exams on one screen, which the company says will increase provider productivity. PracticeWatch, a built-in scheduler fully integrated with Eyecare Advantage, provides users the ability to schedule tasks to automatically run at specified intervals of time, monitor patients and automatically send instant messages.

Visit www.compulinkadvantage.com/products-solutions.

Diagnostic Technology

Single-Use Eye Patches

Haag-Streit has announced the launch of its Mask-it eye patches as an addition to the Octopus line of products. These paper, disposable eye patches are designed for perimetric testing, are size-adjustable and provide fast and effective occlusion, according to Haag-Streit.

Developed for single use, the hygienic patches reliably eliminate the risk of cross infection.

Additionally, the translucent eye patches allow the patient to keep both eyes open during perimetric testing, ensuring natural vision, according to the company.

Visit www.haag-streit.com/products.

New Autorefractor Models

Smart Vision Labs announced the release of two second-generation smart autorefractors. The SVOne Enterprise, a Shack-Hartmann wavefront aberrometer, is a fully automated self-guided objective refraction technology, according to the manufacturer. Additionally, Smart Vision unveiled the SVOne Pro, an upgraded version of Smart Vision's core autorefractor, which touts a new open view channel, an increased range of power and improvements in usability and accuracy.

Visit www.smartvisionlabs.com/autorefractors.

Disposable Applanation Prism

Keeler has introduced the new Tonomate disposable applanation prism for safe and fast Goldmann applanation tonometry, according to the company.

Tonomate prisms are designed to fit most applanation tonometer prism holders, and each prism is individually packed in sterile packaging and can be easily fitted without direct contact, according to the company. The prism is discarded after use to streamline eye exams and prevent cross infection, according to Keeler.

Visit www.keelerusa.com.

Merchandise Offered

Software

Practice For Sale

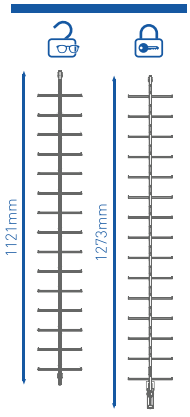
Merchandise Offered

YOUR COLLECTION DESERVES THE ABSOLUTE BEST PRESENTATION!

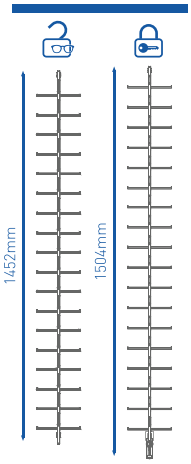
ALUMINA™

DESIGNED TO SHOW, NOT TO BE SEEN.

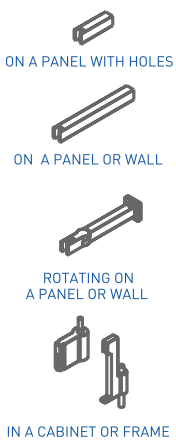
15



18



MOUNTING



Logo Plate

- Easy to change
- Create sections in the panel and organize collections easily

Flexible Mounting Option

- On a panel or wall
- Easy assembly

Alumina key

- The strongest key for optical displays.
- Ergonomic design of the lock allows for easy opening and closing.

April 15-17 | NY
Booth #3608

INTERNATIONAL VISION EXPO & CONFERENCE NEW YORK

Frame Displays .com

An Essilor Company

1-877-274-9300

Merchandise Offered

Continuing Education

21st Annual
KEY WEST
Educational Conference

July 29th & 30th, 2016

9 hours CE/ 8 TQ hours, Cope Approval pending

CASA MARINA RESORT
THE WALDORF ASTORIA COLLECTION
1500 Reynolds Street | Key West, FL 33040
www.casamarinaresort.com
1.888.318.4237

For more information contact:
Gloria Ayan @ 305.491.3747 or E-Mail: gayan@araneye..com

SWFOA.com

SOUTHWEST FLORIDA EDUCATIONAL RETREAT

August 5-7, 2016

SOUTH SEAS ISLAND RESORT
CAPTIVA ISLAND, FLORIDA

Education
Transcript Quality - 6 Hours Continuing Education - 14 hours
Total Hours 20 - 18 Hours COPE approved

Program/ Speakers

Bruce Onofrey, O.D., F.A.A.O.	6 hours TQ/CE
Kim Reed, O.D., F.A.A.O.	8 hours CE
Exhibits	2 hours
April Jasper O.D., F.A.A.O.	2 hours CE/PM & 2 Hrs Medical Errors
Ron Foreman O.D., F.A.A.O.	2 hours CE Optometric Jurisprudence

Information
Visit Our Website:
www.swfoa.com
or
E-mail swfoa@att.net

Registration
Prior to July 10, 2016
AOA members $435
Non members $535
Register online at:
www.swfoa.com

Special convention rates will only be in effect after registering for the meeting

---

OCULAR SYMPOSIUM

Lectures in Ocular Diagnosis and Treatment

Formal Lectures for Optometrists
by Noted Subspecialists in Ophthalmology

Friday, Saturday, Sunday, June 3-5, 2016
24 hours CE credits (8 hours each day) - COPE APPROVAL PENDING

SAN FRANCISCO, CALIFORNIA

Refractive Surgery	Glaucoma	Cataract Surgery
Oculoplastics	Inflammations	Corneal Disease
Neuro-Ophthalmology	Retinal Disease	Ocular Pediatrics

For information call or write:
Ocular Symposium • P.O. Box 640327 • San Francisco • CA • 94164
(415) 278-9940 • FAX (415) 345-1165
e-mail: ocularsymp@aol.com

Do you have Equipment and Supplies for Sale?

REVIEW® OF OPTOMETRY

Contact us today for classified advertising:
Toll free: **888-498-1460** • E-mail: **sales@kerhgroup.com**

REVIEW® OF OPTOMETRY

Do you have CE Programs?

