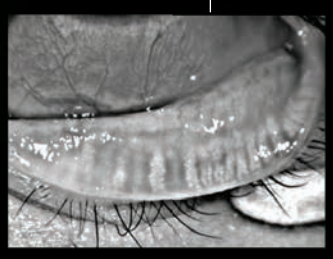
Earn 2 CE Credits: A Stepwise Approach to Evaluating Ocular Motility, **p. 107**

REVIEW® OF OPTOMETRY

May 15, 2016

www.reviewofoptometry.com



17th Annual Dry Eye Report

- Improve Your Understanding of Meibomian Gland Function —and Dysfunction, **p. 36**
- A Better Meibomian Gland Work-up: See What You've Been Missing, **p. 46**
- Tools of the Trade: Current Techniques to Treat MGD, **p. 56**

ALSO INSIDE

Because I know their eyes are prone to discomfort, I prescribe the 1-DAY ACUVUE® MOIST Family.

§ 88% of all BLINK STABILIZED® Design contact lenses were fitted in the first attempt, and 99.5% within 2 trial fittings.

** Based on *in vitro* data. Clinical studies have not been done directly linking differences in lysozyme profile with specific clinical benefits.

* UV-blocking percentages are based on an average across the wavelength spectrum.

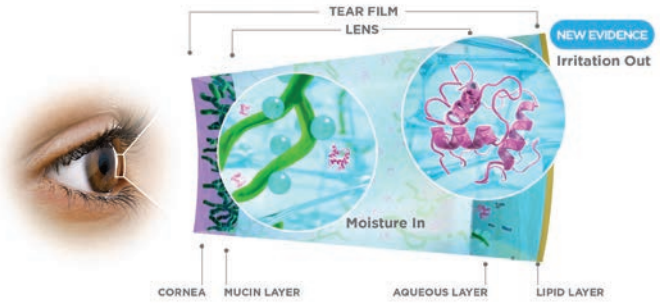
† Helps protect against transmission of harmful UV radiation to the cornea and into the eye.

‡ **WARNING:** UV-absorbing contact lenses are NOT substitutes for protective UV-absorbing eyewear such as UV-absorbing goggles or sunglasses because they do not completely cover the eye and surrounding area. You should continue to use UV-absorbing eyewear as directed. NOTE:Long-term exposure to UV radiation is one of the risk factors associated with cataracts. Exposure is based on a number of factors such as environmental conditions (altitude, geography, cloud cover) and personal factors (extent and nature of outdoor activities). UV-blocking contact lenses help provide protection against harmful UV radiation. However, clinical studies have not been done to demonstrate that wearing UV-blocking contact lenses reduces the risk of developing cataracts or other eye disorders. Consult your eye care practitioner for more information.

EYE-INSPIRED™ Design

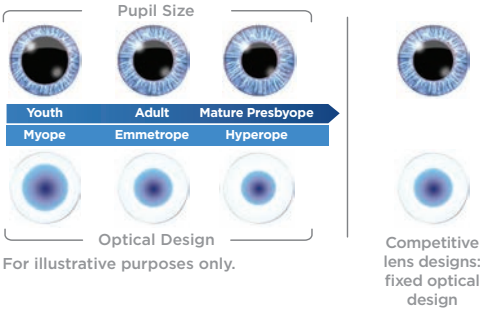
Dual Action Technology helps keep moisture in and irritation out

1-DAY ACUVUE® MOIST Brand Contact Lens Family



- **LACREON® Technology** uses a locked-in wetting agent to create a long-lasting cushion of moisture.
- **New evidence**—Etafilcon A uniquely attracts and retains more lysozyme in its natural state[1],which, along with an INFINITY EDGE™ Design and a low modulus, helps to keep irritation out. **

1-DAY ACUVUE® MOIST MULTIFOCAL



For illustrative purposes only.

Competitive lens designs: fixed optical design

- **INTUISIGHT™ Technology** is the first and only multifocal lens technology that uniquely optimizes the optical design according to age and refractive power
- **A superior vision experience**—for presbyopic patients.

1-DAY ACUVUE® MOIST for ASTIGMATISM

- **BLINK STABILIZED™ Design** harnesses the natural power of a blinking eye, delivering exceptional stability and clear vision for astigmatic patients
- **First fit success**—nearly 90% of the time[§]

for more information visit acuvueprofessional.com

The #1 prescribed daily disposable around the world now satisfies a broader range of patients—available in Sphere, Toric and Multifocal

1-DAY ACUVUE® MOIST BRAND CONTACT LENSES

82% UVA 97% UVB UV BLOCKING*†‡

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 Johnson & Johnson Vision Care, Inc. at 1-800-843-2020.

Reference: 1. Suwala M, Glasier MA, Subbaraman LN, et al. Quantity and conformation of lysozyme deposited on conventional and silicone hydrogel contact lens materials using an in vitro model. *Eye Contact Lens.* 2007;33(3):138-143.

VOL. 153 NO. 5 ■ MAY 15, 2016

IN THE NEWS

Research published in the March issue of *Ophthalmology* shows that approximately 65% of **nuclear cataract** progressions are the result of **environmental factors**. Chief among those factors appeared to be the dietary intake of vitamin C, which, the study says, protects against progression. Another 35% of progression was chalked up to genetic factors.

Johnson & Johnson announced that it will **discontinue its Unilateral Pricing Policy** (UPP) setting minimum prices for contact lenses. This move comes amid sustained pricing and legal battles that have left ODs battling discount sellers like 1-800 Contacts and Costco. The AOA publicly renewed its support of UPP and the Contact Lens Consumer Health Protection Act, introduced by Sen. Bill Cassidy (R-La), suggesting that decisive action is needed to provide stronger protections for patients against the alleged risks of discount sellers. An eye care provider's direct involvement in lens prescribing "is the best way to ensure ocular health and vision are optimally protected," said Justin Bazan, OD, of Park Slope Eye of New York. "UPP helped encourage ECPs to advance their contact lens knowledge," he said, while also helping safeguard against commoditization.

A Phase I-II proof-of-concept study of **Encore Vision's EV06 ophthalmic solution 1.5% for presbyopia** indicates it is safe and effective to use in human subjects, the company says. Patients treated with the drug, which attempts to **reverse the gradual stiffening of the crystalline lens**, displayed DCNVA improvement beginning at day 15 (p=0.017) that continued to the 90-day study completion (p=0.005).

FDA Approves CXL For Keratoconus

By Adrienne Taron, Associate Editor

Collagen crosslinking—a procedure combining ultraviolet light and a topical riboflavin photoenhancer to strengthen collagen bonds in the cornea—now comes to the US, after FDA clearance of three products from Avedro.

"This approval marks a tremendous milestone for the treatment of progressive keratoconus," said Brian Roberts, Avedro's chief operating and financial officer, in a statement. On April 18, the company's KXL System and two photoenhancers, Photrexa and Photrexa Viscous, were cleared for use.

The first studies of corneal crosslinking (CXL) in keratoconic humans date to 1998, and CXL treatment for progressive keratoconus has been available in Canada and Europe for more than 10 years. This recent FDA approval stems from Avedro's NDA submission, comprised of data from three prospective, randomized, parallel-group, open-label, placebo-controlled, 12-month trials performed to assess the safety and efficacy of Avedro's products for use in performing CXL in the eyes of patients with progressive keratoconus. The crosslinked eyes in these studies showed increasing improvements in Kmax (maximum corneal curvature) from month three to month 12. Treated patients had an average Kmax reduction of 1.4D in Study 1 and 1.7D in Study 2 at month 12, compared with average increases among untreated eyes of 0.5D in Study 1 and 0.6D in Study 2. The third study that comprised the Avedro NDA tested safety; no efficacy endpoints were included.

The most common ocular adverse reactions were corneal opacity (haze), punctate keratitis, corneal striae, corneal epithelial defect, eye pain, reduced visual acuity and blurred vision. The studies show that ulcerative keratitis can occur; Avedro advises that patients be monitored for epithelial defects.

Photo: Clark Chang, OD

Avedro's KXL System uses laser crosshairs to align its optical head with the eye in preparation for the procedure.

Calling it "a landmark event that will jump-start a new era of keratoconus management in the United States," Clark Chang, OD, of TLC Laser Eye Centers and a board member of the International Keratoconus Academy, expects CXL to make corneal transplants less common. "As CXL becomes more widely available, we could have our first generation of patients who will not routinely need keratoplasty or suffer progressive vision loss."

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

Alaskan Bill Calls for Scope Expansion

Optometrists defend action to modernize practices, allow more procedures. **By Bill Kekevian, Senior Editor**

Controversy over scope of practice legislation is spilling over into the op-ed pages of the *Alaska Dispatch News*, where dueling commentary pieces address the state's Senate Bill 55. The brouhaha became public after a radio advertisement opposing the bill hit the airwaves in February. In mid-March, an Alaska ophthalmologist published a passionate piece warning of potential complications from noninvasive procedures (such as laser peripheral iridotomy and blepharoplasty). The turf war continued with an op-ed from an OD claiming the bill simply permits optometry to "regulate its own development." While the debate plays out in the public eye, the bill itself provides a detailed explanation of what it will and will not allow.

Indeed, the bill does call for the ability to perform diagnostic and treatment procedures if so authorized by Alaska's optometric board. However, it makes explicit a ban on invasive procedures. As defined by a white paper accompanying the bill, these include: LASIK; PRK; cosmetic lid surgery; any surgery where a scalpel is used to excise abnormal tissue growth on the cornea, any procedure in which a laser is used to remove scar tissue from the cornea; any procedure in which cornea tissue is transplanted from a cadaver; any surgery where a small incision is made in the cornea and two crescent or semi-circular shaped ring segments are inserted between the layers of the cornea.

The same white paper lists procedures ODs will be allowed to perform if Senate Bill 55 passes. They include treatments that do not penetrate the globe, such as procedures where a laser is fired to: create a small hole in the iris to relieve excessive pressure; create a small hole in the membrane that holds a transplanted lens in place; treat areas of tissue at the base of the cornea responsible for draining the aqueous fluid in the eye. They also include procedures that involve: cutting malignant tumors on and around the eye and lid using a scalpel or laser; cutting off excess skin of an upper eyelid or cutting and shortening the lower eyelid using a scalpel or laser; cut the eye tear drainage system using a scalpel.

The bill also says it will expand optometry's injection authority, still prohibiting intravitreal injections but allowing ODs to inject into the front of the eye or into the tissue surrounding the eye.

The bill itself is sponsored by State Senator Cathy Giessel and was written by Jeff Gonnason, OD, a past president of the Alaska Optometric Association, according to the *Alaska Dispatch News*.

Limstrom S, SB 55 Surgery Provision. Alaska State Legislature. www.legis.state.ak.us/basis/get_documents.asp?session=29&docid=3968. March 20, 2015.

Optometry Mourns Loss of Larry Alexander

Optometric educator Larry Alexander, 68, died April 16, 2016 at his home in Venice, Fla. Born in Plainfield, Indiana, he graduated from the school of optometry at Indiana University and later served as an optometrist in the United States Navy. Dr. Alexander also practiced in Elizabeth City, NC; Louisville, KY; and Jeffersonville, IN; and taught at the University of Alabama (UAB) School of Optometry. He most recently was a consultant for Optovue as well as a successful author and lecturer.

"Dr. Larry Alexander was a quintessential educator, with the rare ability to condense complex topics and concepts into easily understandable language that inevitably resonated with clinicians. He had a passion for writing and teaching and was himself a consummate doctor, with a broad patient following. More importantly, his sincerity and unassuming style served as a magnet for friendships throughout the country," said Jimmy D. Bartlett, OD, a long-time faculty colleague at UAB. "Larry gave of himself with no expectation for return. On the dedication page for the latest edition of his classic *Primary Care of the Posterior Segment*, he quotes Drummond: 'I shall pass this way but once. Any good, therefore, that I can do, any kindness I can show any human being, let me do it now, for I shall not pass this way again.'"

Dr. Alexander is survived by his wife, Lynn Alexander; children Kari Alexander and Dan Alexander and grandchildren Kathryn and Nate.


Focus on what matters.
Marchon exceeds expectations with consistent commitment and excellence to both brands and pricing. Marchon me with quality.
– Holly Acebo
Owner
Jonesboro, Arkansas
Marchon me.
MARCHON
FOCUSED ON YOU
Marchon is a registered trademark of Marchon Eyewear Inc. Marchon.com

Canaloplasty Lowers IOP, Avoids Bleb Complications

Canaloplasty may be a suitable alternative to trabeculectomy in patients with open-angle glaucoma, reports a study in the May 2016 *Journal of Glaucoma*. Though trabeculectomy is considered by many to be the gold standard in glaucoma surgery, potential early and late-term complications can occur, including athalamia, hypotonus, choroidal detachment and bleb infection.[1] Other attempts at creating surgical alternatives have yielded techniques that do not provide sufficient intraocular pressure control and may result in other complications.

Researchers considered 218 eyes of 197 glaucoma patients who underwent canaloplasty, a non-perforating blebless technique similar to viscocanalostomy, over 42 months. Success criteria were defined as achieving postoperative IOP≤21mm, ≤18mm or ≤16mm Hg with or without medical treatment. Mean intraocular pressure was 28.4±7.5mm Hg pre-op and 15.9±4.7mm Hg at two-year follow-up. Additionally, after two years, a qualified success rate based on the post-op IOP≤21mm, ≤18mm or ≤16mm Hg success criteria was achieved in 82 (92.1%), 60 (67.4%) and 53 (59.5%) eyes, respectively. Complications included hyphema in 47 eyes (23.7%), detachment of Descemet's membrane in 11 eyes (5.5%) and 12 cases of IOP spikes > 10mm Hg (6.1%).

"One of the most advantageous characteristics of canaloplasty" is the increased safety from avoidance of a filtering bleb, the researchers noted, which reduces post-op treatments, follow-up visits and associated social health costs, they said.

Brusini P, Caramello G, Benedetti S and Tosoni C. Canaloplasty in open-angle glaucoma: mid-term results from a multicenter study. J Glaucoma. 2016 May;25(5):403-7.

Insects' Bacterial Defense May Protect Corneal Transplants

Research presented at the National Meeting & Exposition of the American Chemical Society shows coating synthetic polymers, which are being developed for use in corneal implants, in antibacterial nanopillars may help stave off infection. These pillars are small enough to impale any bacteria that lands on them, eliminating the need for biocidal coating or antibacterial drugs in the construction of poly(methyl methacrylate) based materials. The technology is inspired by similar pointed pillars that cover insect wings, according to the scientists.

In particular, investigators modeled their research on cicada and dragonfly wings. Currently, the researchers have been able to replicate nanopillars like those found on cicada wings, which protect against gram-negative bacteria, such as *E. Coli*. They hope to soon replicate the different kinds of nanopillars found on dragonfly wings, which can also kill gram-positive bacteria, such as MRSA and *Streptococcus*.

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


It's not what you look at that matters, it's what you see.
Quality products I can trust with the designs and brands my patients want. Marchon me with value.
– Brent Bair
Store Manager
Fort Wayne, Indiana
Marchon me.
MARCHON
FOCUSED ON YOU
Marchon is a registered trademark of Marchon Eyewear Inc. Marchon.com

Proactive Medicine: A Focus of Vision Expo East's CE

Lecturers encouraged optometrists to be more attuned to prevention of ocular disease and awareness of systemic health. **By Cheryl G. Murphy, OD, Contributing Editor**

Proactively examining patients for preliminary warning signs of ocular conditions was one key focus of continuing education classes at this year's Vision Expo East. By finding and diagnosing subtle warning signs of looming health conditions, we can sometimes get to the root of the problem and correct it. This may allow us to begin treatment of a patient's disease before irritating symptoms and threatening repercussions manifest.

At the Ocular Surface Disease and Wellness Symposium, Drs. Paul Karpecki, Jack Schaeffer and Marc Bloomenstein discussed how doctors should be looking for signs of dry eye during their annual checkups. This starts with the doctor asking the right questions to probe for symptoms of dryness that the patient may be experiencing, yet overlooking. A dry eye questionnaire in the waiting room can help identify dry eye symptoms and measure severity. "Four things we watch for and treat to ensure ocular surface wellness are obstruction, inflammation, tear stability and biofilm," said Dr. Karpecki at the lecture. Being able to identify which component or combination of those four resulted in dry eye helps to guide practitioners in how to treat it. A careful examination of the lids, lashes, tears and ocular surface each year is recommended and the importance of tear osmolarity testing was also emphasized.

Drs. Schaeffer, Bloomenstein and Karpecki educated attendees about early signs of dry eye as well as factors that can lead to it.

Dr. Thomas stressed the importance of color vision testing.

In Dr. Lisa Renzi-Hammond's course, "Macular Carotenoids and Cognitive and Visual Function Across the Lifespan," the importance of proper nutrition was highlighted. A healthy helping of lutein and zeaxanthin not only improves retinal health, she said; it also allows for optimal retinal functioning. Dr. Renzi-Hammond explained the link between a well-nourished retina and improved visual processing speed and reaction time. Carotenoids, such as lutein and zeaxanthin, are essential to the function of the retina, she noted, and proper supplementation of them can enhance our visual memories, executive functioning and reasoning.

Another speaker who explained how proactive testing can reveal early signs of systemic conditions was Craig Thomas, OD, who lectured on color vision in health and disease. Dr. Thomas said that acquired loss of chromatic discrimination—or dyschromatopsia—can precede more classic signs of glaucoma and can reveal visual functioning changes early in the course of diabetes. "Acquired color vision defects may precede field loss in patients with glaucoma and I have seen this in my own patients," Dr. Thomas noted, "and chromatic disturbances can also precede diabetic retinopathy in some patients."

He went on to explain that the "absence of dot-blot hemorrhages does not mean the retina isn't affected by diabetes. The retina may still have hypoxia and its function can be affected." Dr. Thomas

(Continued on p. 12)

Restasis®
(Cyclosporine Ophthalmic Emulsion) 0.05%

For patients with decreased tear production presumed to be due to ocular inflammation associated with Chronic Dry Eye

THE DRY EYE TREATMENT SHE NEEDS TODAY. BECAUSE TOMORROW MATTERS.

RESTASIS® twice a day, every day, helps patients experience increased tear production

Increased tear production was seen at 6 months.[1]

Indication and Usage

RESTASIS® (cyclosporine ophthalmic emulsion) 0.05% is indicated to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca. Increased tear production was not seen in patients currently taking topical anti-inflammatory drugs or using punctal plugs.

Important Safety Information

Contraindications

RESTASIS® is contraindicated in patients with known or suspected hypersensitivity to any of the ingredients in the formulation.

Warnings and Precautions

Potential for Eye Injury and Contamination: To avoid the potential for eye injury and contamination, individuals prescribed RESTASIS® should not touch the vial tip to their eye or other surfaces.

Use With Contact Lenses: RESTASIS® should not be administered while wearing contact lenses. If contact lenses are worn, they should be removed prior to the administration of the emulsion. Lenses may be reinserted 15 minutes following administration of RESTASIS® ophthalmic emulsion.

Adverse Reactions

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

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

Reference: 1. RESTASIS® Prescribing Information.

Allergan

APC34TC16 160898

VEE CE

(Continued from p. 10)

recommends skipping Ishihara color plates when testing an adult's color vision because they do not measure for blue-yellow defects, which are the most common type of acquired color vision defects. Instead, doctors should employ computer-assisted color vision tests such as ColorDx (Konan), which make testing accurate and scoring faster than Farnsworth D-100 testing, he stated.

Dr. Joe Rappon's course, "Smart Contact Lenses and Other Future Eye Care Technology" showed attendees how breakthrough technologies are helping us to better detect eye conditions and manage illnesses more efficiently. Dr. Rappon said, "Today, one out of every 11 people globally has diabetes" and noted that "people have better control over their diabetes when glucose can be continually monitored." Advances in technology have led to the development of Google's glucose monitoring contact lens containing "a circuit the size of a piece of glitter which allows us to measure and store data and also transmit that data to a smartphone."

Dr. Rappon explained that the future of health monitoring contact lenses is on the way as companies other than Google are developing similar biometric sensing contact lenses, such as Sensimed's Triggerfish for glaucoma patients. These advances will allow clinicians to monitor for daily fluctuations in our patient's disease course. The earlier ODs detect changes in health, the earlier they can intervene to improve overall outcomes. ■

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*

*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.

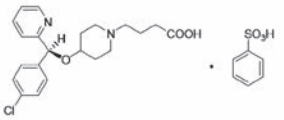
8.3 Nursing Mothers
Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 mcg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection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

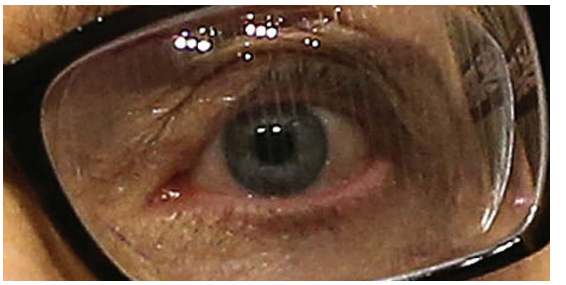
Patients should also be advised to remove contact lenses prior to instillation of BEPREVE. The preservative in BEPREVE, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of BEPREVE.

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

Contents

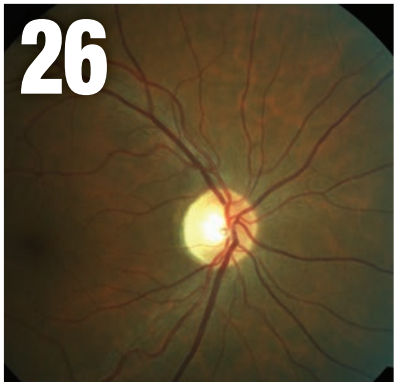
Review of Optometry May 2016

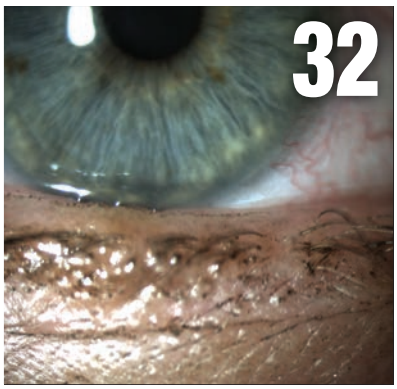
17th Annual Dry Eye Report

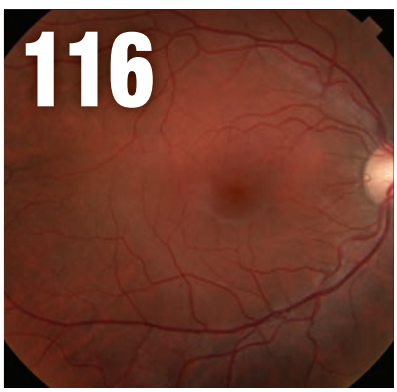


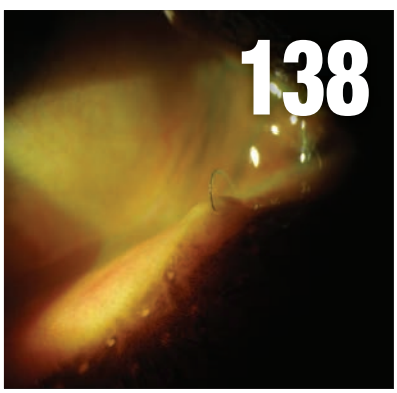
Departments

Review of Optometry May 2016









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.

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

The most comprehensive GP lens care system available.

Introducing LacriPure

Menicon's new rinsing and insertion saline solution.

Indicated for use with soft, hybrid and rigid gas permeable lenses, LacriPure is a sterile, non-preserved saline which provides an alternative to tap water rinsing.

Packaged in a 5ml unit-dose vial, LacriPure has been cleared as a scleral lens insertion solution and provides the patient with exceptional sterility.

Menicon LacriPure joins **Menicon Unique pH®** multi-purpose solution and **Menicon PROGENT** protein remover to complete the industry's most comprehensive GP lens care system.

Menicon

800-636-4266 | meniconamerica.com | information@menicon.com

Letters to the Editor

> *Many diabetic patients are not forthcoming about their blood glucose level or medication use (or non-use).*

Under Pressure? Take Their Blood Pressure

I always enjoy the *Clinical Quandaries* column and the February installment was no exception. In it, Dr. Williams gives a decent review of non-traumatic cranial nerve six palsies. She is correct in noting that 28% are caused by hypertension and 17% by diabetes. I was surprised when she did not recommend taking the patient's blood pressure and doing a stat in-office A1C, the results of which would provide potential etiology for, and immediately dictate how, the patient should be treated, allowing the eye doctor to take control of the patient. I will point out that many patients, especially those with diabetes, are not forthcoming about their blood glucose level or medication use (or non-use). The results of these two tests can potentially save the patient an unnecessary visit to the emergency department.

If both the blood pressure and blood glucose are normal, the patient should be started on an 81mg coated aspirin, one per day (with no contraindications) and followed as Dr. Miller recommends.

If the blood pressure is elevated but not in stroke territory or the A1C is high, or both, the patient can be advised to see their primary care physician on an urgent basis to get these controlled. Start treatment with an 81mg asprin, as above. If the blood pressure is elevated and in "stroke territory" (diastolic 110mm Hg or greater) the patient should be transported to the emergency department. Inform the EMTs that your patient has a right (or left) sixth nerve palsy as a result of uncontrolled hypertension to help avoid confusion in the emergency department. Do not let this patient drive himself, for obvious reasons, and follow after blood pressure is controlled.

These patients are perfect examples of how an astute clinician and two of the simplest tests in medicine can prevent CVAs, blindness and even loss of life; they will be forever grateful.

How to follow them is a story for another time.

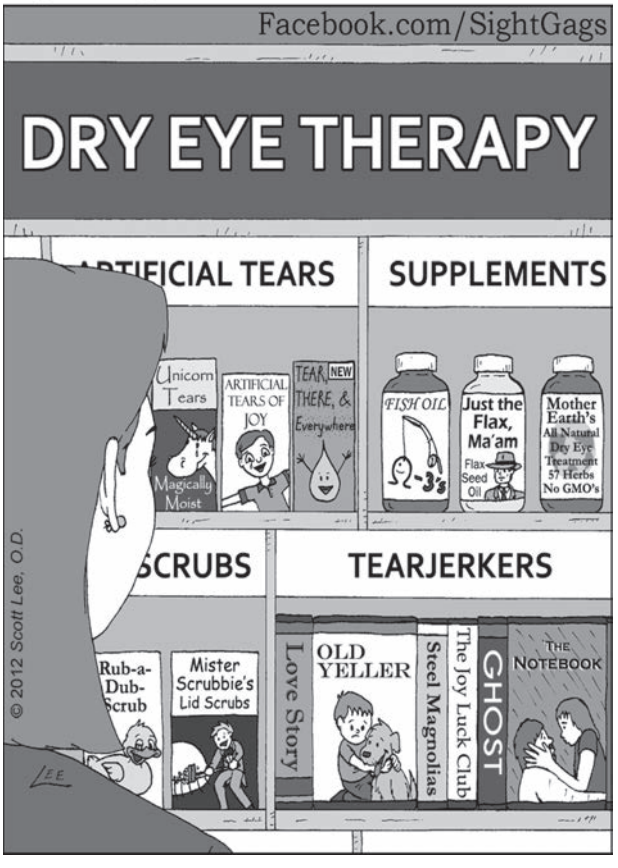
—Mark R. Flora, OD
General Eye Medicine, Disease & Injury
Atlantic Eye Associates

Comment from 'Clinical Quandaries' editor Paul Ajamian, OD:

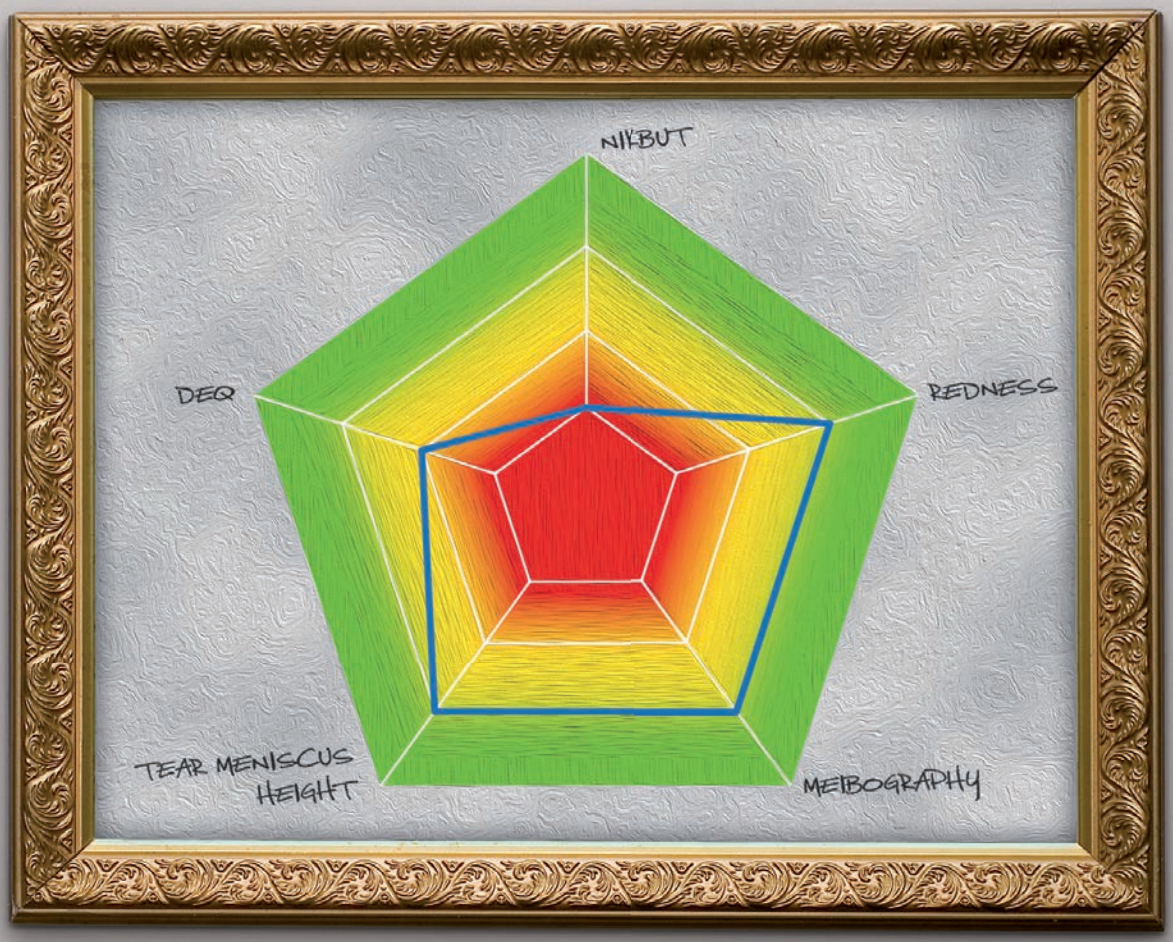
Dr. Flora,
Your detailed advice on handling these patients is very much appreciated. Often, in my experience, a presentation of double vision leads to panic and often a referral to the wrong source, either an ophthalmologist or neurologist. Our role in steering these patients to the correct medical specialist is critical. Thank you for taking the column (which serves as a brief review) a step further on a very important subject!

—Paul Ajamian, OD
Center Director, Omni Eye Services of Atlanta

Sight Gags By Scott Lee, OD



A Masterpiece of Dry Eye Diagnostics



OCULUS Keratograph® 5M with JENVIS Dry Eye Report: See all relevant dry eye information at a glance!

The JENVIS Dry Eye Report is a unique feature of the OCULUS Keratograph® 5M that summarizes all data from your dry eye workup and offers an easy-to-grasp print-out for your patient. Excel with your dry eye diagnosis, combine screening and patient education and improve the bottom line with the OCULUS JENVIS Dry Eye Report!

For more information visit www.dryeyemasterpiece.com

Toll free 888-519-5375 facebook.com/OCULUSusa
ads@oculususa.com www.oculususa.com

OCULUS®

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

The Walking DED

Millions of people have dry eye disease, and countless more are fated to get it. Are you ready?

Although it may seem paradoxical, dry eye disease is so prevalent that it often goes unnoticed. How can something be pervasive and yet invisible? Many people who experience the chronic discomfort brought on by tear film dysfunction simply assume "that's the way it is" and learn to live with it, barely realizing that they have a chance at a better quality of life. But these people suffer in silence needlessly.

They walk among us, the DED. You see plenty in your practice every day—I'll bet one's in the waiting room right now—whether or not the conversation ever happens. Some of the walking DED even edit optometry magazines and should know enough about the topic to bring it up with their own optometrists, but don't. I know of at least one person who fits the bill there.

And, of course, literally millions more cases of DED are inevitable in the coming years, given the condition's links to age-related changes and the ubiquity of digital device use in our lives, which reduces blink frequency and disrupts the tear film, exacerbating dry eye.

Fortunately, eye doctors—and the companies that make products to help them—do seem to be giving dry eye more priority in recent years. Once dismissed as either a nuisance to be brushed off or a genuine problem that lacks good long-term solutions, dry eye disease has increasingly been front and center at research labs, industry R&D departments and optometrists' offices.

Since the prevailing opinion is that meibomian gland dysfunction is the driver of most cases, we've made that component of dry eye the focus of this month's 17th Annual Dry Eye Report. Over the course of three feature articles, our contributors discuss in detail the anatomy of the meibomian glands, causes and consequences of dysfunction, better methods of clinical observation and a wide range of options for prevention and treatment.

We also welcome guest columnist Whitney Hauser, OD, to this month's "Ocular Surface Review" department. Dr. Hauser discusses the relationship between dry eye and depression (in particular, the drugs that treat it).

We hope you come away from this issue's dry eye coverage better prepared to discuss and intervene for your patients, even—perhaps especially—the ones who don't realize they have or may develop DED.

It Was 20 Years Ago Today

This issue also includes the 20th anniversary edition of the *Clinical Guide to Ophthalmic Drugs* by Randall Thomas, OD, and Ron Melton, OD, two names synonymous with clinical expertise. I worked with Drs. Melton and Thomas to put out that first supplement in 1996, when treatment of eye disease by optometrists still seemed a little radical. Now it's the norm. I think it's fair to give credit where credit is due and acknowledge the role these two educators played in moving the profession forward. Many thanks to you both. ■


Sun is on the rise
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.
Be a part of our growing team of world-class professionals.
Rise with us at SunOphthalmics.com/Careers.
Brightening the future of eye care
SUN
OPHTHALMICS
Sun Ophthalmics is a subsidiary of Sun Pharmaceutical Industries Ltd.
© 2016 Sun Ophthalmics. All rights reserved. SUN-OPH-FRA-003-1 03/2016

Super-Marketing

How to win patients and influence people. **By Montgomery Vickers, OD**

I always thought "marketing" meant picking up eggs, bread and milk every week at the supermarket. I never thought about marketing as something that would be used for attracting patients. I assumed patients would just have to call you when they inevitably had non-broccoli related concerns—although there is, I hear, an ICD-10 code for an ocular broccoli burn.

Turns out, this thing called marketing is a big deal. There are millions of books, articles and gurus dealing exclusively with marketing. There's even a science behind the placement and lighting of eggs, bread and milk in the market where you're "marketing" so these staples can best be marketed to you.

But do we optometrists need to think that way? If we are good at what we do, what does marketing mean to us anyway?

50,000,000 Velvet Elvis Fans Could Be Wrong

In the '70s, Pennsylvania College of Optometry was on the cutting edge of medically training optometrists, but we only had one measly practice management course in which the teaching doctor merely showed us slides of how he had redecorated his optometric office. It was very, uh, velvet Elvis meets samurai. This was what I learned about marketing and it took my wife 10 years to convince me not to bring in dragon lanterns and hair pomade as my marketing plan. (OK, I still use the pomade.)

When I graduated from PCO, I went back home to West Virginia and joined a 40-year-old practice. Our marketing plan was simple: everybody in St. Albans knew Dr. Bodie. After all, his folks owned the jewelry store there on Main Street.

Unfortunately, my dad was only a lawyer, so the St. Albanian/Bodie mystique never rubbed off on me. I had to come up with a way to market my practice.

Ther She Blows!

So, I spent several years doing eye screenings and giving speeches at schools and organizations. I spent countless hours in preparation so I could show everyone in town that I was "The Area's Best Eye Doctor," which we had printed on probably a thousand glasses cleaning cloths that I handed out to anyone who crossed my path.

It was a good marketing idea, marred only by the fact that the cloths actually read, "Ther [sic] Area's Best Eye Doctor," which was considered correct English only by the two guys I worked with at the grocery store when I was a teenager. Everyone else who read it figured I was a nincompoop.

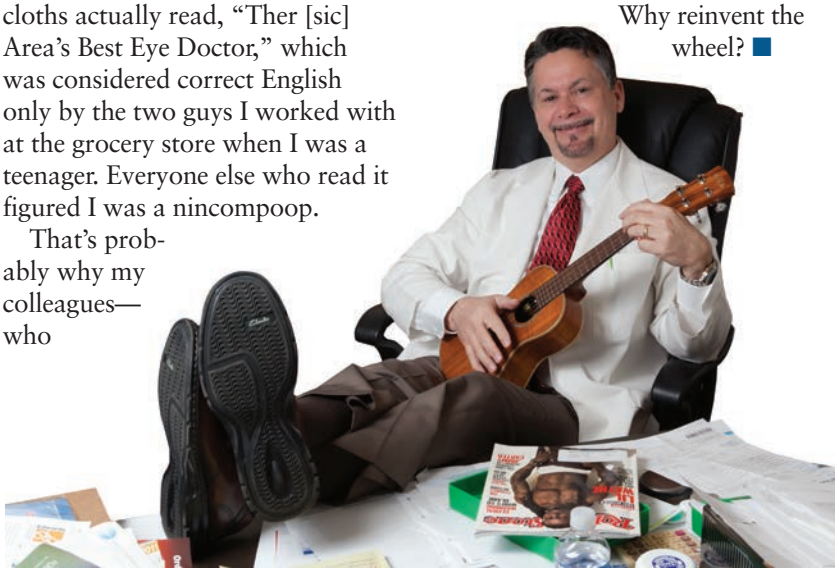
That's probably why my colleagues—who wondered how I became the area's *best*—just let my unfounded pronouncement stand without challenge. If someone asked, they could say, "Him? He can't even spell 'the!'"

Over time, my techniques grew more sophisticated. We handed out T-shirts that read, "My eye doctor loves me" and coffee mugs reading, "Our patients are special," which we had delivered to patients' workplaces so their co-workers would also want to see "ther" best around. That's right—THER—heck, I had tons of the cloths left, why throw them away?

I tried big tri-color spreads in the yellow pages, got a website and a Facebook page and was very appreciative of the 17 patients I acquired through them over the next 10 years.

Now, as an associate in a Texas practice, I am proud to say we're easily "Ther Area's Best Eye Doctors."

Why reinvent the wheel? ■



BAUSCH + LOMB

Biotrue® ONEday lenses

For patients who want to **start and end the day with more moisture** than leading daily disposables[1]

Surface Active Technology™

With its unique dehydration barrier, Biotrue® ONEday maintains **98% of its moisture for up to 16 hours[2]**

Lens Cross Section

- PVP (hydrophilic polyvinylpyrrolidone) allows for a high water lens that is **78% water—the same as the cornea.[3]**
- Poloxamer 407, a Surface Active Macromer, forms a dehydration barrier that helps Biotrue® ONEday **start and end the day with more moisture.[1]**
- Like the lipid layer, Biotrue® ONEday provides a smooth optical surface and **resists dehydration.**

Prescribe Biotrue® ONEday daily disposable contact lenses

For more information, call 1-800-828-9030, contact your Sales Representative or log on to Bausch.com/ecp

Also available for Presbyopia

REFERENCES: 1. Data on file. Bausch & Lomb Incorporated. Rochester NY; 2015. **2.** Data on file. Bausch & Lomb Incorporated. Rochester NY; 2012. **3.** Bergmanson J. Clinical Ocular Anatomy and Physiology, 14th edition, 2007.

BAUSCH + LOMB
See better. Live better.

Seeking Sarcoidosis

Neuro-ophthalmic exam yields manifestations of systemic granulomatous disease.

By Michael Trottini, OD, and Michael DelGiodice, OD

A 54-year-old white female was seen in consultation for a comprehensive ophthalmic evaluation. Her medical history was significant for breast carcinoma (in remission) and hypertension. She was currently medicated with tamoxifen, losartan potassium and aspirin. She reported no pertinent ocular history, social history or drug allergies. Her family history was remarkable for an autosomal dominant inheritance disorder characterized by migraine headache and stroke.

A month prior to her visit, a positron emission tomography (PET) scan revealed multiple lung lesions. Initially read as metastatic lung carcinoma, she was referred to a pulmonologist for pulmonary function tests (PFTs) and excisional biopsy. PFTs were unremarkable, but a bronchoscopy revealed multiple granulomas. She was subsequently sent for ophthalmic assessment.

Her best-corrected visual acuities were 20/30 and 20/40 in her right and left eyes, respectively. Ocular motility was full with no limitation and pupils were equal, round and reactive to light with no afferent defect. Confrontation fields were full to finger counting. Ocular alignment was normal with an orthophoric position in primary and lateral gazes. Additionally, she noted 7/7 color plates in each eye. Intraocular pressure measured 16mm Hg in each eye. The anterior segment was unremarkable.

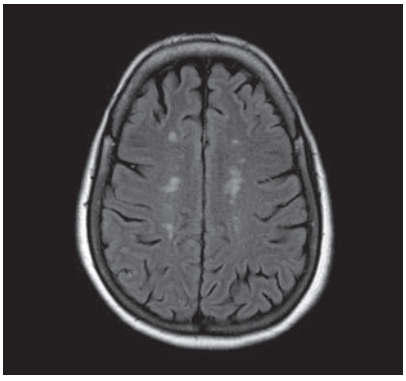


Fig. 1. FLAIR image showing periventricular white matter lesions.

Fundus exam showed healthy lenticular, vitreous, vascular and chorioretinal structures. The optic nerves showed a cup-to-disc ratio of 0.3 with minimal temporal disc pallor in both eyes.

Although she was asymptomatic, both eyes exhibited a loss of best-corrected visual acuity, which raised a red flag. Subsequently, we ordered spectral-domain optical coherence tomography (SD-OCT) and visual field testing. The SD-OCT showed mild temporal retinal nerve fiber layer (RNFL) thinning with corresponding nasal visual field defects. Additional cranial nerve testing revealed partial left facial nerve palsy. In light of her history and clinical findings, our differential diagnosis included inflammatory, demyelinating and neoplastic causes. Subsequently, we ordered magnetic resonance imaging (MRI) of the head and neck with and without contrast and fat suppression.

Intracranial imaging revealed multiple periventricular white matter (PWM) lesions. Causes of PWM lesions are extensive but most commonly include normal senescent changes, hypertension, focal cerebrovascular accidents, demyelination, migraine, vitamin B6 deficiency and infectious or inflammatory-related vasculitis, including but not limited to Lyme disease and sarcoidosis.[1] Additional imaging of the neck revealed swelling of the jugulodigastric and mediastinal lymph nodes. The etiologies of enlarged lymph nodes are numerous but most commonly include infection, neoplasm and inflammation.

In this case, the findings of lung granulomas, bilateral optic atrophy, facial nerve paresis, enlarged mediastinal lymph nodes and PWM lesions led us to a presumptive diagnosis of neuro-sarcoidosis; she was subsequently referred to a neurologist who confirmed the diagnosis.

Discussion

Sarcoidosis is a multi-organ disease resulting from increased cellular immunity of unknown etiology. Activation of T-cell and B-cell lymphocytes results in the production of granulomas and immunoglobulins. The incidence of sarcoidosis in the United States has been reported to range from 0.01 to 0.04%. It typically affects adults within the second to fourth decades of life, and is more frequently found in

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 Optometry's Meeting, Booth 519

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

blacks and females.[2] While the exact mechanism of sarcoidosis is unknown, genetic factors and infectious agents exist that increase susceptibility to developing the disease.[3]

Neuro-sarcoidosis is most often a sequela of systemic sarcoidosis. It primarily affects the meninges, intracranial blood vessels and spinal cord. While its incidence is only reported in 5% of living patients, a postmortem series discovered central nervous system (CNS) involvement in as many as 25% of cases.[4] In rare instances, neuro-sarcoidosis can present as isolated central nervous system disease. These cases are much more difficult to definitively diagnose since a biopsy may not be possible or desirable due to the anatomic location of the granuloma.

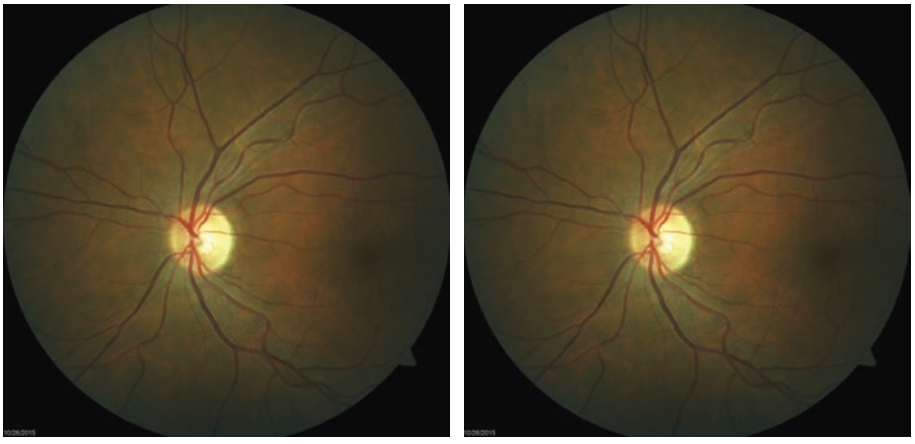


Fig. 2. Fundus images of the patient's left and right eyes, respectively, which revealed mild bitemporal optic nerve pallor.

Seventh nerve palsy is the most common focal manifestation of neuro-sarcoidosis, occurring in up to 50% of patients, by optic and vestibular nerve involvement.[5] In most cases, the clinical presentation of neuro-sarcoidosis is nonspecific, with symptoms that include weakness, paresis, paresthesia, diplopia and dysarthria. In the absence of confirmed systemic granulomas, demyelinating diseases such as multiple sclerosis (MS) and chronic inflammatory demyelinating polyneuropathy may be easily confused.

Imaging of the brain, orbits and spinal cord are invaluable in making a diagnosis of neuro-sarcoidosis since central nervous system involvement may affect the parenchyma, nerve roots, leptomeninges, dura mater, surrounding bone and optic nerve. The most typical neuroimaging finding of neuro-sarcoidosis is enhancement of the leptomeninges; however, this is only present in up to 40% of cases with central nervous system disease.[6] More commonly, neuroimaging of the brain will show nonspecific intraparenchymal abnormalities described as non-enhancing, multiple white matter lesions seen as hyperintense signals on T2-weighted imaging. Often, a diagnosis of probable neuro-sarcoidosis can be considered without confirmed biopsy in the presence of contrast enhancement of the leptomeninges and anterior visual pathway, facial nerve paresis and response to an empiric trial of high-dose corticosteroids.

Understanding Neuro-ophthalmic Sarcoidosis

Neuro-ophthalmic manifestations of sarcoidosis represent a subtype of neuro-sarcoidosis afflicting up to 15% of patients with systemic disease.[7] The most common neuro-ophthalmic findings include optic neuritis, ocular motility disorders, chiasmal involvement and lesions of the optic tract. Patients presenting with any of the above-mentioned neuro-ophthalmic signs and symptoms should initially undergo MRI of the brain and orbits with and without contrast and fat suppression.

Findings consistent with enhancement of the lacrimal gland, meninges, hypothalamus or pituitary stalk are high-risk signs of central nervous system disease. These patients should be evaluated for systemic involvement with chest radiography, serum angiotensin-converting enzyme (ACE), anergy panel, Quantiferon gold tuberculosis test (Cellestis, Australia), 24-hour urine calcium and lumbar puncture.[8] Additional testing through a whole-body gallium scan can also show uptake related to both systemic and central nervous disease but is not a primary test since it lacks specificity.

In all forms of neuro-sarcoidosis, the first line of treatment is systemic corticosteroids dosed at a range of 40mg to 80mg per day, with approximately 50% of patients showing significant improvement.[9] Alternatively, low-dose cyclosporine can be used as a safe and effective treatment in patients who are intolerant to corticosteroids.[10] Other immunomodulary therapies for neuro-

sarcoidosis include azathioprine, cyclophosphamide, chlorambucil and methotrexate.[11]

In our patient, the clinical findings of lung granulomas, facial nerve paresis and optic nerve atrophy prompted urgent MRI of the brain and orbits with and without contrast and fat suppression to discount active central nervous system involvement.

While no evidence of enhancing intracranial lesions or granulomas existed, the presence of PWM lesions in a younger patient without small vessel disease made us suspicious for intraparenchymal inflammation.

Integrating Care

Neuro-sarcoidosis is a rare disease entity, but should be suspected in patients with isolated central nervous system symptoms, including optic atrophy and facial nerve palsy as well as cases of systemic sarcoidosis that present with neuro-ophthalmic findings.

Management of the condition should include urgent neuroimaging and referral to a subspecialist trained in the sufficient management of central nervous system disease. Ophthalmic follow-up should include serial testing of the visual fields and optic nerve with both optical coherence and fundus photography.