CLASSIFIED ADVERTISING WORKS

Contact us today for classified advertising:
Toll free: **888-498-1460**
E-mail: **sales@kerhgroup.com**

kerh group

Career Opportunities

2 VISION SITE PRACTICES FOR SALE
LOCATION: EAST TEXAS

2 Vision Site practices for sale, equipment included in sale is 2 lanes and 2 BIO's, records in EHR, pachymeter, lensometer, 2 Eye Dr. fundus cameras, and 2 computerized acuity charts. Own the website, Facebook, and phone number. Don't think you can afford it, you can.

Good practice for doctor who wishes to be their own boss and own practice.

CONTACT JERRY AT
903-918-3515 OR
TEXASEYEDOC17@GMAIL.COM

PEDIATRIC OPTOMETRIST

Children's Eye Physicians seeking FT Residency Trained Pediatric Optometrist for a unique opportunity within our practice in Beautiful Denver Colorado. Our practice offers services of seven Board Certified Ophthalmologists and four Residency Trained Pediatric Optometrists. Our practice has an exceptional reputation, serving patients for 23 years. **If interested please submit resume to lbridges@cepcolorado.com.**

STAFF OPTOMETRIST

Bard Optical is a leading Midwest vision care organization in business for over 70 years and we are still growing. The company is based in Peoria, IL with 20 retail offices throughout the central Illinois area, as far north as Sterling and as far south as Jacksonville. Once again this year we were named to the Top 50 Optical Retailers in the United States by Vision Monday – currently ranking 37th. A progressive optometric staff is vital to the continued growth of our organization whose foundation is based on one-on-one patient service. We are currently accepting CV/resumes for optometrists focused on full scope primary medical patient care. The candidate must have an Illinois license with therapeutics. The practice includes (but is not limited to) general optometry, contact lenses, and geriatric care. Salaried, full-time positions are available with excellent growth programs and benefits. Some part-time opportunities may be available also. Please email your information to **hr@bardoptical.com** or fax to **309-693-9754**. Mailing address if more convenient is **Bard Optical, Attn: HR, 8309 N Knoxville Avenue, Peoria, IL 61615**. Ask about opportunities within Bard Optical. *We have openings in several existing and new offices opening soon in central Illinois.*

Bard Optical is a proud Associate Member of the Illinois Optometric Association.

BARD OPTICAL

www.bardoptical.com

Here we grow again!

TWO MOTIVATED OPTOMETRISTS
ILLINOIS

One of the largest eye care providers to extended care and assisted living residents in our great state of Illinois needs two motivated Optometrists to join our practice!

Both positions are in the Springfield and Central Illinois areas. One position is full time and one position is part time.

Our physicians are proficient in refracting, diagnosing & treating ocular pathology, and dispensing spectacles on-site. If you are proficient in these areas and you are comfortable driving, here are your benefits: Excellent Pay + bonuses (=145K+), travel bonuses that will exceed expenses incurred, new optical equipment, a personal assistant, but most important helping people in need of our professional services.

Interested? Contact Michael at
Michael@ovitskyvisioncare.com
or at 773-588-3090.

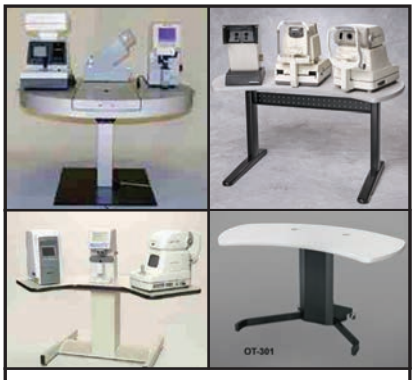
Only serious inquiries please. We will help with relocation expenses, if necessary.

Equipment and Supplies

Motorized Pretesting Tables FOR LESS!

Save hundreds for just shopping on line.

Go to EBAY and search the words PRETESTING TABLES and start saving on all your pretesting needs
or
EMail: eyecareauctions@gmail.com



OPTINOMICS Pretesting Solutions

It's What the Best Pretest on!
(800) 522-2275
www.optinomics.com
sales@optinomics.com

Products and Services

OD ONLINE

COMPLETE PM AND CERTIFIED EHR SOFTWARE
- 2014 Edition

All inclusive solution to enrich patient care and increase profitability for unlimited devices and users.

GET A FREE DEMO AT
WWW.ODONLINE.NET

REVIEW OF OPTOMETRY

Looking to increase sales?

Place Your Ad here.

Contact us today for classified advertising:
888-498-1460
E-mail: **sales@kerhgroup.com**

REVIEW OF OPTOMETRY

Do you have CE Programs?

CONTACT US TODAY
FOR CLASSIFIED ADVERTISING
Toll free: **888-498-1460**
E-mail: **sales@kerhgroup.com**

Contact Lenses

30 YEARS

INTERNATIONAL VISION EXPO & CONFERENCE

NEW YORK

30 YEARS OF GIVING BACK

1,756,768,514 consumer media impressions generated on the topic of digital eye strain and computer eyewear by The Vision Council.

"I love teaching. To have even a small influence on the profession, it's humbling."

DIANA SHECHTMAN, OD; professor, Nova Southeastern University and esteemed speaker

CELEBRATING THE

VISIONARIES

IN EDUCATION + FASHION + TECHNOLOGY

REGISTER TODAY! | **NEW YORK THURSDAY, APRIL 14–SUNDAY, APRIL 17** | **VisionExpo.com/visionaries**

BROUGHT TO YOU BY: THE VISION COUNCIL

PROUD SUPPORTER OF: think about your eyes .com

PRODUCED BY: Reed Exhibitions

BERMUDA

Up to 18 CE Credits (COPE approval pending)

Image courtesy of Hamilton Princess & Beach Club, A Fairmont Managed Hotel

New Technologies and Treatments in Vision Care 2016

REVIEW OF OPTOMETRY®
EDUCATIONAL MEETINGS OF CLINICAL EXCELLENCE

JUNE 9-12, 2016

Superior Education with 3 Interactive Workshops

Fairmont Hamilton Princess
A Fairmont Managed Hotel

76 Pitts Bay Road | Hamilton, BERMUDA HM 08 | 441-295-3000

Discounted room rate $299-$329/NIGHT

Program Chair: **Paul Karpecki, OD**

SPEAKERS:

Marc Bloomenstein, OD

Douglas Devries, OD

Mark Dunbar, OD

Benjamin Gaddie, OD

Jack Schaeffer, OD

REGISTER NOW!

www.ReviewofOptometry.com/Bermuda2016

Or Email **Lois DiDomenico**: **ReviewMeetings@Jobson.com** | Call: **866-658-1772**

REGISTRATION: **4 DAYS - 18 CE CREDITS* - $595**

Please see registration website for a list of sponsors and meeting agenda.

Administered by
Review of Optometry®

cope®
*Approval pending

FAIRMONT HAMILTON PRINCESS

76 PITTS BAY ROAD HAMILTON, BERMUDA HM 08

Up to 18 CE Credits (COPE approval pending)

A limited number of rooms have been reserved at The Fairmont Hamilton Princess.

Discounted Room Rates: $299 - $329 night standard, plus applicable taxes & fees.

Please call the hotel at 441-295-3000 and identify yourself as a participant of "Review of Optometry" for group rate.

Discounted room rates are based on space and availability, so please book early!
Discounted room rates available 3 days pre- and 3 days post- conference based on hotel availability.

Registration Information

Name | NPI # (NPI numbers will only be used for Sunshine reporting purposes) | OE Tracker #

Practice Affiliation

Mailing Address | City | State | Zip Code

Telephone | Fax | E-mail

Name Badge Information (please print clearly)

My Name | My Guest | Additional Guests

Payment Information

	Rate per person		No. in party		Subtotal
OD Registration - $595 (includes up to 18 hours of CE, breakfasts, reception) Call for daily and student rates.	$595	x	_____	=	$_____
Additional Guest(s) - $45 (12 years and older, includes reception)	$45	x	_____	=	$_____
Optional Catamaran/Snorkeling Activity, Saturday, June 11th. Enjoy a catamaran sail and snorkel through the exciting waters of the warm North Atlantic Ocean. Price includes equipment, lunch, and gratuities. Please join us for a fantastic afternoon!	$125	x	_____	=	$_____
			TOTAL	=	$_____

Additional Workshop(s) - 2 CE credits each

❑ Glaucoma Workshop (1pm-3pm) ❑ Ocular Surface Disease Workshop (1pm-3pm) ❑ Retina Workshop (3:15pm-5:15pm)

❑ Check enclosed (make checks payable to *Review of Optometry*)

Charge my: ❑ American Express ❑ Mastercard ❑ Visa

Credit Card Number | Exp Date

Cardholder (print name)

Signature

CONFERENCE CANCELLATION POLICY

- Full refund on registration fee until May 8, 2016
- 50% refund on registration fee until May 23, 2016
- No refund past May 23, 2016

For more information or to register, contact Lois DiDomenico at 866-658-1772 or at ReviewMeetings@Jobson.com.

MAIL FORM : Review Group Meetings c/o Jobson
11 Campus Blvd, Ste. 100
Newtown Square, PA 19073

FAX FORM: Review Meetings Group
610-492-1039

Images courtesy of Hamilton Princess & Beach Club, A Fairmont Managed Hotel

April 2016

■ **21-23.** *Mountain West Council of Optometrists Annual Congress.* Aria Resort & Casino, Las Vegas. Hosted by: MWCO. Key faculty: Jay Haynie, Leo Semes, Michael Stewart, Scot Morris, John McGreal, Jeff Sonsino. CE hours: 72 total, 24 per OD. To register, email Tracy Abel at tracyabel@earthlink.net, call (888) 376-6926 or go to www.mwco.org.

■ **21-26.** *Conference on Comprehensive EyeCare.* Sheraton Hotel, Niagara Falls, NY. 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.

■ **23-24.** *45th Bi-Annual CE Seminar and Optifair Canada Trade Show.* Embassy Grand Convention Centre, Brampton, Ontario, Canada. Hosted by: The Academy of Ophthalmic Education. Key faculty: Mile Brujic. CE hours: 14. To register, email Claudia Marks, CE and Event Coordinator at cmarks@aoece.com or go to www.aoece.com.

■ **23-25.** *2016 KOA Spring Congress.* Hyatt Hotel and Lexington Convention Center, Lexington, KY. Hosted by: Kentucky Optometric Association. CE hours: 20. To register, email Sarah Unger at sarah@kyeyes.org, call (502) 875-3516 or go to www.kyeyes.org.

■ **28-29.** *Great Lakes Eyecare Conference (GLEC).* DeVos Place, Grand Rapids, MI. Hosted by: Michigan Optometric Association/Michigan College of Optometry. CE hours: 13. To register, email Amy Root at amy@themoa.org, call (517) 482-0616 or go to www.themoa.org.

■ **28-30.** *OAOP Vision Summit.* Renaissance Oklahoma City Convention Center Hotel, Oklahoma City, OK. Hosted by: Oklahoma Association of Optometric Physicians. Key faculty: Nathan Lighthizer, Steven Ferrucci, Ken Eakland, Bradley Sutton. CE hours: 25 total, 18 per OD. To register, email Heatherlyn Burton at heatherlyn@oaop.org, call (405) 524-1075 or go to www.oaop.org.