Be sure to keep open the lines of communication between the primary eye provider, pulmonologist and neurologist. In these cases, sufficient communication between specialties is neccesary for integrated care and appropriate management of your patients condition, ensuring that they receive an optimized outcome and quality of life. ■

1. Barkhof F, Scheltens P. Imaging of white matter lesions. Cerebrovasc Dis. 2002;13(Suppl 2):21-30.
2. Newman LS, Rose CS, Maier LA. Sarcoidosis. N Engl J Med. 1997;336:1224–34.
3. Obenauf CD, Shaw HE, Sydnor CF, et al. Sarcoidosis and its ophthalmic manifestations. Am j ophthalmol. 1978;86:648-55.
4. Romero JI, Diaz-Carasco DM. Ataxia como primera manifestacion de neurosarcoidosis. Neurologia Argentina 8, 68-70. [Cross Reference]
5. Stern BJ, Krumholz A, Johns C, et al. Sarcoidosis and its neurological manifestations. Arch Neurol 1985;42:909-17.
6. Smith JK, Matheus MG, Castillo M. Imaging manifestations of neurosarcoidosis. AJR. 2004;182:289-95.
7. Jarnier D, Series C. Neurosarcoidosis. Review of the literature. Neurochirurgie. 1999;45:214-8. [Cross Reference]
8. Frohman LP, Grigorian R, Bielory L. Neuro-ophthalmic manifestations of sarcoidosis: clinical spectrum, evaluation, and management. Journal of Neuroophthalmology. 2001;21(2):132-7.
9. Delaney P. Neurologic manifestations in sarcoidosis: review of the literature, with a report of 23 cases. Ann. Intern. Med. 1977;87(3):336–45.
10. Bielory L, Frohman L. Low-dose cyclosporin therapy of granulomatous optic neuropathy and orbitopathy. Ophthalmology. 1991;98:1732-6.
11. Agbou B, Stern B, Sewell C, et al. Therapeutic considerations in patients with refractory neurosarcoidosis. Arch neurol. 1995;52:875-9.

A GAME-CHANGING APPROACH TO HELP OVERCOME CONTACT LENS DROPOUT

How point-of-care testing can grow your contact lens practice by aiding in lens selection, treatment recommendations and patient education.

By Paul Karpecki, OD, and Ian Benjamin Gaddie, OD

Contact lens dropout rates have not changed appreciably in nearly two decades. Although new materials and preservative-free products have helped, neither was the tipping point we hoped for in contact lens practice. What's more, as clinicians, we now face even greater challenges than we once did. The explosion in digital device use has placed an unprecedented burden on the ocular surface, erecting yet another hurdle to comfort. If there is one thing we have learned about contact lens dropout, it is this: We are less likely than ever to overcome it using traditional strategies. It's time to start thinking outside the box.

In our clinical experience, and in that of many of our forward-thinking colleagues, the most effective way out of what is otherwise sure to be a downward spiral is to catch as many patients as we can as they come in for their annual exams. In other words, we need to identify which patients are at risk of dropping out prior to first fittings and before refits.

In this three-part series, we will explore how osmolarity testing can be the catalyst for change that the contact lens industry has long sought. This surprisingly simple approach is both practical and profitable. In this first installment, we will make the case for how point-of-care osmolarity testing can benefit your contact lens practice. We will also explore different ways you can integrate it into your practice routine. In parts two and three, we will explain how osmolarity can help guide lens selection, setting the stage for better patient education, less dropout and a better bottom line in terms of reimbursements.

STRATEGIES FOR TESTING NEW WEARERS

While many clinicians believe that osmolarity testing is most appropriate for monitoring disease progression, an even better use of tear osmolarity testing is to determine whether a patient has dry eye disease, especially in its early stage when other dry eye signs may give conflicting information. In a recent study by the National Health Service (Great Britain, UK), osmolarity was shown to have the highest positive predictive value for dry eye disease compared to other routine dry eye diagnostic tests.[1] Furthermore, TearLab Osmolarity testing is not only the most predictive test for dry eye, it's also the fastest, requiring fewer than 30 seconds from test to result.

There are several ways to approach dry eye diagnosis at an initial lens fitting. Some practices find that the best approach is to perform osmolarity testing on every new contact lens patient using the TearLab Osmolarity System while others wait to perform osmolarity testing pending other indicators, such as a poor score on a subjective questionnaire.

If your decision to perform osmolarity testing depends on subjective symptoms or surveys, bear in mind that dry eye disease is often asymptomatic—until the ocular surface is "challenged" by a contact lens, so adopting a protocol like this requires greater clinical diligence. In fact, research suggests that relying on symptoms to diagnose dry eye would produce a missed or incorrect diagnosis more than 40% of the time.[2-4]

HOW TO APPROACH REFITS

Have 50% of your current lens wearers mentioned that they have dry eye symptoms? Probably not. Yet dry eye affects nearly 30 million

Americans—including 50% of all contact lens wearers.[5-9] The "don't ask, don't tell" strategy is not working for the contact lens industry and largely explains why about 16% of contact lens wearers drop out every year.[10-11]

A more proactive approach is clearly required. We suggest one of three options: Ask the right questions, perform diagnostic testing on all lens wearers or, better yet, do both. The following probing questions can help tease out information that will let you know whether a patient is at risk of dropping out:

- ***Do your eyes ever feel dry or uncomfortable?***
- ***Are you bothered by changes in your vision throughout the day?***
- ***Are you ever bothered by red eyes?***
- ***Do you ever use or feel the need to use drops, especially after prolonged lens wear?***

A yes to any of these is a red flag. But even if a patient reports none of these problems and is currently asymptomatic, osmolarity testing might reveal early signs of dry eye.

One of the most convenient aspects of the TearLab test is that it can be performed while wearing contact lenses. When this quick test shows that osmolarity is high, you can use this information to guide lens selection and treatment. And, since the TearLab provides an objective score—correlating well with severity—it helps encourage compliance with your recommendations. All you have to say is, "This test shows that your tear chemistry is out of normal range, which indicates that you have dry eye." Then you can detail the steps you'll take to lower the "score" and help patients understand why you recommend a certain lens option, such as a daily disposable modality, which may help with comfort. We'll discuss this in greater detail in Part 2 of this series.

SPECIAL CONSIDERATIONS FOR PRESBYOPES

Multifocal contact lens patients can be one of the greatest profit centers in an optical practice, but can also be one of the most challenging ones since this group is at particularly high risk of developing dry eye. On a case-by-case basis, success with a multifocal contact lens almost always hinges on ocular surface integrity. For this reason, we recommend that all patients who wish to be fit in a multifocal lens be tested first with the TearLab Osmolarity System.

If osmolarity reveals that there's a barrier to successful wear, we treat it first, so we have the best chance of keeping the patient happy in their lenses. The osmolarity score also aids in setting realistic expectations with a multifocal lens. When patients know that their osmolarity score is too high, they're less likely to conclude that multifocal contact lenses—or worse, your clinical skills—are to blame.

In some cases, when scores are high or there is significant disparity between the left and right eye, we may recommend shorter wearing times or simply waiting for the score to improve before moving the patient to a multifocal lens.

THERE'S NOTHING WRONG WITH DOING WHAT'S RIGHT

Whether a patient is male or female, young or old, and wearing a daily or a specialty lens, we can help maximize their contact lens success by proactively identifying and treating patients who have tear film instability—indicating a compromised ocular surface. Osmolarity testing allows us to catch early patients at risk of dry eye, fit patients in lenses that they're most likely to wear with success, and set appropriate expectations. It shows the need to address contact lens fitting from a proper and essential clinical perspective, and differentiates you from the "800 Contact Lens" competition. This, in turn, lessens the likelihood of contact lens dropout and makes for happier, more loyal patients. In fact, the beauty of this approach is that everyone wins. Patients succeed, contact lens practice flourishes and doctors enjoy doing what they do best—offering complete vision and wellness solutions.

1. Wong K, Din N, Ansari E, et al. Tear osmolarity prevalence in general NHS ophthalmic clinics and relation to clinical examination of dry eye. Poster presented at: The XXXII Congress of the ESCRS; London, UK; September 13–17, 2014.
2. Bron AJ, Tomlinson A, Foulks GN, et al. Rethinking dry eye disease: a perspective on clinical implications. Ocul Surf. 2014 Apr;12(2 Suppl):S1-31.
3. Sullivan BD, Crews LA, Messmer EM, et al. Correlations between commonly used objective signs and symptoms for the diagnosis of dry eye disease: clinical implications. Acta Ophthalmol. 2014 Mar;92(2):161-6.
4. Fuerst N, Langelier N, Massaro-Giordano M. Tear osmolarity and dry eye symptoms in diabetics. Clin Ophthalmol. 2014 Mar;8:507-15.
5. National Eye Institute. Facts about dry eye. Available at: https://www.nei.nih.gov/health/dryeye/dryeye. Accessed: January 2015.
6. Begley CG, Caffrey B, Nichols KK, et al. Responses of contact lens wearers to a dry eye survey. Optom Vis Sci. 2000;77(1):40-6.
7. Schaumberg DA, Sullivan DA, Buring JE, Dana MR. Prevalence of dry eye syndrome among US women. Am J Ophthalmol. 2003;136(2):318-326.
8. Paulsen AJ, Cruickshanks KJ, Fischer ME, et al. Dry eye in the beaver dam offspring study: prevalence, risk factors, and health-related quality of life. Am J Ophthalmol. 2014;157(4):799-806.
9. US Census Bureau. Age and sex composition: 2010. www.census.gov/prod/cen2010/briefs/c2010br 03.pdf. Published May 2011. Accessed June 19, 2015.
10. Nichols JJ. 2010 annual report on dry eye diseases. CL Spectrum. 2010;15(8):22.
11. Key JE. Development of contact lenses and their worldwide use. Eye Contact Lens. 2007;33(6 Pt 2):343-5.

OSMOLARITY EXPLAINED

As the volume of the aqueous component of the tear film declines, the salt concentration in tears increases. This brings the tear fluid out of homeostasis, and adds insult to the ocular surface. The TearLab test indicates whether or not the patient has a higher salt content than normal. Therefore, hyperosmolar status, resulting from either decreased tear production or an increased evaporative state, indicates reduced aqueous levels and is an important indicator of ocular surface health.*

**Baudouin C, Aragona P, Messmer EM, et al. Role of hyperosmolarity in the pathogenesis and management of dry eye disease: proceedings of the OCEAN group meeting. Ocul Surf. 2013 Oct;11(4):246-58.*

Mind Games

How optometrists can help dry eye patients who experience symptoms without signs.

By Whitney Hauser, OD

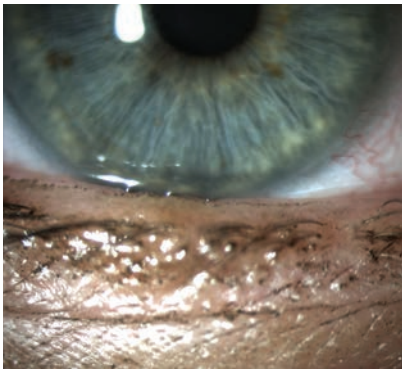
Dry eye disease (DED) can be emotionally trying for doctor and patient. While many patients' mild to moderate complaints can be managed with medications and in-office treatments, others flounder in misery. Often, their symptoms far exceed their signs, raising a "chicken or egg" type of question: Is it the dry eye devastating their lives or are changes in their lives driving the dry eye symptomatology?

Pain and Perception

It is often noted that signs and symptoms of DED do not match. Consider that dry eye syndrome may be the manifestation of a larger disease process rooted—at least in part—within the mind.

Patients' symptoms are frequently driven by ocular surface damage and chronic inflammation. However, the role of pain perception, psychosomatic features triggered by the subconscious or unconscious and overall decline in a patient's sense of well-being can't be discounted. DED is classically more associated with women, aging, hormonal changes, medications and autoimmune disease. Depression and anxiety also correlate with DED.[1,2] Stress mediators, such as cortisol and dehydroepiandrosterone (DHEA), have been identified in the tear film.[3]

Pain perception stems from a complex combination of genetic and environmental factors that can be further influenced by gender, ethnicity and personality.[4] Chronic pain can also be triggered by personality traits.[3] In a study conducted at Duke University Medical Center, more than 2,000 students answered the Minnesota Multiphasic Personality Inventory (MMPI).[4] Thirty years later, participants completed a self-reported questionnaire about chronic pain. Comparison of the MMPI and follow-up survey found correlations between MMPI in college and development of chronic pain.[4]



Tear film reduction, as seen in this rosacea patient, can be related to external stressors.

Psychosomatic conditions are bodily symptoms caused by mental or emotional disturbance. Unfortunately, some may consider psychosomatosis simply "a figment of the patient's imagination" rather than a physiological embodiment of a psychological stressor, but, in fact, psychological stress can provoke neurological suppression of lacrimal gland function.[5,6]

Further research explains that changes to the limbic system—which influences the autonomic nervous system and is responsible for motivation, emotional response, memory and social cognition—due to stressors such as anxiety, fatigue and sleep disruption can decrease basal tear secretion.[7,8]

Treat the Patient, Not Just Symptoms

Some patients present with symptoms that prove difficult to treat. A modest decrease in tear break-up time results in profound symptoms and impact to quality of life (QoL). A study of 229 subjects found tear break-up time and Schirmer's scores were lower in patients diagnosed with DED than those who had dry eye symptoms alone, but no signs. The same patients had significantly lower composite scores on the 25-item National Eye Institute Visual Functioning Questionnaire (NEI VFQ-25) with both subscale scores of ocular pain and mental health measuring lower.[9]

Failure of signs and symptoms to correlate can lead to a disconnect between the doctor and patient. If we appear dismissive of a patient's complaints, the patient will leave disheartened. Consider exploring your patients' symptoms further by using surveys designed to drill deeper into the psychological contributors to their condition. Ocular Surface Disease Index (OSDI) and Standard Patient Evaluation of Eye Dryness (SPEED) are commonly used surveys to give objective value to subjective complaints. While valuable clinically, neither offers insight into the patient's emotional status. Surveys

such as Impact of Dry Eye on Everyday Life (IDEEL), National Eye Institute's Visual Function Questionnaire (NEI VFQ-25), and The Short Form-36 (SF-36) provide information about the patient's quality of life.

• ***IDEEL.*** Comprised of 57 questions consisting of three modules: (1) dry eye symptom bother, (2) impact on daily life (routine activities, emotional status and work) and (3) treatment satisfaction (effectiveness and treatment-related bother/inconvenience).[10] The IDEEL questionnaire is a valid and comprehensive survey specifically directed at dry eye disease.

• ***NEI VFQ-25.*** A general visual function survey consisting of five nonvisual categories (general health, mental health, dependency, social function, role limitations) and seven visual categories: general vision, distance vision, peripheral vision, driving, near vision, color vision and ocular pain. The survey is particularly valuable for evaluation of vision-related QoL.[10]

• ***SF-36.*** A general health-related QoL survey that has been applied to dry eye disease. The questionnaire is comprised of 36 multipurpose questions investigating physical functioning, role limitation due to physical disability, bodily pain, general health, vitality, social functioning, emotional limitation due to emotional disability, and mental health. These items are then divided into a physical component summary score and a mental component survey score.[10] The SF-36 takes approximately 10 minutes to complete.

SSRI Use

A more expansive case history can shed light on treatment-resistant dry eye patients. While a review of systems covers psychiatric conditions, asking specific questions about history of depression and anxiety can be beneficial; DED frequently accompanies both, and increases with longer duration. Precipitating events triggering psychiatric conditions may also precede development of dry eye–related symptoms or increase the level of complaint.[11] This is especially true for older patients with longer psychiatric history and use of selective serotonin reuptake inhibitors (SSRIs).[11] Patients taking SSRIs had decreased Schirmer's testing relative to those taking serotonin-norepinephrine reuptake inhibitors regardless of duration of usage.[12]

The association of dry eye disease with autoimmune conditions is widely accepted. The etiology of autoimmune disease, like dry eye, is multifactorial and not well defined. Potential origins are rooted in genetics, environmental factors, hormone changes and immunological components. However, 50% are considered to have "unknown trigger factors."[13] Retrospective studies have identified up to 80% of patients encountering uncommon emotional stress before the development of autoimmune disease.[13] Candid conversations with patients about dramatic alterations in their lives can help pinpoint the onset of symptoms and foster communication between doctor and patient.

Sleep patterns should also be discussed with patients. Somnolence may be driven by a variety of mental illnesses, including depression. Circadian tear production maintains a heightened tear level in the morning and a subsequent decrease throughout the day. Lowest basal tear secretion is reported while sleeping. Up to 97% of patients with depression report sleep difficulties and 59% note that their QoL was adversely affected. While hypersomnia is less common, some patients can experience both hypersomnia and insomnia in the same depressive event.[14]

Giving extra attention to a patient's emotional history and the onset of dry eye symptoms can provide necessary insight into the disease process. Treatment-resistant patients often transition from practitioner to practitioner in search of a compassionate and patient doctor who will partner with them in their difficult journey. Building that bond often creates a patient for life. ■

Commonly Prescribed SSRIs in the United States

1. Cymbalta, Eli Lilly
2. Pristiq, Wyeth
3. Viibryd, Merck
4. Celexa, Allergan
5. Zoloft, Pzifer
6. Prozac, Eli Lilly
7. Trazodone
8. Lexapro, Forest Laboratories
9. Paxil, GlaxoSmithKline
10. Effexor, Wyeth

1. Kim K, Han S, Han E, et al. Association between depression and dry eye disease in an elderly population. Invest Ophthalmol Vis Sci. 2011;52(11):7954-8.
2. Li M, Gong L, Sun X, Chapin W. Anxiety and depression in patients with dry eye syndrome. Curr Eye Res. 2011;36(1):1-7.
3. Banbury L. Stress biomarkers in the tear film [dissertation]. Lismore, NSW, AU: Southern Cross University; 2009.
4. Jarrett C. Ouch! The different ways people experience pain. The Psychologist. 2011;24:416-20.
5. Applegate K, Keefe F, Siegler I, et al. Does personality at college entry predict number of reported pain conditions at mid-life? A longitudinal study. J Pain. 2005 Feb;6(2):92-7.
6. Nepp J. Psychosomatic aspects of dry eye syndrome. Ophthalmologe. 2016;113(2):111-9.
7. Rajmohan V, Mohandas E. The limbic system. Indian J Psychiatry. 2007; 49(2):132–9.
8. Murube, J, Németh J, Höh H, et al. The triple classification of dry eye for practical clinical use. Eur J Ophthalmol. 2005 Nov-Dec;15(6):660-7.
9. Le Q, Zhou X, Ge L, et al. Impact of dry eye syndrome on vision-related quality of life in a non-clinic-based general population. BMC Ophthalmology. 2012; 12(1):22.
10. Uchino M, Schaumberg D. Dry eye disease: Impact on quality of life and vision. Curr Ophthalmology Reports. 2013; 1(2):51-7.
11. Wen, W, Wu Y, Chen Y, et al. Dry eye disease in patients with depressive and anxiety disorders in Shanghai. Cornea. 2012;31(6):686-92.
12. Koçer E, Koçer A, Özsütçü M, et al. Dry eye related to commonly used new antidepressants. J Clin Psychopharmacol. 2015;35(4):411-3.
13. Stojanovich L, Marisavljevich D. Stress as a trigger of autoimmune disease. Autoimmun Rev. 2008;7(3):209-13.
14. Nutt D, Wilson S, Paterson L. Sleep disorders as core symptoms of depression. Dialogues Clin Neurosci. 2008; 10(3):329–36.

Uveitis: Go Big or Go Home

Don't be afraid to knock it out from the get-go—or it may get back up to fight another round. **Edited by Paul C. Ajamian, OD**

Q I have a patient with moderate anterior uveitis in one eye. Not only has there been no improvement after a week of Pred Forte (prednisolone acetate, Allergan) QID, but now it looks like he is developing posterior synechiae. Where do I go from here?

A Anterior uveitis can be a formidable foe. "One should not take this disease lightly," says Trennda L. Rittenbach, OD, of the Palo Alto Medical Foundation in Sunnyvale, California. Aggressive treatment is necessary, she says, to lower the risk of consequences such as trabecular meshwork damage and glaucoma, among others.

In mild cases, initial treatment with time-honored prednisolone may suffice. However, if the patient does not respond to Pred Forte, Dr. Rittenbach advises calling in the big guns. "I would switch them immediately to Durezol (difluprednate, Alcon) along with dilating agents," says Dr. Rittenbach, noting that it is uncommon for synechiae to develop if the patient is on a cycloplegic agent. "Unless the anterior uveitis is very mild, my go-to regimen is Durezol QID to Q2H and cyclopentolate 1% BID," says Dr. Rittenbach. "And, if the iritis is severe, I will add Tobradex (tobramycin/dexamethasone, Alcon) ung qHS." She notes that the steroid ointment at night will give the patient coverage for those hours they are sleeping, to avoid having them wake up in the middle of the night to instill drops.

Dr. Rittenbach says that, as a reminder, the physician needs to monitor for a steroid response at every follow-up appointment. If frequent topical dosing isn't controlling the inflammation, think about a methylprednisolone dose pack or subconjunctival steroid injection.

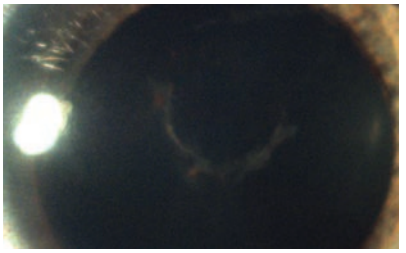
"Blast Away" Posterior Synechiae

If synechiae have developed, the best approach, according to Dr. Rittenbach, is what she calls the blasting technique. "I soak a Weck-Cel sponge in a mixture of 1% atropine and 10% phenylephrine. After giving a drop of proparacaine to the eye, I place the sponge in the inferior fornix, where it remains for about 10 to 15 minutes with the eye closed," says Dr. Rittenbach. She says that she may see some of the synechiae break that day, but more often will see the greatest results the following day. "Don't be afraid to prescribe the atropine and 10% phenylephrine for advanced cases, BID to QID; but, you should probably have these drops on hand, as most pharmacies don't carry them."

Also, remember to use caution with 10% phenylephrine in patients with any heart problems, she says, due to their rare but serious potential cardiovascular effects, reminds Dr. Rittenbach.

Systemic Work-up—Must-Do

In the past, I would do a systemic work-up for anyone with bilateral or recurrent uveitis, Dr. Rittenbach says. "Now, I have a lengthy discussion about the possible underlying causes of uveitis and offer a systemic work up to patient for the first occurrence of an anterior uveitis. I also go over the patient's medical history and ask questions about any joint or back pain and take a thorough family medical history."



This patient will require aggressive management to break their synechiae.

It is extremely important to control any underlying systemic disease that is giving rise to inflammation in the body. To investigate this, one has to order the systemic work-up. "It is also a great idea to establish a relationship with a rheumatologist to refer these patients to if necessary," says Dr. Rittenbach.

What Goes Up, Must Come Down

A patient on an aggressive steroid regimen can expect to see relief quickly. But don't be in a rush to taper once the presentation is under control. A steroid taper differs between patients, says Dr. Rittenbach. There is no set-in-stone protocol to follow. "It depends on how well an individual patient responded to the treatment and how long they have been on the steroid." Just remember—a slow taper is best to avoid a rebound; also, continue to measure the IOP at every visit. ■

Up to 20 CE Credits*

Philadelphia

REVIEW OF OPTOMETRY®
EDUCATIONAL MEETINGS OF CLINICAL EXCELLENCE

New Technologies and Treatments in Vision Care 2016

OCTOBER 7-9, 2016

Superior Education with 4 Interactive Workshops

Philadelphia Marriott Downtown

1201 Market Street | Philadelphia, PA | (215) 625-2900

Discounted room rate: $169/Standard Room

Program Chair: **Paul Karpecki, OD**

$75 OFF! REGISTER BY: AUGUST 15TH

FACULTY

Douglas Devries, OD

Kelly Malloy, OD

Robert Wooldridge, OD

REGISTER NOW!

REGISTRATION COST: $495 • THREE WAYS TO REGISTER

www.ReviewofOptometry.com/PhiladelphiaNTT2016

or Email **Lois DiDomenico: ReviewMeetings@Jobson.com** | Call: **866-658-1772**

Administered by
Review of Optometry®

cope®
*Approval pending

Partially supported by an unrestricted educational grant from
Alcon

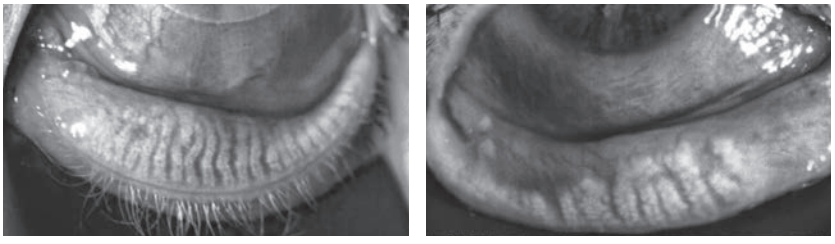
Improve Your Understanding of Meibomian Gland Function—and Dysfunction

To fully appreciate the underpinnings of dry eye, it is important to take a step back and consider both the structure and function of the meibomian glands.

By Leanna Olennikov, OD, Derek Cunningham, OD, and Walter Whitley, OD, MBA

Is it time for us to rethink our dry eye diagnostic and treatment philosophy? In the traditional approach to dry eye disease (DED), the patient's subjective symptoms determine the timing and course of management: treatment starts when the problem is brought to the practitioner's attention. Patient reports of burning, foreign body sensation and daily use of artificial tears often lead to the diagnosis after patients try numerous drops with minimal to no long-term relief. They come to us for better treatment options.

Unfortunately, the first treatment that patients are often given is another artificial tear, which may be effective for mild or episodic dry eye, but addresses none of the underlying pathophysiology. If no improvement is seen, anti-inflammatories, nutraceuticals, antibiotics and punctal occlusion are all options, depending on severity, as recommended by the International Task Force on Dysfunctional Tear Syndrome and the 2007 Dry Eye Workshop.[1,2]



Right photo: Dan Fuller, OD

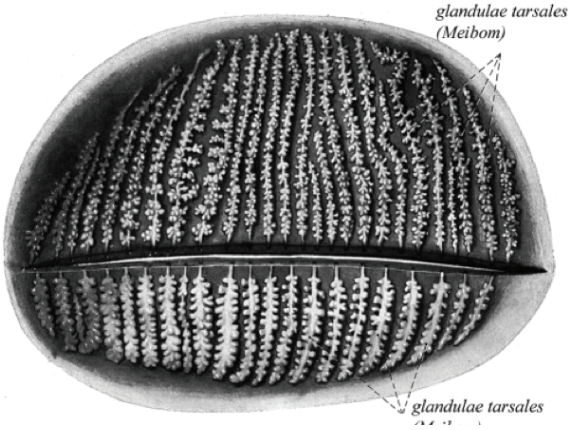
At left: Relatively healthy meibomian glands with piano-key like linear glands running the length of the eyelid. At right: Severe MG drop-out and dilation of the ductal tissues.

Though many patients can experience symptomatic improvement with this approach, the root cause of the condition may not be identified and treated. Let's take another approach to dry eye by considering the role of the meibomian glands in DED and recognizing them as the pivotal factors in its development and long-term prognosis.

According to the International Workshop on Meibomian Gland Dysfunction (MGD), the condition is a chronic, diffuse abnormality of the meibomian glands, commonly characterized by terminal duct obstruction, and qualitative and quantitative changes in the glandular secretion. Meibomian gland dysfunction may result in alterations of the tear film, symptoms of eye irritation, clinically apparent inflammation and ocular surface disease. Additionally, meibomian gland dysfunction may well be the leading cause of DED globally.[3] If this is the case, it demonstrates the importance of addressing the meibomian glands and evaluating all our patients—both the asymptomatic as well as the symptomatic. Here are two things to consider:

(1) If we can restore and optimize meibomian gland function, will our intervention halt the progression of the disease?

(2) Can we promote ocular surface wellness for all our patients? To do this, we need to evaluate every ocular surface disease patient for meibomian gland dysfunction and identify the condition at the earliest stages. The inflammatory component of DED may be the cause, or a result of meibomian gland dysfunction, and use of the appropriate anti-inflammatory therapies may be needed as adjunctive therapy.



All glands are spread vertically throughout the tarsal plates in both the superior and inferior lids.

Let's Talk Meibomian Gland Structure

Let's talk briefly about their anatomy. There are approximately 31 glands in the upper lid and approximately 26 glands in the lower lid, with the upper being roughly 5.5mm in length and the lower being near 2mm in length. All glands are spread vertically throughout the tarsal plates in both the superior and inferior lids. Anterior to the tarsal plates lies the orbicularis oculi muscle, which assists in milking the glands during a blink. Each individual gland contains 10 to 15 acini filled with secretory cells responsible for the production of the meibum, which forms the lipid layer of the tear film upon expression from the glands. The acini in every gland cluster around and empty contents into a long central duct from which the meibum is delivered. Surrounding the terminal part of every gland is Riolan's muscle. During a blink, this muscle—along with the orbicularis oculi—contracts and assists with the delivery of meibum out of the duct and onto the lid margin. This exit point can be described as an orifice.[4]

As a sebaceous gland, the meibomian gland produces meibum via holocrine secretion. The contents of the oily meibum include wax and sterol esters (comprising approximately 77%), including fatty acids, fatty alcohols and cholesterol, phospholipids (8%), and digylcerides, triglycerides and hydrocarbons (9%).[5] Meibocytes located in acini are secretory cells responsible for the production of meibum. During maturation, the meibocytes' nuclei shrink and disintegrate, forming the oily product. Meibocyte production is constant, which accounts for the continual secretion of oil.

It is important to differentiate between secretion and delivery of meibum—secretion refers to oil production and delivery refers to its expulsion out of the gland orifice. Meibum, though constantly secreted, is only delivered to the lid surface during a blink. If blockage of the orifice occurs, meibum builds up and the gland eventually atrophies.[4] Active delivery of meibum occurs in 45% of glands at any given time and decreases by 50% between the ages of 20 and 80 years, which may be due to gland atrophy.[7]

While the anatomy of the meibomian glands and the eyelids contains much greater complexity than described here, the importance of evaluating the meibomian gland structure cannot be emphasized enough. Make sure to assess the dry eye patient or suspect for these two structural deficits of the meibomian glands: (1) gland dropout and (2) duct dilatation. Both findings indicate chronic meibomian gland dysfunction and reduced gland function, and can be staged by severity scale. Several commercially available products can assess the structure of the meibomian glands.

What's the Function?

By understanding the structure of the meibomian glands, both doctors and patients are better able to distinguish normal vs. abnormal gland function. As we know, the meibomian glands secrete the meibum responsible for the formation of the tear film's outer layer. The meibum aids in reducing the evaporation of tears from the front surface of the eye, increasing the surface tension and forming an optically superior tear meniscus.

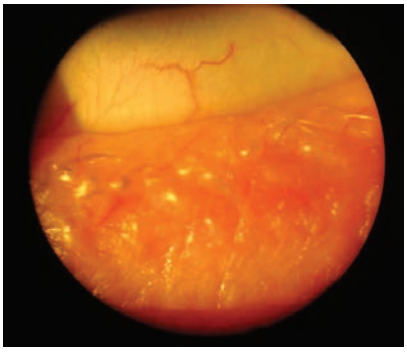
The historical idea of three distinct and independent layers of the tear film—the mucin, aqueous and lipid layers—is not quite accurate. More likely, each of the three layers interacts and blends heavily with each other. The proper proportion of each of these three layers is likely as important to ocular surface disease as a deficiency in just one. Disrupting the balance of any of these layers will lead to a dysfunctional tear film, which is not able to protect and nourish

the surrounding tissues properly, resulting in inflammation of the ocular surface.

Any impact on the function of the meibomian glands initiates a domino effect of dysfunction that ultimately contributes to dry eye signs and symptoms. Hyperkeratinization—the leading cause of MGD—in turn causes obstruction of the gland orifice, resulting in meibum build-up and subsequent dilatation of the gland, loss of secretory meibocytes resulting in acini and gland atrophy, and decreased meibum secretion.[4] Multiple etiologies may be at the root of hyperkeratinization: aging, hormonal changes, medication and chemical toxic effects, products of meibomian lipid breakdown and external factors such as epinephrine eye drops and contact lens wear are all potential culprits.[4] These factors, in addition to blink inhibition, contribute to an increase in evaporative stress that leads to hyperkeratinization and meibomian gland dysfunction.[8]

Here are some of the potential hyperkeratinization and meibomian gland dysfunction drivers:

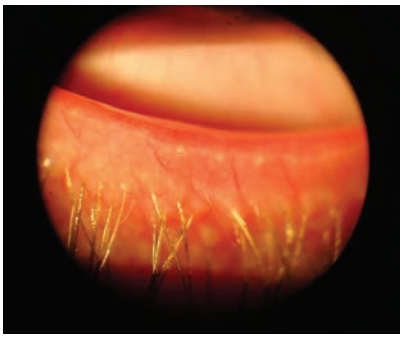
• ***Omega-3 fatty acids.*** Some have theorized that a component of meibomian gland dysfunction is related to decreased lipid levels in the meibum. However, a study evaluating the benefit of dietary omega-3 fatty acid (FA) supplementation on dry eye signs and symptoms in patients with meibomian gland dysfunction found no increased omega-3 levels in the meibum after a year of daily supplementation with approximately 3.5g of omega-3s.[5] This is not to say that no benefit to omega-3 FA supplementation exists. However, the benefit of supplementation lies in the reduction of inflammation, not in reducing an omega-3 deficit within the meibum.[5]



Lid notching from drop out.

• ***Sex steroids.*** It is evident that the sex steroids—androgens, estrogens and progestanes—influence the function of sebaceous glands (which include the meibomian glands) throughout the body. Androgens increase lipid production in the meibomian glands and decrease genetic activity responsible for hyperkeratinization. Estrogens, on the other hand, decrease the activity of sebaceous glands. In meibomian glands specifically, this decrease in activity is seen with lipid and fatty acid catabolism and suppression of lipid production genes. The effect of progestanes on meibomian gland function is unclear. Research suggests that progestanes in females are analogous to testosterone in males with respect to its effect on meibomian gland function. Overall, the consensus is that sex steroids affect the meibomian glands, which can explain the sex-dependent symptomatic differences in patients, as well as provide an explanation for the fact that certain disease states create a greater number of dry eye signs and symptoms.[4,5]

• ***Glaucoma considerations.*** Many studies have looked at the correlation between glaucoma medication usage and meibomian gland dysfunction. Most glaucoma drops contain the preservative benzalkonium chloride (BAK). Due to the chronic nature of glaucoma, patients are expected to be on drops long term. Research shows an increase in epithelial holes, a loss of peripheral microvilli and corneal surface cells wrinkling following administration of BAK. According to researchers, BAK also lowers goblet cell density in the conjunctival epithelium.[9] All of this sets the stage for a chronic, subclinical, inflammatory environment, which contributes to meibomian gland dysfunction.

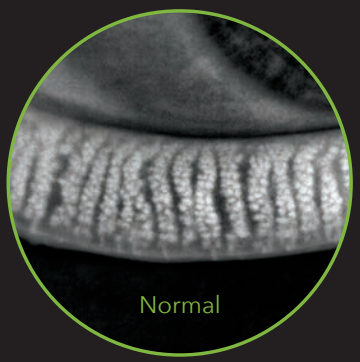


Capped meibomian gland orfices.

• ***Bacteria and lid flora.*** A study that evaluated bacteria cultured from eyelids found that these organisms are able to break down healthy meibum, releasing free fatty acids, which irritate the epithelium, triggering an inflammatory cascade. Research shows patients with blepharitis have increased levels of phospholipase A2, an enzyme that catalyzes phospholipids, leading to production of inflammatory mediators such as prostaglandin and leukotriene.[10] This secondarily contributes to hyperkeratinization of the meibomian glands as well as changes in the lipid profile of the meibum.[11] Although a certain amount of bacteria present on the eyelids is normal, overgrowth may lead to hyperkeratinization and change in the meibum lipid profile.

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.*

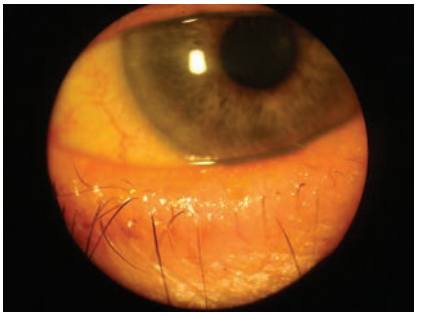
* 31 peer reviewed reports, including 5 large multi-centered, randomized, controlled studies.

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

• ***Contact lens wear.*** Contact lenses have been found to contribute to obstructive meibomian gland dysfunction and symptoms of dry eye disease. The exact pathophysiology behind it remains unknown. Researchers have found contact lens patients in their 30s with gland dropout equal to that of a normal population in their 80s; the finding is independent of contact lens type.[12]

• ***Aging.*** Changes associated with aging are not excluded from a role in the pathophysiology of meibomian gland dysfunction. Research has found acinar atrophy in human meibomian glands without gland distention, which implies a primary cause of secondary atrophy not related to meibum build-up.[13,14] These changes may in fact happen due to aging as it occurs throughout other organs in the body, leading to decreased meibomian gland secretion and increased symptoms of dryness.

• ***Digital devices.*** With the ubiquity of computers, tablets and smart phones, the latest addition to the pathophysiology behind meibomian gland dysfunction is what was once called "computer vision syndrome." The main culprit: decreased blink rate. On average, a person blinks around 15 times per minute. Studies show that during computer use, the blink rate decreases by 60% to about 4.5 blinks per minute.[15] As discussed earlier, the action of blinking releases the meibum from the meibomian gland, delivering it to the lid margin. With less frequent blinking, meibum build-up creates similar long-term issues with acinar and meibomian gland atrophy.[15,16]



Eyelid thickening and lash loss.

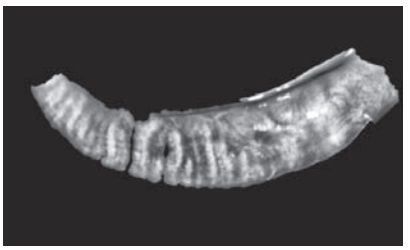
• ***Demodex folliculorum and Demodex brevis.*** *Demodex* colonization of the lid margin can contribute to MGD. *D. folliculorum* live in the lash follicles where they attach to the eyelashes, consume epithelial cells and contribute to lash misdirection and loss. They also cause microabrasions with their claws, triggering epithelial hyperplasia and hyperkeratinization, which accounts for the classic appearance of the collaratte around the eyelash base.

D. brevis live deep within meibomian glands, obstructing the orifice and creating an environment where meibum builds up, creating similar secondary effects as in that lead to meibomian gland dysfunction.

Demodex also act as a vector for bacteria such *Staphylococci* and *Streptococci*, which can trigger an additional inflammatory cascade.[17]

When assessing meibomian gland function, it is important to consider the elements that can contribute MGD, given its nature as progressive condition, and manage them accordingly. Any risk factors that increase evaporative stress and loss of meibomian gland function can lead to the sequelae of dry eye, including inflammation, pain and blurred vision along with the functional and anatomical changes.

Tests that evaluate MG function include the meibomian gland expression, lipid layer thickness (LLT) and, indirectly, tear film break up time (TBUT). During MG expression, the number of functional glands is measured on the lower lid margin, and the type of MG secretions—from liquid oil to granular secretions, to no secreting glands—is also measured. The lipid layer thickness can be measured with in-office interferometry (available on the Lipiview II) with thinner scores indicating an increased the risk of having meibomian gland dysfunction. Tear film break up time can easily be performed to assess for evaporative dry eye.



Meibography of advanced meibomian gland atrophy seen by the lack of the white, column-like glands nasally and the truncation of many temporally.

Conclusions

Meibomian gland dysfunction is one of the hottest topics in eye care today. Having a firm understanding of the role of meibomian gland structure and function is crucial to adequately addressing the all-too-common condition we call dry eye. If we look at the key words in the definition of meibomian gland dysfunction, the terms *terminal duct obstruction* and *changes in glandular secretion* are notable signs of dysfunction. By understanding the proper function of the meibomian gland, we can address, improve and promote a healthy ocular surface, ultimately improving the lives of our patients, who are often desperate for our help.

Is it time for us to rethink our

dry eye diagnostic and treatment philosophy? The answer may very well be yes. By looking specifically at the function of the meibomian gland, we no longer have to rely on the patients' subjective symptoms to determine both the time at which intervention can begin, and the course of management.

With increased attention to the meibomian glands, the root cause of DED can be identified and treated, leaving your patients with the quality of ocular health—and life—that they deserve. ■

Dr. Olennikov is a recent graduate of Pacific University's College of Optometry and an optometric resident at Virginia Eye Consultants in Norfolk, Virginia. After residency, she will be joining Virginia Eye Consultants with a focus on vitreoretinal disease, peri-operative care and clinical research.

Dr. Cunningham is the Director of Optometry at Dell Laser Consultants in Austin, Tx.

Dr. Whitley is the Director of Optometric Services at Virginia Eye Consultants in Norfolk, Va.

1. Behrens A, Doyle JJ, Stern L, et al. The Dysfunctional Tear Syndrome Study Group. Dysfunctional Tear Syndrome: A Delphi Approach to Treatment Recommendations. Cornea. 2006 Sep;25(8):900-7.
2. Management and Therapy of Dry Eye Disease: Report of the Management and Therapy Subcommittee of the International Dry Eye WorkShop. Geerling G, Pflugfelder S, Kinoshita S, et al. Ocular Surface. 2007 Apr;5(2)163-78.
3. Nichols KK, Foulks GN, Bron AJ et al. The international workshop on meibomian gland dysfunction: executive summary. Invest Ophthalmol Vis Sci. 2011;52(4):1922-9.
4. Knop E, Knop, N, Millar T, et al. The International Workshop on Meibomian Gland Dysfunction: Report of the Subcommittee on Anatomy, Physiology, and Pathophysiology of the Meibomian Gland. Invest Ophthalmology & Vis Sci. 2011. 52(4);1938–78.
5. Sullivan D. Androgen Influence On The Meibomian Gland. Investigative Ophthalmology & Visual Science. 2000;41(12):3732-42.
6. Macsai M. The role of omega-3 dietary supplementation in blepharitis and meibomian gland dysfunction (An AOS Thesis). Transactions of the American Ophthalmological Society 2008;106:336.
7. Norn M. Expressibility of meibomian secretion: relation to age, lipid precorneal film, scales, foam, hair and pigmentation. Acta Ophthalmol (Copenh). 1987;65(2):137–42.
8. Suhalim, J, Parfitt, G, Xie, Y, et. al. Evaporative stress affects meibomian gland function. The Ocular Surface. 2014;12:59-68.
9. Whitson J, Varner D, Netland P. Glaucoma drugs and the ocular surface. Review Of Ophthalmology. 2006. Web. 4 Apr. 2016. www.reviewofophthalmology.com/content/d/features/i/1299/c/25020/#sthash.QNTclbRD.dpuf.
10. Meyer MC, Rastogi P, Beckett CS. et al. Phospholipase A2 inhibitors as potential anti-inflammatory agents. Current Pharmaceutical Design, 2005;11(10):1301-12.
11. Dougherty JM, McCulley JP. Bacterial lipases and chronic blepharitis. Invest Ophthalmol Vis Sci. 1986;27(4):486-91.
12. Arita R, Itoh K, Inoue K, et al. Contact lens wear is associated with decrease of meibomian glands. Ophthalmology. 2009;116(3):379–84.
13. Obata H. Anatomy and histopathology of human meibomian gland. Cornea. 2002; 21(Suppl. 2):S70–4.
14. Obata H, Horiuchi H, Miyata K, et al. Histopathological study of the meibomian glands in 72 autopsy cases (in Japanese). Nippon Ganka Gakkai Zasshi. 1994;98(8):765–71.
15. Abelson, Mark. Review Of Ophthalmology. It's time to think about the blink. www.reviewofophthalmology.com/content/d/therapeutic_topics/c/28665.
16. Wu, Huping et al. Meibomian gland dysfunction determines the severity of the dry eye conditions in visual display terminal workers". PLoS ONE 9.8 (2014): e105575. Web. 4 Apr. 2016.
17. Liu J, Sheha, H, Tseng SCG. Pathogenic role of Demodex mites in blepharitis. Curr Opin Allergy and Clin Immunol. 2010;10(5);505-10.

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

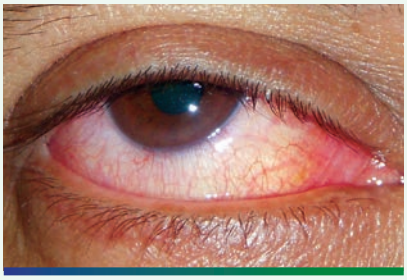


Figure 1 Allergic conjunctivitis.
(Image courtesy of Randall K. Thomas, OD, MPH, and Ron Melton, OD.)

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]

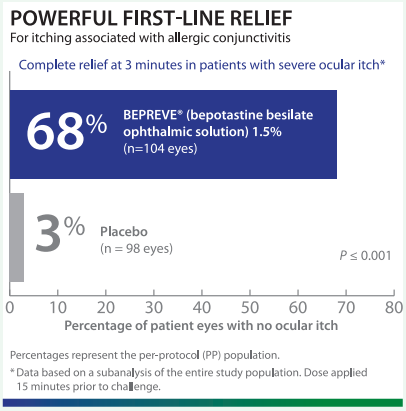


Figure 2 First-line relief. *(Meier reference 12.)*

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*

*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.

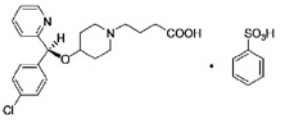
8.3 Nursing Mothers
Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 mcg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection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

A BETTER MEIBOMIAN GLAND WORK-UP: SEE WHAT YOU'VE BEEN MISSING

Develop a protocol for assessing the lids and related structures. **By Dan Fuller, OD**

The past decade has brought eye care practitioners a plethora of new research on dry eye, meibomian gland dysfunction (MGD) and contact lens discomfort. The proliferation of research into these areas is driven by the pervasive nature of ocular surface disease (OSD). The complex and often overlapping nature of the multifactorial conditions that cause dry eye has given rise to a multitude of involved organizational flowcharts, diagnostic tests and treatment paradigms.[1-3]

This article aims to make sense of the available knowledge concerning MGD and the related diagnostic technologies available.[4]

A brief review of the research, clinically available devices and emerging technologies is presented to deepen our understanding.

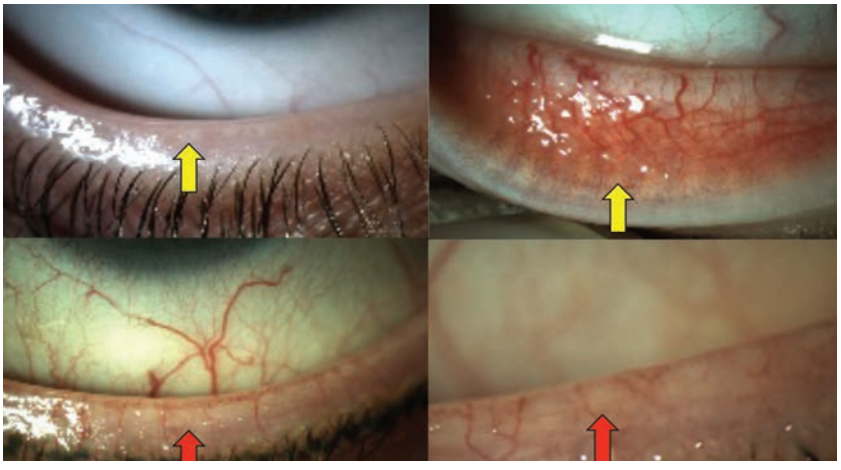


Fig. 1. Normal lower lid appearance, indicating well-defined meibomian gland orifices (top left) and ductal elements (top right) highlighted with yellow arrows. Contrast the normal appearance of the lids above with the telangiectasia, posterior dragging and loss of anatomical detail in the lower images (red arrows) in obstructive MGD.