■ **28-30.** *2016 Kansas Optometric Association Annual Convention and Seminar.* Capitol Plaza Hotel, Topeka, KS. Hosted by: Kansas Optometric Association. CE hours: 13. To register, email Todd Fleischer at todd@kansasoptometric.org, call (785) 232-0225 or go to www.kansasoptometric.org.

■ **28-May 1.** *2016 Arkansas Optometric Association Spring Convention.* Little Rock Marriott, Little Rock, AK. Hosted by: Arkansas Optometric Association. CE hours: 20. To register, email Vicki Farmer at aroa@arkansasoptometric.org, call (501) 661-7675 or go to arkansasoptometric.org.

■ **29.** *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.

■ **29-30.** *Florida Chapter-American Academy of Optometry.* Mission Inn, Howey-in-the-Hills, FL. Hosted by: Florida Chapter-American Academy of Optometry. Key faculty: Paul Karpecki, Dave Woods, John McClane, Joe Pizzimenti, Ben Lambright. CE hours: 16 total (including 6 HRS CE/TQ), 12 per OD (including 6 HRS CE/TQ). To register, email Art Young at eyeguy4123@msn.com or call (239) 542-4627.

■ **29-May 1.** *31st Annual Morgan Symposium.* DoubleTree Hotel, Berkeley, CA. Hosted by: University of California, Berkeley, School of Optometry. Key faculty: Carl Jacobsen, Todd Severin, Mark Dunbar, Joe Sowka. CE hours: 21. To register, email Danni Peck at optoce@berkeley.edu, call (800) 827-2163 or go to http://optometry.berkeley.edu/ce/morgan-symposium.

■ **30-May 1.** *MOS Annual Spring Conference.* Cleveland Marriott East, Cleveland, OH. Hosted by: Midwest Optometric Society and The Ohio State College of Optometry. Key faculty: Elliot Kirstein, Todd Zelczak, Sherry Bass. CE hours: 16. To register, go to www.midwestoptometricsociety.com, or for more information, call Marcy at (513) 321-2020.

■ **30-May 1.** *CE in the Southwest.* Westin Galleria Dallas. Hosted by: University of Houston College of Optometry and the University of the Incarnate Word Rosenberg School of Optometry. Key faculty: Sandra Fortenberry, Pat Segu. CE hours: 16. To register, email optce@central.uh.edu, call (713) 743-1900 or go to http://ce.opt.uh.edu.

May 2016

■ **1.** *Ninth Annual Evidence Based Care in Optometry Conference.* Turf Valley Resort & Conference Center, Ellicott City, MD. Hosted by: Maryland Optometric Association and Johns Hopkins Wilmer Eye Institute. CE hours: 7. To register, email Gala McCray at info@marylandoptometry.org, call (410) 486-9662 or go to marylandoptometry.org.

■ **1-5.** *ARVO.* Washington State Convention Center, Seattle. Hosted by: The Association for Research in Vision and Ophthalmology. For more information, go to www.arvo.org.

■ **4-6.** *MOA Annual Conference & Exposition.* Hilton Garden Inn, Missoula, MT. Hosted by: Montana Optometric Association. CE hours: 18. To register, email Sue Weingartner at sweingartner@rmsmanagement.com or go to www.mteyes.com.

■ **9.** *Coding Update 2016.* St. Louis. Hosted by: University of MO-St. Louis College of Optometry. Key faculty: John McGreal. CE hours: 4. To register, email Lis Ellerbusch at ellerbusch@umsl.edu or call (314) 516-5615.

■ **13-14.** *International Vision Conference East.* Hyatt Regency Pittsburgh International Airport, Pittsburgh, PA. Hosted by: OD Excellence. Key faculty: John McGreal, Paul Chous, Jeffry

Gerson, Valerie Manso. CE Hours: 6. To register, email Johanna Lieblein at johanna@odexcellence.com, call (707) 433-5542 or go to odexcellence.com.

■ **13-15.** *POA Spring Congress.* Radisson Hotel, Camp Hill, PA. Hosted by: PA Optometric Association. CE hours: 14. To register, email Ilene K. Sauertieg at ilene@poaeyes.org, call (717) 233-6455 or go to www.poaeyes.org.

■ **14-15.** *Indiana University CE.* IU School of Optometry, Bloomington, IN. Hosted by: IU School of Optometry. CE hours: 16. To register, email Cheryl Oldfield at coldfiel@indiana.edu or go to www.opt.indiana.edu/ce/seminars.htm.

■ **15.** *Potpourri of CE.* Marshall B. Ketchum University, Fullerton, CA. Hosted by: Marshall B. Ketchum University. CE hours: 8. To register, email Antoinette Smith at ce@ketchum.edu or go to www.ketchum.edu/index.php/ce.

■ **18-22.** *VT/Visual Dysfunction.* Phoenix, AZ. Hosted by: OEP Foundation. Key faculty: Rob Lewis. 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.

■ **19-22.** *Oregon's Meeting.* Sunriver Resort, Portland, OR. Hosted by: Oregon Optometric Physicians Association. Key faculty: Winston Chamberlain, Afshan Nanji, John Clements, Mansi Parikh, Eric Steele, Lori Lombardi. 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.

■ **20-22.** *New Technologies and Treatments in Vision Care.* San Antonio Marriott Rivercenter, San Antonio, TX. Hosted by: *Review of Optometry*. Key faculty: Paul Karpecki (meeting chair). CE hours: 19. To register, email Lois DiDomenico at reviewmeetings@Jobson.com, call (866) 658-1772 or go to www.reviewofoptometry.com/SanAntonio2016.

June 2016

■ **1-5.** *VT/Learning Related Visual Problems.* Nova Southeastern University College of Optometry, Ft. Lauderdale, FL. Hosted by: OEP. Key faculty: Rob Lewis. 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.

■ **2-5.** *Alaska Optometric Association CE Congress.* Lands End Resort, Homer, AK. Hosted by: Alaska Optometric Association. CE hours: 22. To register, email Lisa Johnson at alaskaoptometrics@gmail.com or go to akoa.org. ■

To list your meeting, please send the details to:
Adrienne Taron, Associate Editor
Email: ataron@jobson.com
Phone: (610) 492-1025

Advertisers Index

Alcon Laboratories ..... 72-73 .....137, 140
Phone .....(800) 451-3937
Fax.....(817) 551-4352

Bausch + Lomb .....9, 10, 16-17 .....18-19, 31, 32, 51, 91 .....92,123, 124, 139
Phone .....(800) 323-0000
Fax.....(813) 975-7762

BioD, LLC 45
Phone .....(877) 675-4149
.....contact@biodllc.com
.....www.biodlogics.com

Clear Eyes 87
Phone .....(877) 274-1787
..... www.cleareyes.com

Coburn Technologies .....95 .....97, 99
Phone .....(800) 262-8761
.... www.coburntechnologies.com

CooperVision 55
Phone .....(800) 341-2020

Essilor of America.....13
.....www.essilorusa.com

Icare USA 77
Phone .....(888) 389-4022
.....www.icare-usa.com

Keeler Instruments.....5
Phone .....(800) 523-5620
Fax.....(610) 353-7814

Lacrimedics, Inc 29
Phone .....(800) 367-8327
Fax.....(253) 964-2699
..... info@lacrimedics.com
..... www.lacrimedics.com

Lombart Instruments 115
Phone .....(800) 446-8092
Fax.....(757) 855-1232

M&S Technologies.....61
Phone .....(877) 225-6101
Fax.....(847) 763-9170

Marchon.....23, 25, 27
Phone .....(800) 645-1300
Fax.....(800) 544-1334

Natural Ophthalmics, Inc. 43
Phone .....(877) 220-9710
..... info@natoph.com
.....www.natoph.com

NovaBay Pharmaceuticals, Inc. 59
Phone .....(800) 890-0329
..... sales@avenova.com
..... www.avenova.com

Odyssey Medical (now part of Beaver-Visitec International, Inc.) 15
Phone .....(866) 906-8080
..... www.odysseymed.com

OGI Eyewear 41
Phone .....(888) 560-1060
..... www.ogieyewear.com

Optos North America 85
Phone .....(877) 455-8855 x 100
Fax.....(508) 486-9310

Paragon BioTeck, Inc. 79
Phone .....(888) 424-1192
..... www.paragonbioteck.com

Reichert Technologies ...39, 111
Phone .....(888) 849-8955
Fax.....(716) 686-4545
.....www.reichert.com

Reliance Medical 81
Phone .....(800) 735-0357
Fax.....(513) 398-0256

S4OPTIK 67, 69, 71
Phone .....(888) 224-6012

Shire Ophthalmics 7
..... www.shire.com

Smart Vision Labs 53
.....www.smartvisionlabs.com

Sun Ophthalmics..... 34-35
..... SunIsOnTheRise.com

TearScience 83
Phone .....(919) 459-4891
Fax.....(919) 467-3300

TelScreen 65
..... www.TelScreen.com
..... DryEye@TelScreen.com

U.S. Army.....21
Phone .....(800) 431-6731
www.healthcare.goarmy.com/at66

Veatch.....47
Phone .....(800) 447-7511
Fax.....(602) 838-4934

Vision Source 119
Phone .....(281) 312-1111
Fax.....(281) 312-1153
.....www.visionsource.com

Vistakon 2-3
Phone .....(800) 874-5278
Fax.....(904) 443-1252

This advertiser index is published as a convenience and not as part of the advertising contract. Every care will be taken to index correctly. No allowance will be made for errors due to spelling, incorrect page number, or failure to insert.

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

Tightening the Lid

Medical and cosmetic reasons can lead patients to quietly consider blepharoplasty. Increase opportunities to offer this procedure to your patients. **By Cecelia Koetting, OD**

Often, gradual anatomical changes to the eyelids go unnoticed, or unremarked during exams, yet can significantly affect our patients' vision—and their self-perception. Blepharoplasty can be performed for cosmetic or medical reasons, both of which should be considered when talking to patients. The most common diagnosis leading to blepharoplasty is dermatochalasis, an age-related, progressive and bilateral eyelid droop resulting from redundant, loose eyelid skin and herniation of the orbital fat.

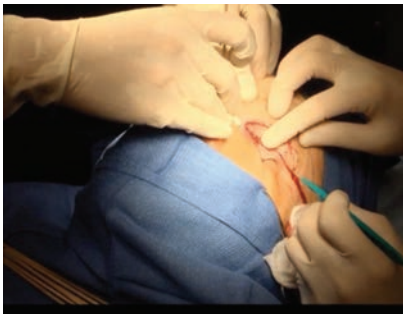
Who Benefits?

Dermatochalasis is often regarded as an independent condition; however, one study found that 51% of patients also complained of dry eye. Of those patients, 86% reported improvements in dry eye symptoms following upper blepharoplasty.[1]

Patients with significant dermatochalasis may lose a portion of their superior vision. Glaucoma patients with the condition may do poorly on visual field testing and present with a pseudo-altitudinal defect, which improves after the procedure.[2]

Many dermatochalasis patients who present to us without a measurable visual defect may be thinking about aesthetic concerns; so, be sure to consider this before writing off the idea that they may be interested in elective procedures.

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



During upper lid blepharoplasty, a crescent of skin and the underlying orbicularis muscle is excised to remove or trim prolapsing, preaponeurotic fat.