Understanding the Elements

Dry eye disease (DED) is one type of OSD and has been broadly classified into two categories: aqueous-deficient and evaporative.[5] MGD largely contributes to the latter, although it is possible to see patients with mixed presentations.[6]

Researchers suggest that MGD may be the leading cause of DED throughout the world.[7] Due to considerable variation in diagnostic criteria and methodological differences in various studies, its exact prevalence has not yet been clearly established.[8]

Classification

A simple classification system has been devised for MGD based on whether or not the glands under- or over-produce meibum of varying quality. These states have been termed "low delivery"—if the patient has an undersecretion of meibum, either with or without obstruction—or "high delivery"—

Table 1. Obstructive Disease Types	
Condition	**Gauging the likelihood of a clinical encounter**
Trachoma	A common cause of cicatricial changes in underdeveloped countries but rare in the United States, with some isolated occurrences in native American populations. One study suggests 22.4% of patients with scarring will have dry eye complaints.[55]
Ocular cicatricial pemphigoid (OCTT)	OCTT occurs at a rate of 1/12,000 to 1/60,000.[17,56]
Erythema multiforme (EM)	Incidence per year is less than 1%; 70% of recurrent EM cases have herpes simplex.[17,57,58]
Acne rosacea	Up to 50% of rosacea patients may have MGD.[59,60]
Atopic dermatitis	Prevalence in adults 10.2%.[39]
Psoriasis	Psoriatic are at risk for obstructive MGD.[40]
Seborrhea	Up to 46% of patients with MGD may have seborrhea.[18,60]

an oversecretion of meibum.[7,9] The end result of either gives rise to a cascade of tear film alteration, irritation, inflammation and OSD we see manifested clinically as dry eye.[7]

Anatomy and Pathophysiology

Approximately 30 meibomian glands can be found in the upper lid and 25 in the lower lid, with a correspondingly higher volume of acinar tissue in the upper lid.[10-12] These sebaceous glands produce the lipids and proteins that are secreted at the lid margin just posterior to the cilia and anterior to the mucocutaneous junction under the control of complex neuromuscular and hormonal interactions (*Figure 1*).[13]

Low delivery states may arise from reduced secretion with or without gland obstruction—the former being more common.[9,14,15] Obstruction of the ducts occurs as tissues undergo keratinization and may or may not involve cicatricial changes which can be differentiated clinically by noting whether the orifices remain in their normal anatomical positions or are displaced posteriorly toward the mucocutaneous junction (*Figure 1*).[4,16] The causes for non-obstructive states have not been well established.[9] Etiological factors observed in cicatricial obstructive disease include infectious (trachoma), autoimmune (ocular pemphigoid), immune (erythema multiforme) and hypersensitivity (atopy) conditions.[17] Non-cicatricial obstructive disease is more commonly associated with inflammatory conditions such as seborrheic or psoriatic dermatoses, atopy and acne rosacea (*Table 1*).[17]

High delivery states represent an excessive release of meibum and have also been associated with acne rosacea, atopy and seborrheic dermatitis, but without signs of obstruction.[18]

Evaluating the Problem

Understanding the organizational schema, cascade of subsequent events and anatomy and pathophysiology, which gives rise to MGD, is the starting point for the work-up. This framework allows clinicians—and industry—to develop tools for its systematic diagnosis and management.

Diagnostic approach—A comprehensive evaluation of the meibomian glands includes a balanced assessment of both the structure and function (*Table 2*).

Your approach should exclude causes of aqueous deficient dry eye (ADDE) prior to arriving at a diagnosis of evaporative dry eye secondary to MGD. You should first perform testing techniques that are noninvasive to avoid distorting your observations. Invasive techiques that manipulate the lids may express meibum and alter the test results. Many of the tests are indirect measures of function. Signs may correlate poorly with symptoms, and correlations between different tests—and repeatability for the same test—may vary.[20-26]

Biomicroscopy and expression—Begin your assessment of the meibomian gland with a careful slit lamp evaluation, looking for telangiectasia, hyperemia, capping and anatomical distortions (*Figure 1*). Assess any tear film debris before attempting to express the glands or performing invasive tests. Gland expression can be done digitally, with cotton tip applicators or with one of a number of devices. The goal is to milk the meibum out of the glands from their point of origin towards the orifices. The control that the clinican is able to exert and the efficacy and discomfort a patient experiences will vary somewhat with each device. The meibum should be clear and flow easily rather than be turbid or paste-like.

Varying scales have been proposed to assess the number of glands expressed and the quality of the secretions in a research environment.[27,28,29] One scale with potential clinical use suggests an approach based on the number of glands which can be expressed on the lower lid in a descending manner:

- 4 (or more)=normal,
- 3=mildly reduced,
- 2=moderately reduced,
- 1 (or less)=severely reduced.[27]

Table 2. Assessing Meibomian Gland Function and Structure

Technique	Purpose	Interpretation
Schirmer and tear film break up time[20,25,62,63]	Exclude causes of aqueous deficient dry eye disease (tear production/evaporation).	Decreased wetting (<5mm in five minutes) and tear film instability (<10 seconds).
Biomicroscopy with expression[27,64]	Identify signs of cicatricial and inflammatory changes, which may lead to either obstructive or non-obstructive dysfunction.	Notching, telangiectasia, hyperemia, capping, turbid or paste-like secretions or an absence of secretions.
Stains and dyes (fluorescein, lissamine green, rose begal)[5,20,65,66]	May be used to assess tear film break up times; apoptosis, dead or devitalized cells and areas where the tight junctions between epithelial cells may be diminished.	Rapid break-up times; punctate, patchy or regional staining of the cornea especially inferiorly or bulbar conjunctiva; staining of the lid-wiper region.
Lipid layer interferometry[39,31,34]	Helps determine if the lipid layer in the tear film is sufficiently thick to avoid evaporation and instability.	A reduced thickness has been correlated with MGD.
Osmolarity[1,67,68]	Nonspecific clinical measure of tear film osmolarity. Research devices are more accurate.	Any decrease in meibum or aqueous secretion contributes to increases in osmolarity.
Meibometry[69,70]	A research technique used to assess basal meibum levels.	Photometric assessments of interaction between the meibum and a reactive substrate on a tape provide insight, but the test is influenced by many factors.
Transillumination[36,71]	Allows visualization of gland and ductal morphology by applying a transilluminator to the epidermal side of an everted lid.	Atrophy, "drop-out," shortening in ductal length, dilation of glands or ducts, and tortuosity may indicate MGD.
Infrared (IR) imaging[35-72]	Enhances the contrast of the image obtained from transillumination or noncontact tests.	Same as transillumination.
Laser confocal microscopy[49,73]	Provides a higher resolution image at a microscopic level than available from IR tests.	Similar to transillumination and IR imaging but also allows detection of inflammatory cells and fibrosis.
Optical coherence tomography[43,54,74]	Allows 2D and 3D assessments of MG volume.	The implication is that a decreased MG volume is a sign of MGD.

Interferometry—This test provides insights into lipid layer thickness, stability of the tear film, proving useful in assessing the contribution of the meibomian glands to DED.[30-31] The only commercially available device within the United States is the LipiView II unit (TearScience). Absolute cut-off values have not been clearly established and may vary over time or be influenced by inadvertent expression of the meibomian glands or blinking.[32,33] However, they are likely in the range from a low of 54nm in Asians to 75nm in a cross section of a clinic population.[33,34]

Transillumination and meibography—Transillumination (meiboscopy) and meibography may be performed in a variety of ways (*Table 2*), using contact or noncontact devices. Regardless of the method, the interpretations are similar. Evaluate the number and morphology of the glands from their point of origin through to the ductal termination at the orifices. As previously noted, anticipate 30 in the upper and 25 in the lower lid.[11-13] Ducts should not be attenuated and atrophied (as indicated by "drop-out") or dilated, which would suggest obstruction with keratinized cells and meibum.[4,16,35-37]

Transillumination (meiboscopy) may be performed easily in office without the need of more expensive or sophisticated devices.[38] After darkening the exam room, evert the lids (upper and lower in sequence), position your transilluminator against the cutaneous side of the lids and make observations from the palpebral conjunctival side using the white light source.[38,39] Note areas where the normal ductal anatomy is absent, tortuous or attenuated as well as areas of drop-out. The shortcomings of this method include a limited field of view, low contrast between structures limiting visualization of details and some discomfort for the patient (*Figure 2*).

Meibography differs from meiboscopy by using photo or video documentation, or both, of examiner views applying either white or infrared light to increase the contrast of the anatomical detail.[39,40] The Lipiview II unit makes use of both reflected infrared light (dynamic reflected illumination) and transilluminated (adaptive high-definition transillumination) images.[41] There is contact made between the transilluminator and the lids. Another device is the Keratograph 5M (Oculus, Wetzlar, GE).[42]

Coding Connection

By John Rumpakis, OD, MBA, Clinical Coding Editor

MGD: The Epidemic that Gets no Love

Despite its high prevalence, clinicians may neglect its impact on quality of life during patient assessment—and coding ambiguities don't help matters.

Epidemic: "An outbreak or unusually high occurrence of a disease or illness in a population or area."

With an incidence and prevalence rate often stated in the 70% to 80% range, meibomian gland dysfunction (MGD) would certainly qualify to be of epidemic proportions in the United States today. But why does it get so little bandwidth from clinicians in practice?

At its core, MGD certainly reduces quality of life for those afflicted, as it exacerbates the symptoms of dry eye: decreasing comfort with contact lens wear, increasing contact lens drop-out rate, increasing end of day irritation for those who spend the majority of the day staring at a screen of some sort and increasing the level of symptom severity in those who also have ocular allergies. I will leave the clinical aspects of the disease to my clinical colleagues, but needed to state these basics to emphasize that MGD is walking into your practice 10, 15, 20 times a day—and it is not getting addressed.

MGD vs. ICD

Caring for your MGD patient adds adjunctive service that you will be providing to your dry eye patients. There are a number of treatment protocols you will want to familiarize yourself with, but from a coding perspective there are just few rules of which we want to be aware. First, it is common to hear terms such as *anterior blepharitis*, *posterior blepharitis* and *MGD* on a daily basis in clinical discourse with our patients and peers; however, none of those terms actually exist in ICD-10 terminology—thus, the first mistake that most clinicians make is in the diagnostic labeling of MGD. Since MGD doesn't have its own ICD-10 code, there are a number of ICD-10 codes being used—mostly incorrectly. The most appropriate diagnosis is Unspecified Blepharitis, H01.001 – H01.009 (remember it is lid specific, so it is likely that you will code 4 ICD-10 codes on a claim).

As far as documentation goes, if you are visualizing and capturing an image of the meibomian glands, then 92285 (external ocular photography with interpretation and report) would be the appropriate code to use. Keep in mind that it is a bilateral code by definition, which must be appropriately reduced with modifiers if you are only performing on a single eye.

Of course there is a wide range of available treatments—some have a specific code, while others are nothing more than an office visit. In the case of the LipiFlow (TearScience), you would use HCPCS Level III code 0207T, defined as "Evacuation of meibomian glands, automated, using heat and intermittent pressure, unilateral." In most cases, an HCPCS Category III code is payable by the patient, even though often you will have to submit the claim to the insurer with a zero balance so they can track utilization.

Please note that this code does not cover probing or manual expression of the meibomian glands. To properly code manual expression of the meibomian glands or debriding the lids with something like the BlephEx (Rysurg), the CPT code 92499 (unlisted ophthalmic procedure) should be used to describe this procedure as there is not a more specific code provided by the CPT. If you are submitting this to a carrier, be aware that unlisted procedure codes generally invite additional scrutiny. Whether you are charging the patient directly or submitting to a carrier, your fee should be consistent to all patients irrespective of their coverage status.

When billing an office visit for assessment of the condition or performing an in-office treatment for lid hygiene, generally a 920X2 (if you meet the definition) or an appropriate 992XX code which represents the level of history, physical exam and medical decision making actually performed will fit the bill, so to speak. In most cases, it would be a 99201 or 99212 because of the limited nature of the presenting problem.

MGD is an extremely prevalent issue that affects the quality of life of many people. It is our responsibility to properly diagnose and treat these patients and avoid falling into the rut of "routine eye care." Management of this chronic condition can transform patients' lives and enhance your practice. Now *that* is a combination worth pursuing. ■

Its Meibo-Scan software analyzes the reflected image from an 840nm diode source to provide a high contrast image of the everted lids.[42] This is a non-contact device (*Figure 3*). The Lipiview II unit is part of a dedicated dry eye diagnosis and treatment platform whereas the Keratograph 5M has multiple configurations, which include dry eye reports, tear film scans, meibomian gland scans, topography, pupilometry, imaging and oxygen transmissibility mapping through a soft contact lens.

Both of these devices are convenient, easy to use and comfortable for the patient.

Multiple grading systems are currently competing for prominence in analyzing meibography images.[43,44] Scales vary widely based on methodology and are primarily used in a research setting. In general, they attempt to assess the amount of drop-out in relation to the area of the lid assessed.[43-49] Some of these scales are fairly complex regarding the angle of deviation of the glandular ducts and whether or not changes in the acini are noted.[44] With the absence of a standard of care, clinicians are more focused on detection and change over time in a qualitative sense. Inter- and intra-reliabilities are "moderate to fair" by some estimates—combining upper with lower lid observations may be the most useful approach.[46,47] Research shows computerized grading systems have the best repeatability in contrast to five- or four-grade scales.[48] As of yet, no commercial device offers an option similar to normative databases used in threshold visual fields and optical coherence tomography of the posterior segment.

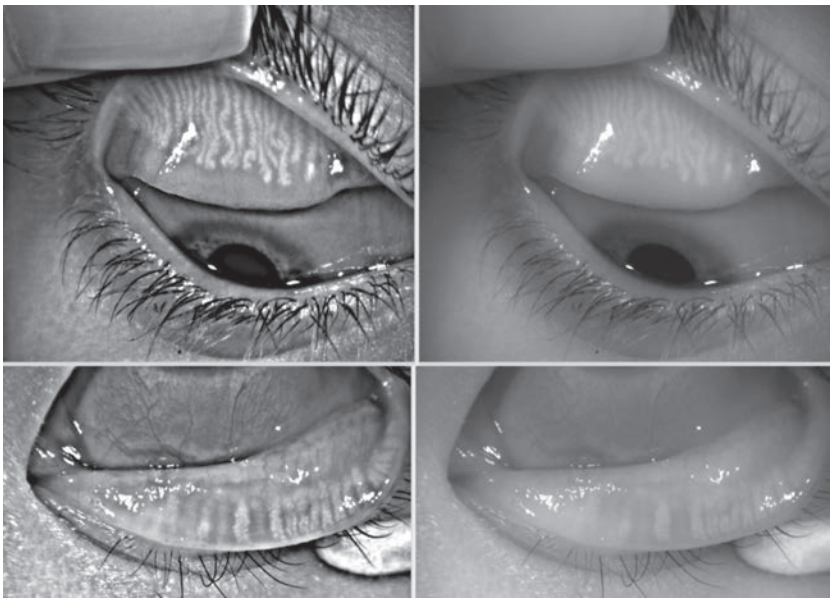


Fig. 3. The reflected IR images (left) and white light images (right) in a patient with MG attenuation and drop-out.

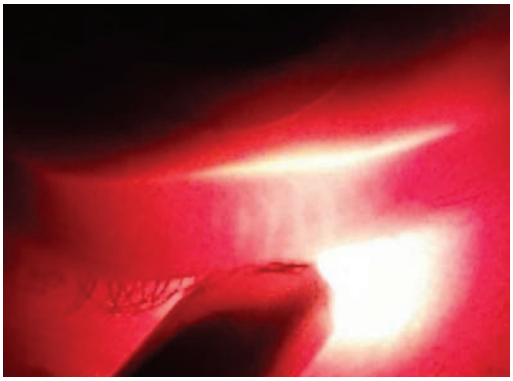


Fig. 2. Transillumination (meiboscopy) of the lower lids shows a normal arrangement of meibomian glands.

The Future, Confocal Microscopy and 3D-OCT

Some of the devices that we may eventually find commonplace are now prominent only in the realm of research and large academic centers. Clinicians frequently see adapted versions of research devices once proven merit gives way to larger scale production that brings down the acquisition cost.

Confocal microscopes, for example, are typically found in large research clinics or teaching programs. With these devices, the lids are everted and a cap with a gel interface is applanated against the lid surface, providing the observer with a view of the acinar structures of the MGs.[49-53] At least one unit is available with software that can quantify morphological changes with a high degree of sensitivity and specificity.[19,52,53]

3D ultrahigh-resolution OCT volumetric imaging of the meibomian glands in healthy and inflamed states was first reported in 2010 and demonstrated a future potential for yet another tool to evaluate morphology.[54]

The "take-away" for eye care clinicians is that meibomian gland dysfunction plays a predominant role in evaporative dry eye and contributes to ocular surface disease. A basic understanding of how to assess the morphological changes underlying the clinical signs and symptoms

VEATCH
OPHTHALMIC INSTRUMENTS

voi2020.com

The Future is Now!

The Ophthalmic Industry Is Going Digital...
FOR GOOD REASON!

- Increased Efficiency
- Patient WOW Factor
- Less Pain for Doctor
- High ROI
- Fewer Errors & Remakes
- Increased Capabilities
- Equipment Connectivity
- EMR Integration*

*Electronic Medical Records

Don't get left behind

IT'S TIME TO GO DIGITAL

Contact Us Today!

Veatch Ophthalmic Instruments

voi2020.com | 800.447.7511

Forget About REPETITIVE DATA ENTRIES

Digital refractors include features such as a dual cross cylinder, programmable sequences and wireless interface with pre-test equipment that allow for effortless, error-free exams.

In fact, switching to digital systems allows doctors to see two to six more patients per day.

So you can focus on what matters... YOUR PATIENT

and establishing clinical benchmarks are excellent ways of tracking the changes over time and assessing the effectiveness of therapies. Staying informed about the scientific evidence, diagnostic and management strategies as they emerge allows us to better serve our patients while expanding growth opportunities for our practices. ■

Dr. Fuller is an associate professor and founding supervisor of the Cornea & Contact Lens – Refractive Surgery residency at The Eye Center, Southern College of Optometry.

1. DEWS. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the international dry eye workshop. Ocul Surf. 2007 Apr;5(2):75-92.
2. Asbell P, Stapleton F, Wickström K, et al. The international workshop on meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011 Mar 30;52:2065-85.
3. Nichols J, Jones L, Nelson D. The TFOS international workshop on contact lens discomfort. Invest Ophthalmol Vis Sci. 2013;54:TFOS1–122.
4. Korb D, Henriquez A. Meibomian gland dysfunction and contact lens intolerance. J Am Optom Assoc. 1980;51:243–51.
5. Lemp M. Report of the national eye institute/industry workshop on clinical trials in dry eyes. CLAO J 1995;21:221–32.
6. The definition and classification of dry eye disease: report of the definition and classification subcommittee of the international dry eye workshop. Ocul Surf. 2007;5:75–92.
7. Nichols K, Foulks G, Bron A, et al. The international workshop on meibomian gland dysfunction: executive summary. Invest Ophthalmol Vis Sci. 2011;52:1922–9.
8. Schaumberg D, Nichols J, Papas E, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on the epidemiology of, and associated risk factors for, MGD. Invest Ophthalmol Vis Sci. 2011;52:1994–2005.
9. Nelson J, Shimazaki J, Benitez-del-Castillo J, et al. The international workshop on meibomian gland dysfunction: report of the definition and classification subcommittee. Invest Ophthalmol Vis Sci. 2011;52:1930–7.
10. Bron A, Tiffany J, Gouveia S, et al. Functional aspects of the tear film lipid layer. Exp Eye Res 2004;78:347–60.
11. Knop N, Knop E, Millar T. The international workshop on meibomian gland dysfunction: Report of the subcommittee on anatomy, physiology and pathophysiology of the meibomian gland. Invest Ophthalmol Vis Sci. 2011 Mar; 52(4): 1938–78.
12. Greiner J, Glonek T, Korb D, et al. Volume of the human and rabbit meibomian gland system. Adv Exp Med Biol 1998;438:339–43.
13. Knop E, Knop N, Millar T, et al. The international workshop on meibomian gland dysfunction: report of the subcommittee on anatomy, physiology, and pathophysiology of the meibomian gland. Invest Ophthalmol Vis Sci. 2011;52:1938–78.
14. Obata H, Horiuchi H, Miyata K, et al. Histopathological study of the meibomian glands in 72 autopsy cases. Nihon Ganka Gakkai Zasshi. 1994;98:765–71.
15. Shimazaki J, Sakata M, Tsubota K. Ocular surface changes and discomfort in patients with meibomian gland dysfunction. Arch Ophthalmol (Chicago, Ill 1960) 1995;113:1266–70.
16. Henriquez A, Korb D. Meibomian glands and contact lens wear. Br J Ophthalmol 1981;65:108–11.
17. Bron A and Tiffany J. The contribution of meibomian disease to dry eye. Ocul Surf. 2004;2:149–65.
18. McCulley J, Dougherty J, Deneau D. Classification of chronic blepharitis. Ophthalmology 1982;89:1173–80.
19. Wise R, Sobel R, Allen R. Meibography: A review of techniques and technologies. Saudi J Ophthalmol Off J Saudi Ophthalmol Soc. 2012;26:349–56.
20. Zeev M, Miller D, Latkany R. Diagnosis of dry eye disease and emerging technologies. Clin Ophthalmol. 2014;8:581–90.
21. Alves M, Reinach P, Paula J. Comparison of diagnostic tests in distinct well-defined conditions related to dry eye disease. PLoS One 2014;9:e97921.
22. Onwubiko S, Eze B, Udeh N, et al. Dry eye disease: Concordance between the diagnostic tests in African eyes. Eye Contact Lens. December 2015.
23. Schiffman R, Christianson M, Jacobsen G, et al. Reliability and validity of the ocular surface disease index. Arch Ophthalmol. 2000;118:615–21.
24. Cox S, Nichols K, Nichols J. Agreement between automated and traditional measures of tear film breakup. Optom Vis Sci. 2015;92:e257–63.
25. Nichols K, Mitchell G, Zadnik K. The repeatability of clinical measurements of dry eye. Cornea. 2004;23:272–85.
26. Powell D, Nichols J, Nichols K. Inter-examiner reliability in meibomian gland dysfunction assessment. Invest Ophthalmol Vis Sci. 2012;53:3120–5.
27. Meadows J, Ramamoorthy P, Nichols J. Development of the 4-3-2-1 meibum expressibility scale. Eye Contact Lens. 2012 Mar;38(2):86-92.
28. Arita R, Itoh K, Maeda S. Proposed diagnostic criteria for obstructive meibomian gland dysfunction. Ophthalmology. 2009;116:2058–63.e1.
29. Bron A, Benjamin L, Snibson G. Meibomian gland disease. Classification and grading of lid changes. Eye(Lond). 1991;5 (Pt. 4):395–411.
30. Eom Y, Lee J, Kang S, et al. Correlation between quantitative measurements of tear film lipid layer thickness and meibomian gland loss in patients with obstructive meibomian gland dysfunction and normal controls. Am J Ophthalmol. 2013;155:1104–10.e2.
31. Blackie C, Solomon J, Scaffidi R, et al. The relationship between dry eye symptoms and lipid layer thickness. Cornea 2009;28:789–94.
32. Finis D, Pischel N, Borrelli M. Factors influencing the measurement of tear film lipid layer thickness with interferometry. Klin Monbl Augenheilkd. 2014;231:603–10.
33. Zhao Y, Tan C, Tong L. Intra-observer and inter-observer repeatability of ocular surface interferometer in measuring lipid layer thickness. BMC Ophthalmol 2015;15:53.
34. Finis D, Pischel N, Schrader S. Evaluation of lipid layer thickness measurement of the tear film as a diagnostic tool for meibomian gland dysfunction. Cornea 2013;32:1549–53.
35. Robin J, Jester J, Nobe J. In vivo transillumination biomicroscopy and photography of meibomian gland dysfunction. A clinical study. Ophthalmology. 1985;92:1423–6.
36. Jester J, Rife L, Nii D. In vivo biomicroscopy and photography of meibomian glands in a rabbit model of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 1982;22:660–7.
37. Koh Y, Celik T, Lee H. Detection of meibomian glands and classification of meibography images. J Biomed Opt. 2012;17:086008.
38. Tapie R. Etude biomicroscopique des glandes de meibomius. Ann Ocul 1977;210:637–48.
39. Wise R, Sobel R, Allen R. Meibography: A review of techniques and technologies. Saudi J Ophthalmol Off J Saudi Ophthalmol Soc. 2012;26:349–56.
40. Ngo W, Srinivasan S, Jones L. Historical overview of imaging the meibomian glands. J Optom 2013;6:1–8.
41. Tear Science Brochure. TearScience Solut MGD 2016:1–6.
42. The Oculus Keratograph 5M. Oculus Prod 2016.
43. Arita R, Itoh K, Inoue K, Amano S. Noncontact infrared meibography to document age-related changes of the meibomian glands in a normal population. Ophthalmology. 2008;115:911–5.
44. Srinivasan S, Menzies K, Sorbara L. Infrared imaging of meibomian gland structure using a novel keratograph. Optom Vis Sci 2012;89:788–94.
45. Bailey I, Bullimore M, Raasch T, Taylor H. Clinical grading and the effects of scaling. Invest Ophthalmol Vis Sci 1991;32:422–32.
46. Nichols J, Berntsen D, Mitchell G, Nichols K. An assessment of grading scales for meibography images. Cornea 2005;24:382–8.
47. Pult H, Riede-Pult B, Nichols J. Relation between upper and lower lids' meibomian gland morphology, tear film, and dry eye. Optom Vis Sci. 2012;89:e310–5.
48. Pult H, Riede-Pult B. Comparison of subjective grading and objective assessment in meibography. Cont Lens Anterior Eye. 2013;36:22–7.
49. Matsumoto Y, Sato E, Ibrahim O, et al. The application of in vivo laser confocal microscopy to the diagnosis and evaluation of meibomian gland dysfunction. Mol Vis. 2008;14:1263–71.
50. Matsumoto Y, Shigeno Y, Sato E, et al. The evaluation of the treatment response in obstructive meibomian gland disease by in vivo laser confocal microscopy. Graefe's Arch Clin Exp Ophthalmol. Albr von Graefes Arch für Klin und Exp Ophthalmol. 2009;247:821–9.
51. Wakamatsu T, Sato E, Matsumoto Y, et al. Conjunctival in vivo confocal scanning laser microscopy in patients with Sjögren syndrome. Invest Ophthalmol Vis Sci 2010;51:144–50.
52. Ngo W, Srinivasan S, Jones L. Historical overview of imaging the meibomian glands. J Optom 2013;6:1–8.
53. Ibrahim O, Matsumoto Y, Dogru M, et al. The efficacy, sensitivity and specificity of in vivo laser confocal microscopy in the diagnosis of meibomian gland dysfunction. Ophthalmology. 2010;117:665–72.
54. Bizheva K, Lee P, Sorbara L, Hutchings N, Simpson T. In vivo volumetric imaging of the human upper eyelid with ultrahigh-resolution optical coherence tomography. J Biomed Opt. 15:040508.
55. Lucena A, Akaishi P, Rodrigues M. Upper eyelid entropion and dry eye in cicatricial trachoma without trichiasis. Arq Bras Oftalmol. 2012;75:420–2.
56. Kirzhner M, Jakobiec F. Ocular Cicatricial Pemphigoid: A Review of Clinical Features, Immunopathology, Differential Diagnosis, and Current Management. Semin Ophthalmol September 2011.
57. Staikuniene J, Staneviciute J. Long-term valacyclovir treatment and immune modulation for Herpes-associated erythema multiforme. Cent J Immunol/Polish Soc Immunol Elev other Cent Immunol Soc 2015;40:387–90.
58. Sokumbi O, Wetter D. Clinical features, diagnosis and treatment of erythema multiforme: a review for the practicing dermatologist. Int J Dermatol 2012;51:889–902.
59. Machalinska A, Zakrzewska A, Markowska A, et al. Morphological and functional evaluation of meibomian gland dysfunction in rosacea patients. Curr Eye Res December 2015:1–6.
60. McCulley J, Dougherty J. Blepharitis associated with acne rosacea and seborrheic dermatitis. Int Ophthalmol Clin 1985;25:159–72.
61. Silverberg J, Hanifin J. Adult eczema prevalence and associations with asthma and other health and demographic factors: a US population-based study. J Allergy Clin Immunol. 2013;132:1132–8.
62. Schirmer O. Studien zur physiologie und pathologie der trenasbsonderung und treabfuhr. Arch Klin Exp Ophthalmol.1903;56:197–291.
63. Lemp M. Breakup of the tear film. Int Ophthalmol Clin. 1973;13:97–102.
64. Korb D and Blackie C. Meibomian gland diagnostic expressibility: correlation with dry eye symptoms and gland location. Cornea 2008;27:1142–7.
65. Yoon K, Im S, Kim H, You I. Usefulness of double vital staining with 1% fluorescein and 1% lissamine green in patients with dry eye syndrome. Cornea. 2011;30:972–6.
66. Bron A, Evans V, Smith J. Grading of corneal and conjunctival staining in the context of other dry eye tests. Cornea. 2003;22:640–50.
67. Gilbard J, Rossi S, Heyda K. Tear film and ocular surface changes after closure of the meibomian gland orifices in the rabbit. Ophthalmology 1989;96:1180–6.
68. Versura P, Profazio V, Campos E. Performance of tear osmolarity compared to previous diagnostic tests for dry eye diseases. Curr Eye Res 2010;35:553–64.
69. Yokoi N, Mossa F, Tiffany J, Bron A. Assessment of meibomian gland function in dry eye using meibometry. Arch Ophthalmol. (Chicago, Ill 1960) 1999;117:723–9.
70. Yokoi N, Komuro A. Non-invasive methods of assessing the tear film. Exp Eye Res 2004;78:399–407.
71. Kohno T, Ohnishi Y. [In vivo transillumination of the meibomian gland in yusho patients]. Fukuoka Igaku Zasshi. 1987;78:355–7.
72. Satjawatcharaphong P, Ge S, Lin M. Clinical outcomes associated with thermal pulsation system treatment. Optom Vis Sci. 2015;92:e334–41.
73. Qazi Y, Aggarwal S, Hamrah P. Image-guided evaluation and monitoring of treatment response in patients with dry eye disease. Graefes Arch Clin Exp Ophthalmol. 2014;252:857–72.
74. Palamar M, Degirmenci C, Ertam I, Yagci A. Evaluation of dry eye and meibomian gland dysfunction with meibography in patients with rosacea. Cornea. 2015;34:497–9.

Classic beta blocker adjunctive therapy for the right patient at the right time[3]

The concomitant use of two topical beta-adrenergic blocking agents is not recommended[4,5]

Indications and Usage

ISTALOL® (timolol maleate ophthalmic solution) is a non-selective beta-adrenergic receptor blocking agent indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.

Preservative-free TIMOPTIC® (timolol maleate ophthalmic solution) in OCUDOSE® (dispenser) is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma. It may be used when a patient is sensitive to the preservative in TIMOPTIC (timolol maleate ophthalmic solution), benzalkonium chloride, or when use of a preservative-free topical medication is advisable.

Important Safety Information for Istalol® and Timoptic® in Ocudose®

- Both ISTALOL® (timolol maleate ophthalmic solution) and TIMOPTIC® (timolol maleate ophthalmic solution) in OCUDOSE® (dispenser) are contraindicated in patients with: bronchial asthma; a history of bronchial asthma; severe chronic obstructive pulmonary disease; sinus bradycardia; second or third degree atrioventricular block; overt cardiac failure; cardiogenic shock; hypersensitivity to any component of the product.
- **The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. Severe respiratory reactions and cardiac reaction, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol maleate.**
- Patients with a history of atopy or severe anaphylactic reactions to a variety of allergens may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.
- Timolol has been reported rarely to increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.
- Beta-adrenergic blocking agents may mask signs and symptoms of acute hypoglycemia or certain clinical signs of hyperthyroidism. Patients subject to spontaneous hypoglycemia, or diabetic patients receiving either insulin or oral hypoglycemic agents, or patients suspected of developing thyrotoxicosis, should be managed carefully, with caution.
- In patients undergoing elective surgery, some authorities recommend gradual withdrawal of beta adrenergic receptor blocking agents because these agents impair the ability of the heart to respond to beta-adrenergically mediated reflex stimuli.
- The most frequently reported adverse reactions have been burning and stinging upon instillation. This was seen in 38% of patients treated with ISTALOL and in approximately one in eight patients treated with TIMOPTIC in OCUDOSE. Additional reactions reported with ISTALOL at a frequency of 4 to 10% include: blurred vision, cataract, conjunctival injection, headache, hypertension, infection, itching and decreased visual acuity.

Please see Brief Summary of Prescribing Information for ISTALOL and TIMOPTIC in OCUDOSE on the following pages.

For the patients who need incremental IOP reduction in a preservative free form[6]

Preservative-Free

TIMOPTIC® in OCUDOSE®
(TIMOLOL MALEATE 0.5% OPHTHALMIC SOLUTION) (DISPENSER)

For the patients who need incremental IOP reduction in a once a day form[6]

Istalol®
(timolol maleate ophthalmic solution) 0.5%

References: 1. Alm A, Stjernschantz J. Effects on Intraocular Pressure and Side Effects of 0.005% Latanoprost Applied Once Daily, Evening or Morning. *Ophthalmology*. 1995;102:1743-1752. **2.** Brubaker R. Flow of Aqueous Humor in Humans. *IOVS*. 1991;32:(13)3145-3166. **3.** Obstbaum S, Cioffi GA, Krieglstein GK, et al. Gold Standard Medical Therapy for Glaucoma: Defining the Criteria Identifying Measures for an Evidence-Based Analysis. *Clin Ther.* 2004;26(12)2102-2119. **4.** Istalol [package insert]. Bridgewater, NJ: Bausch & Lomb Incorporated; 2013. **5.** Timoptic in Ocudose [package insert]. Lawrenceville, NJ: Aton Pharma; 2009. **6.** Stewart W, Day DG, Sharpe ED. Efficacy and Safety of Timolol Solution Once Daily vs Timolol Gel Added to Latanoprost. *Am J Ophthalmol*. 1999;128(6)692-696.

BAUSCH + LOMB

US/TOP/14/0017(1)

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use TIMOPTIC® 0.25% AND 0.5% (timolol maleate ophthalmic solution) in OCUDOSE® (DISPENSER) safely and effectively. See full prescribing information for TIMOPTIC in OCUDOSE.

PRESERVATIVE-FREE STERILE OPHTHALMIC SOLUTION
in a Sterile Ophthalmic Unit Dose Dispenser

TIMOPTIC® 0.25% AND 0.5%
(TIMOLOL MALEATE OPHTHALMIC SOLUTION)
in OCUDOSE® (DISPENSER)

INDICATIONS AND USAGE

Preservative-free TIMOPTIC in OCUDOSE is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma.

Preservative-free TIMOPTIC in OCUDOSE may be used when a patient is sensitive to the preservative in TIMOPTIC (timolol maleate ophthalmic solution), benzalkonium chloride, or when use of a preservative-free topical medication is advisable.

CONTRAINDICATIONS

Preservative-free TIMOPTIC in OCUDOSE is contraindicated in patients with (1) bronchial asthma; (2) a history of bronchial asthma; (3) severe chronic obstructive pulmonary disease (see WARNINGS); (4) sinus bradycardia; (5) second or third degree atrioventricular block; (6) overt cardiac failure (see WARNINGS); (7) cardiogenic shock; or (8) hypersensitivity to any component of this product.

WARNINGS

As with many topically applied ophthalmic drugs, this drug is absorbed systemically.

The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol maleate (see CONTRAINDICATIONS).

Cardiac Failure: Sympathetic stimulation may be essential for support of the circulation in individuals with diminished myocardial contractility, and its inhibition by beta-adrenergic receptor blockade may precipitate more severe failure.

In Patients Without a History of Cardiac Failure continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of cardiac failure, Preservative-free TIMOPTIC in OCUDOSE should be discontinued.

Obstructive Pulmonary Disease: Patients with chronic obstructive pulmonary disease (e.g., chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease (other than bronchial asthma or a history of bronchial asthma, in which TIMOPTIC in OCUDOSE is contraindicated [see CONTRAINDICATIONS]) should, in general, not receive beta-blockers, including Preservative-free TIMOPTIC in OCUDOSE.

Major Surgery: The necessity or desirability of withdrawal of beta-adrenergic blocking agents prior to major surgery is controversial. Beta-adrenergic receptor blockade impairs the ability of the heart to respond to beta-adrenergically mediated reflex stimuli. This may augment the risk of general anesthesia in surgical procedures. Some patients receiving beta-adrenergic receptor blocking agents have experienced protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported. For these reasons, in patients undergoing elective surgery, some authorities recommend gradual withdrawal of beta-adrenergic receptor blocking agents.

If necessary during surgery, the effects of beta-adrenergic blocking agents may be reversed by sufficient doses of adrenergic agonists.

Diabetes Mellitus: Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic receptor blocking agents may mask the signs and symptoms of acute hypoglycemia.

Thyrotoxicosis: Beta-adrenergic blocking agents may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta-adrenergic blocking agents that might precipitate a thyroid storm.

PRECAUTIONS

General: Because of potential effects of beta-adrenergic blocking agents on blood pressure and pulse, these agents should be used with caution in patients with cerebrovascular insufficiency. If signs or symptoms suggesting reduced cerebral blood flow develop following initiation of therapy with Preservative-free TIMOPTIC in OCUDOSE, alternative therapy should be considered.

Choroidal detachment after filtration procedures has been reported with the administration of aqueous suppressant therapy (e.g. timolol).

Angle-closure glaucoma: In patients with angle-closure glaucoma, the immediate objective of treatment is to reopen the angle. This requires constricting the pupil. Timolol maleate has little or no effect on the pupil. TIMOPTIC in OCUDOSE should not be used alone in the treatment of angle-closure glaucoma.

Anaphylaxis: While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge with such allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

Muscle Weakness: Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (e.g., diplopia, ptosis, and generalized weakness). Timolol has been reported rarely to increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.

Information for Patients: Patients should be instructed about the use of Preservative-free TIMOPTIC in OCUDOSE.

Since sterility cannot be maintained after the individual unit is opened, patients should be instructed to use the product immediately after opening, and to discard the individual unit and any remaining contents immediately after use.

Patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second or third degree atrioventricular block, or cardiac failure should be advised not to take this product. (See CONTRAINDICATIONS.)

Drug Interactions: Although TIMOPTIC (timolol maleate ophthalmic solution) used alone has little or no effect on pupil size, mydriasis resulting from concomitant therapy with TIMOPTIC (timolol maleate ophthalmic solution) and epinephrine has been reported occasionally.

Beta-adrenergic blocking agents: Patients who are receiving a beta-adrenergic blocking agent orally and Preservative-free TIMOPTIC in OCUDOSE should be observed for potential additive effects of beta-blockade, both systemic and on intraocular pressure. The concomitant use of two topical beta-adrenergic blocking agents is not recommended.

Calcium antagonists: Caution should be used in the coadministration of beta-adrenergic blocking agents, such as Preservative-free TIMOPTIC in OCUDOSE, and oral or intravenous calcium antagonists, because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension. In patients with impaired cardiac function, coadministration should be avoided.

Catecholamine-depleting drugs: Close observation of the patient is recommended when a beta blocker is administered to patients receiving catecholamine-depleting drugs such as reserpine, because of possible additive effects and the production of hypotension and/or marked bradycardia, which may result in vertigo, syncope, or postural hypotension.

Digitalis and calcium antagonists: The concomitant use of beta-adrenergic blocking agents with digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time.

CYP2D6 inhibitors: Potentiated systemic beta-blockade (e.g., decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g., quinidine, SSRIs) and timolol.

Clonidine: Oral beta-adrenergic blocking agents may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. There have been no reports of exacerbation of rebound hypertension with ophthalmic timolol maleate.

Injectable epinephrine: (See PRECAUTIONS, *General, Anaphylaxis*)

Carcinogenesis, Mutagenesis, Impairment of Fertility: In a two-year oral study of timolol maleate administered orally to rats, there was a statistically significant increase in the incidence of adrenal pheochromocytomas in male rats administered 300 mg/kg/day (approximately 42,000 times the systemic exposure following the maximum recommended human ophthalmic dose). Similar differences were not observed in rats administered oral doses equivalent to approximately 14,000 times the maximum recommended human ophthalmic dose.

In a lifetime oral study in mice, there were statistically significant increases in the incidence of benign and malignant pulmonary tumors, benign uterine polyps and mammary adenocarcinomas in female mice at 500 mg/kg/day (approximately 71,000 times the systemic exposure following the maximum recommended human ophthalmic dose), but not at 5 or 50 mg/kg/day (approximately 700 or 7,000 times, respectively, the systemic exposure following the maximum recommended human ophthalmic dose). In a subsequent study in female mice, in which post-mortem examinations were limited to the uterus and the lungs, a statistically significant increase in the incidence of pulmonary tumors was again observed at 500 mg/kg/day.

The increased occurrence of mammary adenocarcinomas was associated with elevations in serum prolactin which occurred in female mice administered oral timolol at 500 mg/kg/day, but not at doses of 5 or 50 mg/kg/day. An increased incidence of mammary adenocarcinomas in rodents has been associated with administration of several other therapeutic agents that elevate serum prolactin, but no correlation between serum prolactin levels and mammary tumors has been established in humans. Furthermore, in adult human female subjects who received oral dosages of up to 60 mg of timolol maleate (the maximum recommended human oral dosage), there were no clinically meaningful changes in serum prolactin.

Timolol maleate was devoid of mutagenic potential when tested *in vivo* (mouse) in the micronucleus test and cytogenetic assay (doses up to 800 mg/kg) and *in vitro* in a neoplastic cell transformation assay (up to 100 mcg/mL). In Ames tests the highest concentrations of timolol employed, 5,000 or 10,000 mcg/plate, were associated with statistically significant elevations of revertants observed with tester strain TA100 (in seven replicate assays), but not in the remaining three strains. In the assays with tester strain TA100, no consistent dose response relationship was observed, and the ratio of test to control revertants did not reach 2. A ratio of 2 is usually considered the criterion for a positive Ames test.

Reproduction and fertility studies in rats demonstrated no adverse effect on male or female fertility at doses up to 21,000 times the systemic exposure following the maximum recommended human ophthalmic dose.

Pregnancy: *Teratogenic Effects* — Pregnancy Category C. Teratogenicity studies with timolol in mice, rats and rabbits at oral doses up to 50 mg/kg/day (7,000 times the systemic exposure following the maximum recommended human ophthalmic dose) demonstrated no evidence of fetal malformations. Although delayed fetal ossification was observed at this dose in rats, there were no adverse effects on postnatal development of offspring. Doses of 1000 mg/kg/day (142,000 times the systemic exposure following the maximum recommended human ophthalmic dose) were maternotoxic in mice and resulted in an increased number of fetal resorptions. Increased fetal resorptions were also seen in rabbits at doses of 14,000 times the systemic exposure following the maximum recommended human ophthalmic dose, in this case without apparent maternotoxicity.

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

Nursing Mothers: Timolol maleate has been detected in human milk following oral and ophthalmic drug administration. Because of the potential for serious adverse reactions from timolol in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

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

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

ADVERSE REACTIONS

The most frequently reported adverse experiences have been burning and stinging upon instillation (approximately one in eight patients).

The following additional adverse experiences have been reported less frequently with ocular administration of this or other timolol maleate formulations:

BODY AS A WHOLE: Headache, asthenia/fatigue, and chest pain.

CARDIOVASCULAR: Bradycardia, arrhythmia, hypotension, hypertension, syncope, heart block, cerebral vascular accident, cerebral ischemia, cardiac failure, worsening of angina pectoris, palpitation, cardiac arrest, pulmonary edema, edema, claudication, Raynaud's phenomenon, and cold hands and feet.

DIGESTIVE: Nausea, diarrhea, dyspepsia, anorexia, and dry mouth.

IMMUNOLOGIC: Systemic lupus erythematosus.

NERVOUS SYSTEM/PSYCHIATRIC: Dizziness, increase in signs and symptoms of myasthenia gravis, paresthesia, somnolence, insomnia, nightmares, behavioral changes and psychic disturbances including depression, confusion, hallucinations, anxiety, disorientation, nervousness, and memory loss.

SKIN: Alopecia and psoriasiform rash or exacerbation of psoriasis.

HYPERSENSITIVITY: Signs and symptoms of systemic allergic reactions including anaphylaxis, angioedema, urticaria, and localized and generalized rash.

RESPIRATORY: Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), respiratory failure, dyspnea, nasal congestion, cough and upper respiratory infections.

ENDOCRINE: Masked symptoms of hypoglycemia in diabetic patients (see WARNINGS).

SPECIAL SENSES: Signs and symptoms of ocular irritation including conjunctivitis, blepharitis, keratitis, ocular pain, discharge (e.g., crusting), foreign body sensation, itching and tearing, and dry eyes; ptosis; decreased corneal sensitivity; cystoid macular edema; visual disturbances including refractive changes and diplopia; pseudopemphigoid; choroidal detachment following filtration surgery (see PRECAUTIONS, *General*); and tinnitus.

UROGENITAL: Retroperitoneal fibrosis, decreased libido, impotence, and Peyronie's disease.

The following additional adverse effects have been reported in clinical experience with ORAL timolol maleate or other ORAL beta blocking agents, and may be considered potential effects of ophthalmic timolol maleate: *Allergic:* Erythematous rash, fever combined with aching and sore throat, laryngospasm with respiratory distress; *Body as a Whole:* Extremity pain, decreased exercise tolerance, weight loss; *Cardiovascular:* Worsening of arterial insufficiency, vasodilatation; *Digestive:* Gastrointestinal pain, hepatomegaly, vomiting, mesenteric arterial thrombosis, ischemic colitis; *Hematologic:* Nonthrombocytopenic purpura; thrombocytopenic purpura; agranulocytosis; *Endocrine:* Hyperglycemia, hypoglycemia; *Skin:* Pruritus, skin irritation, increased pigmentation, sweating; *Musculoskeletal:* Arthralgia; *Nervous System/Psychiatric:* Vertigo, local weakness, diminished concentration, reversible mental depression progressing to catatonia, an acute reversible syndrome characterized by disorientation for time and place, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics; *Respiratory:* Rales, bronchial obstruction; *Urogenital:* Urination difficulties.

OVERDOSAGE

There have been reports of inadvertent overdosage with Ophthalmic Solution TIMOPTIC (timolol maleate ophthalmic solution) resulting in systemic effects similar to those seen with systemic beta-adrenergic blocking agents such as dizziness, headache, shortness of breath, bradycardia, bronchospasm, and cardiac arrest (see also ADVERSE REACTIONS).

Overdosage has been reported with Tablets BLOCADREN* (timolol maleate tablets). A 30 year old female ingested 650 mg of BLOCADREN (maximum recommended oral daily dose is 60 mg) and experienced second and third degree heart block. She recovered without treatment but approximately two months later developed irregular heartbeat, hypertension, dizziness, tinnitus, faintness, increased pulse rate, and borderline first degree heart block.

An *in vitro* hemodialysis study, using ^{14}C timolol added to human plasma or whole blood, showed that timolol was readily dialyzed from these fluids; however, a study of patients with renal failure showed that timolol did not dialyze readily.

DOSAGE AND ADMINISTRATION

Preservative-free TIMOPTIC in OCUDOSE is a sterile solution that does not contain a preservative. The solution from one individual unit is to be used immediately after opening for administration to one or both eyes. Since sterility cannot be guaranteed after the individual unit is opened, the remaining contents should be discarded immediately after administration.

Preservative-free TIMOPTIC in OCUDOSE is available in concentrations of 0.25 and 0.5 percent. The usual starting dose is one drop of 0.25 percent Preservative-free TIMOPTIC in OCUDOSE in the affected eye(s) administered twice a day. Apply enough gentle pressure on the individual container to obtain a single drop of solution. If the clinical response is not adequate, the dosage may be changed to one drop of 0.5 percent solution in the affected eye(s) administered twice a day.

Since in some patients the pressure-lowering response to Preservative-free TIMOPTIC in OCUDOSE may require a few weeks to stabilize, evaluation should include a determination of intraocular pressure after approximately 4 weeks of treatment with Preservative-free TIMOPTIC in OCUDOSE.

If the intraocular pressure is maintained at satisfactory levels, the dosage schedule may be changed to one drop once a day in the affected eye(s). Because of diurnal variations in intraocular pressure, satisfactory response to the once-a-day dose is best determined by measuring the intraocular pressure at different times during the day.

Dosages above one drop of 0.5 percent TIMOPTIC (timolol maleate ophthalmic solution) twice a day generally have not been shown to produce further reduction in intraocular pressure. If the patient's intraocular pressure is still not at a satisfactory level on this regimen, concomitant therapy with other agent(s) for lowering intraocular pressure can be instituted taking into consideration that the preparation(s) used concomitantly may contain one or more preservatives. The concomitant use of two topical beta-adrenergic blocking agents is not recommended. (See PRECAUTIONS, *Drug Interactions, Beta-adrenergic blocking agents.*)

Distributed by:
Bausch + Lomb, a division of
Valeant Pharmaceuticals North America LLC
Bridgewater, NJ 08807 USA

Manufactured by:
Laboratoire Unither
ZI de la Guérie
F-50211 Coutances Cedex
France

Rev. 05/14
Based on 65NOT8557/A 9390301
US/TOP/14/0018(1)

* TIMOPTIC and OCUDOSE are trademarks of Valeant Pharmaceuticals International, Inc. or its affiliates.

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use ISTALOL® (timolol maleate ophthalmic solution) 0.5% safely and effectively. See full prescribing information for ISTALOL.

Istalol® (timolol maleate ophthalmic solution) 0.5%

Initial U.S. Approval: 1978

STERILE

INDICATIONS AND USAGE

Istalol (timolol maleate ophthalmic solution) 0.5% is a non-selective beta-adrenergic receptor blocking agent indicated in the treatment of elevated intraocular pressure (IOP) in patients with ocular hypertension or open-angle glaucoma.

CONTRAINDICATIONS

4.1 Asthma, COPD: Istalol is contraindicated in patients with bronchial asthma; a history of bronchial asthma; severe chronic obstructive pulmonary disease (see **WARNINGS AND PRECAUTIONS, 5.1, 5.3**).

4.2 Sinus Bradycardia, AV Block, Cardiac Failure, Cardiogenic Shock: Istalol is contraindicated in patients with sinus bradycardia; second or third degree atrioventricular block; overt cardiac failure (see **WARNINGS AND PRECAUTIONS, 5.2**); cardiogenic shock.

4.3 Hypersensitivity Reactions: Istalol is contraindicated in patients who have exhibited a hypersensitivity reaction to any component of this product in the past.

WARNINGS AND PRECAUTIONS

5.1 Potentiation of Respiratory Reactions Including Asthma: Istalol contains timolol maleate; and although administered topically, it can be absorbed systemically. Therefore, the same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions and cardiac reactions including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol maleate (see **CONTRAINDICATIONS, 4.1**).

5.2 Cardiac Failure: Sympathetic stimulation may be essential for support of the circulation in individuals with diminished myocardial contractility, and its inhibition of beta-adrenergic receptor blockade may precipitate more severe failure. In patients without a history of cardiac failure, continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of cardiac failure, Istalol should be discontinued (see also **CONTRAINDICATIONS, 4.2**).

5.3 Obstructive Pulmonary Disease: Patients with chronic obstructive pulmonary disease (e.g., chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease [other than bronchial asthma or a history of bronchial asthma in which Istalol is contraindicated (see **CONTRAINDICATIONS, 4.2**)] should, in general, not receive beta-blocking agents, including Istalol.

5.4 Increased Reactivity to Allergens: While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge with such allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

5.5 Potentiation of Muscle Weakness: Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (e.g., diplopia, ptosis, and generalized weakness). Timolol has been reported rarely to increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.

5.6 Masking of Hypoglycemic Symptoms in Patients with Diabetes Mellitus: Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic receptor blocking agents may mask the signs and symptoms of acute hypoglycemia.

5.7 Masking of Thyrotoxicosis: Beta-adrenergic blocking agents may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta-adrenergic blocking agents that might precipitate a thyroid storm.

5.8 Contamination of Topical Ophthalmic Products After Use: There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface (see **PATIENT COUNSELING INFORMATION, 17**).

5.9 Impairment of Beta-adrenergically Mediated Reflexes During Surgery: The necessity or desirability of withdrawal of beta-adrenergic blocking agents prior to major surgery is controversial. Beta-adrenergic receptor blockade impairs the ability of the heart to respond to beta-adrenergically mediated reflex stimuli. This may augment the risk of general anesthesia in surgical procedures. Some patients receiving beta-adrenergic receptor blocking agents have experienced protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported. For these reasons, in patients undergoing elective surgery, some authorities recommend gradual withdrawal of beta-adrenergic receptor blocking agents. If necessary during surgery, the effects of beta-adrenergic blocking agents may be reversed by sufficient doses of adrenergic agonists.

5.10 Angle-Closure Glaucoma: In patients with angle-closure glaucoma, the immediate objective of treatment is to reopen the angle. This may require constricting the pupil. Timolol maleate has little or no effect on the pupil. Istalol should not be used alone in the treatment of angle-closure glaucoma.

5.11 Cerebrovascular Insufficiency: Because of potential effects of beta-adrenergic blocking agents on blood pressure and pulse, these agents should be used with caution in patients with cerebrovascular insufficiency. If signs or symptoms suggesting reduced cerebral blood flow develop following initiation of therapy with Istalol, alternative therapy should be considered.

5.12 Choroidal Detachment: Choroidal detachment after filtration procedures has been reported with the administration of aqueous suppressant therapy (e.g. timolol).

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 practice.

The most frequently reported adverse reactions have been burning and stinging upon instillation in 38% of patients treated with Istalol. Additional reactions reported with Istalol at a frequency of 4 to 10% include: blurred vision, cataract, conjunctival injection, headache, hypertension, infection, itching and decreased visual acuity. The following additional adverse reactions have been reported less frequently with ocular administration of this or other timolol maleate formulations.

Timolol (Ocular Administration): *Body as a whole:* Asthenia/fatigue and chest pain; *Cardiovascular:* Bradycardia, arrhythmia, hypotension, syncope, heart block, cerebral vascular accident, cerebral ischemia, cardiac failure, worsening of angina pectoris, palpitation, cardiac arrest, pulmonary edema, edema, claudication, Raynaud's phenomenon and cold hands and feet; *Digestive:* Nausea, diarrhea, dyspepsia, anorexia, and dry mouth; *Immunologic:* Systemic lupus erythematosus; *Nervous System/Psychiatric:* Dizziness, increase in signs and symptoms of myasthenia gravis, paresthesia, somnolence, insomnia, nightmares, behavioral changes and psychic disturbances including depression, confusion, hallucinations, anxiety, disorientation, nervousness and memory loss; *Skin:* Alopecia and psoriasiform rash or exacerbation of psoriasis; *Hypersensitivity:* Signs and symptoms of systemic allergic reactions, including angioedema, urticaria, and localized and generalized rash; *Respiratory:* Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), respiratory failure, dyspnea, nasal congestion, cough and upper respiratory infections; *Endocrine:* Masked symptoms of hypoglycemia in diabetic patients (see **WARNINGS AND PRECAUTIONS, 5.6**); *Special Senses:* Signs and symptoms of ocular irritation including conjunctivitis, blepharitis, keratitis, ocular pain, discharge (e.g., crusting), foreign body sensation, itching and tearing, and dry eyes; ptosis, decreased corneal sensitivity; cystoid macular edema; visual disturbances including refractive changes and diplopia; pseudopemphigoid; choroidal detachment following filtration surgery (see **WARNINGS AND PRECAUTIONS, 5.12**); *Urogenital:* Retroperitoneal fibrosis, decreased libido, impotence, and Peyronie's disease.

6.2 Postmarketing Experience

Oral Timolol/Oral Beta-blockers: The following additional adverse effects have been reported in clinical experience with ORAL timolol maleate or other ORAL beta-blocking agents and may be considered potential effects of ophthalmic timolol maleate: *Allergic:* Erythematous rash, fever combined with aching and sore throat, laryngospasm with respiratory distress; *Body as a Whole:* Extremity pain, decreased exercise tolerance, weight loss; *Cardiovascular:* Worsening of arterial insufficiency, vasodilatation; *Digestive:* Gastrointestinal pain, hepatomegaly, vomiting, mesenteric arterial thrombosis, ischemic colitis; *Hematologic:* Nonthrombocytopenic purpura; thrombocytopenic purpura, agranulocytosis; *Endocrine:* Hyperglycemia, hypoglycemia; *Skin:* Pruritus, skin irritation, increased pigmentation, sweating; *Musculoskeletal:* Arthralgia; *Nervous System/Psychiatric:* Vertigo, local weakness, diminished concentration, reversible mental depression progressing to catatonia, an acute reversible syndrome characterized by disorientation for time and place, emotional lability, slightly clouded sensorium and decreased performance on neuropsychometrics; *Respiratory:* Rales, bronchial obstruction; *Urogenital:* Urination difficulties.

DRUG INTERACTIONS

7.1 Beta-Adrenergic Blocking Agents: Patients who are receiving a beta-adrenergic blocking agent orally and Istalol® should be observed for potential additive effects of beta-blockade, both systemic and on intraocular pressure. The concomitant use of two topical beta-adrenergic blocking agents is not recommended.

7.2 Calcium Antagonists: Caution should be used in the co-administration of beta-adrenergic blocking agents, such as Istalol, and oral or intravenous calcium antagonists because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension. In patients with impaired cardiac function, co-administration should be avoided.

7.3 Catecholamine-Depleting Drugs: Close observation of the patient is recommended when a beta blocker is administered to patients receiving catecholamine-depleting drugs such as reserpine, because of possible additive effects and the production of hypotension and/or marked bradycardia, which may result in vertigo, syncope, or postural hypotension.

7.4 Digitalis and Calcium Antagonists: The concomitant use of beta-adrenergic blocking agents with digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time.

7.5 CYP2D6 Inhibitors: Potentiated systemic beta-blockade (e.g., decreased heart rate) has been reported during combined treatment with CYP2D6 inhibitors (e.g., quinidine) and timolol.

7.6 Clonidine: Oral beta-adrenergic blocking agents may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. There have been no reports of exacerbation of rebound hypertension with ophthalmic timolol maleate.

USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic Effects: Pregnancy Category C: Teratogenicity studies have been performed in animals. Teratogenicity studies with timolol in mice, rats, and rabbits at oral doses up to 50 mg/kg/day (7,000 times the systemic exposure following the maximum recommended human ophthalmic dose) demonstrated no evidence of fetal malformations. Although delayed fetal ossification was observed at this dose in rats, there were no adverse effects on postnatal development of offspring. Doses of 1000 mg/kg/day (142,000 times the systemic exposure following the maximum recommended human ophthalmic dose) were maternotoxic in mice and resulted in an increased number of fetal resorptions. Increased fetal resorptions were also seen in rabbits at doses of 14,000 times the systemic exposure following the maximum recommended human ophthalmic dose, in this case without apparent maternotoxicity. There are no adequate and well-controlled studies in pregnant women. Istalol should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers: Timolol has been detected in human milk following oral and ophthalmic drug administration. Because of the potential for serious adverse reactions from Istalol in nursing infants, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

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

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

OVERDOSAGE

There have been reports of inadvertent overdosage with Istalol resulting in systemic effects similar to those seen with systemic beta-adrenergic blocking agents such as dizziness, headache, shortness of breath, bradycardia, bronchospasm, and cardiac arrest. An *in vitro* hemodialysis study, using ^{14}C timolol added to human plasma or whole blood, showed that timolol was readily dialyzed from these fluids; however, a study of patients with renal failure showed that timolol did not dialyze readily.

NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility: In a two-year study of timolol maleate administered orally to rats, there was a statistically significant increase in the incidence of adrenal pheochromocytomas in male rats administered 300 mg/kg/day (approximately 42,000 times the systemic exposure following the maximum recommended human ophthalmic dose). Similar differences were not observed in rats administered oral doses equivalent to approximately 14,000 times the maximum recommended human ophthalmic dose. In a lifetime oral study in mice, there were statistically significant increases in the incidence of benign and malignant pulmonary tumors, benign uterine polyps and mammary adenocarcinomas in female mice at 500 mg/kg/day, (approximately 71,000 times the systemic exposure following the maximum recommended human ophthalmic dose), but not at 5 or 50 mg/kg/day (approximately 700 or 7,000, respectively, times the systemic exposure following the maximum recommended human ophthalmic dose). In a subsequent study in female mice, in which post-mortem examinations were limited to the uterus and the lungs, a statistically significant increase in the incidence of pulmonary tumors was again observed at 500 mg/kg/day. The increased occurrence of mammary adenocarcinomas was associated with elevations in serum prolactin which occurred in female mice administered oral timolol at 500 mg/kg/day, but not at doses of 5 or 50 mg/kg/day. An increased incidence of mammary adenocarcinomas in rodents has been associated with administration of several other therapeutic agents that elevate serum prolactin, but no correlation between serum prolactin levels and mammary tumors has been established in humans. Furthermore, in adult human female subjects who received oral dosages of up to 60 mg of timolol maleate (the maximum recommended human oral dosage), there were no clinically meaningful changes in serum prolactin. Timolol maleate was devoid of mutagenic potential when tested *in vivo* (mouse) in the micronucleus test and cytogenetic assay (doses up to 800 mg/kg) and *in vitro* in a neoplastic cell transformation assay (up to 100 mcg/mL). In Ames tests the highest concentrations of timolol employed, 5,000 or 10,000 mcg/plate, were associated with statistically significant elevations of revertants observed with tester strain TA100 (in seven replicate assays), but not in the remaining three strains. In the assays with tester strain TA100, no consistent dose response relationship was observed, and the ratio of test to control revertants did not reach 2. A ratio of 2 is usually considered the criterion for a positive Ames test. Reproduction and fertility studies in rats demonstrated no adverse effect on male or female fertility at doses up to 21,000 times the systemic exposure following the maximum recommended human ophthalmic dose.

PATIENT COUNSELING INFORMATION

Patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second or third degree atrioventricular block, or cardiac failure should be advised not to take this product. (see **CONTRAINDICATIONS, 4.1, 4.2**) Patients should also be instructed that ocular solutions, if handled improperly or if the tip of the dispensing container contacts the eye or surrounding structures, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions. (see **WARNINGS AND PRECAUTIONS 5.8**) Patients should also be advised that if they have ocular surgery or develop an intercurrent ocular condition (e.g., trauma or infection), they should immediately seek their physician's advice concerning the continued use of the present multidose container. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five minutes apart. Patients should be advised that Istalol® contains benzalkonium chloride which may be absorbed by soft contact lenses. Contact lenses should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following Istalol® administration.

Rx Only

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

Based on 9401500 US/IST/14/0007 Issued 06/2013

17th Annual Dry Eye Report

Tools of the Trade:

Current Techniques to Treat Meibomian Gland Dysfunction

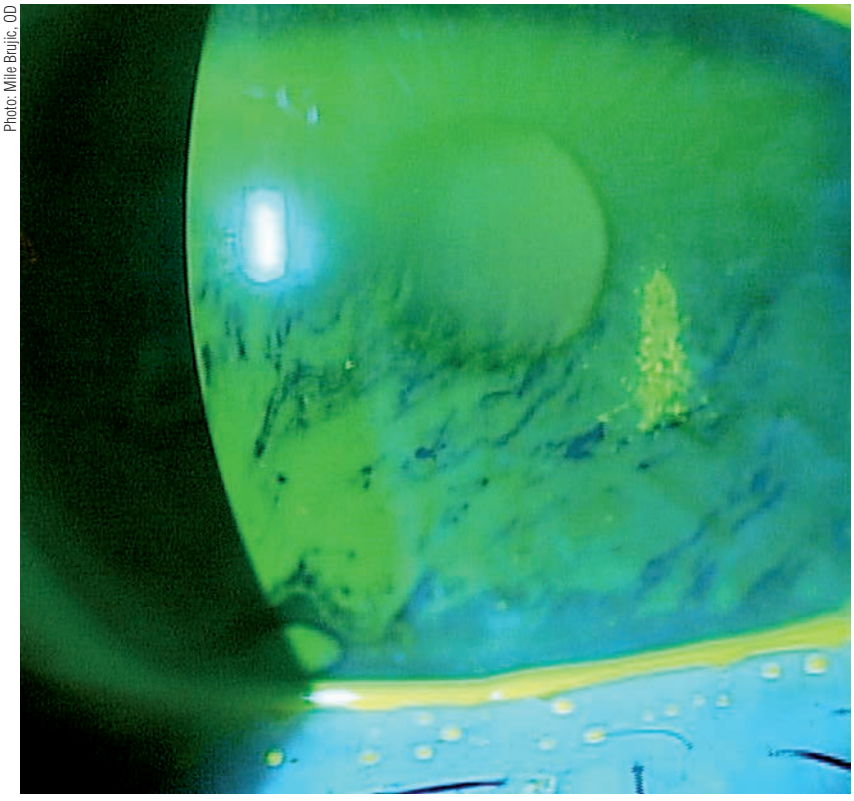
With new techniques and technologies emerging, optometrists have more ways than ever to combat this pervasive problem. By Gregory Moore, OD

Because dry eye disease (DED), like its associated pathologies, most often involves an inflammatory process, logic may dictate that successful treatment requires nothing more than eliminating the inflammation. However, treatment is rarely so simple. Clinicians no longer concern ourselves solely with treating the inflammation—today, we aim to treat its underlying cause.

Dry eye and its components are not always easy to diagnose. As we learned from the DEWS report, DED is a multifaceted disease of the tears and ocular surface that results in symptoms such as dryness, itching, stinging, burning, blurry vision, a gritty or sandy sensation, excessive tearing, photophobia and, last but not least, visual disturbance.[1-3]

Once a diagnosis is made, subsequent treatment should include an evaluation for systemic or environmental factors, especially if the presentation is not consistent with the patient's age or overall health.

Photo: Mile Brujic, OD



Corneal staining in this dry eye patient shows epithelial barrier disruption. A variety of new tools to combat the factors associated with dry eye pathogenesis have hit the market in the last few years.

This article provides an overview of the latest methods and devices available for optometrists to treat dry eye, specifically those involving evaporative dry eye.

The Rising Tide

Dry eye typically stems from one of two etiologies: aqueous deficiency or meibomian gland dysfunction (MGD).[3] The curveball in diagnosing is that both can be present at once.[3] Years ago, when dry eye was considered simply a nuisance, aqueous-deficient dry eye (ADDE) treatment included artificial tears and punctal occlusion, while MGD care was limited to a low-dose, long-term, oral doxycycline or tetracycline and warm compresses. Then, Restasis (cyclosporine, Allergan) came along and upended the conventional wisdom. Suddenly, the eye care community had a demonstrably efficacious way to increase tear production. Since then, the discipline has shown a growing interest in tackling what was often dismissed as a nuisance complaint.

And it's a nuisance not just for MGD patients—who experience a lasting impact on their quality of life—but for clinicians as well, who are seeing a dramatic rise in DED prevalence.[3-6] A 2012 Gallup study of dry eye sufferers projected growth of 10.2% over the next 10 years.[6]

Research shows that DED is present in approximately half of patients who wear contact lenses.[7] In patients with diabetes, it is reportedly as high as 54%.[8] In those with glaucoma or ocular hypertension, it is as high as 59%.[9] A recent prospective study of patients scheduled for DED using the International Task Force scale—where two is considered moderate level of DED—indicated that 80.9% of patients scheduled for cataract surgery scored a two or higher.[10] Yet, only 22.1% of these patients were previously diagnosed with DED.[10]

Add to these statistics the realization that the dry eye prevalence increases with age, and our aging population continues to grow, and it's reasonable to be on the lookout for this disease process in all patients older than 65 years.[11]

The bottom line: you're quite likely to encounter dry eye at an increasing rate, and with so many treatment methods available, you can be responsible for restoring quality of life to patients whether they developed dry eye after surgery, years of contact lens use or simply due to age.

Something in the Air

A 24-year-old white male presented in the morning with complaints of red, irritated eyes after working on a computer all day. However, upon examination, his eyes looked remarkably healthy. Another optometrist previously diagnosed him with computer eyestrain and prescribed computer glasses, which offered only some relief.

The patient was rescheduled for an end-of-day appointment, during which he presented with highly irritated eyes with a 3+ conjunctival edema and 1++ injection OU. He was prescribed Lotemax (loteprednol etabonate, Bausch + Lomb) OU QID for two weeks.

Upon follow up, the patient reported improvement of his symptoms; however, it was clear something in his workplace was causing the problem. He denied awareness of any window or vent creating airflow. He was asked to investigate any possible airflow in his work environment and taper the Lotemax over the next two weeks.

At follow up, he reported that he stopped using the Lotemax the day after his last visit and had not had any problems since. He had found an air vent that was indirectly creating airflow on his face at work, and had adjusted the vent accordingly, which resolved the issue.

The lesson: despite our ever-increasing arsenal of sophisticated therapies for dry eye, sometimes paying careful attention to the conditions under which our patients work, live and play will yield simple adjustments that can make lasting improvements.

Tear Film Anatomy

To properly treat MGD, clinicians should first have a firm grasp of the anatomy of the tear film and the origins of each layer—critical elements that help you determine the most appropriate treatment to resolve the underlying disease process that resulted in DED.

To briefly review, the tear film is made up of three layers: mucin, aqueous and lipid.[12]

The mucin layer, which is about 0.02µm to 0.05µm thick, is the innermost and thinnest layer. It maintains tear film stability and is a product of the conjunctival goblet cells.[12] Epithelial cells produce glycocalyx to help bind the mucin layer to the epithelial surface.[12]

The aqueous layer, about 0.7µm thick, is the thickest of the three. This middle layer is formed from the secretions of the lacrimal and accessory glands. It contains electrolytes, proteins, antibodies, oxygen, carbon dioxide, minerals and glucose.[12]

The outer layer, which is comprised of lipids, is approximately 0.1µm thick and contains esters and glycerol as well as fatty acids. Its function is to prevent the evaporation of aqueous. This layer is a product of the meibomian glands and the glands of Zeiss.[12]

Investigators have shown that MGD is present in as many as 86 out of 100 cases of dry eye.[5] The exact etiology of MGD is unknown.

It is clear, however, that two pathologies seem to be key: decrease in the lipid layer due to keratinization of the terminal duct anatomy and an accumulation of cellular and lipid material within the duct lamina.[13]

Much of the research—and product development—has focused on enhancing the meibomian gland function by reversing or eliminating these two pathologies.

Clinical Approach

After diagnosing a patient with DED, clinicians must then determine whether it is ADDE, MGD or (as is common) a combination of the two. Next, determine which process is the most significant contributor to the presentation and direct your approach to therapy appropriately.

Most patients who present with 2+ dry eye disease have minimal expression of oil from the meibomian glands, according to the DEWS report.[3] Initially, an accurate differential diagnosis based upon staining and meibomian gland expression can be difficult to determine because the inflammatory process will create findings consistent with both ADDE and MGD. Too often, this can be misleading and start the practitioner and the patient on the wrong management path if the underlying cause is more significantly ADDE as opposed to MGD. Given that treatments for both of these diagnoses can take months to produce results, it is obviously essential to make the best initial diagnosis before long-term treatment is attempted.

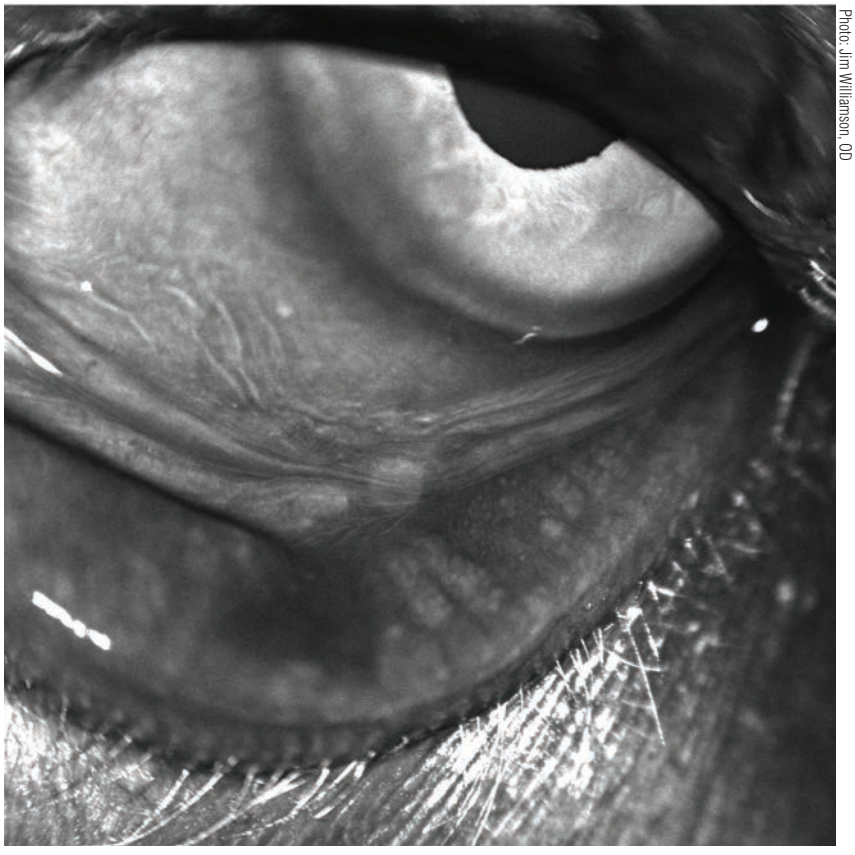


Photo: Jim Williamson, OD

This patient clearly demonstrates meibomian gland dropout.

The initial use of a topical steroid QID for two to four weeks can reduce the inflammation, allowing the clinician to make a more accurate initial diagnosis and initial treatment plan. The Report of the International Dry Eye Workshop states that, at least in some instances, periglandular inflammation contributes to MGD.[3]

In our practice, we typically initiate short-term use of a topical steroid to reduce the inflammation in and around the meibomian glands and help to restore the free flow of oil via digital expression. If this is successful, we'll continue with reasonable confidence that treating the ADDE will improve the overall DED. Since this patient has ADDE, our medical regimen typically would be to taper the steroid over the first month's treatment, introduce cyclosporine 0.5% OU BID and follow up in three months. These patients are given thorough education at diagnosis on the chronic nature of the disease and understand they will need to be treated and/or monitored routinely.

When reduction of the periglandular inflammation does not result in the desired clearance of meibomian gland blockage, we act more aggressively to improve the production of the lipid layer.

Many practitioners initiate treatment with both a steroid and topical cyclosporine. A 2012 study indicates that treatment with a combination of methylprednisolone 1% and cyclosporine 0.5% resulted in improved clinical findings at one month compared with patients who were treated with cyclosporine alone.[14] This suggests that initial treatment with a steroid can help better address the underlying cause of the inflammatory process.

Lotemax gel (loteprednol etabonate, Bausch + Lomb) is par-

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®

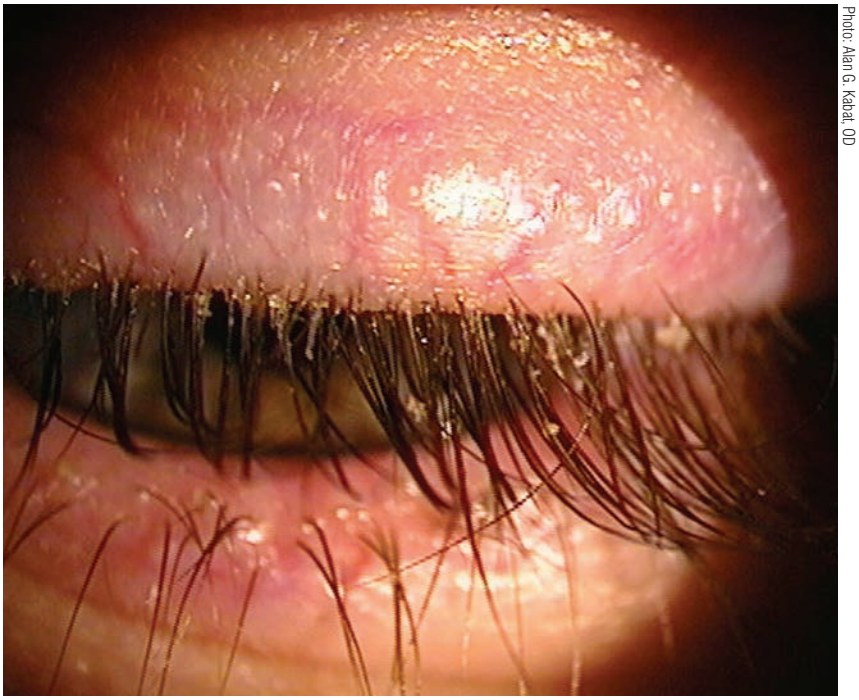


Photo: Alan G. Kabat, OD

Blepharitis is an inflammatory infection that can lead to dry eye disease. Several products on the market aim to treat this condition.

ticularly useful in this initial stage of treatment. An advantage of the drug's gel form is that the suspension maintains an equal distribution of the active ingredient throughout the bottle without having to shake before using, which patients are apt to forget before instilling an eye drop. In non-gel drug delivery vehicles, this can result in a dilution of the active ingredient during the initial phase of the application and an oversaturation of the active ingredient toward the end of the treatment.

Therapy Beyond the Bottle

Several new treatment options have come along recently with the purpose of eliminating the constant need for drops, and mainstays like punctal occlusion continue to play a role. However, even with the added control these interventions offer, DED patients need to be advised that they will likely be treated for life.

Unless you have a practice limited to dry eye, it is rare that any one practice would support purchasing all available options. These products are in various stages of FDA approval, but each shows some degree of promise for dry eye treatment, and MGD specifically.

Punctal plugs have of course been in use for years as a treatment for DED as a way to decrease tear drainage and maintain adequate tear volume. Dextenza (Ocular Therapeutix), a promising new development that's similar in concept though not truly a punctal plug, is an intracanalicular drug depot that will time-release a tapered dose of dexamethasone over a four-week period. By avoiding the sizable variations in drug concentration typical of topically administered drugs, this sustained-release approach is believed to provide more consistent therapy. It is currently under FDA review.

BlephEx (Rysurg), an in-office procedure akin to an aggressive lid scrub, is another promising MGD intervention. Though blepharitis is not the same as MGD, its presence also can interfere with meibomian gland secretions. This treatment looks similar to an alger brush used for foreign body removal, but uses a microsponge instead of a diamond head. BlephEx is a procedure performed by the clinician to exfoliate debris from the lid margin, usually following application of a topical anesthetic. It takes about six to eight minutes.

Avenova (NovaBay) is a newer lid hygiene method to be used by the patient at home, although it does require a prescription. It contains a stable formulation of hypochlorous acid 0.01%—the same molecule used by white blood cells to inactivate pathogens—in saline said to be designed for daily use. Avenova has broad-spectrum activity against common lid microorganisms, including *Serratia marcescens*, Methicillin-resistant *Staphylococcus aureus*, *Staphylococcus epidermis* and *Staphylococcus haemolyticus*.[16] The patient sprays Avenova on the surface of the lids with their eye closed, then gently massages it into the lid with their finger.

LipiFlow (TearScience), is a thermal pulsation treatment system to improve meibum mobility. The device delivers heat to the inner eyelid along with adaptive pressure that cleans the glands without putting pressure on the globe. The procedure is done bilaterally in the office and takes about 12 minutes to elicit an expression of the meibomian gland. It can be performed just once or repeated based on the patient's response.

Intense pulsed light therapy (IPL) has been FDA approved for more than 15 years to treat rosacea and

One Plug
One Size

SnugPlug™

That's *all* you need!

One-size-fits-all punctum plug
eliminates sizing and **simplifies stocking**

Pre-stretched shape (on inserter)
avoids dilation and **facilitates insertion**

Expanded shape (once inserted)
assures snug fit and **virtually eliminates pop-out**

Soft collar prevents migration
and **provides patient comfort**

Ophthalmics
FCI

FCI-Ophthalmics.com
800.932.4202

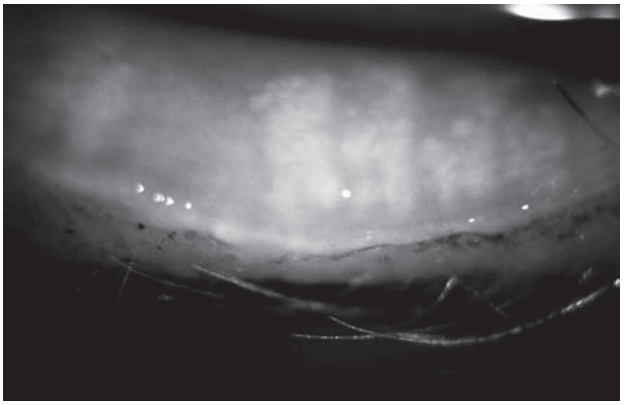
Plug into FCI for Dry Eye Treatment and watch the SnugPlug insertion video.

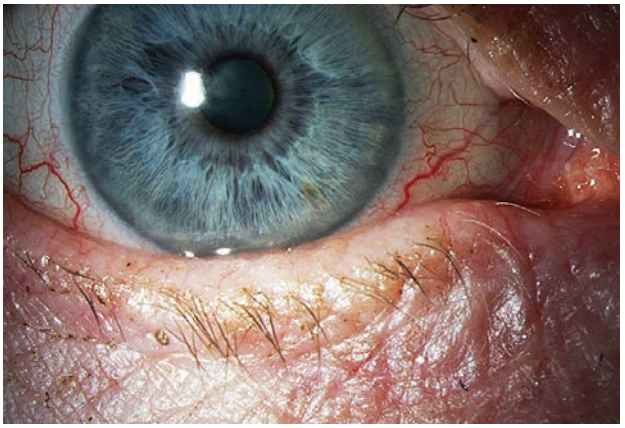
Visit PlugintoFCI.com for promotional pricing

remove superficial skin lesions. Such a device is commonly found in dermatology offices.

Ophthalmologist Rolando Toyos, MD, originated the idea of using IPL in eye care after a series of DED patients presented in his office demonstrating improved tear film characteristics without any change in their treatment regimen—all had been treated for rosacea with IPL.[15] The device uses a xenon flash-lamp to emit wavelengths of light from 400nm to 1200nm. When placed on the light, a filter restricts the wavelength to the visible light range of 500nm. When applied to the skin, this band of light causes the blood cells in telangiectatic vessels to absorb the light, coagulate and, finally, to close the blood vessels.[16] Some studies hypothesize that IPL treatment near the lid causes the abnormal blood vessels to close and note a positive effect on patients with MGD.

IPL is contraindicated in patients with darker pigmentation in that the pigment absorbs the light, making it ineffective. While IPL shows promise in treating MGD, scope of practice laws may hamper its widespread use by optometrists. However, numerous state optometry boards interpret the laws of that state as allowing this technology to be within optometry's scope of practice. Prior to implementing any IPL treatment in-office, clinicians should check with their state board to make sure there is no prohibitive language that would prevent optometric use.





Above, significant meibomian gland structural loss in a patient with moderate to severe MGD. Below, the clinical appearance of the ocular surface and lid in the same eye.

The management of MGD in clinical practice remains challenging, as patient compliance with doctor-recommended self-administered therapies is notoriously poor.[17] So, to provide more effective dry eye management, practitioners should investigate in-office options that may offer clinical improvement that is both immediate and independent of patient compliance (or lack thereof). Some manufacturers offer a trial period to ensure their patient demographics will support the added out-of-pocket expense and cover the initial overhead. Once you hone in on how to best treat DED in your particular population, you can begin improving the quality of their lives for years to come. ■

Dr. Moore is senior clinical instructor for the Kentucky College of Optometry in Pikeville, KY and is currently vice president of the Association of Regulatory Boards of Optometry.

1. Market Scope. 2011 Comprehensive Report on The Global Dry Eye Products Market. St. Louis, MO: Market Scope, November 2011.
2. National Eye Institute. Facts about dry eye. www.nei.nih.gov/health/dryeye/dryeye. Accessed April 7, 2016.
3. The definition and classification of dry eye disease: Report of the Definition and Classification Subcommittee of the International Dry Eye Workshop (2007) Ocul Surf. 2007;5:75–92.
4. Kim KW, Han SB, Han ER, et al. Association between depression and dry eye disease in an elderly population. Invest Ophthalmol Vis Sci. 2011 Oct 10;52(11):7954-8.
5. Lemp M, Crews L, Bron A, et al. Distribution of aqueous deficient and evaporative dry eye in a clinic-based patient population. Cornea. 2012 May;31(5):472-8.
6. The Gallup Organization, Inc. The 2012 Gallup Study of Dry Eye Sufferers. Princeton, NJ: Multi-Sponsor Surveys, Inc; 2012.
7. Doughty M, Fonn D, Richter D, et al. A patient questionnaire approach to estimating the prevalence of dry eye symptoms in patients presenting to optometric practices across Canada. Optometry and Vision Science. 1997;74(8):624-31.
8. Manaviat M, Rashidi M, Afkhami-Ardekani M, Reza Shoja M. Prevalence of dry eye syndrome and diabetic retinopathy in type 2 diabetic patients. BMC Ophthalmology. 2008 June 2;8:10.
9. Leung E, Medeiros F, Weinreb R. Prevalence of ocular surface disease in glaucoma patients. J Glaucoma. 2008 Aug;17(5):350-5.
10. Trattler W, Reilly C, Goldberg D, et al. Cataract and dry eye: Prospective Health Assessment of Cataract Patients Ocular Surface Study. 2011 American Society of Cataract and Refractive Surgery Annual Meeting, San Diego, Calif.
11. Schaumberg DA, Sullivan DA, Buring JE, Dana MR. Prevalence of dry eye syndrome among US women. Am J Ophthalmol. 2003 Aug; 136(2):318-26.
12. Creech J, Do L, Fatt I, Radke C. In vivo tear film thickness and implications for tear film stability. Curr Eye Res. 1998 Nov 17(11)1058-66.
13. Tomlinson A, Bron A, Korb D. The International Workshop on Meibomian Gland Dysfunction: Report of the Diagnosis Subcommittee. Investigative Ophthalmology & Visual Science. March 2011;52:2006-49.
14. Byun Y, Kim T, Kown S, et al. Efficacy of combined 0.05% cyclosporine and 1% Methylprednisiline treatment for chronic dry eye. Cornea, 2012 May;31(5):509-13.
15. Papageorgiou P, Clayton W, et al. Treatment of rosacea with intense pulsed light: Significant improvement and long-lasting results. Br J Dermatol 2008:159;3;628-32.
16. Toyos R, McGill W, Briscoe D. Intense Pulsed Light Treatment for Dry Eye Disease Due to Meibomian Gland Dysfunction; A 3-Year Retrospective Study. Photomed Laser Surg. 2015 Jan 1;33(1):41–6.
17. Geerling G, Tauber J, Baudouin C, et al. The International Workshop on Meibomian Gland Dysfunction: report of the subcommittee on management and treatment of meibomian gland dysfunction. Invest Ophthalmol Vis Sci. 2011; 52: 2050–2064.


Take10Vision
WATCH LEARN GROW
855-504-8152 | info@take10vision.com
Home
About Us
Introduction
Mission
Strategy
Sponsors
Updates
Contact Us
LOGIN
Education & Training Videos
in 10 Minutes or less.
A website offering concise, to-the-point education and training videos supplemented with implementation support provided in a user-friendly time saving and entertaining format.
CONTACT US
OR
VIEW SAMPLE VIDEOS
WATCH ONLINE
take10vision.com
Increase your office's productivity and efficiency with Take10Vision
STAFF TRAINING + NICHE MARKETING + OFFICE SURGERY + PEDIATRICS + MUCH MORE...!
POWERED BY EYE iQ


Take10Vision
WATCH LEARN GROW
EYE iQ
DIGITAL MEDIA PLATFORM
BOOST YOUR IQ
855.504.8152 OR EYE-IQ.COM
Take10Vision is Powered by Eye IQ
TRAINING + VIDEO + EMAIL + LOBBY + SOCIAL MEDIA + WEBSITES
Eye IQ is a product of EyeMotion

Blephadex™
Science Based Lid Care

NEXT-GENERATION
Treatment For:

- DRY EYE SYNDROME
- MEIBOMIAN GLAND DYSFUNCTION
- BLEPHARITIS/DEMODEX

Lunovus™
innovating your future

1-800-980-6551

www.Blephadex.com
www.MacularHealth.com

Dry Eye Breakthroughs

(Advertisement)

Key Industry Leader Discussion

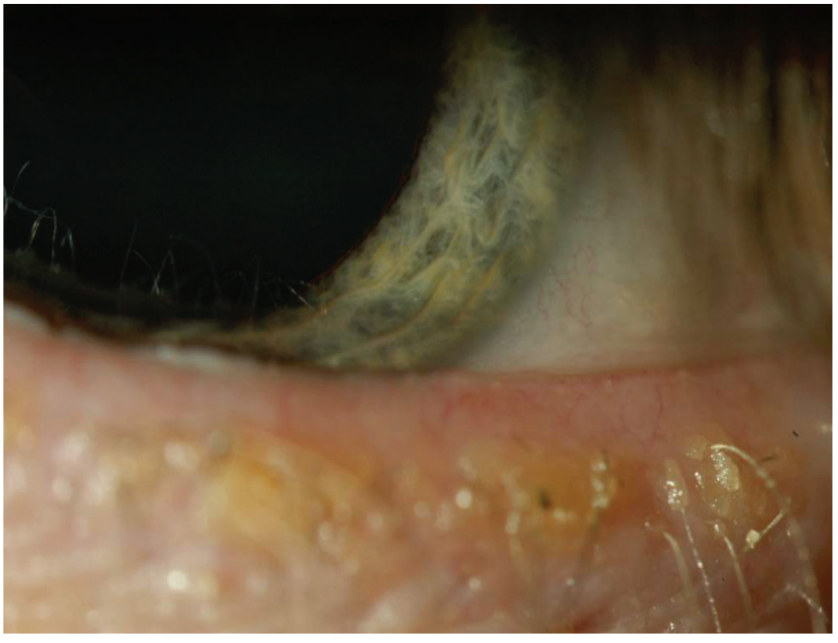
Ben Gaddie, O.D.

Blephadex Leads Evolution In Non RX Treatments for Dry Eyes and Blepharitis

Dry Eye is the most common anterior segment disease presenting to eyecare providers world-wide and represents the easiest pathway for medical eyecare management. Approximately 40 million Americans have dry eye disease.

Blepharitis and Meibomian Gland Dysfunction are common findings in ocular surface disease in up to 86% of patients. Lemp MA, et al. Distribution of aqueous deficient and evaporative dry eye in a clinic-based patient cohort: a retrospective study. Cornea. 2012:31(5):472-478. Blepharitis and MGD result in mechanical blockage of the meibomian gland orifice which can manifest as dry eye disease. Removal of bacterial and Demodex biofilms on the eyelid/meibomian line margin is crucial for restoring normal function to the glands. (See photo below for example of lid margin build up of biofilms and demodex debris blocking meibomian gland function.)

> *"Blephadex is one of the best Non-RX products I have used with patients."*



The leading cause of blepharitis is Demodex infestation. Demodex can be found in higher numbers amongst contact lens wearers versus non contact lens wearers. Jalbert I1, Rejab S. Increased numbers of Demodex in contact lens wearers. Optom Vis Sci. 2015 Jun;92(6):671-8. doi: 10.1097/OPX.0000000000000605.

The combination of Tea Tree Oil and Coconut Oil found in Blephadex has been an effective, comfortable and easy-to-use treatment for patients with symptoms of blepharitis and Demodex. Patients' symptoms like watering and itching eyes are remarkably better after 3-4 weeks of use. It's become our go-to product for blepharitis and is great for ongoing maintenance as a lid hygiene product.

DOCTOR, MY EYES... ARE TIRED!

With ubiquitous tech comes asthenopia, but your patients may not be reporting it. To keep patients safe in this digital world, gain greater clarity in defining and discussing eyestrain. **By Dawn Meyer, OD and Pete Kollbaum, OD, PhD**

Photo: iStock

Those of you old enough to remember the Jackson Browne song "Doctor, My Eyes" may now have the tune stuck in your head; however, it brings to mind a serious question: How many times have you, as a practitioner, heard from your patients that their eyes are tired? It is troubling that you may not hear patients make mention of it as often as you should. Even worse, why are patients saying it and what can you do about it?

We all work hard each and every day; so do our eyes. Likewise, as the rest of the body experiences fatigue throughout the day, our eyes follow suit. This all makes sense, but why does this happen? The answer may not be as simple as you might think.

Usage Patterns

Tired eyes, referred to in the medical literature as *asthenopia*, may also be known by a variety of terms such as *eyestrain*, *computer vision syndrome* or the now-preferred *digital eyestrain*. Nonetheless, the terms themselves, and the variety used to describe the condition, hint at an underlying etiology and a lack of its true understanding.

Digital eyestrain is a diagnosis of exclusion. Patients may complain of one or a combination of multiple symptoms, such as tired eyes, shoulder pain, headache, fatigue, eye irritation and pain, blurred or double vision, light sensitivity, tearing, dry eyes and trouble focusing. These complaints may differ between patients and can vary for an individual over time.

Asthenopia has been well reported in the literature; however, we have only recently seen its resurgence, potentially in association with the increase of digital device use.[1-5] In particular, according to a recent Vision Council survey, upwards of 90% of Americans use digital devices at least two hours per day, with 60% using them five or more hours per day and 70% using two or more devices at a time—a staggering figure with respect to the potential implications for eyestrain.[6] In fact, 73% of all American adults own a computer and 68% own a smartphone.[7]

Devices are rapidly replacing

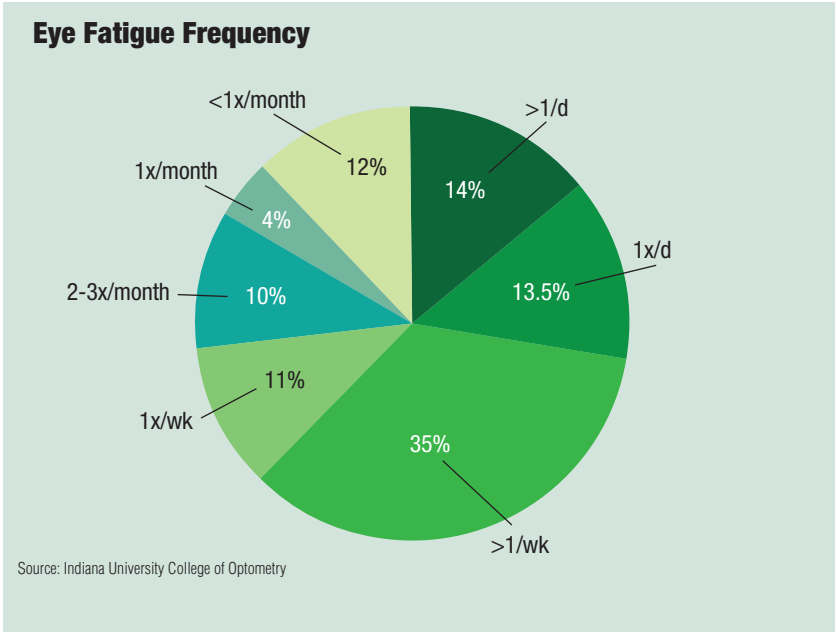


Fig. 1. Frequency with which eye fatigue is experienced by 609 respondents to an online survey. Subjects were told, "Eye fatigue is the physical discomfort of your eyes after spending periods of time throughout the day in front of a digital screen, like a computer or smartphone." Based on that definition, subjects were asked how often they experienced eye fatigue, with options ranging from 'multiple times per day' to 'I never experience eye fatigue.'

other forms of communication media; 63% of Americans use a smartphone, computer, tablet or e-reader as opposed to traditional printed paper.[8] This is only one task capable of being completed on the devices, and they are performing it for an average of 60 hours per week.[9]

To add to this, 84% of smartphone and tablet owners say they also use their devices as second screens while watching television.[9] Chalk that up to the rise of social media and a desire to share the experience with friends and family as it happens.

Sounding a cautionary note about our digital device habits, the Vision Council survey reported that 65% of Americans experience symptoms of eyestrain while using these devices, with even more frequent reports occurring in adults younger than 30 years of age.[6] Comparable numbers have been reported by other studies.[4,8] Millennials and the generations who will follow them live in a world where the use of digital screens for many aspects of communication and education is their default experience.

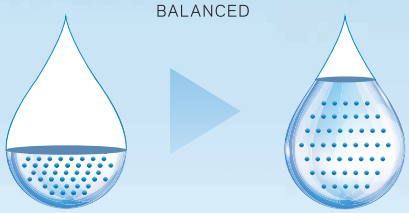
Similarly, we at Indiana University School of Optometry recently surveyed a random sample of 18- to 39-year-old adults who do not currently wear multifocal correction or gas permeable contact lenses. We questioned the 609 respondents on how often they experienced eye fatigue, which was defined as physical discomfort of their eyes after spending periods of time throughout the day in front of a digital screen. More than one-quarter of respondents stated they experienced eye fatigue at least one

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

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

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

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



HYPEROSMOLARITY

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

HEALTHY TEAR

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

RESTORE + CLEANSE + NOURISH

thera tears®
THERAPY FOR YOUR EYES™

DRY EYE THERAPY

Restores Eyes Natural Balance™

theratears.com

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

AKORN Consumer Health

time per day and more than half reported experiencing it more than once per week *(Figure 1)*.

Causes and Consequences

While it is possible that we are all just working our eyes harder than ever before, the possibility exists that digital devices are increasing the incidence of eye strain. The visual demands and effects of digital devices on the ocular system are inherently different from traditional print in many ways.

• ***Screen size.*** Mobile device screen sizes are smaller than typical newspaper formats. Although text sizes are theoretically easily increased on digital devices, people most often choose to view text at considerably smaller point size than newspaper print and at the smaller end of the ISO recommendations.[10-12] Small text and screens, and the associated closer viewing distance seen with digital device use may require a sustained, increased accommodative and convergence demand, stressing the muscles of these systems.

• ***Posture.*** When viewing smaller character sizes on digital devices, posture may also be frequently altered to compensate for the limits of visual acuity. These postural adjustments include flexing the thoracic and lumbar spine and lowering torso height, resulting in incorrect posture. When viewing small characters at a far viewing distance, the head is also frequently moved forward, resulting in increased muscle load on the upper vertebrae, which is balanced by an increased load on the muscles in the neck, shoulders and upper back.[13] Reflective glare from screens is also a frequent complaint of users of digital devices, which is not seen when using traditional print. These reflections may also result in altered head and neck postures when working on digital devices.[11]

• ***Blink rate.*** Any task with a high cognitive demand results in a decreased blink rate, regardless of the medium.[14] Digital device use has been shown to decrease the blink fullness—an increase in incomplete blinks—over completing the same task on hardcopy.[15] Increased corneal exposure may occur, which can result in increased evaporation of the tear film, leading to more symptoms.

• ***Blue light.*** Many of these digital devices have been shown to emit high levels of short-wavelength blue light, which research shows has a negative impact on melatonin production. Repeated, prolonged exposure to blue light can result in altered circadian rhythms and the possibility of increased general fatigue which, in turn, impacts the frequency and amount of eye fatigue.[16,17]

Although it is clear that many ways exist for digital devices to impact our visual system, and the demands on our eyes are different than they were only a few decades ago (when Jackson Browne was well known), it may not be an exaggeration to question whether or not we truly understand what it means when someone says they have tired eyes. Importantly, the underlying etiology of eyestrain must be better understood.