Facial rejuvenation via blepharoplasty can also improve the aesthetics of both the brow and cheek. Don't be afraid to address these topics with patients—they will be glad you did.

Screening

Many patients who can benefit from a blepharoplasty may not know it, or assume the procedure is elective so they don't consider it. For example, a patient who has difficulty opening their eyes at the slit lamp is an optimal patient with whom to initiate a discussion.

Obtain a thorough history regarding current systemic conditions and medications, and pay attention to a history of keloid scarring, and drugs or supplements that are anticoagulants. Screen patients for dry eye, glaucoma, pre-existing ptosis, lagophthalmos and thyroid eye disease.

The upper margin-reflex distance (MRD-1) indicates the dermatochalasis is severe if the distance from center of the pupil to the eyelid margin is 2.5mm or less. The superior, 36-point screening test with and without taping is standard to show the visual significance of dermatochalasis and is often used by insurers to determine coverage.

Surgical Overview

Blepharoplasty can be performed in-office under local anesthesia or under sedation at a surgical center. Upper lid blepharoplasty uses an external incision to create and remove a small crescent of skin, along with any prolapsing medial or central fat pads. Resection with absorbable sutures of retro-orbicularis oculi fat helps decrease the upper lid and lateral brow weight.

Lower lid blepharoplasty uses either an external incision below the lash line for dermatochalasis excision or an internal incision through the conjunctiva below the lid margin to conservatively remove fat.

Significant swelling and bruising is likely after surgery. Advise patients to use ice packs for 15 minutes each hour in the two to three days following surgery to reduce edema. Topical antibiotic ointment is applied twice daily until sutures are removed, and pain is managed with acetaminophen 1000mg. Vitamin E ointment can be massaged into the skin after suture removal to minimize scar formation. At the one-month follow up, assess positioning and symmetry between the eyelids. ■

1. Vold S, Carroll RP, Nelson JD. Dermatochalasis and dry eye. Amer J Ophthalmol. 1993;115(2):216-20.
2. Alan KS, Wishart PK, Birch MK. Apparent glaucomatous visual field defects caused by dermatochalasis. Eye. 1997;11(Pt 5):682-6.

Pazeo™

(olopatadine hydrochloride ophthalmic solution) 0.7%

BRIEF SUMMARY

PAZEO (olopatadine hydrochloride ophthalmic solution) 0.7%. For topical ophthalmic administration.

The following is a brief summary only; see full prescribing information for complete product information.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Contamination of Tip and Solution

As with any eye drop, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle to prevent contaminating the tip and solution. Keep bottle tightly closed when not in use.

Contact Lens Use

Patients should not wear a contact lens if their eye is red.

The preservative in PAZEO solution, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and whose eyes are not red, should be instructed to wait at least five minutes after instilling PAZEO before they insert their contact lenses.

ADVERSE REACTIONS

Clinical Trials Experience

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

In a randomized, double-masked, vehicle-controlled trial, patients at risk for developing allergic conjunctivitis received one drop of either PAZEO (N=330) or vehicle (N=169) in both eyes for 6 weeks. The mean age of the population was 32 years (range 2 to 74 years). Thirty-five percent were male. Fifty-three percent had brown iris color and 23% had blue iris color. The most commonly reported adverse reactions occurred in 2-5% of patients treated with either PAZEO or vehicle. These events were blurred vision, dry eye, superficial punctate keratitis, dysgeusia and abnormal sensation in eye.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no adequate or well-controlled studies with PAZEO in pregnant women. Olopatadine caused maternal toxicity and embryofetal toxicity in rats at levels 1,080 to 14,400 times the maximum recommended human ophthalmic dose (MRHOD). There was no toxicity in rat offspring at exposures estimated to be 45 to 150 times that at MRHOD. Olopatadine should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Animal Data

In a rabbit embryofetal study, rabbits treated orally at 400 mg/kg/day during organogenesis showed a decrease in live fetuses. This dose is 14,400 times the MRHOD, on a mg/m^2 basis.

An oral dose of 600 mg/kg/day olopatadine (10,800 times the MRHOD) was shown to be maternally toxic in rats, producing death and reduced maternal body weight gain. When administered to rats throughout organogenesis, olopatadine produced cleft palate at 60 mg/kg/day (1080 times the MRHOD) and decreased embryofetal viability and reduced fetal weight in rats at 600 mg/kg/day. When administered to rats during late gestation and throughout the lactation period, olopatadine produced decreased neonatal survival at 60 mg/kg/day and reduced body weight gain in offspring at 4 mg/kg/day. A dose of 2 mg/kg/day olopatadine produced no toxicity in rat offspring. An oral dose of 1 mg/kg olopatadine in rats resulted in a range of systemic plasma area under the curve (AUC) levels that were 45 to 150 times higher than the observed human exposure [9.7 ng·hr/mL] following administration of the recommended human ophthalmic dose.

Nursing Mothers

Olopatadine has been identified in the milk of nursing rats following oral administration. Oral administration of olopatadine doses at or above 4 mg/kg/day throughout the lactation period produced decreased body weight gain in rat offspring; a dose of 2 mg/kg/day olopatadine produced no toxicity. An oral dose of 1 mg/kg olopatadine in rats resulted in a range of systemic plasma area under the curve (AUC) levels that were 45 to 150 times higher than the observed human exposure [9.7 ng·hr/mL] following administration of the recommended human ophthalmic dose. It is not known whether topical ocular administration could result in sufficient systemic absorption to produce detectable quantities in the human breast milk. Nevertheless, caution should be exercised when PAZEO is administered to a nursing mother.

Pediatric Use

The safety and effectiveness of PAZEO have been established in pediatric patients two years of age and older. Use of PAZEO in these pediatric patients is supported by evidence from adequate and well-controlled studies of PAZEO in adults and an adequate and well controlled study evaluating the safety of PAZEO in pediatric and adult patients.

Geriatric Use

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity

Olopatadine administered orally was not carcinogenic in mice and rats in doses up to 500 mg/kg/day and 200 mg/kg/day, respectively. Based on a 35 µL drop size and a 60 kg person, these doses are approximately 4,500 and 3,600 times the MRHOD, on a mg/m^2 basis.

Mutagenesis

No mutagenic potential was observed when olopatadine was tested in an *in vitro* bacterial reverse mutation (Ames) test, an *in vitro* mammalian chromosome aberration assay or an *in vivo* mouse micronucleus test.

Impairment of fertility

Olopatadine administered at an oral dose of 400 mg/kg/day (approximately 7,200 times the MRHOD) produced toxicity in male and female rats, and resulted in a decrease in the fertility index and reduced implantation rate. No effects on reproductive function were observed at 50 mg/kg/day (approximately 900 times the MRHOD).

PATIENT COUNSELING INFORMATION

• Risk of Contamination: Advise patients to not touch dropper tip to eyelids or surrounding areas, as this may contaminate the dropper tip and ophthalmic solution.

• Concomitant Use of Contact Lenses: Advise patients not to wear contact lenses if their eyes are red. Advise patients that PAZEO should not be used to treat contact lens-related irritation. Advise patients to remove contact lenses prior to instillation of PAZEO. The preservative in PAZEO solution, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted 5 minutes following administration of PAZEO.

Patents: 8,791,154

Alcon®

ALCON LABORATORIES, INC.
Fort Worth, Texas 76134 USA

6/15 PAZ15093JAD

Changes to the System

By Andrew S. Gurwood, OD

History

A 39-year-old black male presented to the emergency department complaining of worsening blurred vision in both eyes over the course of one week.

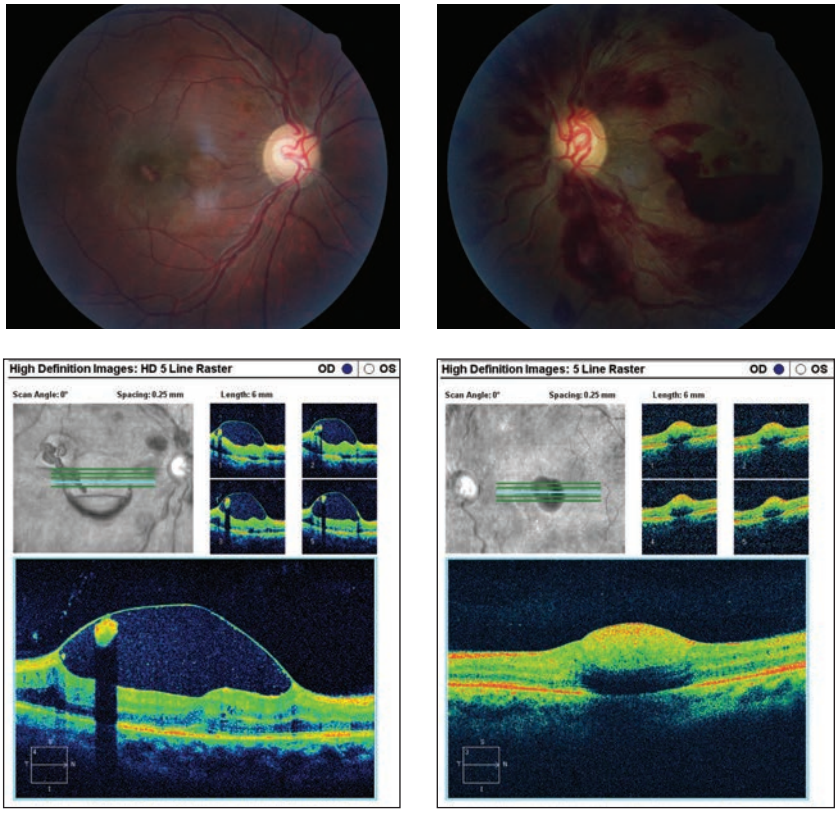
He also noted weight loss, palpitations and night sweats. A cursory work up uncovered pancytopenia (deficiency of red blood cells, white blood cells and platelets) and splenomegaly. The patient was referred to an ophthalmologist to investigate the ocular issues.

On the initial presentation, entering visual acuity without correction was 20/200 OD with no improvement upon pinhole testing and counting fingers at 10 feet with pinhole improvement to 20/200 OS.

There was a 15% red cap color desaturation present in the patient's right eye.

Pupils were round, equal, reactive, and there was no presence of a relative afferent pupillary defect.

Confrontation fields were blurry, but full-to-finger counting in each eye and extraocular muscle movements were full and smooth in both of his eyes.



Can these fundus photos and OCT images help explain our 39-year-old patient's worsening vision blur? What can his systemic changes tell you about his diagnosis?

Diagnostic Data

Biomicroscopic anterior segment examination found normal structures with deep anterior chambers, no evidence of inflammation, open angles and intraocular pressures measuring 8mm Hg OD and 10mm Hg OS by Goldmann applanation tonometry.

The pertinent fundus findings are demonstrated in the photographs.

Your Diagnosis

Does this case require additional tests? What is your diagnosis? How would you manage this patient? What's the likely prognosis? To find out, please visit www.reviewofoptometry.com. ■

Retina Quiz Answers *(from page 112):* 1) b; 2) c; 3) c; 4) d.