Sorting Out the Symptoms

In an effort to better understand what patients mean when they say they have eye fatigue, our survey asked respondents to report the frequency and severity of symptoms they experience during instances of eye fatigue. In general, the frequency and severity of these symptoms fall into three main groups or factors

(Figure 2). Symptoms of eyestrain, soreness, tired eyes and headache all fall together in one grouping called *primary global sensations*. A second group is comprised of blurred vision and "floating" text, which we refer to as *visual sensations*. The final group—irritation, dryness, burning and tearing—we refer to as *secondary surface sensations*.

The results of our survey indicate that regardless of frequency or severity, a respondent reports concerning an individual symptom, each eyestrain symptom can be reliably differentiated from one another, even as they occur simultaneously. We believe this categorization scheme helps uncover the underlying etiology and direct our efforts toward appropriate treatment options.

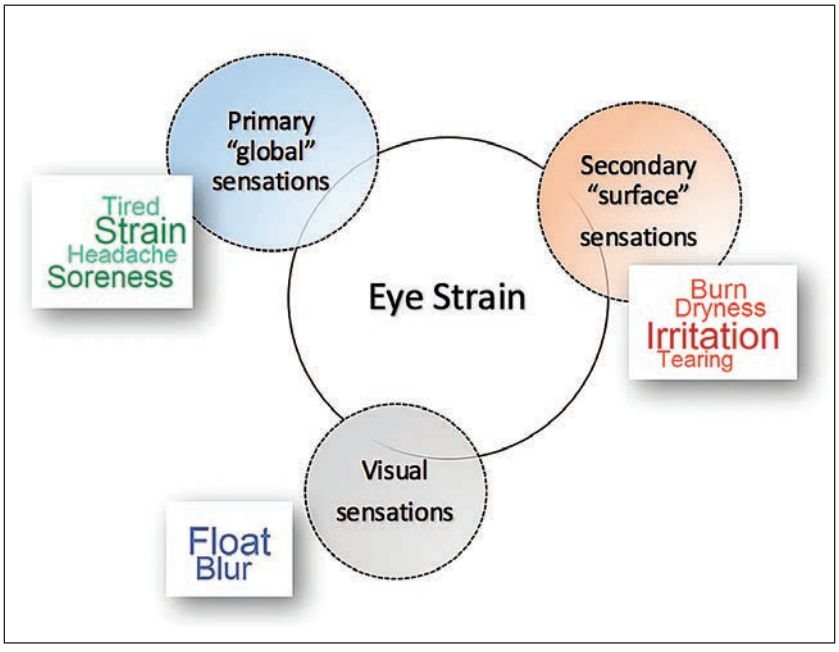


Fig. 2. A diagram demonstrating the results of a confirmatory factor analysis, where both symptom frequency and severity as described by subjects with eye strain fall into three distinct groups, where the relative symptom importance within each group is described by the text size.

What Can We Do?

Although better categorization of symptoms can provide greater clarity of mind, questions remain about the underlying etiologies. Do issues of accommodation, convergence, environment, surface dryness, blue light or a combination of these factors cause eye fatigue? Ultimately, treatments need to match causes and be tailored to the individual's usage habits and symptoms. For now, we can take advantage of symptom categorizations to direct our management. For example, the primary global sensations that individuals describe may be aided by more holistic lifestyle changes or overall aids, such as attention to ergonomic factors, taking frequent breaks or reducing blue light exposure.

Establishing an ergonomic working environment should be emphasized to our patients. Ideally, the head and neck will upright, face will be directed at the screen, reflections will be minimal and the patient will either be standing up or using an ergonomically supportive chair. Strategies to reduce blue light include spectacle lenses with blue-blocking filters or coatings available from many manufacturers, and software on digital devices that limits blue light emission, like Apple's Night Shift feature for iOS devices. These can also positively impact the patient's duration and quality of sleep, helping to mitigate the elements of eyestrain that derive from a state of general fatigue.

The secondary surface sensations that individuals describe may be addressed by encouraging them to take more breaks, blink more often and use lubricating eye drops. Additionally, specific soft contact lens materials or surface coatings may minimize surface sensations related to tear evaporation that stems from reduced blink rates during device use.

Clinicians can address the visual sensations individuals describe with a variety of optical manipulations to their corrective lenses such using as low-add progressive addition lenses, or aspheric or zonal contact lenses, all with some variation of lens power to supplement the eyes'

Strategies to reduce blue light include spectacle lenses with blue-blocking filters or coatings available from many manufacturers, and software on digital devices that limits blue light emission, like Apple's Night Shift feature for iOS devices.

natural accommodative system.

Given the surprising complexity at work in how our eyes interact with digital screens, we should keep all options in mind, and in the conversation. A mix of common sense advice and targeted optical remedies can ensure uneventful long-term device use for patients.

It is clear that a potentially large percentage of our patients struggle with symptoms of eye fatigue of high frequency and severity. Many, although struggling, are not voicing their concerns during visits. This highlights the need for practitioners to proactively ask our patients if they are experiencing symptoms and, if so, work with them toward minimizing them insofar as that is possible in this digital age. And we too should practice what we preach, being mindful of our own device use. After all, without digital devices, how could younger readers Google to find out who Jackson Browne was, or maybe even read this article?

The rewards of having access to the world's resources at the touch of a button outweigh the symptoms that accompany digital device use, but with a change in the times comes the need for practitioners to keep pace with changing patient needs in this brave new world of bytes and blue light. ■

Dr. Kollbaum is Associate Dean for Research, and Director of the Borish Center for Ophthalmic Research at the Indiana University School of Optometry. His areas of research interest encompass contact lens optics, contact lens fitting and design, presbyopia, keratoconus, refractive surgery optics, corneal topography, and predictive modeling. Dr. Kollbaum worked in a private multidisciplinary practice prior to returning to IU where he now teaches and performs research in the areas of contact lenses and optics.

Dr. Meyer received her doctorate in optometry in 2012 from Indiana University where she completed a primary care residency. In 2013, she joined Dr. Kollbaum and the rest of the Clinical Optical Research Lab. Dr. Meyer holds membership to the AOA, the Indiana Optometric Association and her local Stonebelt Optometric Society. Her areas of research interests include contact lens fitting and design, patient education and compliance, presbyopia and keraoconus.

1. Sheedy, JE, Hayes JN, Engle J. Is all asthenopia the same? Optom Vis Sci, 2003. 80(11):732-9.
2. Drew SA, Borsting E, Escobar AE, et al. Can chronic visual discomfort measures accurately predict acute symptoms? Optom Vis Sci. 2013. 90(10):1149-55.
3. Riva MA, Arpa C, Gioco M. Dante and asthenopia: a modern visual problem described during the Middle Ages. Eye. 2014;28(4):498.
4. Han CC, Liu R, Liu RR, et al. Prevalence of asthenopia and its risk factors in Chinese college students. Int J Ophthalmol. 2013;6(5):718-22.
5. Chu C, Rosenfield M, Portello JK, et al. A comparison of symptoms after viewing text on a computer screen and hardcopy. Ophthalmic Physiol Opt. 2011;31(1):29-32.
6. Council, TV. Eyes Overexposed: The Digital Device Dilemma. 2016.
7. Anderson, M. Technology Device Ownership: ww.pewinternet.org/2015/10/29/device-ownership-2015-about-this-report. Updated: 10/29/2015. Accessed: 4/2016.
8. Association, A.O., American Eye-Q Survey. 2015.
9. The U.S. Digital Consumer Report T.N. Company, Editor. 2014.
10. Bababekova Y, Rosenfield M, Hue JE, et al. Font size and viewing distance of handheld smart phones. Optom Vis Sci, 2011;88(7):795-7.
11. Ko P, Mohapatra A, Bailey IL, et al. Effect of font size and glare on computer tasks in young and older adults. Optom Vis Sci. 2014;91(6):682-9.
12. Standardization, I.O.f., Ergonomics of human-system interaction VPart 303: requirements for electronic visual displays. 2011. p. 1-43.
13. Rempel D, Willms K, Anshel J, et al. The effects of visual display distance on eye accommodation, head posture, and vision and neck symptoms. Hum Factors. 2007;49(5):830-8.
14. Patel S, Henderson R, Bradley L, et al. Effect of visual display unit use on blink rate and tear stability. Optom Vis Sci. 1991;68(11):888-92.
15. Argilés M, Cardona G, Pérez-Cabré E, et al. Blink rate and incomplete blinks in six different controlled hard-copy and electronic reading conditions. Blink Rate and Incomplete Blinks. Invest Ophthal & Vis Sci. 2015;56(11):6679-85.
16. Gringras P, Middleton B, Skene DJ, et al. Bigger, Brighter, Bluer-Better? Current Light-Emitting Devices – Adverse Sleep Properties and Preventative Strategies. Frontiers in Public Health. 2015;3:233.
17. Chang AM, Aeschbach D, Duffy JF, et al. Evening use of light-emitting eReaders negatively affects sleep, circadian timing, and next-morning alertness. Proc Nat Acad Sci. 2015;112(4):1232-7.

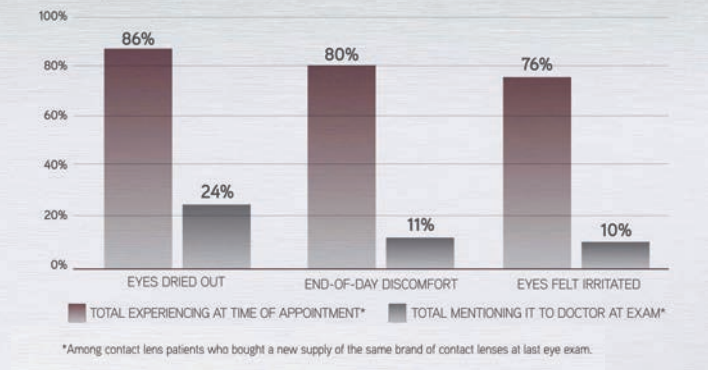
Do You Have Silent Sufferers in Your Practice?

Be a Problem Solver *and* a Problem Preventer for Your Patients

From the moment DAILIES TOTAL1® contact lenses first became available, eye care professionals (ECPs) have been relying on them for patients who experience end-of-day discomfort with their lenses.[1,2] However, there are two types of patients often overlooked for DAILIES TOTAL1® who can especially benefit from its novel material with Water Gradient Technology—*the silent sufferer* and the *new contact lens patient*.[3,4]

A 2006 survey showed that 80% of patients who bought a new supply of the same brand of contact lenses at their last eye exam experienced end-of-day discomfort with their lenses, but only a small percentage (11%) mentioned this symptom to their ECP during the exam.[5]

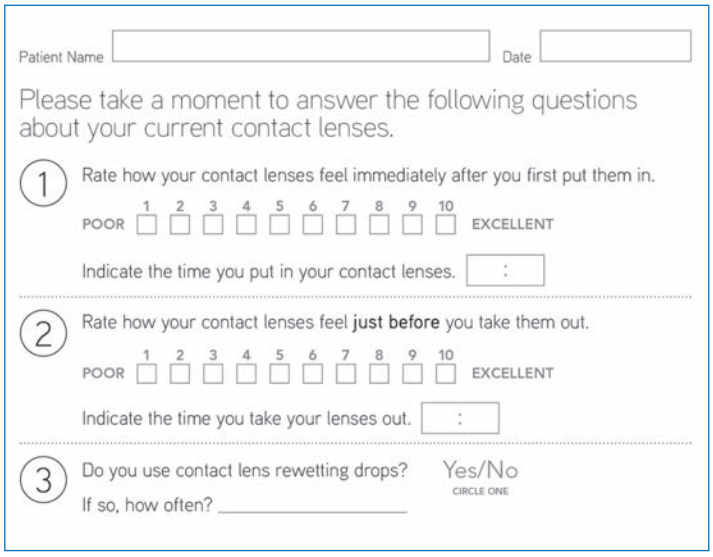
The Silent Sufferer. Every practice has them. The patients who either do not realize their symptoms are related to their contact lenses, or who are simply resigned to the (false) belief that symptoms such as end-of-day discomfort and irritation are an unavoidable part of lens wear. Many ECPs, however, may be surprised to learn just how many silent sufferers they have in their practices. In fact, a 2006 survey showed that 80% of patients who bought a new supply of the same brand of contact lenses at their last eye exam experienced end-of-day discomfort with their lenses, but only a small percentage (11%) mentioned this symptom to their ECP during the exam.[5]



Most patients silently struggle with lens discomfort.[3]

Identifying silent sufferers is a vital part of good patient management, and

Asking a few simple questions can help identify the silent sufferer.



Patient Name _____ Date _____

Please take a moment to answer the following questions about your current contact lenses.

1. Rate how your contact lenses feel immediately after you first put them in.

POOR ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 EXCELLENT

Indicate the time you put in your contact lenses. ☐ :

2. Rate how your contact lenses feel **just before** you take them out.

POOR ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 EXCELLENT

Indicate the time you take your lenses out. ☐ :

3. Do you use contact lens rewetting drops? Yes/No (CIRCLE ONE)

If so, how often? _____

benefits the practice as well. Silent sufferers are at risk for dropout, and each patient who drops out of contact lens use has a financial impact on the practice.[6] Therefore, it is critical to ask the right questions in order to encourage silent sufferers to open up about any problems or discomfort that they may be experiencing with their current lenses. An effective approach is to ask patients how they feel both when they first put their lenses in, and just before they take them out. Also, ask patients if they are using rewetting drops to alleviate end-of-day dryness or discomfort. Simply asking these questions gives ECPs the opportunity to be problem solvers for their patients and to build patient loyalty to their practices.

The New Contact Lens Patient. ECPs may look at DAILIES TOTAL1® contact lenses as a problem solver, and rightfully so given the ability of DAILIES TOTAL1® lenses to help alleviate end-of-day discomfort*.[1,7] It may be just as important, however, to recommend DAILIES TOTAL1® to new contact lens wearers so as to help prevent problems associated with discomfort. Patients who leave the office happy with their contact lenses are more likely to return and to refer others. And more than 80% of DAILIES TOTAL1® contact lens wearers were "extremely" or "very likely" to recommend these lenses to friends or family.[8]

The first contact lens offered to patients should be the lens they will love. Treat this as an opportunity to be proactive with all patients by making a strong recommendation for DAILIES TOTAL1® contact lenses.

**Percentage of wearers agreeing with the statement "With these lenses I sometimes forget I have them on".*

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. In a survey of 280 wearers, based on the increase in number of wearers agreeing with the statement "My/these lenses feel comfortable at the end of the day". Alcon data on file, 2012.
3. Thekveli S, Qui Y, Kapoor Y, et al. Structure-property relationship of delefilcon A lenses. *Cont Lens Anterior Eye.* 2012;35(Suppl 1):e14.
4. Based on laboratory measurement of unworn lenses; Alcon data on file, 2011.
5. Contact Lens Wearers Decision Flow Quantitative Research. Alcon data on file, 2006.
6. Rumpakis J. New data on contact lens dropouts: An international perspective. *Rev Optom.* 2010;147:37-42.
7. Alcon data on file, 2014.
8. Dailies Difference Survey Dashboard. Alcon data on file, 2014.

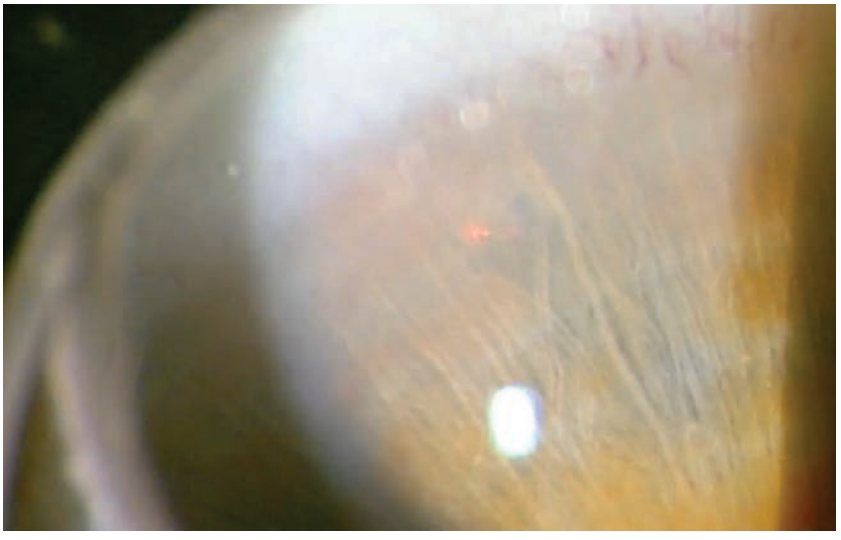
Breaking Down Barriers:
Iridotomy in Optometric Practice

Progressive states allow it, and others are likely to follow. Here's how it's done.

By Joseph Shetler, OD, Jeff Miller, OD, and Nathan Lighthizer, OD

You don't have to look to "a galaxy far, far away" to find optometrists manning the battle stations with lasers. Due to recent optometric scope expansions in Louisiana and Kentucky, added to the prior-existing scope-of-practice law in Oklahoma, clinicians using neodymium:yttrium-aluminum-garnet (Nd:YAG) lasers (1064 nanometers) to treat anatomically narrow angles can be found right here in the Milky Way.

For new graduates, recently trained optometric residents and seasoned clinicians alike, the opportunity to treat anatomically narrow angles or angle closure using Nd:YAG lasers is growing. This article provides a step-by-step account of how to perform this procedure when the laws in your state permit.



In this right eye, at approximately 11 o'clock the clinician aims the laser directly to the left of the visible vessel to assure the laser doesn't cause bleeding.

The Four Angle Closures

The first step in disease management is a proper diagnosis. Taking careful steps at the beginning to fully understand the disease etiology and the orientation of the structures will make for a more predictable and positive outcome. Anatomically narrow angles can be sub-divided into four basic forms:

1. Pupillary block
2. Plateau iris configuration
3. Phacomorphic glaucoma
4. Malignant glaucoma

The end result of each abnormality is approximately the same; a blocked or narrow angle impeding the flow of aqueous humor entering and exiting the anterior chamber and increasing the intraocular

To see a narrated video of this procedure from Dr. Lighthizer, visit www.reviewofoptometry.com.

"Educate Patients,
Inspire Positive Behaviors!"

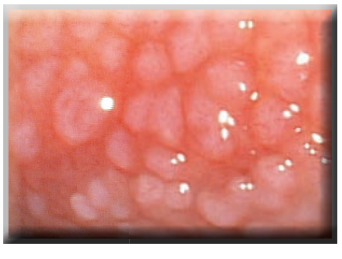
TelScreen

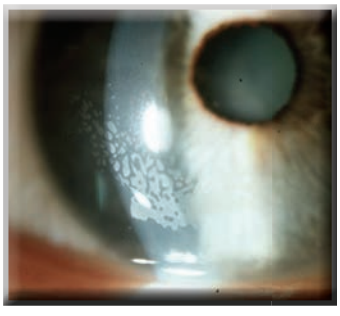
EyeRes™

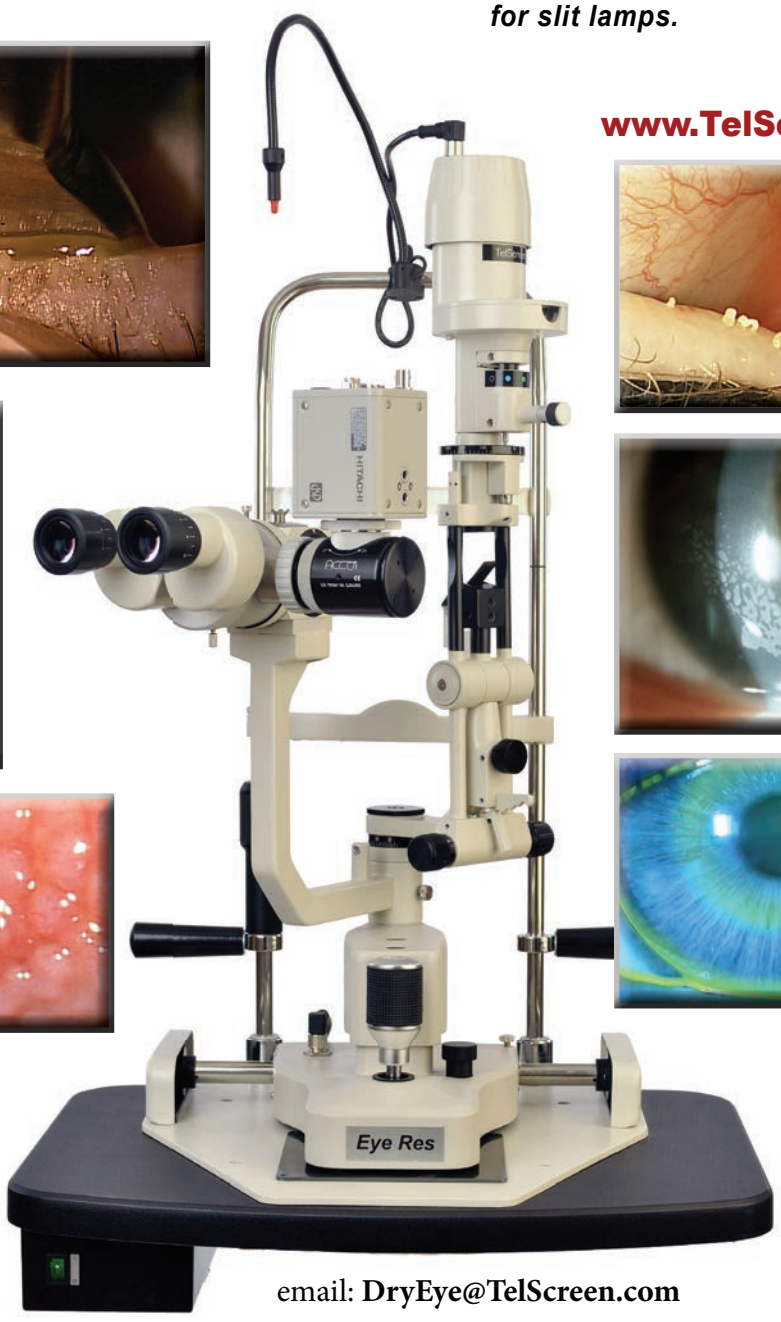
Digital Imaging Systems

for slit lamps.

www.TelScreen.com







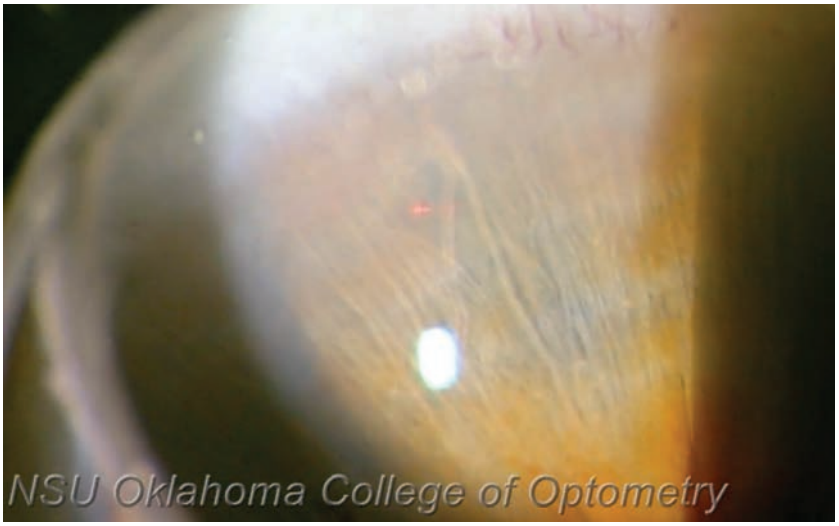
email: **DryEye@TelScreen.com**

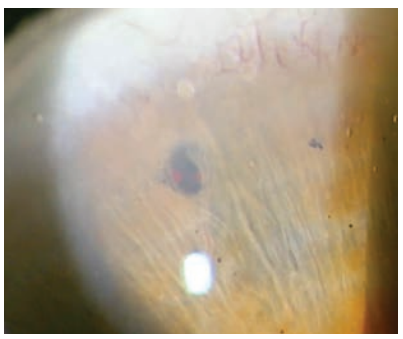
pressure (IOP) by varying and, often, significant amounts. The appropriate diagnosis is a critical element to appropriate treatment.

Pupillary Block

The most common form of angle closure, and the type most commonly associated with positive outcomes, is attributed to pupillary block.[1] A pupillary block occurs when the pupil border comes in contact with the lens and shuts down the flow of the aqueous humor into the anterior chamber. The resultant iris bombé often forms, closing the angle and elevating the IOP. The application of a laser peripheral iridotomy (laser PI) is an immediate need in these cases and a successful procedure will typically lower the pressure within minutes after the procedure. The fellow eye should be carefully evaluated in this case as its angle formation may be similar. The opacification of the lens and anatomical structure, however, may be quite asymmetrical, placing one eye in jeopardy of a closed angle and not the fellow eye.

In many cases, the laser peripheral iridotomy (PI) is performed as a preventative procedure to prevent an acute closed angle.[2] The old adage "an ounce of prevention is worth a pound of cure" is certainly true for this condition. If the standard Van Herrick angle estimation indicates a narrow angle, it is prudent to perform gonioscopy to visualize the angle and make a clinical judgment regarding the necessity of a PI. Anterior segment imaging is also particularly helpful in making a determination regarding the necessity of a preventative PI. Typically an angle less than 10 degrees is judged to be narrow and an indication to proceed with a PI. An angle less than 10 degrees as determined by anterior segment imaging typically corresponds to an angle in which the posterior pigmented trabecular meshwork cannot be observed by standard gonioscopy techniques. This gonioscopic view in which the posterior trabecular meshwork is not visible should be present in at least two quadrants before elevating the case to high closure risk and indicating the need for preventative PI.[3] Another way of stating this is that if you can see the entire trabecular meshwork in three to four quadrants, then a laser PI is likely not indicated.





Above, the clinician prepares to fire the first shot. Before beginning the procedure, we put Alphagan (brimonidine tartrate, Allergan) and pilocarpine in the eye. At left, after two shots, the impact of the laser is clearly visible as is much of the fluid rushing through the hole into the anterior chamber and helping to open up the patient's angle.

Plateau Iris Configuration

Another, much less common, angle closure occurs when the insertion of the iris root is displaced anteriorly. This is called plateau iris configuration. Due to the location of the iris root, a fold is created in the angle and bunched tissue places the angle at risk for closure. In previously undiagnosed cases, the patient may present with alarmingly elevated IOP (in the range of 40mm to 60mm) due to closed angles. A laser PI is usually performed within one to three days of closure onset, depending on the severity of the case and its initial response to medical management. Topical beta-blockers in one dose and brimonidine in one dose accompanied by topical steroids may be used as initial medical management. Carbonic anhydrase inhibitors are indicated if an IOP decrease is urgent. Pilocarpine should be used only in cases of phakic pupillary block or angle crowding.[5]

It is prudent to treat the other eye prophylactically, assuming the

Ask Yourself This Question...

"Why Prescribe?"

OTC Savings Compared to Rx Costs

Kills Bacteria on Contact -"0" Eye Irritation

Stable 18 Months Opened or Unopened

www.whyprescribe.com

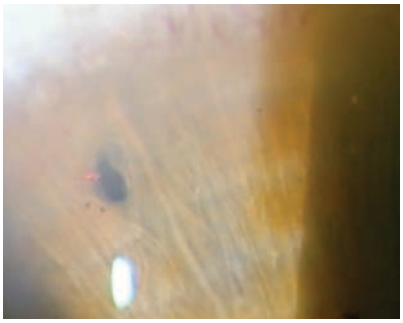
For more information and to order,
call (800) 233-5469 or visit www.ocusoft.com

OCuSOFT®

Procedural Checklist

- ❑ Gonioscopy to visualize the angle anatomy in all quadrants.
- ❑ Consent form and review of risks vs. benefits.
- ❑ Instill pilocarpine and Alphagan (brimonidine tartrate, Allergan) to eye(s) undergoing the procedure 20 minutes prior.
- ❑ Instill proparacaine.
- ❑ Be sure both patient and clinician are in a comfortable position.
- ❑ Under moderate magnification (16x to 25x), identify target crypt.
- ❑ Set power (2.0mJ to 5.0mJ), set pulse 1-2, no offset.
- ❑ Place iridotomy lens, aligning the magnification insert with target.
- ❑ Focus visual beams on selected iris crypt target.
- ❑ Fire with thumb or finger trigger.
- ❑ Continue at same location until plume is visualized.
- ❑ Widen peripheral area to 0.5mm to 1mm.
- ❑ Remove center strands.
- ❑ Remove iridotomy lens.
- ❑ Record total energy, shots fired, outcome of procedure and patient condition.
- ❑ Instill one drop Alphagan in treated eye immediately after the procedure.
- ❑ Check IOP 30 minutes post-op.
- ❑ Prescribe topical steroid for BID-QID use for one week.

patient responds well to the initial PI. If angle closure continues to be present after a patent PI the practitioner must have an elevated concern about plateau iris syndrome as opposed to plateau iris configuration. A PI will typically cure angle closure attacks in plateau iris configuration. In plateau iris syndrome, the peripheral iris bunches up in the angle and obstructs outflow without evidence of pupillary block. Often the diagnosis of plateau iris syndrome cannot be made until after evaluating the benefit of a PI. When treating suspected plateau iris configuration patients, be mindful



More than two shots will be required, as a hole that is too small will heal easily and reclose the angle. The hole should be approximately 500µm, or about a 0.5mm.

that if the angle remains obstructed or recloses, the diagnosis of plateau iris syndrome must be carefully considered. Continued angle closure episodes even after a patent PI is a strong indication of plateau iris syndrome and a laser iridoplasty is the next clinical step to break the attack and prevent subsequent ones.

Phacomorphic Glaucoma

A rare form of angle narrowing or closure that occurs when the lens continues to pathologically enlarge and pushes the iris forward, narrowing the angle, is called phacomorphic glaucoma. A PI remains a strong component of early management but ultimately cataract surgery will be required.[6]

Malignant Glaucoma

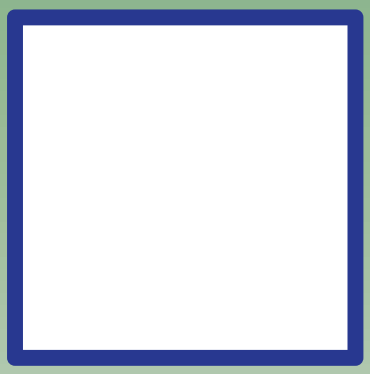
An extremely rare malady, malignant glaucoma, occurs when a misdirection of the flow of aqueous actually rotates in a cyclic pattern and pushes the vitreous forward, narrowing the angle. Typically this occurs after intraocular surgery in eyes with small anterior segments.[7]

Diagnosis

Good gonioscopy skills are necessary to visualize and appropriately evaluate the angle. Evaluate all 360 degrees of the angle. If the posterior trabecular meshwork is the most posterior structure visible, the angle can be assumed to be between 10 degrees and 20 degrees and is described as narrow—putting the patient at risk for angle closure. Clinical judgment and correlation with other symptoms and risk factors will be critical to advising these patients on the necessity of a PI. If only the anterior portion of the trabecular meshwork is visible, the angle is typically 10 degrees or smaller and the risk of closure is probable.[8] This is the time to make recommendations to proceed with the PI. It is also relevant to evaluate pigment in the trabecular meshwork and check for neovascularization in the angle, as well as the presence of anterior synechiae. Prolonged, recurrent or subacute closed angle attacks that have occurred previously may be evident by residual peripheral anterior synechiae.

Thoroughly evaluate for contraindications before proceeding with PI treatment. Carefully consider corneal opacifications and abrasions. Ocular lasers typically cause intraocular inflammation, so be certain the eye is free from inflammatory disorders. The patient must be physically able to hold a steady fixation throughout the procedure. Although the patient cannot be dilated the day of the procedure, it is vital to assess the macula and retina prior to proceeding.

A risk-vs.-benefit dilemma is created when a narrow angle is identified in the initial slit lamp examination. Assessing the macula and retina is critical in most cases prior to proceeding with the procedure, but the question must arise: what if the dilation procedure creates the angle occlusion? If the patient presents with a closed angle, the standard of care and risk-vs.-benefit protocol would be to manage the most obvious and visually destructive condition, the closed



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:

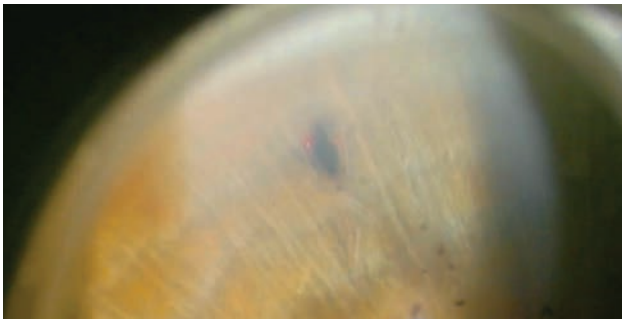
- Unique glycerin formula with **hyaluronic acid** for advanced comfort
- Low actuation force with 1 drop control
- 90 day open bottle stability
- Up to 12 hours of soothing comfort
- Available over-the-counter

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

angle. If the cornea is too cloudy to focus the laser beam, medical steps would need to be taken to reduce corneal edema. In severe cases, proceeding through a hazed cornea may be in the patient's best interest if medical management will not quickly decrease the pressure and edema. When addressing prophylactic concerns, dilate one eye at a time under carefully monitored conditions to assess the retina's and macula's condition prior to proceeding with the PI procedure. Monitor the patient carefully using only a minimal dilating agent, such as phenylephrine, and be certain a immediate danger has passed before scheduling the laser procedure.

Inform the patient that non-perforation or re-closure of the opening with time is a possibility. IOP spikes and inflammation are common and will be medically managed during the post-op period. Approximately 10% of patients undergoing the procedure will experience post-op pressure spikes.[9] Also, inform the patient that, although unlikely, other risks include hyphema, synechiae, peaked pupil, floaters, monocular diplopia, retinal detachment and permanent vision loss.

After education and a signed consent form, pilocarpine is instilled prior to the procedure in an effort to constrict and tighten the iris for easy penetration. Typically, Alphagan or iopidine is instilled to retard pressure spikes. The decision to do both eyes at the same encounter is a personal one and calls for careful judgment. In many cases, it is in the patient's best interest to do both eyes at the same setting. Barring any complications, this is more efficient both in terms of time and monetary expense. The patient's health and visual welfare is always foremost and it is often prudent to do one eye and gauge the results in terms of complications, energy required and desired outcome before proceeding to the second eye.



Here, the clinician fires several more shots, allowing more pigment to come through the hole, equalizing the pressure between the posterior chamber and the anterior chamber.

Procedure Steps

After proparacaine is instilled in both eyes, both the patient and clinician should be seated, and adjustments should be made for comfort and decreased movement. Historically, the PI location is typically at 11 o'clock or 1 o'clock and should be tucked successfully under the upper lid. Although the PI location is still based primarily on personal preference and experience, an increasing amount of surgeons are placing the opening on the temporal meridian in an effort to reduce visual side effects such as dysphotopsia.[10] It is best to identify a crypt or thinner area of the iris as the target.

Place the iridotomy lens on the anesthetized eye, cushioned with Celluvisc (carboxymethylcellulose sodium, Allergan) or a similar agent. Location of the 10mm 66D magnification insert section of the iridotomy lens is critical and should be aligned with the targeted area of the iris. After selecting the target, the optometrist's goal is to create an opening approximately 0.5mm to 1mm in diameter in a peripheral location that will not create a visual disturbance. The optometrist will observe a plume when penetration of the iris has occurred. The fluid behind the iris will rush forward through the opening, looking a bit like a cloud. Although this indicates penetration and can be dramatic, it is not the desired endpoint. Several additional shots will usually be necessary to widen the opening and prevent reclosure. The actual endpoint will come with experience and clinical judgment. The important aspect is to visualize the initial plume. The edges should be widened to 0.5mm to 1mm in diameter. Removing central strands will also prevent collection of debris in the center of the opening that may serve to eventually clog the created opening.

The YAG laser has a 95% penetration rate, making it the laser of choice. The spot size and duration are fixed. The energy necessary will vary tremendously based on iris thickness and pigmentation. Lighter, thinner irises are easier to penetrate. The numerical millijoules (mJ) value is typically between 2.0mJ and 5.0mJ. No focus offset is needed. Commonly the pulse is set on two. This means that with each fire of the trigger, two bursts of energy are delivered in rapid sequence. The power of each pulse of energy delivered is equivalent to the prescribed power set in millijoules. If 2.0mJ are set the laser will deliver 2.0mJ per pulse for a total energy power of 4.0mJ with the pulse counter set at two. The upper limit of total energy per eye applied in one setting is typically 150mJ, but can vary tremendously depending on clinical judgment and the energy necessary to create a patent opening.

The rule of thumb is to use the

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

In the end, this patient's angles went from only being able to see the anterior trabecular meshwork in two quadrants to being able to see scleral spur in all four quadrants, thanks to the procedure.

lowest energy and least number of shots to get the job done.

During the Procedure

There are a few caveats to be aware of that will make the experience more pleasant for both the doctor and the patient. A small amount of bleeding is quite common when a blood vessel is inadvertently struck by the laser. The blood will cascade momentarily, like a red waterfall, but with slight pressure applied to the eye with the iridotomy lens, the bleeding will typical cease and the procedure can be continued. On some occasions the doctor may have to pause momentarily to allow the field to clear.

The field can also be clouded by pigmentation, but this should not be confused with the plume described earlier. Although 150mJ of energy is considered the upper level, in a quiet eye nearing completion, it is often more prudent to finish the procedure with a few additional shots rather than have the patient return. Total energy in the eye should always try to be minimized as that reduces potential complications. Clinical experience has shown energy levels between 15mJ and 200mJ to be optimal for most laser PIs, with lighter colored blue eyes often having thinner irides and requiring much less energy.

Always try to eliminate strands of tissue crisscrossing the opening, as this will often clog the opening with time and decrease the effectiveness. Patients will often feel slight pain if the per-shot energy level is higher than their tolerance threshold. Patients should be instructed to report pain or uncomfortable sensations during the procedure so that the energy can be decreased accordingly in small increments.

Postoperative Care

After successfully creating a patent opening, one drop of Alphagan or iopidine should be instilled postoperatively. The patient should remain in the clinic for approximately 30 minutes to evaluate for postoperative pressure spikes. If the pressure is rising, instill more pressure reducing medication and keep the patient in the office until the pressure is under control. Upon dismissal the patient should be placed on prednisolone acetate four times daily for one week followed by a rapid taper to decrease the inflammatory response. Alphagan is typically not needed after the first hour, but if the pressure is still of concern Alphagan can be used twice a day until the return visit one week later. In cases when Alphagan is contraindicated, consider timolol or oral acetazolamide.

May the Force Be With Your Patients

As with any procedure, education can help alleviate the patient's concerns. Educate the patient of the possible common side effects, such as IOP elevations and inflammation, and how these will be addressed. Also, review the rare complications, such as retinal detachment, and the signs and symptoms to watch for. After reviewing any concerns the patient may have and addressing those, evaluation at the one-week visit should include visual acuities, IOPs, slit lamp evaluation, gonioscopy and retinal inspection. Anterior segment imaging and quantifying the angle will also assist in determining the overall benefit of the procedure. If no complications are identified at the one-week follow-up, the patient can then be returned back to primary eye care.

Recognizing patients who would benefit from this procedure, providing quality education and preventing permanent sight loss is a win/win in any galaxy. ■

Dr. Miller is a professor of optometry at the NSU Oklahoma College of Optometry where he oversees the glaucoma clinics and course.

Dr. Shetler is an assistant professor and chief of the university clinic facilities at the Oklahoma College of Optometry.

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.

1. Allingham R, Damji K, Freedman S, et al. Shields Textbook of Glaucoma 6th ed. Philadelphia: Lippincott, 2011.
2. Al-Aswad L, Tsai J. Managing the Narrow-angle patient. Review of Ophthalmology. 2004;4(6):45-50.
3. Foster P,Buhrmann R, Quigley HA, Johnson GJ. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmology 2002;86:238-42.
4. Allingham R, Damji K, Freedman S, et al. Shields Textbook of Glaucoma 6th ed. Philadelphia:Lippincott, 2011.
5. Wills Eye Hospital, The Wills Eye Manual 3rd ed. Lippincott Williams & Wilkins,1999. 10;10 :252-3.
6. Tomey K, al-Rajhi A. Neodymium:YAG laser iridotomy in the initial management of phacomorphic glaucoma. Ophthalmology. 1992;99(5):660–5.
7. Allingham R, Damji K, Freedman S, et al. Shields Textbook of Glaucoma 6th ed. Philadelphia: Lippincott, 2011.
8. Foster P, Buhrmann R, Quigley H, Johnson G. The definition and classification of glaucoma in prevalence surveys. Br J Ophthalmol. 2002;86:238-42.
9. Jiang Y, Chang D, Foster P, et al. Immediate changes in intraocular pressure after laser peripheral iridotomy in primary angle-closure suspects. Ophthalmology. 2013;119(2):283-8.
10. Vera V, Naqi A, Belovay G, et al. Dysphotopsia after temporal versus superior laser peripheral iridotomy: a prospective randomized paired eye trial. Am J Ophthalmol. 2014; 157(5):929-35.

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

Spectacle Dispensing: How Do You Solve These Tough Refraction Challenges?

Patients who wear rigid gas permeables, are diagnosed with diabetes or are in need of prism can be some of the most difficult to fit with spectacles. These tips can help you succeed with hard-to-refract cases. **By William B. Potter, OD**

Clinicians can think of the art and science of refraction on two levels: Simplistically, we are measuring the state of an eye's focus and binocularity in order to attain best possible vision for our patients. But more than that, we are also directly and indirectly evaluating the quality of the ocular media, including cornea, aqueous humor, crystalline lens and vitreous humor. Even the condition of the retina can influence refractive results; for example, if there is edema or elevation from other causes. This article explores diagnosing and prescribing at the interface of refractive findings and ocular health by looking at some tough refractive cases commonly encountered in practice.

Fig. 1. Halberg clips are a great aid for measuring and demonstrating proposed refractive changes.

Prescribing Prism

As optometrists, we all know that refraction and binocular function are intimately related, and prescribing for patients who have a deviation of the visual axes is both challenging and rewarding. These patients present with a variety of asthenopic and diplopic symptoms. Extensive use of digital devices and sedentary occupations certainly haven't helped. Given that patients cannot always regulate their visual tasks and device use— productivity demands and available technologies may limit patient comfort, in terms of ergonomics and duration of use— prescribing prism can have a huge impact on a patient's well-being.

At the primary care level, clinicians must first rule out pathological processes prior to incorporating prismatic correction into the spectacle Rx. Although patients often expect the primary care eye doctor to provide treatment upon the initial visit, the possibility of pathologic origin requires a team approach. The most important step is to ensure that phorias and tropias are not due to pathology of the eye muscles or cranial nerves. This may involve consulting with the patient's pediatrician, pediatric ophthalmologist, neurologist or neuro-ophthalmologist and blood testing and neuroimaging. Any new-onset binocular deviation that is noncomitant (i.e., variable according to gaze position) merits medical investigation. These consultations, along with a complete review of systems and an exam by the primary care OD, can help uncover potential systemic causes for extraocular muscle dysfunction.

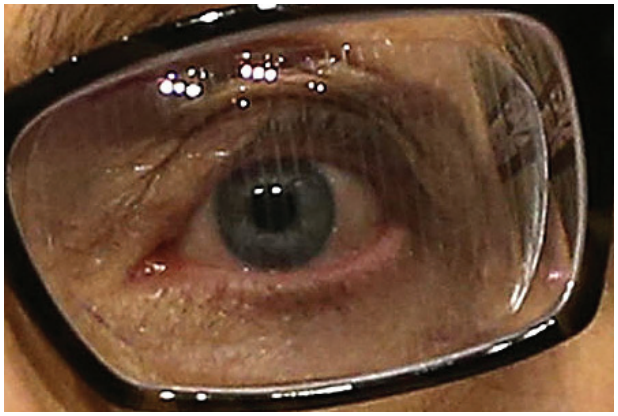


Fig. 2. Fresnel prism is an economical way to demonstrate prism without permanently fabricating it into the patient's lenses.

There are many methods for measuring phorias and tropias, with von Graefe prisms and prism-bar neutralization being among the most common in our practice. Maddox Rod testing is helpful in quickly identifying a deviation as comitant vs. noncomitant, and prism can be incorporated to aid in quantitative measurement.

However, the method of measurement is not as critical as trial-framing the result. Practitioners can use Halberg clips to attach the proposed prism to the patient's own spectacle frame (*Figure 1*). It may be helpful to ask the patient to read at near or to view a distance target, based on the nature of symptoms, for an appropriate period of time. While positive results of prismatic correction may be apparent immediately, allowing patients a little time with the trial Rx in place can be even more revealing. Using Halberg clips in-office may solve the issue for a limited timeframe, but if symptoms are variable or if they develop over several hours, Fresnel prism might be the better choice. Address the chief complaint at the specific working distance with prismatic trial.

Fusional reserves are also helpful in ascertaining the right degree of prism. For example, a patient who is symptomatic for near tasks may have unremarkable phorias, yet becomes diplopic when challenged by a minimal amount of base-out prism. If the eyes are unable to converge enough to overcome this base-out challenge, and the patient is symptomatic, a prescription of base-in prism for reading may be an effective and efficient remedy. Again, trial framing the prismatic Rx with a small amount of prism is helpful. Allow time for adaptation in the office, and present a near task similar to the one that generates the reading complaint. Having the patient test with a personal device such as a cell phone or tablet can be beneficial.

The degree and direction of visual axis deviation can help the primary care optometrist determine if prism is appropriate. We usually prescribe prism equal to one third to half of the binocular deviation. If the deviation is large, especially greater than 10 prism diopters, the prism can make the lenses unsightly with difficult adaptation. For example, a patient presenting with an 8 prism diopter exophoria may do well with an initial Rx of 1.5 prism diopters base-in for each eye. A larger prescription, in this case, may neutralize the deviation but present adaptation difficulties. A 20 diopter exodeviation would call for an unwearable amount of prism, if it had not been worn previously.

Patients who are unsuccessful trialing this prism should consult with a vision therapy specialist or eye muscle surgeon. Patients with binocular dysfunction may have difficulty with the most accurately prescribed prism, or find that the lenses are unacceptably thick or asymetrical in appearance. The key for the primary care optometrist is realizing when specialty care is needed. The true art of prescribing prism is shaping patient expectations, with a clear explanation of the diagnosis, treatment and expected outcomes. As with any other therapeutic procedure, the patient's input is paramount in making the decision.

Other challenges the primary care optometrist might face include oblique prism and patients who have had multiple extraocular muscle surgeries without total success. The oblique prism tends to have variable results that may be best undertaken by a specialist. Binocular vision optometrists or pediatric ophthalmologists have experience prescribing prism of this nature. It is best to establish these experts in advance of the consultation. The multiple-surgery patient has a special set of needs, including muscle scarring and very poor fusional abilities. Clinicians may struggle with patients who do not appreciate induced diplopia on testing, as imbedded suppression would tend to indicate specialty care. A team approach of vision therapy—and possibly repeat surgery—is often indicated, in addition to a prismatic Rx.

Case Example

A 91-year-old pseudophakic white male with medication-controlled hypertension and diabetes presented with a four-year history of intermittent horizontal diplopia while driving. He carried a diagnosis of right sixth nerve paresis from another practice, when the diplopia occurred initially.

Comfortear® Lacrisolve™ 180

ABSORBABLE PUNCTUM PLUG

"The Comfortear® Lacrisolve™ 180 Absorbable Punctum Plugs ***deliver approximately 180 days of dry eye relief*** *and are available in two diameters for a* ***secure fit and better patient comfort."***

Leslie O'Dell, OD, FAAO
Director, Dry Eye Center of PA
Manchester, PA

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.

M075-0416-01

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.

Neurologic work-up was negative for occult pathology. von Graefe testing revealed 8 prism diopters of esophoria at distance and orthophoria at near. Maddox Rod testing showed an eso deviation that increased on right gaze and decreased on left, confirming the original diagnosis.

Surgery and vision therapy were not practical options; thus, prismatic correction became a plausible choice. Patients tend to accept an initial prismatic correction equal to approximately half of the deviation measured. In this case, a trial of 2 diopters base-out in each eye produced a disorienting sensation that did not improve with office trial. The prism was reduced to 1 diopter base-out in each eye, resulting in better acceptance of the prescription and significant improvement of symptoms.

The patient had recently purchased new spectacles, creating a great opportunity to use Fresnel prisms (*Figure 2*). As a temporary plastic applique, we could test the efficacy of prism prior to having the spectacles remade. With the Fresnel prism in place, the patient's acceptance at follow-up was fine, and he reported significant reduction of diplopic symptoms while driving. We issued a new spectacle Rx incorporating the prism. While Fresnel prisms are great for trial and demonstration, the polymer applique and adding surfaces through which the patient sees can reduce objective and subjective acuity.

Prescribing Spectacles for the Rigid Gas Permeable Wearer

Patients who wear rigid gas permeables (RGP) and want spectacles represent one of our most challenging refraction scenarios. Even the perfectly-fit RGP can alter the corneal shape, thus altering refractive error. Simplistically, the spherical base curve of the RGP cannot match the complexity of the aspheric cornea, and compression of the corneal epithelium is inevitable. In the days after the lens is removed, the effect of this compression gradually reduces, creating a variable refractive error. Add in any issues with corneal edema and inflammation, and the refraction becomes a moving target. At least one line of reduction in best-corrected acuity is not unusual.[1]

In my practice we measure the spectacle prescription about 20 minutes after the RGP is removed, which may be done in concert with routine pupillary dilation. While this does not account for all variability produced when a lens is removed, it accommodates the patient's need when removing lenses. That is, the patient wants to wear the spectacles in real time—upon removing the lenses. The precorneal tear film has somewhat stabilized during the 20 minute wait, and any wetting solution and mucin has blinked away. Often, prior generations of clinicians asked patients to remove lenses three days before the exam to allow the cornea to return to its "normal" shape. However, patients want to wear spectacles immediately, not three days after removing the lenses.

The key when prescribing spectacles for the RGP patient is to consider the sphere and cylinder powers and axes of the prior Rx. A simple prescription of the current subjective refraction is a formula for a spectacle remake. A diopter change in subjective refraction might result in an Rx of half that amount. Similarly, cylindrical adjustments should be a fraction of the change measured. RGP patient counseling on the variability of spectacle vision is another key to success and should be emphasized at each visit.

Case Example

A 60-year-old white female has a long history of contact lens wear, having switched from PMMA lenses to RGPs when they became available in the '80s. She corrects to 20/20 in each eye with her contact lenses. Her chief complaint is that she cannot see well with last year's spectacles. The lenses themselves fit in a superior, lid-controlled fashion, with base curves 0.75 diopter flatter than the flat central keratometric reading. The patient's prior eye care practitioner performed spectacle refraction after the lenses were removed for a three-day period. Her habitual spectacles were -3.75-1.00x180, 20/40 OD and -4.00-1.25x180, 20/30 OS.

Our spectacle refraction, performed 20 minutes after lens removal, produced OD -3.00-1.00x180, 20/30 OD and -3.50-0.75x180, 20/25 OS. The reduced minus seems to be associated with the timing of the refraction on last year's exam. Contact lenses fitted "flat" centrally tend to have an orthokeratologic effect that begins to unwind itself during the three days that the prior doctor had indicated for a rest from the lenses. The

Practice Pearls

- Obtain a detailed history of symptoms and systemic and ocular health.
- Identify and quantify the binocular defect, including possible paresis.
- Trial frame prism, split binocularly, amount totaling one third to half of the measured defect.
- Use Fresnel prism to trial with current glasses for one to two weeks, then follow up.
- Finalize new Rx.

xoma

FORM AND FUNCTION MEET STYLE AND BEAUTY.

The XOMA® Exam Room System.

There's so much to appreciate in our Xoma Exam Room System, it's difficult to know where to begin. XOMA's unique and beautifully designed, all-in-one, patient positioning and instrument delivery system is truly a sight to behold. Its exciting design displays stunning lines while maximizing efficiency through extraordinary functionality. XOMA…the all-in-one innovation from the one-and-only Reliance.

800.735.0357
xomasystem.com

RELIANCE INTERNATIONAL
REMARKABLE. RELIABLE. RELIANCE.

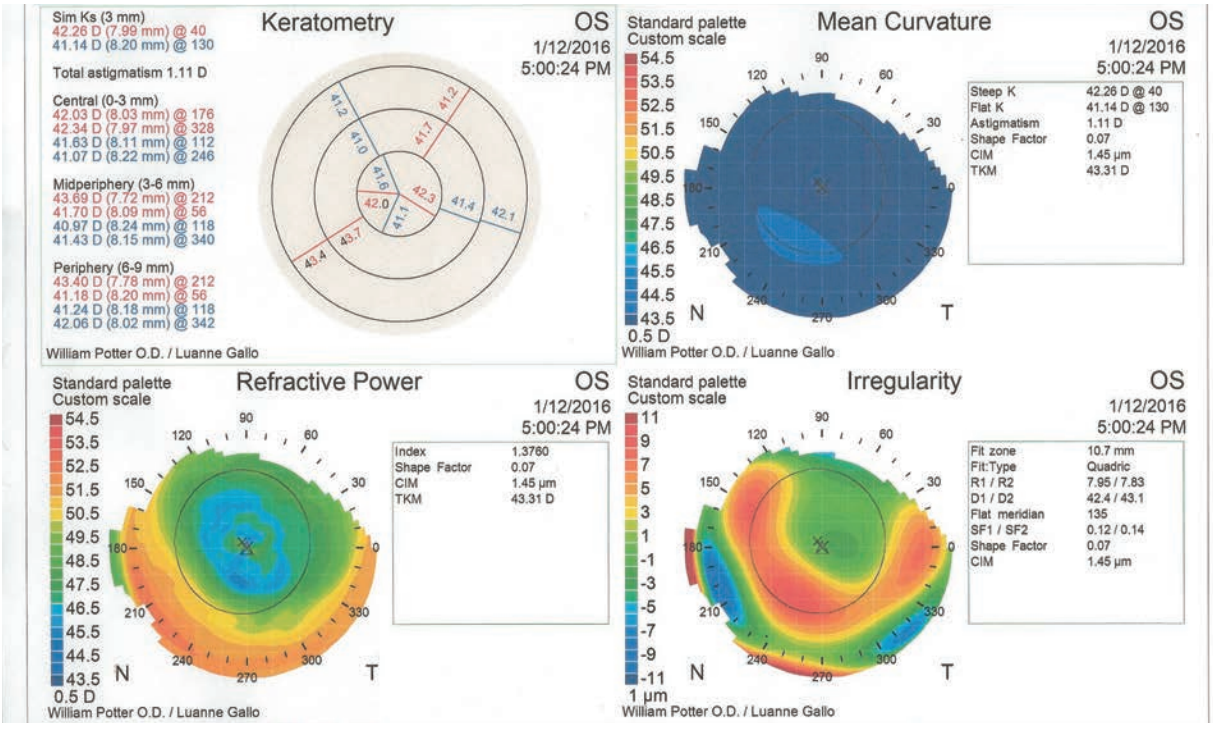


Fig. 3. Post-removal corneal topography shows distortion and some inferior corneal steepening that could be misinterpreted as keratoconus. The eccentricity value does not support a keratoconus diagnosis.

cornea begins to return to its more natural, steeper shape, thus affecting the spectacle refraction.

Figure 3 shows the patient's corneal topography immediately post-removal of the contact lenses. At a glance, the graphics would seem to indicate keratoconus, with inferior steepening and irregularity of the cornea. However, the statistical indices reveal no suspicion of keratoconus, and the molded corneal shape corresponds to the high-riding contact lens position.

Practice Pearls

- Don't refract immediately upon lens removal. Allow time for the tear film to re-establish.
- Check corneal topography for unusual distortion, as a refit may be indicated.
- Shape RGP patient expectations on variability and lower visual acuity with spectacles.
- Prescribe half to two thirds of the refractive change to compensate for variability and aid in adaptation, while assuring that the patient's driving needs are met.

Prescribing Spectacles for the Diabetic Patient

Patients with diabetes often present challenges when prescribing spectacles as well. Elevated blood sugar can produce changes in the crystalline lens, altering clarity, refractive index and curvature. Blur from diabetic pathology itself can be a confounding factor. Visual variability can be due to optic neuropathy, which can be frank or subtle, and may not be apparent on clinical exam. Patients with diabetes may also be susceptible to dry eye syndrome, causing further difficulty with visual acuity and function.[2,3] Diabetic retinopathy—with its hemorrhages, microaneurisms and neovascularization—tends to have little influence on refractive results unless there is significant macular edema, which can cause a hyperopic shift due to its shortening of axial length.

There is much debate regarding refractive change in these patients. Is there a myopic shift, or hyperopic? Literature evidence is sparse, though discussion with colleagues and some texts suggest a consensus for myopic shift.[4] The classic Borish text, *Clinical Refraction*, refers to osmotic dehydration of the crystalline lens as a cause for these changes.[5] There is also the possibility of a temporary hyperopic shift as control is attained.[6] Researchers who evaluated risk factors and the direction of refractive change in diabetic patients found that, over time, type 1 diabetics were likely to be more myopic than those with type 2 diabetes.[7] However, a longer duration of type 1, and the presence of proliferative

For Dry Eye/MGD Patients

MGD can cause the lipid layer to break down. Soothe® XP helps replenish this layer.

The eye's outer protective lipid layer keeps in moisture. 74% of patients reporting dry eye symptoms have a compromised lipid layer (Meibomian Gland Dysfunction or MGD).[1] Only Soothe® XP contains Restoryl® mineral oils that help restore this layer, seal in moisture, and protect against further irritation.

BAUSCH + LOMB
See better. Live better.

To request samples, please call 1-800-778-0980

[1]Blackie CA et al. Cornea 2009 (v0.1) p.1.

Practice Pearls

- Be alert to sudden refractive shifts of 1.0D or more as a possible indicator of incipient or uncontrolled diabetes
- Refer the patient to their PCP for a physical examination and labs to rule out diabetes mellitus.
- Initiate patient education on the variability of Rx and the possible six to eight week course to resolution.
- Prescribe a simple, temporary spectacle Rx, and alert the optician it is a courtesy Rx.
- Finalize the spectacle Rx when fasting blood sugar is well below 200 and A1C is below 8.0.

retinopathy, indicated more strongly for hyperopic shifts.[7] Acutely, refractive shifts tend to be in the myopic direction, although hyperopic shifts can occur during aggressive attempts at controlling blood sugar.[7]

Our practice has experienced a number of large hyperopic shifts on initial presentation, with some support in the literature.[8] As the natural history of the patient's blood glucose control is usually not specific, many may have been seen when their control was improving. Again, the poorly understood pathophysiology of the diabetic refractive shift leaves these events subject to speculation.

The typical diabetes patient with refractive changes will present with a chief complaint of a profound visual change in each eye. The sudden onset and the relatively extreme dioptric change can help differentiate diabetic involvement from physiologic changes that naturally occur in myopes and hyperopes. A cursory refraction will typically reveal two or more diopters of variability in sphere power compared with the patient's habitual Rx. In our experience in a large OD/MD practice, patients whose fasting blood sugars regularly touch the 200 range are prime candidates for sudden refractive shift.

The challenge is meeting the patient's visual needs following initial diabetic treatment. Stability may take six weeks to attain, and patients may have driving or reading needs.[5] We prescribe a "temporary" installation of lenses. Patient education is key to ensure they understand the Rx will change, and family practitioners usually help reinforce the notion of variable vision. Keep the features of the temporary lens simple, usually without progressive, tint or antireflection features. In many cases, a pre-fabricated, OTC spectacle can be specified as a temporary Rx. Schedule a follow up in six weeks to check for the resolution of visual findings. Patients occasionally return and indicate that vision has long since returned to the baseline. In the meantime, we feel that our strongest obligation is to provide for the patient's visual needs to drive safely, both in terms of comfort level and being able to pass a state motor vehicle department vision exam.

Case Example

A 48-year-old white male first-time patient presented with the unusual complaint that he "could suddenly read without his reading glasses, and street signs were blurry." The patient reports hydrochlorothiazide for systemic hypertension as his only medication. He had a significant history of type 2 diabetes mellitus in the family. His uncorrected acuity was 20/80 OD and 20/80 OS, with manifest refraction of -2.00 sphere in each eye, to 20/20. Unaided near acuity was 20/20 in each eye, and was not helped by his habitual reading Rx of +1.75 spheres in each eye.

During the examination, we contacted the patient's prior eye care provider, who revealed that last year's examination showed a plano sphere Rx in each eye for distance, with a +1.75 add for reading, and a normal dilated examination with no cataract or other health issues. Similarly, our current exam was essentially normal and revealed no cataract and no diabetic retinopathy or optic neuropathy.

Clearly, a sudden two diopter refractive shift is cause for concern. While incipient nuclear sclerosis cataracts can cause significant myopic changes, this patient's crystalline lenses were perfectly clear. We sent the patient off to his primary care physician (PCP), requesting that she rule out diabetes mellitus. The patient's laboratory testing revealed a fasting blood sugar of 210 and a hemoglobin A1C of 9.7. His PCP initiated diabetic therapy in the form of dietary education, exercise regimen and oral Metformin. The patient's laboratory values returned to the more acceptable fasting blood sugar of 110, with A1C of 6.9, in the ensuing six-week period.

This patient was well-served by temporary use of OTC readers, recommended at +1.75. As there was no cataract formation or retinal pathology, vision returned to baseline after six weeks of treatment. ■

Dr. Potter is chief of optometry and contact lens services at Millennium Eye Care in West Freehold, NJ, a multi-subspecialty optometry/ophthalmology practice.

1. Ruiz-Montenegro J, Mafra CH, Wilson SE, et al. Corneal topographic alterations in normal contact lens wearers. Ophthalmology. 1993 Jan;100(1):128-34.
2. Milton H. Diabetes and Dry Eye: The Forgotten Connection. Review of Optometry. 2010 Sept;147(9). 94-105.
3. Tong L, Waduthantri S, Wong TY, et al. Impact of symptomatic dry eye on vision-related daily activities: The Singapore Malay Eye Study. Eye. 2010;24:1486-91.
4. Milder B, Rubin M. The Fine Art of Prescribing Glasses Without Making a Spectacle of Youself. 3rd ed. Gainsville, FL: Triad Scientific Publishers;2004:96.
5. Borish I. Clincal Refraction. 3rd ed. Chicago, IL: The Professional Press; 1975:1048-9.
6. Sonmez B, Bozkurt B, Atmaca A, et al. Effects of glycemic control on refractive changes in diabetic patients with hyperglycemia. Cornea. 2005 July;24(5):531-7.
7. Klein B, Lee KE, Klein R, et al. Refraction in adults with diabetes. Arch Ophthalmol. 2011 Jan;129(1):56-62.
8. Tai MC, Lin SY, Chen JT, et al. Sweet hyperopia: refractive changes in acute hyperglycemia. Eur J Ophthalmol. 2006 Sept-Oct;16(5):663-3.


The Covington
SERAPHIN™
An Ogi Eyewear Brand • www.seraphineyewear.com • 1.888.560.1060

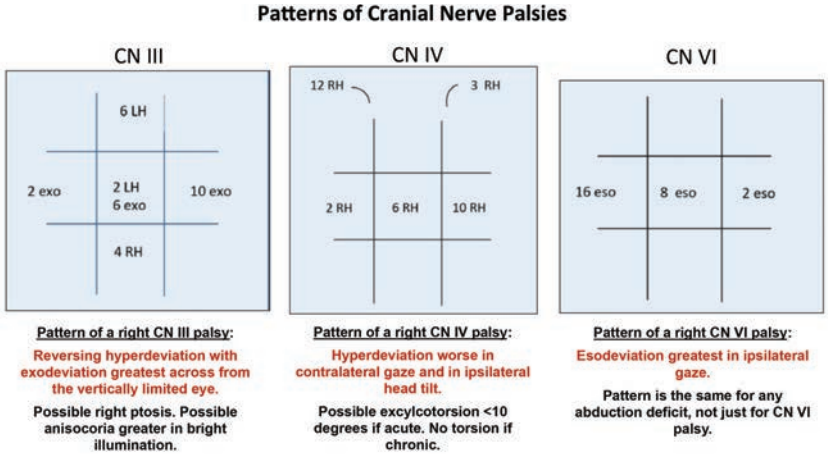
2 CE Credits
(COPE approval pending)

A Stepwise Approach to Evaluating Diplopia and Other Ocular Motility Abnormalities

Optometrists can carefully localize patients' ocular misalignments by employing a particular order of operations. **By Kelly A. Malloy, OD, Erin M. Draper, OD, Ashley K. Maglione, OD**

When patients present with ocular misalignment or diplopia, the number of possible etiologies can be overwhelming. It requires a systematic, stepwise approach to both examination techniques and differential diagnoses to attain a greater level of comfort with these patients.

To establish this stepwise approach, first review some basic anatomy. This will help localize the problem. Once acheived, you can narrow in on a particular anatomical structure and evaluate for known etiologies to that region.



For a stepwise approach to identifying the cause of diplopia, think of four distinct categories. First, consider if the findings localize to the brain, including the cerebral cortex and brainstem. Second, consider whether the findings localize to a specific cranial nerve (CN) or a combination of nerves and if a specific

Release Date: May 2016
Expiration Date: May 1, 2019
Goal Statement: Issues of ocular motility or diplopia can be symptoms of a broad range of neuro-ophthalmic conditions. To narrow down the suspects, optometrists should follow a particular process of elimination based on the patient's symptoms as well as brain scanning technology. This article provides a detailed overview of that process and defines conditions optometrists may encounter.

Faculty/Editorial Board: Kelly A. Malloy, OD, Erin M. Draper, OD, Ashley K. Maglione, OD, and Kelsey L. Moody, 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: The authors have no relationships to disclose.

location along the CN course can be pinpointed. Third, evaluate for features that suggest localization to the neuromuscular junction. Fourth, look for suggestions of localization to the orbit. Evaluating diplopia or ocular misalignment in this manner ensures all possible options for the clinical presentation are considered.

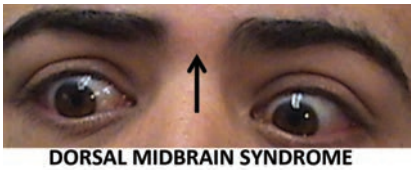
A careful examination of the efferent visual system is necessary in all patients with diplopia or ocular misalignment. For more information on the basics of performing the efferent visual system evaluation, refer to the February 2015 *Review of Optometry* article on that topic.[1]

This article provides an anatomical review of the structures key to ocular motility followed by four main sections, each dedicated to a specific anatomic location (brain, nerve, junction, orbit). Each of these sections discuss clinical features that may be present at that anatomic location, potential abnormalities that may occur there and subsequent work-up needed to make a diagnosis.

Anatomy Review

Recall there is cortical, or supranuclear, input from several areas, including the frontal and parietal lobes of the brain. The brainstem plays a major role in ocular motilities, housing not only CNs III, IV and VI nuclei and beginning segments of each corresponding CN, but also important anatomic regions that coordinate movements between eyes. Understand the pathway that each CN takes after it exits the brainstem on its way to the orbit to innervate specific extraocular muscles (EOMs), as these nerves ultimately control eye movements. For the EOMs to receive signals from their corresponding CNs, the neuromuscular junction (NMJ) must be intact and functioning properly.

With so many components working together for normal ocular motility, it can be a daunting task to determine the location of the system's breakdown. However, if approached in a stepwise fashion, it is less overwhelming.


DORSAL MIDBRAIN SYNDROME

These images portray patients displaying brainstem motility disorders.

First, assess the patient's ability to perform ductions. Do this by having the fellow eye occluded and looking only at one eye, assessing in which positions of gaze the eye is not able to achieve full range of motion. Next, carefully perform cover testing in all positions of gaze to identify whether the deviation is comitant or non-comitant, and to look for any classic pattern suggesting a CN palsy or other identifiable process. Signs or symptoms can help narrow your focus, but familiarity with neuroanatomy is key to diagnosis here.

EOM Disorders Stemming From the Brain

When patients present with EOM issues, the clinician should first evaluate them for disorders related the brain, since this is where the efferent pathways begin. Here is a list of likely diagnoses and how to identify them.

Gaze palsy—If the patient experiences an inability to look to one side, as well as weakness of the lower face and arms or legs on the same side, they may be suffering from a gaze palsy. This is a reduced ability of both eyes to move in the direction of lateral gaze.

The frontal eye fields are regions located anterior to the motor areas in the cerebral cortex. Their function allows contralateral gaze. Damage to these fields results in contralateral gaze palsy, and possibly ipsilateral gaze preference.[2,3] Because of their proximity to the motor cortex, these lesions in the frontal eye fields could also cause contralateral weakness.

An intact cerebral cortex communicates through the contralateral paramedian pontine reticular formation (PPRF) with the contralateral CN VI nucleus in the pons. This is the horizontal gaze center, coordinating both eyes in ipsilateral gaze. The contralateral CN VI nucleus gives rise to two populations of fibers. One becomes CN VI, innervating its ipsilateral lateral rectus muscle, and the other travels through an interneuron to the contralateral medial longitudinal fasciculus (MLF), the subnucleus of CN III, and ultimately the medial rectus muscle. A lesion of the CN VI nucleus results in ipsilateral gaze palsy. Pontine lesions large enough to also affect the ventral motor tracts could cause limb weakness both contralateral to the lesion and to the direction of gaze palsy.

This differs from cortical lesions, where weakness and gaze palsy are on the same side. Another difference is that nuclear lesions cannot be overcome with doll's head technique or vestibulo-ocular reflex (VOR), whereas supranuclear lesions can.[3,4]

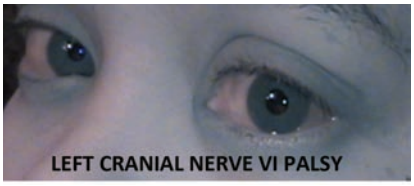
Abduction deficit (CN VI damage in the pons)—Damage to CN

VI in the pons (sparing VI nucleus) produces a CN VI palsy, or abduction deficit. These deficits are not specific to CN VI palsy; they can occur at all four anatomic regions. An abduction deficit with associated ipsilateral facial weakness, contralateral extremity weakness or reduced contralateral sensation significantly increases suspicion for a pontine lesion. Look for facial asymmetry; ask patients to raise their eyebrows, frown, puff out their cheeks and smile. As CN VI travels through the pons, dorsal damage near the sensory fibers (medial lemniscus) causes decreased contralateral sensation of the limbs due to sensory decussation in the medulla.[5,6] Ventrally, CN VI can be damaged near the motor fibers, resulting in contralateral extremity weakness.[5,6]

Internuclear ophthalmoplegia—When the medial longitudinal fasciculus (MLF) is damaged in the pons or midbrain, the medial rectus does not get the signal from the horizontal gaze center of the contralateral VI nucleus. The result is an adduction deficit and exo deviation increasing in the direction of attempted lateral gaze. Associated abducting nystagmus in the fellow eye is pathognomonic for internuclear ophthalmoplegia (INO). To further localize INO to the pons or midbrain, assess the convergence. Convergence is spared in pontine lesions; convergence may be affected in midbrain lesions if the medial rectus subnuclei of CN III are also affected.[7]

BILATERAL DUANE'S RETRACTION SYNDROME

When CN VI does not develop properly in utero, the lateral rectus gets innervated by CN III, leading to a congenital cranial dysinnervation disorder called Duane's retraction syndrome. It can present as unilateral or, as in this case, bilateral.



LEFT CRANIAL NERVE VI PALSY

This patient was determined to have a left CN VI palsy only after complete work-up. Without knowing any other information, this abduction deficit could be associated with any of the four locations: brain, nerve, neuromuscular junction or orbit. A detailed clinical examination can help sort this out.

One and a half syndrome—A lesion affecting CN VI nucleus (or PPRF) and ipsilateral MLF results in an ipsilateral gaze palsy and INO. The latter is named for the eye with the adduction deficit. A lesion of the right CN VI nucleus and the right MLF results in a right gaze palsy and right INO.[7]

Duane's retraction syndrome—When CN VI does not develop properly *in utero*, the lateral rectus gets innervated by CN III and the patient has an ipsilateral abduction deficit. In contralateral gaze—because of co-contraction of medial and lateral recti—the globe is pulled back in the orbit, giving an enophthalmic appearance and decreased palpebral aperture, pathognomonic for type I Duane's retraction syndrome. This congenital cranial dysinnervation disorder may be unilateral or bilateral and does not require workup or treatment.[8-10]

CN IV damage in the brainstem—The CN IV nucleus is located in the lower dorsal midbrain. Unlike other CNs, CN IV has a short course in the brainstem because it exits posteriorly; it is not associated with contralateral weakness or numbness. After CN IV exits the midbrain, it crosses in the isthmus pons. Damage to the anterior medullary velum, where both CN IV cross, can result in bilateral CN IV palsy.[5,6]

Brainstem CN palsy and Horner's syndrome—With any CN palsy from a brainstem lesion, there may be an associated Horner's syndrome, due to sympathetic involvement. With CN VI and CN III involvement, Horner's syndrome only presents ipsilateral to the palsy, since the sympathetic fibers do not cross. With CN IV involvement, Horner's syndrome is contralateral.

Dorsal midbrain syndrome—Damage to the posterior commissure, results in pathognomonic features, including difficulty with upgaze, eyelid retraction, light-near dissociation pupils and convergence retraction nystagmus. With lesions also affecting surrounding anatomic areas, unilateral or bilateral CN IV palsy or skew deviation may also be present.[3,11,12]

Skew deviation—This phenomenon is a vertical misalignment of the eyes, with the higher eye intorted and lower eye extorted; a head tilt is often seen toward the lower eye. This occurs with damage to the pathway connecting the vestibular and ocular motor systems. This pathway involves semicircular canals, vestibular nerve and nuclei in lateral medulla and the MLF that interconnects CN IV nucleus and CN III subnuclei to control vertical alignment and torsion.[3] Since the MLF also is involved in coordination of horizontal movements, it is not uncommon to see an INO and skew deviation together.

CN III damage in the midbrain—The CN III nucleus, or ocular motor complex, sits midline in the midbrain tegmentum. Nuclear lesions are rare, resulting in bilateral deficits. During its course, CN III can be affected with sensory fibers, resulting in a loss of contralateral sensation. CN III can be affected ventrally

with the crus cerebri motor tracts, resulting in contralateral weakness. CN III travels near the red nucleus, which is involved with motor coordination; there may be contralateral ataxia and difficulty with motor control.[5,6]

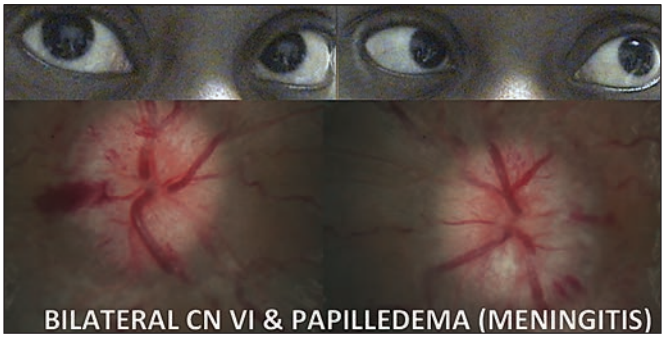
If features that localize to the cortex or brainstem are found, referral to neurology or neuro-ophthalmology is warranted. Patients need neuroimaging (preferably MRI with contrast if not contraindicated) to look for infarct, hemorrhage, demyelination, primary tumor or metastatic disease.

Evaluating for EOM Disorders Stemming from the Nerves

Once CNs III, IV and VI leave the brainstem, they travel through the subarachnoid space to the cavernous sinus prior to entering the orbit through the superior orbital fissure. This section follows the nerves along this pathway, where they are subject to damage from various etiologies.

Subarachnoid space—Within the subarachnoid space, the CNs are subject to trauma; CN IV is most likely to incur damage, due to its thin caliber, long course from the dorsal aspect of the brainstem and position in the tentorial margin.[6] Always ask patients about their trauma history.

Additionally, within the subarachnoid space, each CN may be affected by a subarachnoid hemorrhage, compressive mass, cerebral spinal fluid (CSF) inflammation (i.e., sarcoidosis) or CSF infection (i.e., meningitis, Lyme disease, syphilis and fungal).[5,17-19] Any of these processes could result in increased intracranial pressure (ICP). CN VI is most affected by increased ICP. One or both CN VI may be compressed by the petroclinoid ligament while traveling through Dorello's canal to the cavernous sinus.[20] Always consider increased ICP with an abduction deficit. Carefully assess the optic discs for features of even subtle papilledema, which constitutes a medical emergency. Necessary work-up includes brain MRI and MRV (to rule out cerebral venous sinus thrombosis), followed by a lumbar puncture to measure opening pressure and rule out infectious or inflammatory CSF processes. It is also possible to see a CN VI palsy with a sudden decrease in ICP, such as with a CSF leak after lumbar puncture.



In cases of CN VI, always assess the optic discs for features of even subtle papilledema, since this constitutes a medical emergency.

While in the subarachnoid space, CN VI traverses up the clivus in route to the cavernous sinus. Here, one or both CN VI may be subject to damage from bone metastases, most commonly seen in lung, breast or prostate cancers.[21] The cisternal and cavernous sinus segments of CNs are also subject to paresis from schwannomas and metastatic spread in CSF.[22]

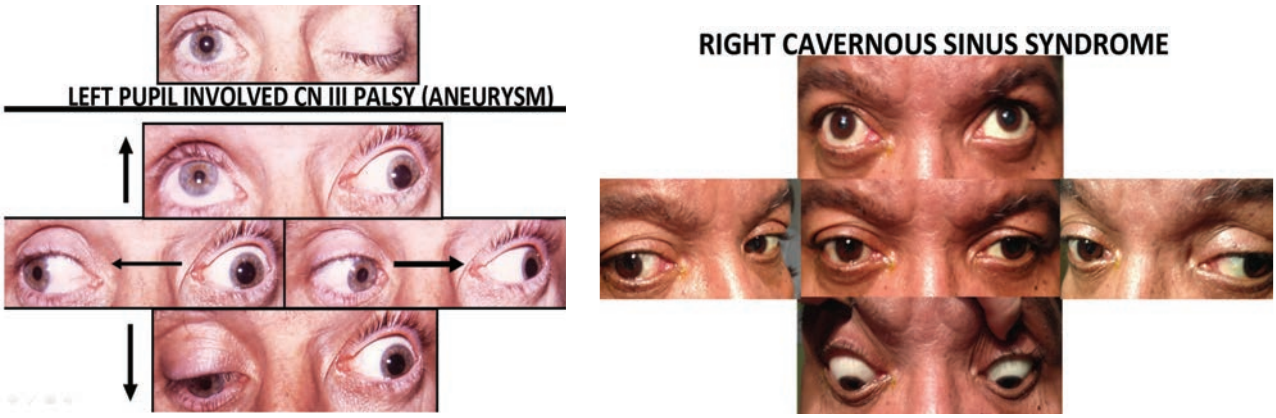
Another condition that emerges from the subarachnoid space is aneurysm. Although aneurysms may affect any artery and compress any adjacent CN, CN III is most commonly affected.[23] Since the parasympathetic preganglionic fibers travel on the outside of CN III, external compression of CN III results in pupillary dilation in addition to the tell-tale reversing hyper deviation pattern on cover testing. Any painful or pupil-involved CN III palsy is considered an aneurysm of the posterior communicating artery until proven otherwise. Due to the high risk of mortality, emergent work-up is necessary and should include MRA, CTA or formal angiography.

Cavernous Sinus—CNs III, IV, and VI converge in the cavernous sinus. With multiple cranial nerve involvement, be suspicious of an orbital apex or cavernous sinus lesion such as neoplasm, carotid artery aneurysm, inflammation, fistula or thrombosis.[24]

Patients with cavernous sinus syndrome may complain of pain, since the first division of the trigeminal nerve (V1) may be affected. If a cavernous sinus lesion is suspected, test for decreased facial sensation in the regions innervated by CN V1 and CN V2, above and below the orbit respectively. While V1 and V2 travel in the lateral wall of the cavernous sinus, V3 is not in the cavernous sinus. Therefore, the preservation of sensation in the chin region may help confirm localization. Depending on the nature of the lesion, chemosis, proptosis or Horner's syndrome may also be present.

Neoplasms—Cavernous meningiomas are common lesions of the base of the skull. Although they're benign, they can be invasive and difficult to treat.[25] If lesions extend into the orbital cavity, you may observe optic atrophy. Of course, malignant tumors, such as lymphoma, and even metastases may also result in cavernous sinus syndrome. Be suspicious of a metastatic process in patients with a history of cancer.

The pituitary gland sits between the two cavernous sinuses; it is not



At left, evidence of pupil-involved CN III palsy requires an emergent work up, due to the risk of mortality associated with aneurysm. At right, the combination of a right CN III pattern as well as a right abduction deficit, localizes the lesion to the cavernous sinus. These findings may be subtle, which underscores the need for cover testing in all positions of gaze. Also, testing for decreased facial sensation in V1 and V2 also helps with localization.

uncommon for a pituitary macroadenoma to compress or extend into one or both sinuses. Rarely, a pituitary hemorrhage or infarction, termed pituitary apoplexy (another emergent condition), may result in not only diplopia, but also sudden vision loss and headache.[26]

Cases of painful ophthalmoplegia that exhibit enhancement of the cavernous sinus on neuroimaging and respond to steroids are often misdiagnosed as Tolosa-Hunt syndrome. A diagnosis of idiopathic Tolosa-Hunt syndrome should be considered only after ruling out neoplasm, infection and other inflammatory etiologies.[27]

Cavernous sinus aneurysm—Within the cavernous sinus, the internal carotid artery (ICA) is surrounded by the sympathetic fibers. Additionally, unlike CN III and CN IV, which lie in the lateral wall of the cavernous sinus (along with V1 and V2), CN VI is proximal to the carotid artery. Thus, an abduction deficit with ipsilateral Horner's syndrome may lead you to suspect an intracavernous ICA aneurysm. Aneurysmal rupture is uncommon and typically not life threatening (unlike aneurysm in the subarachnoid space), but may cause a carotid cavernous fistula.

Carotid cavernous fistula—Direct carotid cavernous fistulas occur with communication between the arterial and venous system within the cavernous sinus, often from trauma or aneurysm rupture. The venous system is unable to drain the high-pressure influx of blood from the arterial system, leading to acute cavernous sinus syndrome, and possibly proptosis, chemosis and pulsatile exophthalmos. Indirect fistulas have a more insidious onset and tend to occur spontaneously.

As demonstrated, CN palsy localizing to the subarachnoid space or cavernous sinus may indicate a medical emergency, requiring immediate hospitalization. Newer steady-state free precession (SSFP) MRI Images sequences (e.g., FIESTA/CISS) are best at imaging the CNs in the subarachnoid space.[28]

A common cause of isolated CN palsies occurring in patients older than 50 years is microvascular ischemia (i.e., diabetes and hypertension), which should resolve within three to six months. Recent research recommends all patients presenting with acute, isolated ocular motor neuropathies undergo additional work-up.[29,30]

In addition, any diplopia or ocular misalignment in a patient older than 50 years should prompt concern for giant cell arteritis (GCA), and urgent ESR, c-reactive protein and CBC is recommended.[24]

Evaluating for EOM Disorders Stemming from the Neuromuscular Junction

If you do not find any features that definitively localize to the brain or a specific point along a CN, the next step is to consider a disease process of the neuromuscular junction (NMJ). Myasthenia gravis (MG), which often mimics CN palsies, is the most common NMJ disorder.[19]

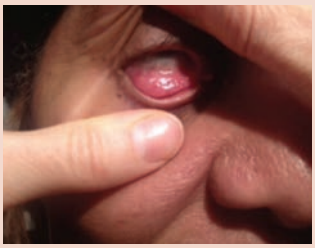
In cases of MG, waves of depolarization arrive at the presynaptic neuron terminal initiating the release of acetylcholine, similar to that in patients without MG. However, in MG, as acetylcholine makes its way across the synaptic cleft it is unable to fuse with its receptor due to the presence of antibodies. These antibodies may affect the receptor in three ways; antibodies may:

1. Bind to the receptor and initiate an inflammatory reaction.

2. Block the receptor and simply prevent acetylcholine attachment.

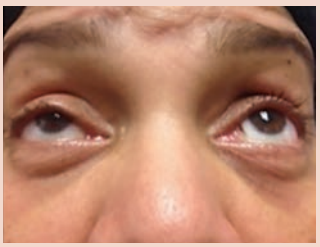
Myasthenia Gravis Testing Techniques

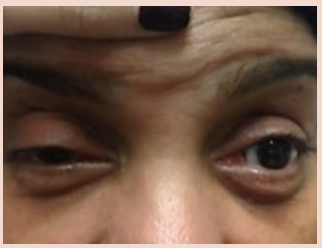
Orbicularis Weakness



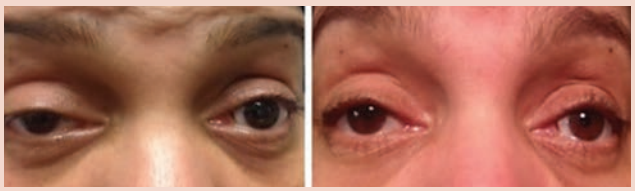
At left, ask the patient to forcefully close their eyes; in a normal patient, the eyelids cannot be pried open. In a patient with MG, the eyelids may be easily opened.

Eyelid Fatigue





Pre- and Post-ice Pack



Above, fatigue the levator by sustaining up-gaze for two minutes and/or fatigue the extraocular muscles by performing 100 saccades. Compare measures of palpebral aperture or magnitude of ocular misalignment pre- and post-fatigue; assess for interval chance. At left, to perform ice pack testing, hold ice on the eyelids for two minutes. At least 2mm increase in palpebral aperture is considered a positive result, suggestive of MG.

3. Modulate by cross-linking, thereby causing engulfment of the receptor.

Therefore, acetylcholine is unable to initiate contraction of the intended muscle cell. In a smaller percentage of patients, antibodies are produced against the Muscle Specific Kinase (MuSK) receptor, which is responsible for regulating the population of acetylcholine receptors.[31] In both cases, the receptor is the limiting factor. However, if the availability of the acetylcholine is also decreased, the effects are compounded. Consequently, MG is characterized by patients who have weakness, which worsens with fatigue.

The majority of patients with MG present with ptosis and ocular misalignment. To explain the increased susceptibility of the muscles within and around the orbit, investigators propose that the acetylcholine receptors are antigenically different in this area.[32] MG is subdivided into ocular MG, which is isolated to the ocular muscles and generalized MG, which involves head, limb and respiratory muscles. Patients with ocular MG have roughly a 50% chance of developing generalized MG within two years of onset.[33]

Diagnosis of MG—In all patients with diplopia or ocular misalignment, regardless of the pattern, myasthenia gravis must be in your differential diagnosis. Three in-office tests aid in the diagnosis of MG (*above*). These tests check for an increased ptosis after fatigue, improvement in ptosis when acetylcholinesterase enzyme is deactivated by cold, and general weakness of the orbicularis muscles.

To further confirm the suspected diagnosis, test serologically for the acetylcholine receptor antibodies (binding, blocking and modulating), and for the less common Anti-MusK antibodies. If these fail to confirm a diagnosis, a more sensitive test for MG is the single fiber electromyogram (sfEMG), which employs an electrode to record the action potentials of individual muscle cells. If testing for ocular MG, the sfEMG should be performed on the frontalis or orbicularis oculi muscle. A positive result shows increased jitter.

Patients diagnosed with systemic or ocular MG need a chest CT to rule out thymoma. Referral can then be made to neurology/neuro-ophthalmology for systemic treatment that may include cholinesterase inhibitors, immunosuppressants and corticosteroids. A careful review of medications is necessary as there are many which can incite or worsen MG, these include statins, antibiotics, anticonvulsants, antiarrhythmics, beta blockers (both systemic and topical) and botulinum toxin.

EOM Disorders Stemming From the Orbit

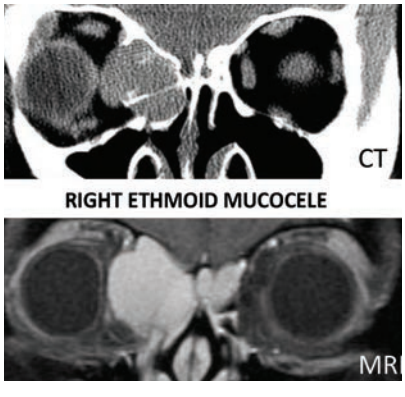
Clinically, two tests can localize diplopia to the orbit. They are exophthalmometry and forced duction testing. The eye can either be exophthalmic or enophthalmic, depending on the cause. A positive forced duction test (when the eye is unable to be manually moved in the direction of limited gaze) suggests orbital localization. There may be associated eye pain, injection or chemosis, as well as features to suggest afferent visual system compromise. If an orbital cause for diplopia is suspected, referral to an orbital/oculoplastic specialist is often warranted.

Lab Testing for Thyroid Eye Disease

- TSH
- T3
- T4
- Thyroperoxidase antibodies
- Thyroglobulin antibodies
- Thyroid stimulating immunoglobulin

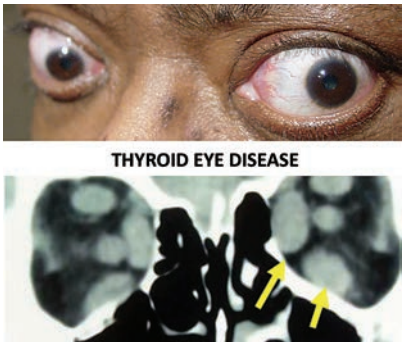
Orbital fracture—Blowout fractures of the orbit are commonly caused by blunt trauma and frequently cause diplopia. EOM restriction in the setting of recent trauma should cause suspicion for orbital fracture. Most commonly, the orbital floor is affected, causing entrapment of the inferior rectus and subsequent supraduction deficit. Since the infraorbital nerve runs through the inferior orbital groove, hypoesthesia of the lower eyelid increases suspicion of an orbital floor fracture. Enophthalmos is seen in floor fractures if orbital contents sublux into the maxillary sinus. Less commonly, the medial rectus can become entrapped with medial wall fractures, as the ethmoid is the thinnest bone of the orbit. An orbital CT allows visualization of the fracture.[34]

Mucocele—Mucus lines the paranasal sinuses adjacent to the orbits. When there is scarring and obstruction of the sinus ostium, a mucocele can develop, eroding the bony sinus wall and invading the brain and orbit with potential for abscess and rupture. Diplopia combined with proptosis, pain, chronic sinusitis or history of endoscopic surgery should prompt suspicion of mucocele. Work-up includes neuroimaging of the orbits; CT will assess for bony destruction.[34,35]



RIGHT ETHMOID MUCOCELE

Diplopia combined with proptosis, pain, chronic sinusitis or history of endoscopic surgery should prompt suspicion of mucocele.



THYROID EYE DISEASE

Thyroid eye disease is the most common cause of ocular motility restrictions in adults. The arrows show enlarged bellies of the extraocular muscles.

Thyroid eye disease—Thyroid eye disease is the most common cause of motility restriction in adults, involving inflammation of the EOMs.[36,37] The inferior rectus (supraduction deficit) and medial rectus (abduction deficit) are most commonly affected. Exophthalmos, eyelid retraction and eyelid edema are also possible, but not necessarily present. Positive forced duction testing and increased intraocular pressure in affected gazes supports the diagnosis. Work-up for thyroid eye disease includes lab testing (thyroid functions and antibodies) and neuroimaging of the orbit (CT or MRI) looking for extraocular muscle belly enlargement.[36-41]

Other Conditions with Orbital Mass Effect

Inflammatory Conditions—The spectrum of orbital inflammatory disease ranges from nonspecific inflammation of one orbital structure to widespread inflammation from systemic disease. Usually, patients present with diplopia (any pattern possible), proptosis, eye pain and possibly eyelid edema, chemosis or injection. A thorough history regarding onset, associated symptoms and systemic health conditions is critical in guiding differentials.

Idiopathic orbital inflammatory syndrome—IOIS can affect many structures of the orbit and is a diagnosis of exclusion. It commonly presents with unilateral symptoms with variable degree of inflammation, fibrosis and mass effect based on the structure involved. This condition should improve quickly with corticosteroids. If not, or in cases of recurrence, alternate etiologies should be considered.[39-41]

Sarcoidosis—This condition can affect any part of the orbit. Although it usually presents with enlargement of the lacrimal gland(s), it can also manifest as a diffuse, solid mass with infiltration of orbital fat, lacrimal sac or extraocular muscles. Abnormal skin lesions, chronic cough, shortness of breath or uveitis may raise suspicion for sarcoidosis. Although a mass may be seen on neuroimaging, or angiotensin converting enzyme may be positive, definitive diagnosis is made by biopsy, often of the lacrimal gland or lung.[42,43]

Granulomatosis with polyangiitis (GPA)(formerly Wegener's)—Ocular manifestations can occur with or without symptoms of systemic GPA,

Lab Testing for Orbital Inflammations

Sarcoid
- ACE

GPA
- C-ANCA
- P-ANCA

GCA
- ESR
- C-reactive protein
- CBC

although they are more common later in the disease course. Ocular findings are commonly associated with adjacent paranasal sinus or nasal granulomatous disease. History of chronic sinusitis, rhinitis or epistaxis or a saddle nose deformity indicate possible GPA.[44,45]

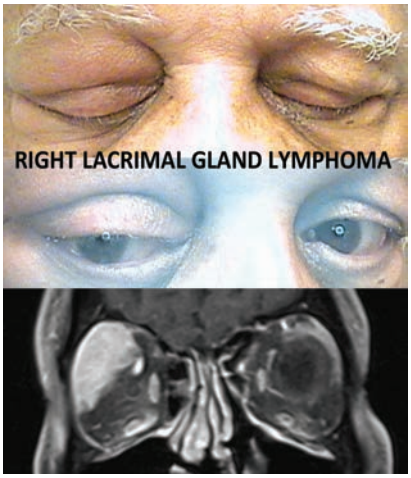
Giant cell arteritis (GCA)—Orbital inflammatory disease is an uncommon yet underdiagnosed finding in GCA despite being the most common vasculitis in patients older than 50. In addition to symptoms of orbital inflammatory disease, these patients might present with other classic features of GCA: headache, malaise, weight loss and vision loss.[46-47]

Infectious conditions—Orbital infections include orbital cellulitis, subperiosteal or orbital abscess. Bacterial infections are more common than fungal, but both etiologies are possible. In addition to the features found in inflammatory orbital disorders, infectious causes may present with fever or secondary infection. The most common bacterial causes of orbital infections are *Staphyococcus aureus*, *Streptococcus pneumoniae* and anaerobic Gram negative bacilli, such as *Prevotella, Porphyromonas*, and *Fusobacterium*. In addition, mucormycosis, aspergillosis and *Mycobacterium tuberculosis* have been implicated, more commonly in immunocompromised hosts.[34,48-49]

Cancers

Primary and secondary orbital malignancy must be considered in the setting of persistent progression or inflammation despite treatment.

Lymphoma—Lymphocytic lesions of the orbit include both benign lymphoid hyperplasia and malignant lymphoma, which is almost exclusively B-cell lymphoma. These usually manifest in the orbit as painless masses; they may affect specific structures such as the lacrimal gland. Painful lymphomas are rare, tend to progress more rapidly and have worse prognosis. MRI demonstrates a well-defined soft-tissue mass affecting, but not destroying, surrounding tissues. Biopsy is required to confirm the diagnosis.[34,50]



Lymphomatic lesions usually manifest in the orbit as painless masses that affect specific structures, such as the lacrimal gland, as noted in this patient. The MRI demonstrates a well-defined soft-tissue mass affecting, but not destroying, surrounding tissue.

Metastases—These can occur to specific orbital structures, including the EOMs. When an isolated muscle is enlarged in the setting of a history of cancer, consider metastasis before jumping to a diagnosis of thyroid eye disease. Proptosis is common when mass effect is present. However, there is also possibility of enophthalmos if the metastasis causes fibroblast contraction and globe retraction. This can be seen with scirrhous breast cancer, among others. Consider mammogram, colonscopy and imaging of the chest, abdomen and pelvis in any unexplained non-traumatic enophthalmos.[34,50-51]

A step-wise approach will increase your comfort level in dealing with diplopia and ocular motility abnormalities. Use your history and clinical examination to localize the lesion to the brain, nerve, junction or orbit. This will streamline the process and help you understand potential urgency, necessary work-up and the most appropriate referral. ■

Dr. Malloy is the director of the Neuro-ophthalmic Disease Service at Pennsylvania College of Optometry, Salus University.

Dr. Draper teaches neuro-ophthalmic disease at Salus University and practices in the Neuro-Ophthalmic Disease and Low Vision Specialty Services at The Eye Institute.

Drs. Maglione and Moody are in the process of completing the new two-year advanced residency program in neuro-ophthalmic disease at Salus under the direction of Drs. Malloy and Draper.