REVIEW OF OPTOMETRY (ISSN 0147-7633) IS PUBLISHED MONTHLY, 12 TIMES A YEAR BY JOBSON MEDICAL INFORMATION LLC, 100 AVENUE OF THE AMERICAS, NEW YORK, NY 10013-1678. PERIODICALS POSTAGE PAID AT NEW YORK, NY AND ADDITIONAL MAILING OFFICES. POSTMASTER: SEND ADDRESS CHANGES TO REVIEW OF OPTOMETRY, PO BOX 81, CONGERS, NY 10920-0081. SUBSCRIPTION PRICES: US: ONE YEAR $56; TWO YEARS $97, CANADA: ONE YEAR $88, TWO YEARS $160, INT'L: ONE YEAR $209, TWO YEARS $299. FOR SUBSCRIPTION INFORMATION CALL TOLL-FREE (877) 529-1746 (USA); OUTSIDE USA, CALL (845) 267-3065. OR EMAIL US AT REVOPTOMETRY@CAMBEYWEST.COM. PUBLICATIONS MAIL AGREEMENT NO: 40612608. CANADA RETURNS TO BE SENT TO BLEUCHIP INTERNATIONAL, P.O. BOX 25542, LONDON, ON N6C 6B2.

Bausch + Lomb ULTRA® for Presbyopia

- **MoistureSeal® technology:** helps maintain 95% of lens moisture for a full 16 hours[1]
- **3-Zone Progressive™ Design:** provides outstanding near, intermediate, and distance vision[2]
- **Easy, predictable fitting:** 80% of patients were successfully fit in one visit[2,3*]

Provide your patients
clarity through consistency

Learn more at www.Bausch.com/UFP

*When the ECP followed the fitting guide for the 3-Zone Progressive™ Design of PureVision®2 for Presbyopia lens.

REFERENCES: 1. Data on file. Bausch & Lomb Incorporated. Rochester, NY; 2013. **2.** Data on file. Bausch & Lomb Incorporated. Rochester, NY; 2015. **3.** Thirty-nine ECPs (from 10 countries) refitted 422 existing soft contact lens wearing presbyopes into PureVision®2 Presbyopia lenses. Patients returned for follow-up visits after 1-2 weeks. ECP assessment of lens performance including ease of fit, and patient satisfaction with lenses in real-world conditions, were measured using a 6-point agreement survey.

BAUSCH + LOMB
See better. Live better.

Once-Daily **PAZEO™ Solution**

24 HOURS OF OCULAR ALLERGY

ITCH RELIEF IN ONE DROP

Once-Daily **PAZEO™ Solution** for relief of ocular allergy itch:

- The first and only FDA-approved once-daily drop with demonstrated 24-hour ocular allergy itch relief[1]
- Statistically significantly improved relief of ocular itching compared to **PATADAY® (olopatadine hydrochloride ophthalmic solution) 0.2%** at 24 hours post dose (not statistically significantly different at 30-34 minutes)[1]
- Statistically significantly improved relief of ocular itching compared to vehicle through 24 hours post dose[1]

Study design: Two multicenter, randomized, double-masked, parallel-group, vehicle- and active-controlled studies in patients at least 18 years of age with allergic conjunctivitis using the conjunctival allergen challenge (CAC) model (N=547). Patients were randomized to receive study drug or vehicle, 1 drop per eye on each of 2-3 assessment days. On separate days, antigen challenge was performed at 27 (±1) minutes post dose to assess onset of action, at 16 hours post dose (Study 1 only), and at 24 hours post dose. Itching scores were evaluated using a half-unit scale from 0=none to 4=incapacitating itch, with data collected 3, 5, and 7 minutes after antigen instillation. The primary objectives were to demonstrate the superiority of **PAZEO™ Solution** for the treatment of ocular allergy itch. Study 1: **PAZEO™ Solution** vs vehicle at onset of action and 16 hours. Study 2: **PAZEO™ Solution** vs vehicle at onset of action; **PAZEO™ Solution** vs **PATADAY® Solution**, PATANOL® (olopatadine hydrochloride ophthalmic solution) 0.1%, and vehicle at 24 hours.[1-3]

Give your patients 24 HOURS OF OCULAR ALLERGY ITCH RELIEF with once-daily PAZEO™ Solution[1]

PAZEO™ Solution: Safety Profile

- Well tolerated[1]
- The safety and effectiveness of **PAZEO™ Solution** have been established in patients two years of age and older[1]
- The most commonly reported adverse reactions, occurring in 2% to 5% of patients, were blurred vision, dry eye, superficial punctate keratitis, dysgeusia, and abnormal sensation in eye[1]

Once-daily dosing[1]

INDICATION AND DOSING

PAZEO™ Solution is indicated for the treatment of ocular itching associated with allergic conjunctivitis. The recommended dosage is to instill one drop in each affected eye once a day.

IMPORTANT SAFETY INFORMATION

As with any eye drop, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle to prevent contaminating the tip and solution. Keep bottle tightly closed when not in use.

Patients should not wear a contact lens if their eye is red. PAZEO™ Solution should not be used to treat contact lens-related irritation. The preservative in PAZEO™ Solution, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses and whose eyes are not red should be instructed to wait at least five minutes after instilling PAZEO™ Solution before they insert their contact lenses.

The most commonly reported adverse reactions in a clinical study occurred in 2%-5% of patients treated with either PAZEO™ Solution or vehicle. These events were blurred vision, dry eye, superficial punctate keratitis, dysgeusia, and abnormal sensation in eye.

For additional information on PAZEO™ Solution, please refer to the brief summary of the full Prescribing Information on the following page.

References: 1. PAZEO™ Solution Package Insert. **2.** Data on file, 2011. **3.** Data on file, 2013.

From Alcon, committed to providing treatment options for patients.

Alcon
a Novartis company

Olopatadine is licensed from Kyowa Hakko Kirin Co., Ltd. Japan

 6/15 PAZ15093JAD

Pazeo™
(olopatadine hydrochloride ophthalmic solution) 0.7%