1. Malloy K. Neuro-ophthalmic disease basics: Focus on the efferent visual system evaluation. Rev Optom. 2015. Feb;152:74-83.
2. Bourne S, Duhaime A. Transient horizontal gaze palsy in a one-month-old boy after a fall. Pediatr Neurosurg. 2016;51(1):42-7.
3. Eggenberger E. Supranuclear eye movement abnormalities. Continuum (Minneap Minn). 2014 Aug;20(4 Neuro-ophthalmology):981-92.
4. Strupp M, Kremmyda O, Adamczyk C, et al. Central ocular motor disorders, including gaze palsy and nystagmus. J Neurol. 2014 Sep;261 Suppl 2:S542-58.
5. Koskas P, Heran F. Towards understanding ocular motility: III, IV, and VI. Diagnostic and interventional imaging. 2013; 94: 1017-1031.
6. Brazis P. Isolated palsies of cranial nerves III, IV, and VI. Semin Neurol. 2009;29:14-28.
7. Bronstein A, Rudge P, Gresty M, et al. Abnormalities of horizontal gaze. Clinical oculographic and magnetic resonance imaging findings. II gaze palsy and internuclear ophthalmoplegia. Journal of Neurology, Neurosurgery and Psychiatry. 1990;53:20-207.
8. Gutowski N, Chilton J. The congenital cranial dysinnervation disorders. Arch Dis Child. 2015 Jul;100(7):678-81.
9. Xia S, Li R, Li Y, et al. MRI findings in Duane's ocular retraction syndrome. Clin Radiol. 2014 May;69(5):e191-8.
10. Oystreck D. Congenital and genetic ocular motility disorders: update and considerations. Am Orthopt J. 2015;65:58-66.
11. Gnanapavan S, Sillery E, Acheson J, Toosy A. Parinaud's syndrome—A rare presentation of clinically isolated syndrome. Mult Scler Relat Disord. 2014 May;3(3):398-401.
12. Alemdar M, Kamaci S, Budak F. Unilateral midbrain infarction causing upward and downward gaze palsy. J Neuroophthalmol. 2006 Sep;26(3):173-6.
13. Eggenberger E. Eight and-a-half syndrome: one-and-a-half syndrome plus cranial nerve VII palsy. J Neuroophthalmol 1998;18(2) 114-116.
14. Rosini F, Pretegiani E, Guideri F, Cerase A, Rufa A. Eight and a half syndrome with hemiparesis and hemihypesthesia: the nine syndrome? J Stroke Cerebrovasc Dis. 2013 Nov;22(8):e637-8.
15. Connors R, Ngan V, Howard J. A case of complete lateral gaze paralysis and facial diplegia: the 16 syndrome. J Neuroophthalmol. 2013 Mar;33(1):69-70.
16. Lee H, de Kort PL. 16 syndrome in a patient with multiple sclerosis. J Neuroophthalmol. 2013 Jun;33(2):203-4.
17. Howard V, Barrow D. Neuro-ophthalmology and intracranial aneurysms. World neurosurg. 2015 Mar;83(3):291-3.
18. Ramgopal S, Obeid R, Zuccoli G, et al. Lyme-disease-related intracranial hypertension in children: clinical and imaging findings. J Neurol. 2016 Mar;263(3):500-7.
19. Neil R. Miller NR, Newman NJ, Biousse V, Kerrison JB, Editors.

Walsh and Hoyts Clinical Neuro-ophthalmology. Lippincott Williams & Wilkins, Philadelphia, 2005.
20. Umansky F, Elidan J, Valarezo A. Dorello's Canal: a microanatomical study. J Neurosurg. 1991 Aug;75(2):294-8.
21. Malloy KA. Prostate cancer metastasis to clivus causing cranial nerve VI palsy. Optometry. 2007 Feb;78(2):55-62.
22. Adams ME, Linn J, Yoursry, I. Pathology of the ocular motor nerve III, IV and VI. Neuroimag Clin N Am. 2008 May;18(2):261-82.
23. Biousse V, Newman N. Aneurysms and subarachnoid hemorrhage. Neurosurg Clin N Am. 1999 Oct;10(4):631-51.
24. Biousse V and Newman N. Neuro-ophthalmology Illustrated. Thieme Medical Publishers, Inc. New York. 614pp.
25. Sindou M, Nebbal M, Guclu B. Cavernous sinus meningiomas: imaging and surgical strategy. Adv Tech Stand Neurosurg. 2015: 42:103-21.
26. Simon S., Torpy D, Brophy B, Blumbergs P, Selva D, Crompton JL. Neuro-ophthalmic manifestations and outcomes of pituitary apoplexy—alife and sight-threatening emergency. N Z Med J. 2011 May 27;124(1335):52-9.
27. Igen Uslu F, Özkan M. Painful ophthalmoplegia: a case report and literature review. Agri. 2015;27(4):219-23.
28. Sheth S, Branstetter BF 4th, Escott EJ. Appearance of normal cranial nerves on steady-state free precession MR images. Radiographics. 2009 Jul-Aug;29(4):1045-55.
29. Kung NH, Van Stavern GP. Isolated ocular motor nerve palsies. Semin Neurol. 2015 Oct;35(5):539-48.
30. Tamhankar MA, Volpe NJ. Management of acute cranial nerve 3, 4 and 6 palsies: role of neuroimaging. Curr Opin Ophthalmol. 2015 Nov;26(6):464-8.
31. Hoch, W. McConville J, Helms S, et al. Auto-antibodies to the receptor tyrosine kinase MuSK in patients with myasthenia gravis without acetylcholine receptor antibodies. Nature Medicine. 2001;7:365-8.
32. Kaminski H, Zhuyi L, Richmonds C, et al. Susceptibility of ocular tissues to autoimmune diseases. Ann N Y Acad Sci. 2003;998:362-74.
33. Patil-Chhablani, P, Devendrav V, Rashminanilkumar G, Akshaygopinathan N. Ocular myasthenia gravis: A review. Indian J Ophthalmol 2014; 62(1): 985.
34. Rose G, Verity D. Neuro-ophthalmology of orbital disease. Handbook of Clinical Neurology. 2011;102(3):467-91.
35. Venugopal M, Sagesh M. Proptosis: The ENT surgeon's perspective. Indian J Otolaryngol Head Neck Surg. 2013. Aug;65(Suppl 2):247-50.
36. Barrio-Barrio J, Sabater A, Bonet-Farriol E, et al. Graves' Ophthalmopathy: VISA versus EUGOGO classification, assessement, and management. Journal of Ophthalmology. 2015 Feb;2015:1-16.
37. McAlinden C. An overview of thyroid eye disease. Eye Vis (Lond). 2014;1(9):1-4.
38. Lutt J, Lim L, Phal P, et al. Orbital inflammatory disease. Semin Arthritis Rheum. 2008; 37:207-222.
39. Costa R, Dumitrascu O, Gordon L. Orbital myositis: diagnosis and management. Current Allergy and Asthma Reports. 2009;9:316-23.
40. Pakdaman M, Sepahdari A, Elkhamary S. Orbital inflammatory disease: pictorial review and differential diagnosis. World J Radiol. 2014; 6(4):106-15.
41. Gordon L. Orbital inflammatory disease: a diagnostic and therapeutic challenge. Eye. 2006;20:1196-206.
42. Demirci H, Christianson M. Orbital and adnexal involvement in sarcoidosis: analysis of clinical features and systemic disease in 30 cases. Am J Ophthalmol. 2011;151:1074-80.
43. Mavrikakis I, Rootman J. Diverse clinical presentations of orbital sarcoid. Am J Opthalmol 2007;144:769-75.
44. Holle J, Voigt C, Both M, et al. Orbital masses in granulomatosis with polyangiitis are associated with refractory course and a high burden of local damage. Rheumatology. 2013;52:875-82.
45. Provenzale J, Mukherji S, Allen N, et al. Orbital involvement by Wegener's granulomatosis: imaging findings. AJR. 1996;166:929-34.
46. Lee A, Tang R, Feldon S, et al. Orbital presentations of giant cell arteritis. Graefe's Arch Clin Exp Ophthalmol. 2001;239:509-13.
47. Gonzalez-Gay M, Carros S, Lopez-Diaz M, et al. Giant cell arteritis. Medicine. 2005;84:269-76.
48. Warburton R, Brookes C, Golden B, et al. Orbital apex disorders: a case series. Int J Oral Maxillofac Surg. 2015;Oct:1-10.
49. Kirszrot J, Rubin PAD. Invasive fungal infections of the orbit. International Ophthalmology Clinics. 2007; 47(2):117-132.
50. Bonavolonta G, Strianese D, Grassi, P, et al. An analysis of 2,480 space-occupying lesions of the orbit from 1976 to 2011. Ophthal Plast Reconstr Surg. 2013; 29:79-86.
51. Ahmad S, Esmaeli B. Metastatic tumors of the orbit and ocular adnexa. Curr Opin Ophthalmol. 2007;18:405-13.
52. Manley D, Alvi R. Brown's syndrome. Curr Opin Ophthalmol. 2011 Sep;22(5):432-40.
53. Currie S, Goddard T. MR imaging features of acquired Brown syndrome. AJNR. 2009 Oct;30:1778-9.

OSC QUIZ

You can obtain transcript-quality continuing education credit through the Optometric Study Center. Complete the test form *(page 103)*, 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. A left abduction deficit with decreased sensation of the right upper and lower extremity localizes to which of the following?
a. Right pons.
b. Left pons.
c. Neuromuscular junction.
d. Subarachnoid space.

2. A left gaze palsy with left sided upper and lower extremity weakness localizes to which of the following?
a. Right pons.
b. Left pons.
c. Right frontal eye fields.
d. Left frontal eye fields.

3. A stroke involving the right CN VI nucleus and the right MLF would result in which of the following?
a. Right gaze palsy and right INO.
b. Right gaze palsy and left INO.
c. Left gaze palsy and left INO.
d. Left gaze palsy and right INO.

4. Which of the following is not a feature of a right Duane's Type 1 Retraction Syndrome?
a. Right palpebral aperture decreases on left gaze.
b. Reduced exophthalmometry reading OD on left gaze.
c. Right abduction deficit.
d. Right adduction deficit.

5. All of the following are features of skew deviation except:
a. Vertical ocular misalignment.
b. Head tilt.
c. Exotropia.
d. Higher eye intorted.

6. Which of the following is least likely associated with Dorsal midbrain syndrome?
a. Ptosis.
b. Light-near dissociated pupils.
c. Convergence retraction nystagmus.
d. Difficulty looking up.

7. Which of the following is least helpful in localizing an abduction deficit?
a. Testing motor function of extremities.
b. Testing CN XII.
c. Forced duction testing.
d. Fatigue testing.

8. Which of the following does not localize to the cavernous sinus?
a. Multiple cranial nerve involvement.
b. Weakness of muscles of mastication.
c. Reduced corneal sensation.
d. Horner's syndrome with ipsilateral CN IV palsy.

9. An isolated pupil-involved CN III palsy is what until proven otherwise?
a. Cavernous sinus thrombosis.
b. Carotid cavernous fistula.
c. Posterior communicating artery aneurysm.
d. Orbital apex syndrome.

10. What is the most important clinical test in the setting of an abduction deficit, which could localize the problem to the subarachnoid space?
a. Dilated fundus examination.
b. Pupil testing.
c. Testing motor function.
d. Exophthalmometry.

11. A bilateral abduction deficit in the setting of a history of prostate cancer causes greatest suspicion for which localization?
a. Pons.
b. Subarachnoid space.
c. Clivus.
d. Suprasellar cistern.

12. All of the following require emergent work-up, except:
a. CN VI palsy and papilledema.
b. Partial CN III palsy.
c. Acute skew deviation.
d. Bilateral proptosis and eyelid retraction.

13. Which of the following is an in-office test, that when positive, is not suggestive of myasthenia gravis?
a. Orbicularis oculi weakness.
b. Forced duction test.
c. Ice pack test.
d. Fatigue test.

14. What is the most common inflammatory disease of the orbit?

OSC QUIZ

a. Thyroid eye disease.
b. Sarcoidosis.
c. Giant cell arteritis.
d. Granulomatosis with polyangiitis.

15. Enophthalmos secondary to contraction from fibrosis is seen in which condition?
a. Sarcoidosis.
b. Brown's syndrome.
c. Metastatic cancer.
d. Thyroid eye disease.

16. Which part of the orbit is most commonly fractured and what is the associated deficit?
a. Floor of the orbit: limitation of downgaze.
b. Floor of the orbit: limitation of up gaze.
c. Roof of the orbit: limitation of downgaze.
d. Roof of the orbit: limitation of up gaze.

17. What blood work is indicated in proptosis, limitation of abduction and a saddle-nose bridge deformity?
a. ANCA.
b. ACE.
c. TSH.
d. CRP.

18. What is the most common cause of infectious orbital disease?
a. *S. Aureus.*
b. *Aspergillus.*
c. *S. Epidermidis.*
d. *Mycobacterium.*

19. Which of the following is considered the most sensitive test for diagnosing myasthenia gravis?
a. Serologic acetylcholine receptor antibodies.
b. Single fiber electromyography.
c. In office ice-pack test.
d. In office fatigue test.

20. Roughly what percent of patients who present with the ocular form of myasthenia gravis develop the generalized form within two years of onset?
a. 10%.
b. 30%.
c. 50%.
d. 80%.

TAKE THE TEST ONLINE TODAY!
www.reviewofoptometry.com/continuing_education/

Examination Answer Sheet

Valid for credit through May 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.

A Stepwise Approach to Evaluating Diplopia and Other Ocular Motility Abnormalities

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

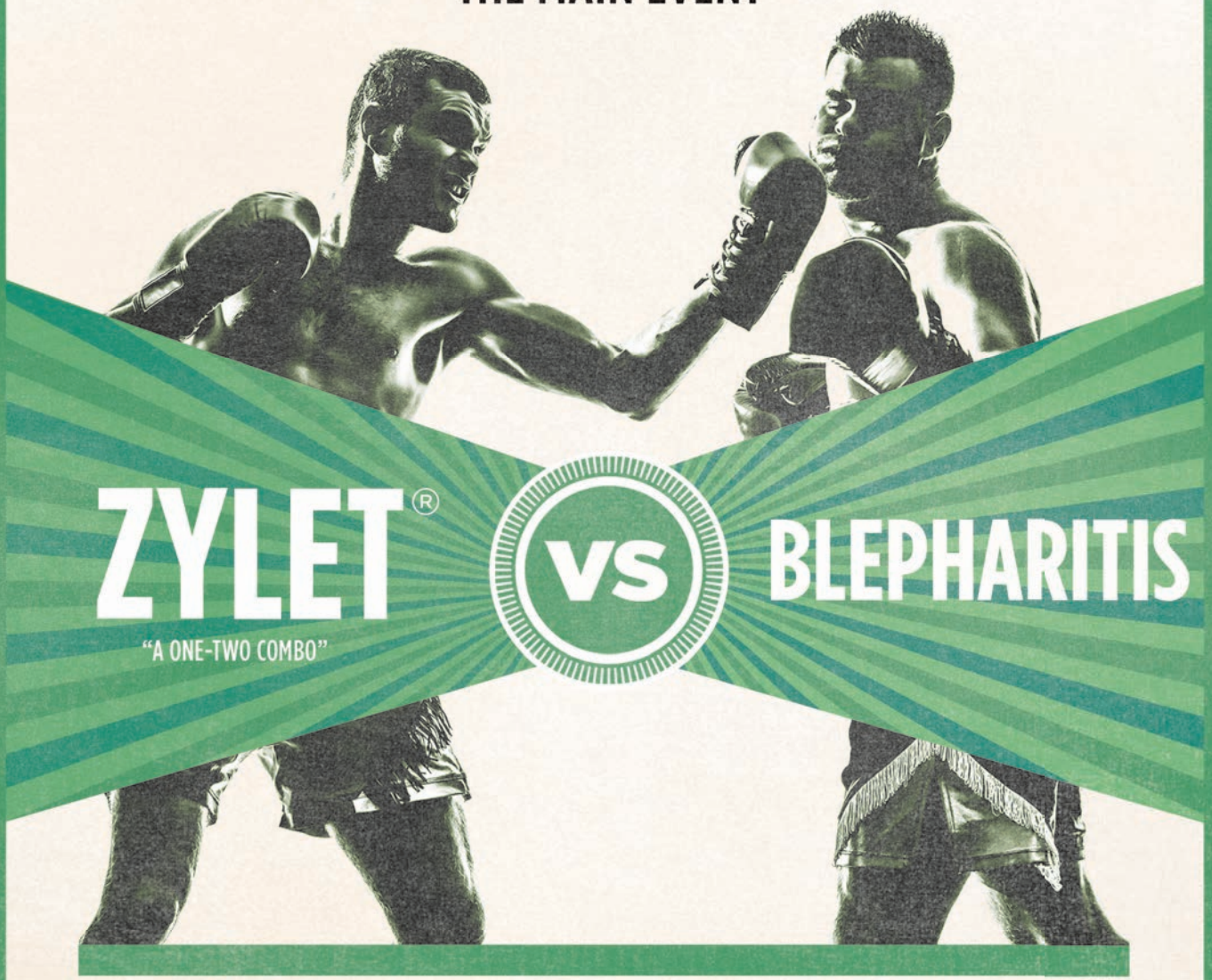
Business Name
Address
City State
ZIP
Telephone # - -
Fax # - -

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 112955 RO-OSC-0516

★ ★ ★ THE MAIN EVENT ★ ★ ★



HELP PUT RELIEF IN YOUR CORNER

INDICATIONS AND USAGE

ZYLET® (loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension) is a topical anti-infective and corticosteroid combination for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists.

Please see additional Indications and Usage information on adjacent page, including list of indicated organisms.

INDICATIONS AND USAGE (continued)

Ocular steroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, and where the inherent risk of steroid use in certain infective conjunctivitides is accepted to obtain a diminution in edema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns, or penetration of foreign bodies.

The use of a combination drug with an anti-infective component is indicated where the risk of superficial ocular infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye.

The particular anti-infective drug in this product (tobramycin) is active against the following common bacterial eye pathogens: *Staphylococci*, including *S. aureus* and *S. epidermidis* (coagulase-positive and coagulase-negative), including penicillin-resistant strains. *Streptococci*, including some of the Group A-beta-hemolytic species, some nonhemolytic species, and some *Streptococcus pneumoniae*, *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes, Proteus mirabilis, Morganella morganii*, most *Proteus vulgaris* strains, *Haemophilus influenzae*, and *H. aegyptius, Moraxella lacunata, Acinetobacter calcoaceticus* and some *Neisseria* species.

IMPORTANT SAFETY INFORMATION

- ZYLET® 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. 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.
- Use of corticosteroids may result in posterior subcapsular cataract formation.
- 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 a slit lamp biomicroscopy and, where appropriate, fluorescein staining.
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infections. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
- Employment of corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and exacerbate the severity of many viral infections of the eye (including herpes simplex).
- Fungal infections 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.
- Most common adverse reactions reported in patients were injection and superficial punctate keratitis, increased intraocular pressure, burning and stinging upon instillation.

Please see Brief Summary of Prescribing Information on the following page.

With a one-two combo in the treatment of blepharitis and other steroid-responsive ocular conditions with the risk of bacterial infection, PRESCRIBE ZYLET® TODAY.

BAUSCH+LOMB

Zylet®
loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use Zylet safely and effectively. See full prescribing information for Zylet.

Zylet® (loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension)

Initial U.S. Approval: 2004

DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

Apply one or two drops of Zylet into the conjunctival sac of the affected eye every four to six hours. During the initial 24 to 48 hours, the dosing may be increased, to every one to two hours. Frequency should be decreased gradually as warranted by improvement in clinical signs. Care should be taken not to discontinue therapy prematurely.

2.2 Prescription Guideline

Not more than 20 mL should be prescribed initially and the prescription should not be refilled without further evaluation [*see Warnings and Precautions (5.3)*].

CONTRAINDICATIONS

4.1 Nonbacterial Etiology

Zylet, as with other steroid anti-infective ophthalmic combination drugs, 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

5.1 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.

5.2 Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

5.3 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 a slit lamp biomicroscopy and, where appropriate, fluorescein staining.

5.4 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. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

5.5 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).

5.6 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.

5.7 Aminoglycoside Hypersensitivity

Sensitivity to topically applied aminoglycosides may occur in some patients. If hypersensitivity develops with this product, discontinue use and institute appropriate therapy.

ADVERSE REACTIONS

Adverse reactions have occurred with steroid/anti-infective combination drugs which can be attributed to the steroid component, the anti-infective component, or the combination.

Zylet:

In a 42 day safety study comparing Zylet to placebo, ocular adverse reactions included injection (approximately 20%) and superficial punctate keratitis (approximately 15%). Increased intraocular pressure was reported in 10% (Zylet) and 4% (placebo) of subjects. Nine percent (9%) of Zylet subjects reported burning and stinging upon instillation.

Ocular reactions reported with an incidence less than 4% include vision disorders, discharge, itching, lacrimation disorder, photophobia, corneal deposits, ocular discomfort, eyelid disorder, and other unspecified eye disorders.

The incidence of non-ocular reactions reported in approximately 14% of subjects was headache; all other non-ocular reactions had an incidence of less than 5%.

Loteprednol etabonate ophthalmic suspension 0.2% - 0.5%:

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.

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.

Tobramycin ophthalmic solution 0.3%:

The most frequent adverse reactions to topical tobramycin are hypersensitivity and localized ocular toxicity, including lid itching and swelling and conjunctival erythema. These reactions occur in less than 4% of patients. Similar reactions may occur with the topical use of other aminoglycoside antibiotics.

Secondary Infection:

The development of secondary infection has occurred after use of combinations containing steroids and antimicrobials. Fungal infections of the cornea are particularly prone to develop coincidentally with long-term applications of steroids.

The possibility of fungal invasion must be considered in any persistent corneal ulceration where steroid treatment has been used.

Secondary bacterial ocular infection following suppression of host responses also occurs.

USE IN SPECIFIC POPULATIONS

8.1 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 fixtures) 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 at 0.5 mg/kg/day (6 times the maximum daily 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.

Reproductive studies have been performed in rats and rabbits with tobramycin at doses up to 100 mg/kg/day parenterally and have revealed no evidence of impaired fertility or harm to the fetus. There are no adequate and well controlled studies in pregnant women. Zylet 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 administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemic steroids that appear in human milk could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when Zylet is administered to a nursing woman.

8.4 Pediatric Use

Two trials were conducted to evaluate the safety and efficacy of Zylet® (loteprednol etabonate and tobramycin ophthalmic suspension) in pediatric subjects age zero to six years; one was in subjects with lid inflammation and the other was in subjects with blepharoconjunctivitis.

In the lid inflammation trial, Zylet with warm compresses did not demonstrate efficacy compared to vehicle with warm compresses. Patients received warm compress lid treatment plus Zylet or vehicle for 14 days. The majority of patients in both treatment groups showed reduced lid inflammation.

In the blepharoconjunctivitis trial, Zylet did not demonstrate efficacy compared to vehicle, loteprednol etabonate ophthalmic suspension, or tobramycin ophthalmic solution. There was no difference between treatment groups in mean change from baseline blepharoconjunctivitis score at Day 15.

There were no differences in safety assessments between the treatment groups in either trial.

8.5 Geriatric Use

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

NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate or tobramycin.

Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma TK assay, a chromosome aberration test in human lymphocytes, or in an *in vivo* mouse micronucleus assay.

Oral treatment of male and female rats at 50 mg/kg/day and 25 mg/kg/day of loteprednol etabonate, respectively, (500 and 250 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender. No impairment of fertility was noted in studies of subcutaneous tobramycin in rats at 100 mg/kg/day (1700 times the maximum daily clinical dose).

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 suspension. If pain develops, redness, itching or inflammation becomes aggravated, the patient should be advised to consult a physician. As with all ophthalmic preparations containing benzalkonium chloride, patients should be advised not to wear soft contact lenses when using Zylet.

MANUFACTURER INFORMATION

BAUSCH & LOMB INCORPORATED

TAMPA, FLORIDA 33637 USA

Based on 9007705-9004405 Revised 08/2013 US/ZYL/15/0014

Conditions in Context: Ventilator-induced Proptosis

Not all cases of 'the bulge' result from of autoimmune disease, trauma or tumor. Sometimes ocular conditions arise in the context of emergent circumstances.

By Jen Lesniewski, BSc, Brian S. Lilien, BA, A.S. Gurwood, OD, and Mark Street, OD

Some patients experience profound decompensation of the respiratory system requiring airway protection. While the thought of intubation is not pleasant, it is warranted in emergent cases such as acute trauma; septic shock; acute and chronic respiratory difficulties; respiratory compromise secondary to cerebrovascular accident, respiration failure secondary to neurological diseases (i.e., Guillain-Barre); respiratory distress following an asthmatic event; and acute hemorrhagic event (i.e., ruptured aneurysm).

In cases like these, patients may be intubated to protect the vulnerable airway from collapse or interruption.[1] Intubation of the airway is accomplished via use of a laryngoscope blades to position plastic tubing into the trachea, through which respiration can be automatically driven by a positive pressure instrument known as a ventilator.[2,3] All ventilators can be adjusted to create specific tidal volumes—volume of air per breath—in the setting of adjustable positive pressure (i.e., inflow push) and frequency of respiration (i.e., respirations per minute).[4] Ventilators breathe for the patient to protect and preserve the air pathway, as well as removing the muscular responsibility from individuals who lack the strength or neurologic control to complete respiration.[4,5]

The process works by creating positive pressure within the lungs.[5,6] Ventilators may be set to two modes: volume mode and pressure mode.[5] *Volume mode* permits the titration of each breath, and is referred to as tidal volume.[5,7] *Pressure mode* regulates the force of air introduced into the lungs.[5,6]

Respiration frequency can also be adjusted to control respirations per minute. The combination of these three variables can be used to control the peak airway pressure and inspiratory flow, generating a flow pattern that is customizable for each individual and situation.[4,7]

The mode of respiration can also be defined. *Triggered Respiration* is selected to permit respiration based on an inspiratory effort by the patient within a time boundary. *Cycled Respiration* is selected to deliver breaths following the reaching of a set tidal volume.[6]

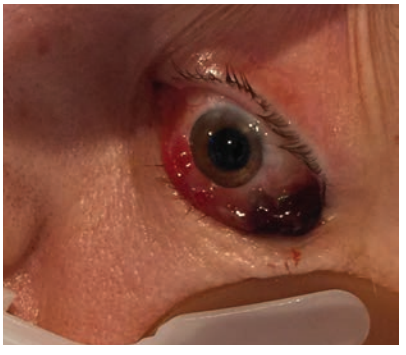


Fig. 1. After introduction of the ventilator, this patient developed acute and intractable bilateral proptosis.

To intubate the trachea, the base of the neck must be aligned so that the three principle axes are located in their proper positions:[3,4]

- The oral axis line—the plane of the tongue and the hard palate.
- The posterior pharyngeal—which defines the pharyngeal axis.
- The tracheal axis.[3,4]

When a patient is supine, the oral axis is perpendicular to the surface of the bed, the pharyngeal axis sits on an angle from the posterior wall of the pharynx to the larynx and the tracheal axis is positioned at downward angle from the larynx.[3,4] Pillows and pads along with techniques designed to preserve the safety of cervical spinal alignment are used to bring the head and neck into position for placement of the tubing.[3,4]

To bring the oral axis into alignment, a jaw-thrust technique preserves neutral head position as the supportive aids stabilize the pharyngeal and tracheal axes. A clear line of sight permits the passage of the intubation tubing into the airway.[3,4]

Intubation Technique

1. The endotracheal tube is held in the provider's right hand and introduced into the right side of the patient's mouth along with the laryngoscope blade.
2. The curve of the endotracheal intubation tube is directed anteriorly.
3. It is advanced toward the glottis from the right side of the mouth so as not to obscure visualization of the glottic opening.
4. Once the proximal end of the tube's cuff is 1cm to 2cm past the vocal cords, placing the distal end of the tube midway between the vocal cords and carina the laryngoscope blade is removed from the patient's mouth.
5. Once in place, the cuff of the endotracheal tube is inflated with air to create a seal against the tracheal mucosa. This seal facilitates positive-pressure ventilation of the lungs and decreases the likelihood of aspiration of pharyngeal or gastric contents, protecting the airway.
6. Upon correct placement (confirmation made via end-tidal CO_2, auscultation for bilateral breath sounds, ballottement of cuff in the suprasternal notch), the endotracheal tube is secured in position externally with tape.
7. Use of the minimum volume of air in a low-pressure high-volume cuff will typically prevent leaks during positive ventilation pressure (20cm to 30cm H_2O). It also minimizes the likelihood of mucosal ischemia resulting from prolonged pressure against the tracheal wall.
8. Serious complications attributable to prolonged or excessive endotracheal cuff pressures include tracheal stenosis, tracheal rupture, tracheoesophageal fistula, tracheocarotid fistula and formation of tracheoinnominate artery fistula.

Ventilator-induced Ocular Complications

The circulatory system is cyclic, owing its efficiency to an uninterrupted circle of movement. Whenever alteration occurs to the physical pathway (blood vessel impingement by thrombosis, blood cell pathology, restriction or compression) or to the pressure within the circulatory system, perfusion can be altered.[8,9]

Ventilation in the setting of excessive positive pressure, excessive volume per breath or increased frequency of respiration has the potential to increase cardiopulmonary congestion, as efficient communication between the heart and lungs is altered. When this occurs, blood can be prevented from filling the right ventricle, with the net effect of increasing systemic venous pressure.[8,9]

Additional circumstances that increase net systemic venous pressure include poor air exchange, in which the lungs cannot expel carbon dioxide efficiently, and cases when the jugular veins are mechanically occluded by the tie back used to externally stabilize the intubation apparatus.[8,9]

Case Report

A 58-year-old woman was admitted to the critical care unit of the hospital secondary to septic shock caused by candidiasis. She obtained the infection from leg sores that had developed as a result of poorly controlled non-insulin dependent diabetes mellitus. As the condition worsened, she developed respiratory compromise necessitating protection of the airway through intubation. Three days following introduction of the ventilator she developed acute and intractable bilateral proptosis *(Figure 1)*. Following neuroimaging that demonstrated normal intracranial structures and vasculature, an ophthalmic consult was requested by the medical team. At the time of the consult, the patient's diabetes and hypertension had been controlled and the systemic sepsis was declining. The chart demonstrated no allergies.

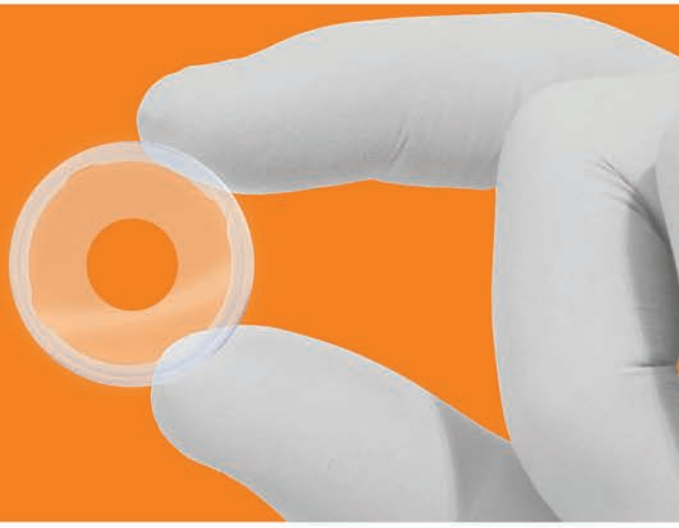
The bedside consult found the patient's eyes covered with gauze pads that had been saturated with Polymyxin B/bacitracin ophthalmic ointment. Her best-corrected visual acuities measured 20/200 using a calibrated near-point card and her near vision spectacles. Extraocular muscle motilities were restricted in all fields of gaze in both eyes. The confrontation visual field test was normal. No afferent pupillary defect existed. No ability existed to retropulse the eyes and there was limited movement upon forced duction testing. Portable biomicroscopy revealed diffuse-exposure keratoconjunctivitis without frank corneal abrasions in both eyes. No evidence of iris

NEW

INTRODUCING

PROKERA® | Clear

Biological Corneal Bandage: *"See More Clearly"*



New PROKERA® Clear helps heal the cornea and maintains visual acuity

HAPPINESS IN SIGHT

PROKERA® Clear goes beyond hydration to:

- ✓ Rejuvenate the cornea
- ✓ Simultaneously reduce inflammation and promote quality healing
- ✓ Treat chronic dry eye cases DEWS level 2, as well as levels 3 and 4

See us at Optometry's Meeting Booth 700

SM-267, Rev 5, 4/21/2016

biotissue®

Optometry's meeting®

LEARN. LEAD. CONNECT.

Exciting New Formats for Education Courses

JOIN US FOR OPTOMETRY'S MEETING® IN BOSTON, JUNE 29 – JULY 3, 2016

Education is the #1 reason you come to Optometry's Meeting®

Our expanded education program means five full days of in-depth, diverse content delivered in new, interesting formats designed to keep your attention! Earn 30+ hours of accredited education from a vast selection of new and unique courses – choose from more than 200 sessions.

What sets our education apart?

Our INTERACTIVE COURSE FORMATS allow you to drive the content. Audience participation is encouraged, and opposing views will be discussed. Don't miss:

- Presentations by the top speakers in the industry
- "OD Talks: Through a Patient's Eyes" – Inspired by TED Talks
- Hands-on workshops for mastering new skills – 11 workshops for doctors of optometry and 5 workshops for optometric staff
- Rapid-fire format debates that address current treatment and diagnostic challenges
- NEW IN 2016: Education in the Round – where we bring the speakers to the center of the audience!
- NEW IN 2016: Expert Perspectives in the Fast Lane – 15 minute presentations to keep the knowledge fast and furious!

Register now for Optometry's Meeting®, the ONLY event that brings the optometry community together to shape the future of the profession. Optometry's Meeting offers doctors of optometry and their staff the opportunity to impact the future of optometric practice and connect with peers, while getting the BEST continuing education in the industry.

Register today at
optometrysmeeting.org

REGISTER BY MAY 2 FOR BEST RATES

AMERICAN OPTOMETRIC ASSOCIATION

AOSA

neovascularization or iritis was present. Tonopen (Reichert) intraocular pressures (IOP) measured 28mm Hg in both eyes. Dilated fundus examination found 0.3/0.3 round optic nerves with no evidence of notching or disc edema. No choroidal folds or peripheral pathologies were present and there was no evidence of *Candida* retinitis. The patient had mild non-proliferative diabetic retinopathy without macular edema in both eyes.

Without evidence of neuro-opthalmologic disease (e.g., tumor, hemorrhage, orbital cellulitis, varicocele, carotid cavernous fistula, venous sinus thrombosis or acute proptosis from thyroid storm), a hypothesis was proffered implicating the pressure effect on the venous system exerted by the ventilator.

An acute strategy of topical antibiotic ointment patching was continued. With permission from the medical team, a topical anti-glaucoma agent (brimonidine 0.15%) TID in both eyes was added to lower the IOP to protect the nerves.

Following a conference with all of the members of the medical team, it was decided that extubation would commence when a determination of safety was made. Following extubation, the proptosis resolved and ocular motility, IOP and visual function normalized. The topical antibiotic ointments were reduced to in frequency from TID to BID and the topical anti-glaucoma agent was removed. The patient's visual acuities returned to pre-disease levels (i.e., 20/40) and the untreated IOP was measured at 16mm Hg.

Differential Diagnosis of Proptosis

1. Mass

Any type of mass in the orbit can cause proptosis. If the mass is in the intraconal fat, it causes a straightforward proptosis; if it is in the extraconal fat, it causes proptosis induced at an angle. Examples: neoplasms resulting from lymphoproliferative disorders, leukemia or metastatic disease.

2. Thyrotoxicosis

Thyrotoxicosis, also known as Grave's disease, is the eye's response to an autoinflammatory disorder of the thyroid gland. Women are affected four to five times more frequently than men and the symptoms range from mild to rapidly progressing. The extraocular muscles can be infiltrated with lymphocytes, macrophages, plasma cells, mast cells and mucopolysaccharides, resulting in proptosis, increased tendon-sparing extraocular muscle (EOM) mass, eye lid inflammation, swelling, eye lid retraction and EOM motility restrictions.

3. Carotid cavernous fistula

A carotid cavernous fistula is defined by arterialization of the internal carotid artery and the cavernous sinus. This abnormal communication results in retrograde flow of arterial blood into the orbit from the ophthalmic veins. This fistula can occur spontaneously or secondary to trauma that tears the internal carotid artery. As arterial blood floods the venous sinus, pressure builds and proptosis occurs.

4. Orbital cellulitis

Orbital cellulitis results from infection that has spread from the maxillary sinuses or ethmoid bone through the ophthalmic and facial veins to the orbital cavity. The walls of the sinus cavity are thin, and are incapable of serving as strong barriers against infection movement. When the pathogens reach the orbit, the orbital contents become inundated, infected and edematous, resulting in pain and loss of function. Proptosis results with hallmark decreased ocular motility.

5. Retrobulbar hemorrhage

A retrobulbar hemorrhage can be accidental or a result of surgical trauma. It can develop very quickly or over minutes to hours. The blood can accumulate in several different locations. The signs and symptoms depend the volume and location of the hemorrhage. The rapid blood fixed against the rigid boundaries of the orbital cavity results in proptosis, pain, decreased ocular motility, nausea, vomiting and increased in intraorbital pressure with secondary elevation of intraocular pressure.

Ocular Vascular Anatomy

The ocular venous system, like the systemic venous system, contains limited valves.[10,11] The choroidal blood supply exits the eye via four to 12 venous voticosae, or vortex veins and the intraretinal blood supply exits the eye via the central retinal vein.

Ocular venous blood exits the eye depending on its anterior or posterior location:

- The majority of internal ocular venous blood exits the eye using the superior and inferior ophthalmic veins.
- The vortex veins, which drain blood from the choroid, join the superior and inferior ophthalmic veins depending upon their position.
- The inferior ophthalmic vein has an anastomosis with the inferior ophthalmic and infraorbital vein and generally drains blood from the adnexa and conjunctivae to the pterygoid plexus of veins in the face.[10,11]

• The superior ophthalmic and inferior ophthalmic veins drain into the cavernous sinus in the middle cranial fossa.[10,12]

• The central retinal vein can drain into the superior ophthalmic vein or drain directly into the cavernous sinus.[10,12]

• The pterygoid plexus of veins in the face return blood to the heart via the external jugular system.[12]

• The anterior muscular veins drain the extraocular muscles. They are variable in location and merge with one another, but ultimately connect with the superior and inferior ophthalmic veins.[10,11]

The Role Of The Improperly Set Ventilator

All ventilators maintain ventilation based upon three general principles: They supply a prescribed volume of air mixed with oxygen at an adjustable rate, pressure and frequency.[6,16] Once intubation is established, the patient's physiology is analyzed to calculate initial ventilation values.

The ventilator has the potential to directly disrupt the pressure gradient of pulmonary blood flow as the air mixture is forced into the lungs.[5,6] When the values are set in such a way that the system cannot compensate, homeostasis is lost.

Ventilation settings resulting in excessively high pulmonary pressure have the potential to disturb the equilibrium of the circulatory system by increasing central venous pressure via congestion.[6] Venous congestion begins in the pulmonary arteries and transmits itself through the entire cardiopulmonary system. Superior systemic blood flow backs up into the superior vena cava through the brachiocephalic vein, to the internal and external jugular veins, which drain all of the cranial contents.[13]

Systemic Complications of Ventilator Use

Pulmonary
- Barotrauma (eg, pneumothorax, pneumomediastinum, systemic gas embolism, etc)
- Ventilator-induced lung injury (ie, volutrauma, atelec-trauma, biotrauma)
- Oxygen toxicity
- Ventilator-associated pneumonia
- Tracheal stenosis

Cardiac
- Reduced cardiac output/hypotension
- Right ventricular ischemia
- Propagation of right-to-left interatrial shunt

Gastrointestinal
- Ileus
- Gastrointestinal hemorrhage

Renal
- Fluid retention
- Hyponatremia

Cerebrovascular
- Increased intracranial pressure

Increased central venous pressure affects the body system wide. It directly affects the ocular venous system and its ability to sustain equilibrium, reducing venous return and arteriole in-flow.[13] While the ocular venous system is a limited valve network capable of tolerating bidirectional blood flow, in extreme cases compensation is not adequate, and back pressure is able to build.

When the ocular venous system does not drain appropriately, fluid and blood is trapped in ocular tissues and the orbit. This reduces egress of fluid and blood from the eye. Consequences of this include increased IOP due to reduced aqueous egress secondary to limited trabecular meshwork drainage and uveal scleral outflow-pathway restriction from interrupted episcleral venous flow. Conjunctival injection and edema, and proptosis can occur.[10,17]

The orbital contents consist of the globe, extraocular muscles, optic nerve, retrobulbar fat and the lacrimal gland. When back-pressure builds in the cavernous sinus, the rigid structures remain stable while the globe slips forward and proptosis occurs.[17-24]

Gravity's effect on fluid pressure is another determinant in positive pressure ventilation and can change the vascular system's performance. Changes in head height can produce pressure differences, affecting blood flow in the lungs as the body changes position.[7,13] Head position can be used therapeutically to decrease blood flow to abnormal areas of the lung, such as in unilateral pneumonia, improving gas exchange, and in contradistinction can be used to increase flow.[7,13]

Lessons Learned

Ventilator-induced proptosis is a diagnosis of exclusion. Ventilator mechanics and cardiopulmonary physiology as they relate to ocular vascular flow create the potential for hemodynamic stasis and poor cardiac return, resulting in cases that range from the mild conjunctival fluid retention to the extreme, cavernous sinus congestion contributory to globe proptosis. Fortunately, the condition is rapidly reversible following either extubation or ventilator reset. ■

Ms. Lesniewski and Mr. Lilien are recent graduates of Salus University.

Dr. Gurwood is Co-Chief of Suite 3 at The Eye Institute and a professor of clinical sciences at Salus University.

Dr. Street serves as Assistant Professor at Salus University.

1. Kritek P, Choi A. Approach to the Patient With Disease of the Respiratory System. In: Longo DL, Fauci AS, Kasper DL, et al. Eds. Harrison's Principles of Internal Medicine. McGraw-Hill, New York, NY 2012:2084-2086.
2. Epstein S, Hite R, Truwit J. Invasive Mechanical Ventilation. In: Epstein S, Hite R, Truwit J. Eds. Practical Guide to Mechanical Ventilation. John Wiley & Sons, Hoboken, NJ 2011:106-251.
3. Butterworth JF, Mackey DC, Wasnick JD. The Airway Management. In: Morgan GE, Mikhail MS, Murray MJ, Eds. Morgan & Mikhail's Clinical Anesthesiology. McGraw-Hill, New York, NY 2013:108-141.
4. Henderson J. Airway Management in an Adult. In: Miller RD, Eriksson LI, et al. Eds: Miller's Anesthesiology. Churchill-Livingstone, Philadelphia, PA 2010:1573-1610.
5. Hall JB, Schmidt GA. Management of the Ventilated Patient. In: Hall JB, Schmidt GA, Wood LH, Eds. Principles of Critical Care. McGraw-Hill, New York, NY 2005:481-498.
6. Celli BR. Mechanical Ventilatory Support. In: Longo DL, Fauci AS, Kasper DL, et al. Eds. Harrison's Principles of Internal Medicine. McGraw-Hill, New York, NY 2012:2210-2214.
7. Grasso S, Mascia L, Ranieri VM et al. Respiratory Care. In: Miller RD, Eriksson LI, Fleisher LA, et al. Eds: Miller's Anesthesiology. Churchill-Livingstone, Philadelphia, PA 2010:2879-2998.
8. Eskaros SM, Papadakos PJ, Lachmann B. Respiratory Monitoring. In: Miller RD, Eriksson LI, Fleisher LA, et al. Miller's Anesthesiology: Churchill-Livingstone, Philadelphia, PA 2010:1411-1442.
9. Prendergast TJ, Chesnutt MS. Pulmonary Disease. In: McPhee SJ, Hammer GD, Eds. Pathophysiology of Disease. McGraw-Hill, New York, NY 2010:1120-1345.
10. Snell RS, Lemp MA. The orbital blood vessels. In: Snell RS, Lemp MA.
Clinical anatomy of the eye. Blackwell Science Inc, Malden, MA 1998:277-293.
11. Remington LA. Orbital Blood Supply. In: Remington LA, Ed. Clinical Anatomy and Physiology of Visual System. Butterworth-Heinmann, United States 2012:202-217.
12. Netter FH. Head and Neck. In: Hansen JT, Benninger B, Brueckner JK, Carmichael SW, Granger NA, Tubbs RS, Eds. Atlas of Human Anatomy. Saunders, Philadelphia, PA 2011:1-148.
13. Hedenstierna G. Respiratory Physiology. In: Miller RD, Eriksson LI, Fleisher LA, et al. Eds: Miller's Anesthesiology. Churchill-Livingstone, Philadelphia, PA: 2010:361-392.
14. Barrett KE, Boitano S, Barman SM, Brooks HL. Introduction to Pulmonary Structure and Mechanics. In: Barrett KE, Boitano S, Barman SM, Brooks HL, Eds. Ganong's Review of Medical Physiology. McGraw-Hill, New York, NY 2012:621-640.
15. Netter FH. Thorax. In: Hansen JT, Benninger B, Brueckner JK, et al. Eds. Atlas of Human Anatomy. Saunders, Philadelphia, PA 2011:175-239.
16. Fessler MB, Fessler MB, Welsh CH, Welsh CH. Mechanical Ventilation: Invasive and Noninvasive. In: Hanley ME, Welsh CH. Eds. Current Diagnosis & Treatment in Pulmonary Medicine. McGraw-Hill, New York, NY 2003:280-291.
17. Oyster CW. The orbit. In: Oyster CW. The human eye structure and
function. Cinaur Associates Inc., Sunderland, MA 1999:111-131.
18. Kanski JJ. Orbit. In: Kanski JJ, Bowling B, Eds. Clinical Ophthalmology: A Systemic Approach. Elsevier Limited, Philadelphia, PA 2011:79-120.
19. Dutton JJ. Orbital diseases. In: Yanoff M, Duker JS. Ophthalmology.
Mosby-Elsevier, St. Louis, MO 2009:1450-1464.
20. Rootman J. An approach to diagnosis. In: Rootman J. Ed. Disease of the Orbit: A Multidisciplinary Approach. Lippincott Williams and Wilkins, Philadelphia, PA 2003:92-103.
21. Rootman J. Inflammatory Diseases. In: Rootman J. Ed. Disease of the Orbit: A Multidisciplinary Approach. Lippincott Williams and Wilkins, Philadelphia, PA 2003:462-514.
22. Marotta TR, Graeb DA, Vascular Lesions. In: Rootman J. Ed. Diseases of the Orbit: A Multidisciplinary Approach. Lippincott Williams and Wilkins, Philadelphia, PA 2003:514-554.
23. Bauer DC, McPhee SJ. Thyroid Disease. In: McPhee SJ, Hammer GD, Eds. Pathophysiology of Disease. McGraw-Hill, New York, NY 2010: 2846-3976.
24. Rubenstein JB, Virasch V. Allergic conjunctivitis. In: Yanoff M, Dukerm JS. Ophthalmology. Mosby-Elsevier, St. Louis, MO 2009:259-263.

Sweeping Away the Doubt

An expert sheds light on the potential role of swept-source OCT technology in corneal imaging. **Edited by Joseph P. Shovlin, OD**

Q Can you provide details on swept-source imaging technology for the cornea? What are the advantages to having this technology in a refractive surgery practice?

A "Swept-source optical coherence tomography (SS-OCT) is the latest technology in the evolution of OCT," explains Karen Yeung, OD, senior optometrist at the Arthur Ashe Student Health & Wellness Center at the University of California Los Angeles. In this technology, "a photodetector detects wavelength-resolved interference signals from a swept-source monochromatic laser (with wavelength of 1,310µm). Commercially available SS-OCTs scan up to 30,000 A-scans per second, with a longitudinal and transverse resolution of 10µm and 30µm, respectively."[1,2] Typically, she adds, the technology creates a 360-degree scan of the anterior segment, which is divided into 128 cross-sections comprised of 512 A-scans each. These cross-section images are processed through a computer analysis program to create three-dimensional representations of the patient's cornea, including both the anterior and posterior portions; the anterior chamber; and angle; bleb segments of the sclera and iris thickness; cornea curvature and surface area.

But is this technology beneficial for a refractive surgery practice? Yes, says Dr. Yeung, citing its accuracy with provision of reliable measurements of corneal curvature, thickness and elevation prior to and following a refractive surgery procedure.[3] "Precise evaluation of the cornea is important in refractive surgery to preclude complications such as post-surgical corneal ectasia," she explains, adding that SS-OCTs may provide the highest accuracy in screening for subclinical keratoconus and measuring corneal thickness in keratoconic eyes.[4-6] A nomogram developed for use in SS-OCT machines can also be used to differentiate normal, forme fruste and early keratoconus, further determining whether a patient is eligible for refractive surgery.[7]

Dr. Yeung points out that SS-OCT technology could be useful for measuring corneal thickness in patients with corneal dystrophies, as its three-dimensional mapping capabilities can record the size, depth and location of granular corneal dystrophy deposits to guide phototherapeutic keratectomy and monitor for corneal changes.[8,9] Additional research indicates the combination of posterior corneal measurements from the SS-OCT device and anterior autokeratometry measurements may allow for accurate prediction of residual astigmatism following surgery.[10,11]

SS-OCT technology can also help with evaluating the ocular surface for pre- and postoperative signs of dry eye. Research has indicated a high correlation in tear meniscus measurements between OCT, vital staining scores, Schirmer test values and tear film breakup time.[12]

In addition to imaging the cornea, Dr. Yeung notes, SS-OCT technology may also help with the improvement of accommodative technologies in pseudophakes and in scleral contact lens fittings.[13] ■

1. SH Yun, GJ Tearney, JF De Boer, et al. High-speed optical frequency-domain imaging. Optics Express. 2003;11(22):2953-63.
2. Yasuno Y, Madjarova VD, Makita S, et al. Three-dimensional and high-speed swept-source optical coherence tomography for in vivo investigation of human anterior eye segments. Optics Express. 2005;13(26):10652-80.
3. Lee YW, Choi CY, Yoon GY. Comparison of dual rotating Scheimpflug-Placido, swept-source optical coherence tomography and Placido-scanning-slit systems. J Cataract Refract Surg. 2015;41;1018-29.
4. Steinburg J, Casagrande MK, Frings A, et al. Screening for subclinical keratoconus using swept-source fourier domain anterior segment optical coherence tomography. Cornea 2015 Nov;34(11):1413-9.
5. Jhanji V, Yang B, Yu M, et al. Corneal thickness and elevation measurements using swept-source optical coherence tomography and slit scanning topography in normal and keratoconic eyes. Clin Experiment Ophthalmol. 2013 Nov;41(8):735-45.
6. Szalai E, Berta A, Hassan Z, et al. Reliability and repeatability of swept-source Fourier domain optical coherence tomography and Scheimpflug imaging in keratoconus. J Cataract Ref Surg. 2012 Mar;38(3):485-94.
7. Rabinowitz YS, Li X, Canedo A, et al. Optical coherence tomography (OCT) combined with videokeratography to differentiate mile keratoconus subtypes. J Refrat Surg. 2014;30(2):80-7.
8. Nowinska AK, Teper SJ, Janiszewska DA, et al. Comparative study of anterior eye segment measurements with spectral swept-source and time-domain optical coherence tomography in eyes with corneal dystrophies. BioMed Research International. 2015 Sept. [Epub].
9. Mori H, Mirua M, Iwasaki T, et al. Three-dimensional optical coherence tomography-guided phototherapeutic keratectomy for granular corneal dystrophy. Cornea. 2009;28(8):944-7.
10. Hoffman PC, Abraham M, Hirnschall N, et al. Prediction of residual astigmatism after cataract surgery using swept source fourier domain optical coherene tomography. Current Eye Research. 2014 Dec:39(12):1178-86.
11. Hoffman PC, Jutz WW, Analysis of biometry and prevalence data for corneal astigmatism in 23,239 eyes. J Cataract Surgery. 2010;36:1479-85.
12. Akiyama-Fukuda R, Usui T, Yoshida T, et al. Evaluation of tear meniscus dynamics using anterior segment swept-source optical coherence tomography after topical solution instillation for dry eye. Cornea 2016;35:654-8.
13. Neri A, Ruggeri M, Protti A, et al. Dynamic imaging of accommodation by swept-source anterior-segment optical coherence tomography. J Cataract Refract Surg. 2015 Mar;41(3):501-510.

EXCEED EXPECTATIONS

Recommend PeroxiClear: Superior all day comfort in only 4 hours[1*].

Provides Superior All-Day Comfort[1*]

Lenses Feel Cleaner and Moister for Longer[1*]

Triple-Moist Technology® Maintains Moisture for up to 20 Hours

Lenses are Ready to Wear in Only 4 Hours

MONEY BACK GUARANTEED SATISFACTION

For more information or to request care kits, visit Bausch.com/Peroxiclear.

*Compared to Clear Care.

^To learn more about the Satisfaction Guarantee, go to www.peroxiclearsolution.com. Terms and conditions apply, see website for full details and instructions.

References: 1. Data on file. 2. A total of 324 eye care practitioners asked Clear Care patients to use PeroxiClear for at least 7 days resulting in 1,447 responses to an online survey. The results of these survey questions are accurate at a 95% confidence level to + or – 2% points.

BAUSCH + LOMB
See better. Live better.

A Ghostly Diagnosis

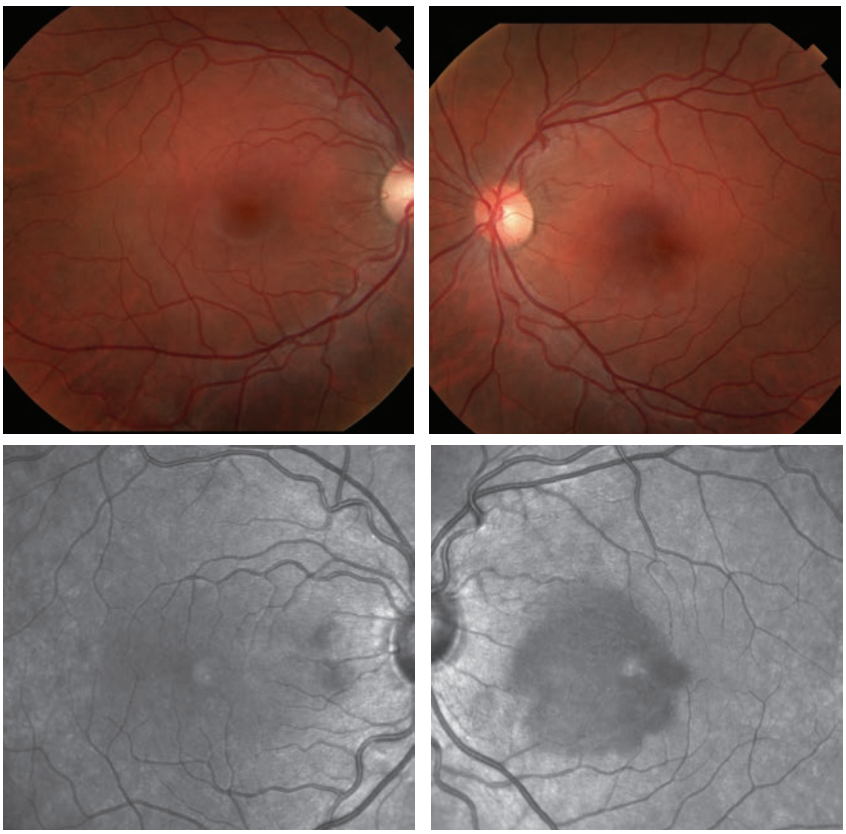
A young patient is haunted by a poor choice, but is it related to her visual symptoms?

By Mark T. Dunbar, OD, and Elliott Brafman, OD

A 26-year-old female presented for an evaluation of blurry vision and floaters that began four weeks prior. She stated that after eating a ghost pepper, she developed an allergic reaction and became unconscious. She was taken to the hospital where she developed aspiration pneumonia, myocarditis and hypotension. She was subsequently intubated and given 1mL epinephrine injection for the evident type 1 hypersensitivity reaction. Since then, she reported, her blood pressure has returned to normal levels and her other systemic problems have resolved. She no longer notices floaters but still complains of blurry vision in her left eye.

Upon examination, the patient's best-corrected vision was 20/20 OD and 20/30 OS. Confrontational visual fields were full in the right eye and revealed a temporal paracentral scotoma in the left. Evidence of the temporal paracentral visual field scotoma was also found in Amsler grid and visual field testing. Her pupils were equally round and reactive to light; no afferent pupillary defect was found. Intraocular pressure (IOP) was 13mm Hg in both eyes. Slit lamp examination of both eyes was unremarkable.

A dilated fundus exam of the right eye was normal. The left eye revealed very subtle pigmentary changes nasal to the fovea (*Figures 1 and 2*). The remainder of the fundus exam was otherwise normal. Red-free fundus photography was performed (*Figure 3*) as well as SD-OCT (*Figure 4*). Multifocal ERGs (mfERG) and FAF was also obtained.



Figs. 1 and 2. At top, fundus photos of the right and left eye of our patient. Below are red-free versions. Look carefully at the left eye images.

Take the Retina Quiz

1. What are the findings on the retinal photograph of the left eye?
a. Trace optic nerve pallor.
b. Choroidal neovascular membrane.

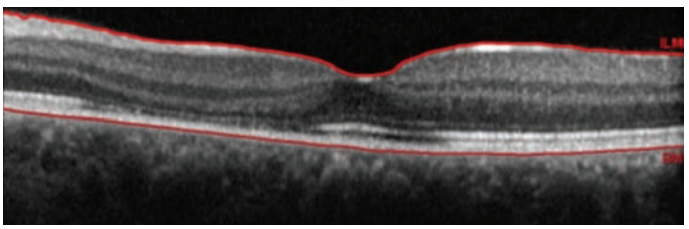


Fig. 3. Can this SD-OCT of the patient's left eye help yield the diagnosis?

THE POWER OF VISION

Since our inception a quarter of a century ago, Vision Source® has remained focused on unlocking the full power of vision — **for network members and patients alike.** And it all began with this insight — *by forming a collaborative network, independent ODs will enjoy the economies and buying power of national chains, while still preserving their independence and relationships with their patients.*

Vision Meets Potential — for 25 Years and Counting

2015 – 100+ relationships with managed care organizations
3,260 offices

2014 – 3,000 offices

2013 – Recognized as 2nd largest optical retailer in US

2009 – 2,000 offices

2007 – Exclusive, proprietary spectacle lenses created for members

TRUclear®

2004 – 1,000 offices

2001 – 500 offices

2002 – Exclusive, proprietary contact lenses created for members

1991 – Founded in Humble, TX
3 offices

Vision Source® SIGNATURE EYE CARE™ 25TH ANNIVERSARY

For more information on joining Vision Source®, go to
www.VisionSourcePlan.com

Vision Source® SIGNATURE EYE CARE™

c. Macular edema.
d. Essentially normal.

2. What layer(s) of the retina seem to be affected on the OCT of the left eye?
a. Outer nuclear layer.
b. Outer plexiform layer.
c. Ellipsoid zone.
d. All of the above.

3. What is the correct diagnosis?
a. Branched artery occlusion.
b. Acute macular neuroretinopathy.
c. Pattern dystrophy.
d. Multiple evanescent white dot syndrome.

4. What is the appropriate treatment?
a. Observe.
b. Topical steroids.
c. Anti-VEGF injections.
d. Refer for an MRI.

5. What are known risk factors for this condition?
a. Sun exposure.
b. High cholesterol.
c. Sympathomimetics.
d. Genetic predisposition.

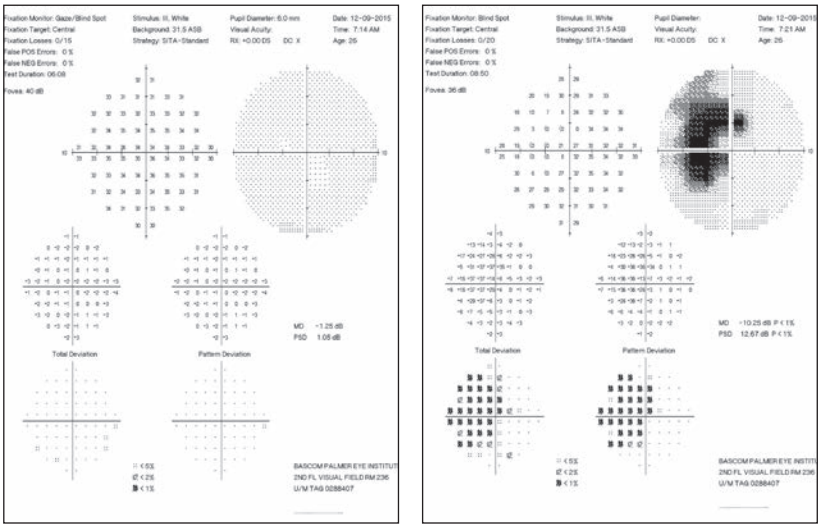


Fig. 4. What information can be gleaned from this patient's visual fields?

Diagnosis

Even though the fundus of the left eye appeared normal, subtle RPE changes could be seen. The OCT of the left eye showed obvious ellipsoid zone disruption as well as nasal hyper-reflective OPL/ONL and ONL thinning. The red-free photos of the left eye showed a dramatic paracentral dark grey, nasal hyporeflective lesion pointing toward the foveal center. The multifocal ERG was normal in the right eye, but indicated impaired responses in the retinal area around the blind spot in the left.

Based on the history, clinical findings and imaging studies, we suspected that our patient had acute macular neuroretinopathy (AMN), an idiopathic, rare disease that most commonly affects young to middle-aged females.[1-3] It was initially believed to involve the inner retina, but since the advent of SD-OCT, it is now known to be located in the outer retina with characteristic ellipsoid zone disruption, which has forced authors to refer to AMN as acute macular outer retinopathy (AMOR).[2,3,5]

Discussion

The condition can present unilaterally or bilaterally with acute onset of a paracentral scotoma and photopsias, typically without involvement of central visual acuity.[1,3] Paracentral location has been proposed simply due to the increased capillary network in this area.[4] The fundus can appear normal as was the case with our patient, but days to months after initial onset of symptoms there are usually one or more red/brown perifoveal petalloid-like or wedge-shaped lesions with the tip pointing towards the fovea.[1,3] Though these may be difficult to see on clinical exam, red-free light and near-infrared reflectance may allow better visualization.[5] OCT of these lesions typically reveal disruptions of the ellipsoid zone.[1]

Many AMN cases have been associated with an acute viral illness preceding the onset of symptoms. It has also been reported to occur after the use of oral contraceptives, IV contrast medium injections, excessive amounts of caffeine intake, allergic reactions to prawns followed by administration of vasoconstricting drugs, shock, trauma, severe blood loss and episodes of acute systemic hypotension.[2-4] Our patient noted her symptoms following an epinephrine injection.

The pathophysiology of AMN is not completely understood, but it may occur as a result of an acute episode of choroidal ischemia.[2] However, many authors refute this notion and argue that it is due to an acute retinal ischemic event, and due to the fact that central vision is often unaffected, it is assumed that the ischemia is to the deep capillary plexus of the central retinal artery rather than to the choroid or choriocapillaris.[3]

On high magnification fluorescein angiography, dilation of the deep capillary plexus has been seen, which further supports an ischemic etiology.[4] In addition, it is not uncommon to see the presence of one or more flame-shaped hemorrhages, which further supports a vascular occlusive event.[2,4]

Comorbidities

There may be an association of AMN with multiple evanescent white dot syndrome (MEWDS), acute idiopathic blind spot enlargement syndrome (AIBSE) and a condition called pseudo presumed ocular histoplasmosis (pseudoPOHS). Some authors recommend these disorders be grouped under the umbrella term of acute zonal occult outer retinopathy (AZOOR).[3]

Paracentral acute middle maculopathy (PAMM) is a newly identified variant of AMN that involves the middle layers of the retina, above and below the OPL.[4] Type 1 AMN, now know as PAMM, refers to hyper-reflectivity of the OPL/INL on OCT with subsequent INL thinning.[4,6] It is usually seen in older men with vascular disease around 60 years of age, but now is also being seen in young women.[4,6] Type 2 AMN, which is more common in young, healthy women around 30 years of age, involves the OPL/ONL. When hyper-reflectivity on OCT of the OPL/ONL resolves, evidence of ONL and subsequent ellipsoid zone thinning is seen, because 10% to 15% of the oxygen supply to the photoreceptors is by the deep capillary plexus.[4,5,6]

AMN tends to be non-recurrent and self-resolving, but symptoms may persist. There is no current treatment for this condition.[1,3]

We chose to closely monitor our patient. She was seen monthly for three months and showed steady improvement back to 20/20. However, a paracentral scotoma persisted on Amsler grid. Interestingly, the pigmentary changes became more evident. ■

Dr. Brafman is an optometric resident at the Bascom Palmer Eye Institute in Miami.

1. Kirkpatrick C. Acute Macular Neuroretinopathy (AMN). University of Iowa Health Care: Ophthalmology and Visual Sciences (2015). http://www.eyerounds.org/atlas/pages/Acute-macular-neuroretinopathy/index.htm. Accessed April 7, 2016.
2. Hughes E, Siow Y, Hunyor A. Acute macular neuroretinopathy: anatomic localization of the lesion with high-resolution OCT. Eye. 2009;23:2132-4.
3. Douglas I, Cockburn D. Acute macular neuroretinopathy. Clinical and Experimental Optometry. 2003;2:121-6.
4. Sarraf D, Rahimy E, Fawzi A, et. al. Paracentral acute middle maculopathy: a new variant of acute macular neuroretinopathy associated with retinal capillary ischemia. Jama Ophthalmol. 2013;131(10):1275-87.
5. Joseph A, Rahimy E, Freund B, Sarraf D. Multimodal Imaging in Acute Macular Neuroretinopathy. Retinal Physician 2013 June;10:40-4.
6. Tsui, I, Sarraf D. Paracentral Acute Middle Maculopathy and Acute Macular Neuroretinopathy. Ophthalmic Surg Lasers Imagine Retina. 2013;44(6):S33-S35.

Smoke (or Vapor) Gets in Your Eyes: Part One

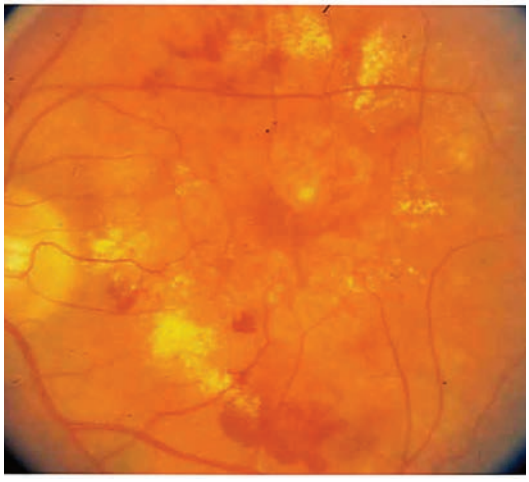
We all know the ocular and systemic harms of cigarettes, but what about cigars, pipes, e-cigarettes and other tobacco delivery methods?

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

Clinicians and scientists have long noted a strong correlation between cigarette smoke and myriad health concerns, including cancer, respiratory disease and cardiovascular disease. Tobacco use is projected to kill a billion people during the 21st century.[1,2]

Cigarette smoke contains toxic chemicals such as nicotine, cyanide, benzene, formaldehyde, methanol, acetylene and ammonia, not to mention tar, carbon monoxide and nitrogen oxide.[1] Nicotine in particular can have many different effects on the body, including:[3]

- Decreases appetite; fear of weight gain makes some people unwilling to stop smoking
- Boosts mood, giving people a sense of well-being
- Increases intestinal activity
- Creates more saliva and phlegm
- Increases heart rate by about 10 to 20 beats per minute
- Increases blood pressure by 5mm Hg to 10mm Hg
- Stimulates memory and alertness; people who use tobacco often depend on it to help them accomplish certain tasks and perform well



Wet AMD in a life-long smoker. Smoking reduces cellular antioxidants in various ocular tissues, especially the retina.

Beyond Cigarettes

Cigarettes are not the only delivery method for tobacco—there are many non-cigarette forms of tobacco and nicotine, and their use varies regionally and globally. Smoked forms of tobacco such as cigars, traditional pipes and water pipes are highly popular and are often perceived as significantly less hazardous than cigarettes. Novel nicotine delivery systems not directly reliant on tobacco, such as electronic cigarettes, are becoming increasingly popular, and their emergence presents challenges and opportunities for public health.

Research suggests that some tobacco and nicotine products may pose less of a health hazard than cigarette smoking, potentially playing a role in reducing morbidity and mortality due to smoking.[4] However, evidence also suggests the public broadly misperceives the relative risks of smoking, tobacco use and nicotine, erroneously thinking smoked tobacco products other than cigarettes, such as cigars and pipes, are harmless.[5]

Cigars

According to the Centers for Disease Control and Prevention, cigar consumption more than doubled in the United States from 2000 to 2011, from slightly less than 6.2 billion in 2000 to more than 13.7 billion in 2011.[6] Unlike nearly all cigarette smokers, most cigar smokers do not inhale. However, even if a cigar smoker doesn't intentionally inhale, potentially harmful amounts of nicotine can be absorbed through the lining of the mouth.[11] For some, switching from cigarettes to cigars can be particularly harmful because they might inhale cigar smoke the way they inhaled cigarette smoke.[11]

Although cigar smokers have lower rates of lung cancer, coronary heart disease and lung disease

ALREX®:

TREATS THE ITCH AND MORE.

SHORT-TERM TREATMENT FOR THE FULL SPECTRUM OF SAC* SIGNS AND SYMPTOMS[1-3]

*Seasonal allergic conjunctivitis.

INDICATION

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

IMPORTANT SAFETY INFORMATION

ALREX® 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, and exacerbation or prolongation of viral ocular infections (including herpes simplex).

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 reexamination of the patient with the aid of magnification. Fungal infections of the cornea may develop with prolonged use of corticosteroids.

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, infection, and photophobia.

Please see brief summary of full Prescribing Information on the following page.

References: 1. ALREX [package insert]. Tampa, FL: Bausch & Lomb Incorporated; 2013. **2.** Dell SJ, Lowry GM, Northcutt JA, Howes J, Novack GD, Hart K. A randomized, double-masked, placebo-controlled parallel study of 0.2% loteprednol etabonate in patients with seasonal allergic conjunctivitis. *J Allergy Clin Immunol.* 1998;102(2):251-255. **3.** Shulman DG, Lothringer LL, Rubin JM, et al. A randomized, double-masked, placebo-controlled parallel study of loteprednol etabonate 0.2% in patients with seasonal allergic conjunctivitis. *Ophthalmology.* 1999;106(2):362-369.

BAUSCH + LOMB

Alrex®
loteprednol etabonate
ophthalmic suspension 0.2%

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

than cigarette smokers, they do have higher rates of these diseases than those who do not smoke cigars.[6,7]

Cigar smoke contains many of the same toxic constituents as cigarette smoke, and research shows cigar smoke has higher levels of tobacco-specific nitrosamines (TSNAs) than cigarette smoke, due to cigar tobacco's curing and fermentation process.[7] Many of these TSNAs, such as N-nitrosonornicotine and nicotine-derived nitrosamine ketone, are known carcinogens.[7] Investigators have also found that cigar smoke has higher levels of carbon monoxide and nitrogen oxide than cigarette smoke.[7] The International Agency of Research on Cancer found that cigar smoking, pipe smoking or both is causally connected to cancers of the pancreas, stomach, urinary tract and bladder, lung and upper digestive tract, including the oral cavity, oropharynx, hypopharynx, larynx and esophagus.[8,9]

More specifically, a systematic review of published studies on current cigar smoking and all-cause and cause-specific mortality risks found that primary cigar smoking (i .e.,current, exclusive cigar smoking with no history of previous cigarette or pipe smoking) was associated with all cause-mortality; oral, esophageal, pancreatic, laryngeal and lung cancers; coronary heart disease and aortic aneurysm.[10]

The researchers also noticed strong dose trends by cigars per day and inhalation level for primary cigar smoking for oral, esophageal, laryngeal and lung cancers. Among primary cigar smokers reporting no inhalation, relative mortality risk was still elevated for oral, esophageal and laryngeal cancers.[10]

Although mortality risks from cigar smoking vary by level of exposure (cigars per day) and inhalation level, evidence suggests cigar smoking carries many of the same health risks as cigarette smoking.[10] Future studies will hopefully collect detailed information on cigar type, exposure level and biomarkers of exposure and potential harm.[10]

Ocular Considerations

Repeated exposure to tobacco smoke accelerates the body's aging process, including that of ocular tissues (*Table 1*).[12] The chemicals in cigarette smoke reduce the body's ability to protect itself by concurrently increasing the levels of oxidants and decreasing the levels of antioxidants.[1] Smoking causes blood vessels throughout the body to narrow and stiffen, known as arteriolar sclerosis. It also reduces the amount of oxygen in the blood, thus reducing the amount of oxygen reaching the retina. Research suggests that cigarette smoke-related tar triggers the formation of drusen.[11]

Inhaling these toxic chemicals, even briefly, significantly increases the risk for cataract, age-related macular degeneration (AMD) and ocular ramifications of cardiovascular disease—and the more a person smokes, the higher the risks. Added to that, tobacco smoke, including second-hand smoke, is an irritant that worsens dry eye disease.[1,2]

For patients diagnosed with AMD and diabetic retinopathy, smoking increases their risk of serious vision loss.[12,13] Patients with Graves' disease who smoke have a fourfold increased risk of developing ocular complications compared with non-smokers.[13]

Fortunately, after people quit smoking, their risk for these ocular diseases becomes almost as low as for people who never smoked.[1,2,3]

In our next column, we will discuss pipes, hookahs, e-cigs and smoking cessation strategies. ■

Table 1. Ocular Conditions Directly or Indirectly Related to Smoking[11]

- Cataract
- Age-related macular degeneration
- Dry eye disease
- Diabetic retinopathy
- Ocular ischemic syndrome
- Retinal vascular occlusions
- Anterior ischemic optic neuropathy
- Thyroid eye disease
- Metastatic carcinoma to the uvea

1. Centers for Disease Control and Prevention. 2010 Surgeon General's Report—How Tobacco Smoke Causes Disease: The Biology and Behavioral Basis for Smoking-Attributable Disease. Atlanta, GA:2010.
2. Benowitz NL, Brunetta PG. Smoking hazards and cessation. In: Broaddus VC, Mason RJ, Ernst JD, et al., eds. Murray and Nadel's Textbook of Respiratory Medicine. 6th ed. Philadelphia, PA: Elsevier Saunders; 2016:chap 46.
3. Rakel RE, Houston T. Nicotine Addiction. In: Rakel RE, Rakel DP, eds. Textbook of Family Medicine. 9th ed. Philadelphia, PA: Elsevier Saunders; 2016:chap 49.
4. Le Houezec J, McNeill A, Britton J. Tobacco, nicotine and harm reduction. Drug Alcohol Rev. 2011 Mar;30(2):119–23.
5. O'Connor RJ, McNeill A, Borland R, et al. Smokers' beliefs about the relative safety of other tobacco products: findings from the ITC collaboration. Nicotine Tob Res. 2007 Oct;9(10):1033–42.
6. Centers for Disease Control and Prevention (CDC). Consumption of cigarettes and combustible tobacco—United States, 2000–2011. MMWR Morb Mortal Wkly Rep 2012;61:565–9.
7. Hoffmann D, Hoffmann I. Chemistry and Toxicology. National Cancer Institute, Smoking and Tobacco Control, Monograph 9: Cigars Health Effects and Trends. 1998:55-104. http://cancercontrol.cancer.gov/brp/tcrb/monographs/.
8. IARC Working Group on the Evaluation of Carcinogenic Risks to Humans. Tobacco smoke and involuntary smoking. IARC Monogr Eval Carcinog Risks Hum. 2004;83:1–1438.
9. Sasco AJ, Secretan MB, Straif K. Tobacco smoking and cancer: a brief review of recent epidemiological evidence. Lung Cancer. 2004;45 Suppl 2:S3–9.
10. Chang CM, Corey CG, Rostron BL, Apelberg BJ. Systematic review of cigar smoking and all cause and smoking related mortality. BMC Public Health. 2015;15:390.
11. Hurt RD, Murphy JG, Dunn WF. Did we finally slay the evil dragon of cigarette smoking in the late 20th century?: unfortunately, the answer is no - the dragon is still alive and well in the 21st century and living in the third world. Shame on us! Chest. 2014;146(6):1438-43.
12. Khan JC, Thurlby DA, Shahid H, et al. Smoking and age-related macular degeneration: The number of pack years of cigarette smoking is a major determinant of risk for both geographic atrophy and choroidal neovascularization. Br J Ophthalmol. 2006;90:75-80.
13. Solberg Y, Rosner M, Belkin M. The association between cigarette smoking and ocular diseases. Survey of ophthalmology. 1998;42(6):535-47.

Lifting the Curtain on Lifitegrast

An update on the status of this potential new dry eye therapy.

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

For the last 13 years, Restasis (0.05% cyclosporine ophthalmic emulsion, Allergan) has reigned as the only FDA-approved prescription pharmaceutical product for the treatment of dry eye disease. Technically, it is indicated "to increase tear production in patients whose tear production is presumed to be suppressed due to ocular inflammation associated with keratoconjunctivitis sicca." Since the launch of Restasis in 2003, numerous companies have filed Investigational New Drug (IND) applications for similar consideration by the FDA, including anakinra, bromfenac, diquafosol, ecabet sodium, isunakinra (EBI-005), lifitegrast, rebamipide, tavilermide (MIM-D3) and tofacitinib. Yet only two of these—diquafosol and lifitegrast—have yielded clinical trials successful enough to warrant submission of a New Drug Application (NDA). Inspire Pharmaceuticals filed an NDA for diquafosol in mid-2003, but despite additional studies, subsequent amendments and numerous discussions with the FDA, the drug was never approved in the US. Merck acquired Inspire and its holdings in 2011, but has made no additional attempts to gain FDA approval of diquafosol.

Currently, diquafosol 3% ophthalmic solution is approved for the treatment of dry eye disease in Japan and is marketed as Diquas by Santen Pharmaceuticals.

Shire, the company developing lifitegrast for the treatment of dry eye disease, submitted its NDA for the drug in early 2015. Last October, the FDA requested an additional clinical study, and Shire responded in January 2016. The FDA acknowledged receipt of the additional data and assigned a six-month review period for the NDA, with a Prescription Drug User Fee Act (PDUFA) goal date of July 22, 2016.

Should the FDA rule favorably, a new therapy for dry eye disease may be available shortly thereafter.

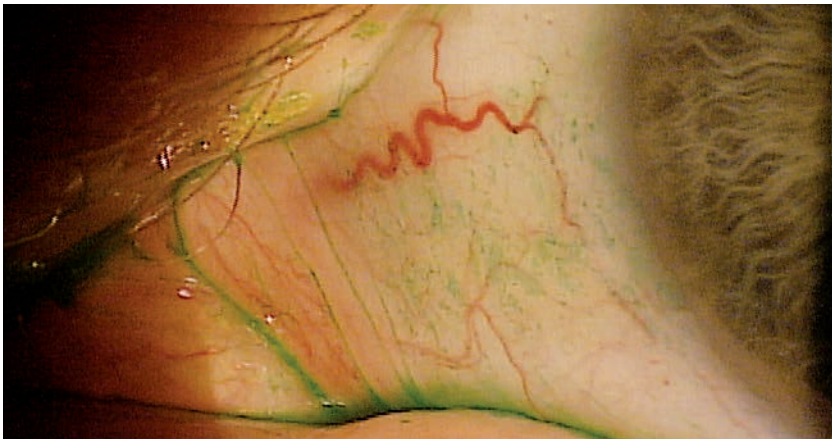


Photo: Mile Brujic, OD

Combating inflammation in dry eye is the focus of a new investigational therapy.

The Role of Inflammation

Trade publications and scientific journal articles have described lifitegrast as an "integrin antagonist," "ICAM-1 decoy" and "LFA-1 inhibitor," yet these terms are lost on many of us in the clinical trenches of optometry. To understand the role of this therapeutic agent, we need to first examine the etiology of dry eye disease. While many contributory factors have been proposed and identified, most experts consider one that is universally present in dry eye disease: inflammation.[1-5] Whether the initiating event is due to mechanical, environmental, autoimmune or other insult, the ocular surface in dry eye patients ultimately displays characteristic inflammatory changes.[6-9]

Inflammation of the ocular surface in dry eye disease is mediated, at least in part, by CD4+ lymphocytes, also known as T-cells.[3,10] Recruitment and activation of these T-cells leads to the release of effector cytokines, which directly contributes to the ocular tissue damage seen in patients with dry eye disease.[10] Research shows that T-cells are attracted to, and subsequently bind with, receptors on the ocular surface due to the presence of a signaling transmembrane protein known as intercellular adhesion molecule (ICAM-1).[7,11]

Strength in Numbers

THINK ABOUT YOUR EYES

18 Leadership Partners

Alcon®
essilor
LUXOTTICA®
AMERICAN OPTOMETRIC ASSOCIATION
THEVISIONCOUNCIL
WestGroupe
CHEMISTRIE EYEWEAR THAT CLICKS
specialeyes
GUNNAR ADVANCED COMPUTER EYEWEAR
ESCHENBACH
WALMAN
ALL ABOUT VISION.com
Hilco Smart Optical Solutions
Transitions®
SPY+
SHAMIR
NATIONAL VISION INC
Jobson Optical Group

Thanks to the support of these organizations, Think About Your Eyes is generating strong numbers. In 2015 alone, Think About Your Eyes drove **over 828,000** incremental eye exams.

thinkaboutyoureyes.com®
Brought to you by the AOA
AMERICAN OPTOMETRIC ASSOCIATION

Will your company be the 19th to join?

If you are interested in joining, please contact Rick Holt at rholt@thinkaboutyoureyes.com

ICAM-1 is normally expressed on epithelial cells, endothelial cells and immune function cells, but may be significantly upregulated when tissues are stressed.[7,10,12] T-cells are attracted to and bind with ICAM-1 on the ocular surface by virtue of a specific integrin, a protein attached to the T-cell's cytoskeleton, designated lymphocyte function-associated antigen (LFA)-1.[7,10-16] LFA-1's affinity for ICAM-1 can be likened to a histamine receptor's capacity to attract and bind its ligand, histamine. The interaction of LFA-1 with ICAM-1 on the ocular surface facilitates a complex cascade of events, beginning with T-cell adhesion, followed by migration into the tissue, T-cell activation (upon binding with antigen presenting cells) and ultimately, cytokine release.[10,12] Inflammatory cytokines such as tumor necrosis factor (TNF)-α and interleukin (IL)-1 serve to stimulate additional expression of ICAM-1.[10] This in turn leads to further proliferation and recruitment of T-cells, and perpetuates the cycle of inflammatory dry eye disease.

Pharmacology

Lifitegrast was engineered specifically to interfere with the binding of LFA-1 to ICAM-1.[10,12-14] Researchers believe that this small molecule exerts its effects by outcompeting ICAM-1 binding to LFA-1 in a dose-dependent fashion.[10] When key sites on the LFA-1 integrin are blocked by lifitegrast, the affinity for ICAM-1 is disrupted, and the T-cell is unable to adhere to the tissue surface. Thus, the subsequent cascade of events is prevented. To use the previous analogy, lifitegrast functions in inflammatory dry eye disease much in the same way that a histamine-antagonist functions in allergic conjunctivitis; by initiating a blockage of the receptor sites, the drug effectively derails the pathological process.

Clinical evaluation of lifitegrast in dry eye patients has been extensive. With more than 2,200 subjects completing four multicenter, randomized, prospective clinical trials, it represents the most thoroughly investigated drug in this category to date.[12,14,15,17] Its two Phase III studies, which employed 5% lifitegrast dosed twice daily for 12 weeks, demonstrated mixed results. In the first of these, subjects treated with the investigational drug demonstrated statistically significant improvement with regard to corneal staining (inferior corneal staining score, mean change from baseline). This was one of the study's two co-primary endpoints. There was also statistically significant improvement in ocular discomfort and dryness in the treatment group.

However, the second of the co-primary endpoints,

specified as the visual-related function subscale of the Ocular Surface Disease Index (VR-OSDI) was not met.[14]

OPUS-2 employed a similar clinical protocol; however, in this trial the subjective primary outcome measure was changed from the VR-OSDI to a less complex Eye Dryness Score (EDS). Subjects treated with lifitegrast 5% in the OPUS-2 demonstrated statistically significant improvement in the EDS, but unfortunately did not achieve the same results when compared to placebo in its co-primary endpoint of corneal fluorescein staining.[15] And, since the FDA stipulates that both an objective (sign) and subjective (symptom) endpoint must be met in at least two separate clinical trials, it was no surprise that lifitegrast did not receive approval upon its initial NDA.

Since that time, however, Shire has submitted additional data from its one-year, multicenter safety study as well as results from another Phase III clinical trial, which has yet to be published.[16,17] Interestingly, it appears that trial had only a single primary endpoint of EDS, which was met in the treatment group (p=0.0007).[17,18] Perhaps more impressive, patients using lifitegrast demonstrated symptom improvement as early as two weeks after initiating therapy.[17] ■

1. Javadi M, Feizi S. Dry eye syndrome. J Ophthalmic Vis Res. 2011 Jul;6(3):192-8.
2. Stevenson W, Chauhan SK, Dana R. Dry eye disease: an immune-mediated ocular surface disorder. Arch Ophthalmol. 2012 Jan;130(1):90-100.
3. Stern M, Schaumburg C, Pflugfelder S. Dry eye as a mucosal autoimmune disease. Int Rev Immunol. 2013 Feb;32(1):19-41.
4. Hessen M, Akpek E. Dry eye: an inflammatory ocular disease. J Ophthalmic Vis Res. 2014 Apr;9(2):240-50.
5. Wei Y, Asbell P. The core mechanism of dry eye disease is inflammation. Eye Contact Lens. 2014 Jul;40(4):248-56.
6. Stern M, Gao J, Schwalb T, et al. Conjunctival T-cell subpopulations in Sjögren's and non-Sjögren's patients with dry eye. Invest Ophthalmol Vis Sci. 2002;43:2609–2614.
7. Gao J, Morgan G, Tieu D, et al. ICAM-1 expression predisposes ocular tissues to immune-based inflammation in dry eye patients and Sjögrens syndrome-like MRL/lpr mice. Exp Eye Res. 2004 Apr;78(4):823-35.
8. Chotikavanich S, de Paiva CS, Li de Q, et al. Production and activity of matrix metalloproteinase-9 on the ocular surface increase in dysfunctional tear syndrome. Invest Ophthalmol Vis Sci. 2009 Jul;50(7):3203-9.
9. Yoon K, Park C, You I, et al. Expression of CXCL9, -10, -11, and CXCR3 in the tear film and ocular surface of patients with dry eye syndrome. Invest Ophthalmol Vis Sci. 2010 Feb;51(2):643-50.
10. Perez V, Pflugfelder S, Zhang S, et al. Lifitegrast, a Novel Integrin Antagonist for Treatment of Dry Eye Disease. Ocul Surf. 2016 Jan 22. [Epub ahead of print]
11. Tsubota K, Fujihara T, Saito K, Takeuchi T. Conjunctival epithelium expression of HLA-DR in dry eye patients. Ophthalmologica. 1999;213(1):16-9.
12. Semba C, Torkildsen G, Lonsdale J, et al. A Phase II randomized, double-masked, placebo-controlled study of a novel integrin antagonist (SAR 1118) for the treatment of dry eye. Am J Ophthalmol. 2012;153:1050-1060.
13. Sun Y, Zhang R, Gadek T, et al. Corneal inflammation is inhibited by the LFA-1 antagonist, lifitegrast (SAR 1118). J Ocul Pharmacol Ther. 2013 May;29(4):395-402.
14. Sheppard J, Torkildsen G, Lonsdale J, et al. Lifitegrast ophthalmic solution 5.0% for treatment of dry eye disease. Results of the OPUS-1 Phase III study. Ophthalmology. 2014;121:475-483.
15. Tauber J, Karpecki P, Latkany R, et al; OPUS-2 Investigators. Lifitegrast Ophthalmic Solution 5.0% versus Placebo for Treatment of Dry Eye Disease: Results of the Randomized Phase III OPUS-2 Study. Ophthalmology. 2015 Dec;122(12):2423-31.
16. Donnenfeld E, Karpecki P, Majmudar P, et al. Safety of Lifitegrast Ophthalmic Solution 5.0% in Patients With Dry Eye Disease: A 1-Year, Multicenter, Randomized, Placebo-Controlled Study. Cornea. 2016 Apr 6. [Epub ahead of print]
17. Shire's OPUS-3 Phase 3 trial with lifitegrast meets primary and key secondary endpoints, significantly reducing patient-reported symptoms for dry eye disease. Available at: www.shire.com/newsroom/2015/october/shires-opus-3-phase-3-trial-with-lifitegrast-meets-primary-and-key-secondary-endpoints. Accessed April 9, 2016.
18. ClinicalTrials.gov. A study to evaluate efficacy and safety of lifitegrast in subjects with dry eye (OPUS-3). Available at: https://clinicaltrials.gov/show/NCT02284516. Accessed April 9, 2016.

REVIEW OF OPTOMETRY®
EDUCATIONAL MEETINGS OF CLINICAL EXCELLENCE

New Technologies and Treatments N T & T IN VISION CARE 2016

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 | 866-540-4447

Discounted room rate $299-$329/NIGHT

Program Chair: **Paul Karpecki, OD**

FACULTY:

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 - UP TO 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 866-540-4447 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

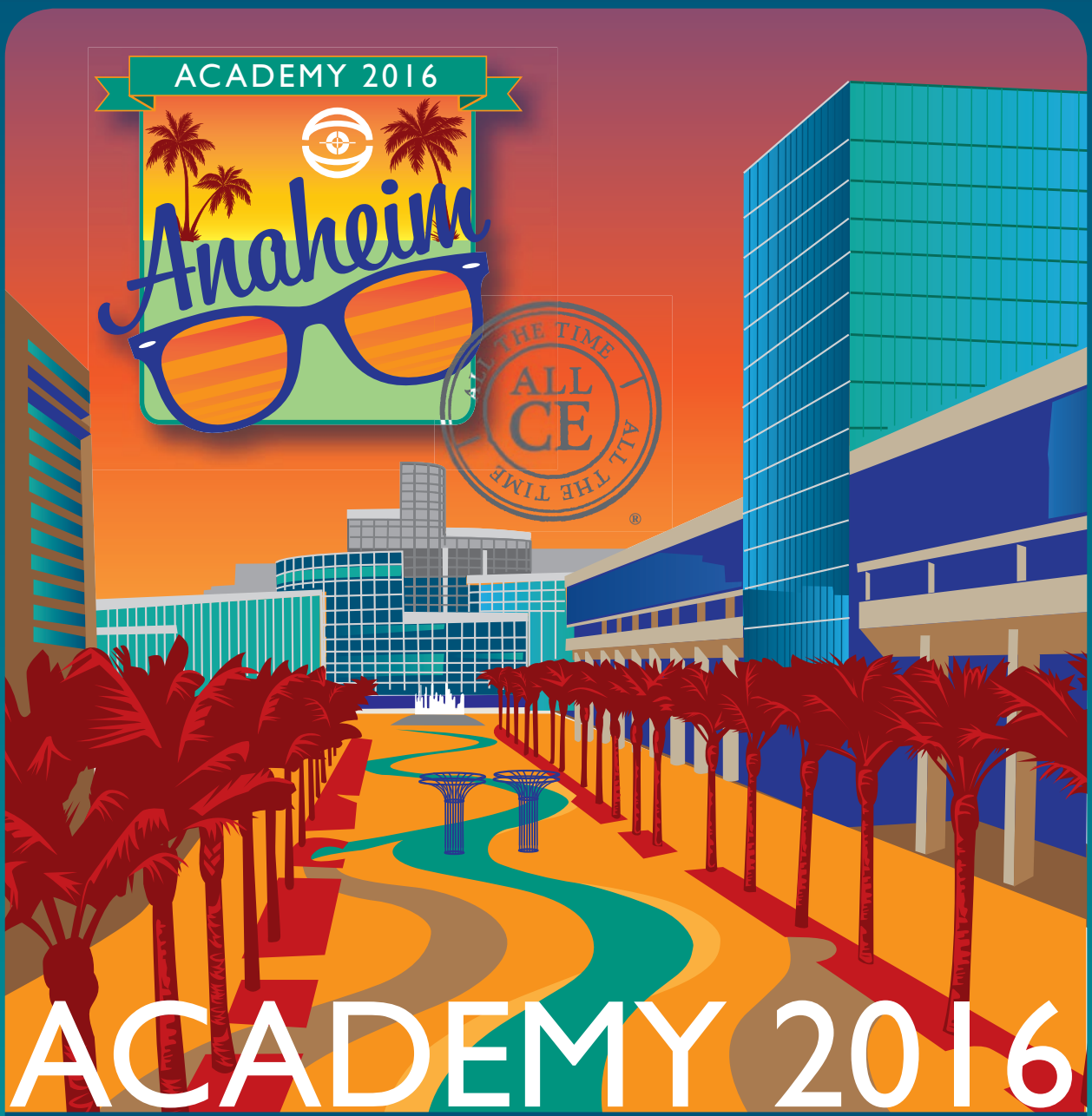
For more information or to register, contact Lois DiDomenico at 866-658-1772 or at ReviewMeetings@Jobson.com.

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

Save the Date!



Anaheim

NOVEMBER 9 - 12, 2016

Anaheim Convention Center

The Academy meeting is traveling to Southern California to offer attendees plenty of sun, fun and exceptional cutting-edge CE! Join us in Anaheim for four days of superb speakers, clinically-relevant sessions, an exceptional exhibit hall, fascinating papers and posters and unforgettable social events.

Registration and housing open May 23, 2016!
Visit http://www.aaopt.org/regsite for more information.

Ophthalmic Lenses

Clear Lens Protection

A new lens protection option from Essilor gives patients greater ability to protect their eyes from the potential hazards of blue light.

The embedded Smart Blue Filter is available in all Transitions adaptive lenses and in select Varilux Digital (PAL) and Eyezen+ (enhanced SV) products—at no additional cost to the patient, the company says.

The feature blocks 20% of blue light while allowing light in the blue-turquoise spectrum to pass through.

Visit www.essilorusa.com/bluelight.

On-The-Go Saline

Alcon now offers a new saline solution for your contact lens patients. Clear Care Rinse & Go allows for quick, gentle contact lens rinsing at home or away.

After cleaning and disinfection, it removes loosened debris and trace amounts of cleaning and disinfecting solution. Alcon says it can be used for up to 30 days of contact lens storage.

It does not replace daily cleaning and disinfection of contact lenses, but is intended as a companion product.

Clear Care Rinse & Go is available in two sizes: 12 fl. oz. and 4 fl. oz.

Visit www.alcon.com.

Practice Management

New MGD Education Website

A new dry eye education resource is now online to help you educate your patients.

TearScience says its new website DryEyeandMGD.com features:

- An intuitive user interface.
- A wealth of educational resources.
- Search function to help patients locate ODs who offer TearScience's LipiFlow MGD treatment.
- An MGD quiz and expert forum for patients to ask questions about their symptoms and treatment options.

Visit www.TearScience.com.

New Speaker Series at Vision Expo

OcuSoft has launched a new speakers series program at this year's International Vision Expo East. "Eyelids & Eyelashes: A Focus on Growth For Your Practice" allows optometrists to share outlooks and views with experts in the field, according to OcuSoft. The goal of the series is to discuss the developments in optometry, including in cosmetics and skin care, and how to effectively incorporate them into everyday practice, according to OcuSoft.

Visit www.ocusoft.com for future meeting dates.

Diagnostic Technology

Improved Handheld Tonometer Model

Optometrists can now take advantage of a new, user-friendly handheld tonometer from Icare USA.

The ic100 model uses the same rebound technology as its successor, TA01i, with added ergonomic features and an improved user interface that makes it easier to obtain consistent, repeatable IOP measurements, according to the company.

The ic100 model includes:

- The ability to be used without callibration, eye drops, air or special training.
- Intelligent positioning. Red and green lights help operators guide the tonometer into the correct position for testing. Optometrists can simply load, align and measure.
- An automated measuring sequence, which takes a series of six measurements with one touch.

Visit info@icare-usa.com.

Post-Op Ocular Pain Drug

Optometrists may now have another choice of pain medication to offer post-op cataract surgery patients. BromSite by Sun Pharma is the first NSAID approved to prevent pain, not just treat it, according to the company.

Two well-controlled studies indicated that more BromSite-treated patients were pain-free at day one post-surgery compared with controls, and more were inflammation-free at day 15 post-surgery, according to Sun Pharma.

Expect Bromsite to be made available in the second half of 2016.

Visit www.sunpharma.com. ■

Meetings + Conferences

May 2016

■ **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, Alaska. Hosted by: Alaska Optometric Association. CE hours: 22. To register, email Lisa Johnson at alaskaoptometrics@gmail.com, call or go to akoa.org.

■ **2-6.** *2016 Annual Congress.* Midway, Utah. Hosted by: Utah Optometric Association. CE hours: 18. To register, email Alyssa White at alyssa@utaheyedoc.org, call (801) 364-9103 or go to www.utaheyedoc.org.

■ **3-5.** *Ocular Disease Update.* Branson, MO. Hosted by: Northeastern State University, Oklahoma College of Optometry. Key faculty: Leonid Skorin, Rich Castillo. CE hours: 13. To register, email Callie McAtee at mcateec@nsuok.edu.

■ **3-5.** *Ocular Symposium: Pearls in Ocular Diagnosis.* Holiday Inn Golden Gateway, San Francisco. Hosted by: Ocular Symposium. Key faculty: H. Richard McDonald, David F. Chang, Andrew G. Iwach, Rona Z. Silkiss, Marc Levin, William F. Good. CE hours: 24. To register, email Lorraine Geary at ocularsymp@aol.com or call (415) 278-9940.

■ **4.** *South Carolina Chapter of the American Academy of Optometry Inaugural Meeting.* Dorn Veterans Hospital, Columbia, SC. Hosted by: South Carolina Chapter of the American Academy of Optometry. Key faculty: Ron Melton, Randall Thomas, Julie Anne Roper, Christian Jordan, Anthony Van Alstine. CE hours: 5. To register, email Anthony Van Alstine at SouthCarolina.AAO@gmail.com.

■ **4-5.** *Everything Therapeutic: Houston.* Health and Biomedical Sciences Building at the University of Houston College of Optometry, Houston. Hosted by: University of Houston College of Optometry. Key faculty: Bruce Onofrey. CE hours: 16. To register, email optce@central.uh.edu.

■ **6-9.** *Indian Health Service: Biennial Healthcare Meeting.* Marshall B. Ketchum University, Fullerton, CA. Hosted by: Marshall B. Ketchum University. CE hours: 25. To register, email Antoinette Smith at ce@ketchum.edu, call (714) 449-7495 or go to www.ketchum.edu/index.php/ce.

■ **10-12.** *Spring Congress.* Embassy Suites Kingston Plantation, Myrtle Beach, SC. Hosted by: North Carolina State Optometric Society. CE hours: 18. To register, email Adrianne Drollette at adrianne@nceyes.org, call (919) 977-6964 or go to www.nceyes.org.

■ **8-12.** *VT/Learning Related Visual Problems.* Listowel, Ontario, Canada. Hosted by: OEP Foundation. Key faculty: Robert Hohendorf. CE hours: 35. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org/oepf_calendar.

■ **8-12.** *The Art + Science of Optometric Care.* Burlington, Ontario, Canada. Hosted by: OEP Foundation. Key faculty: Steen Aalberg. CE hours: 35. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org/oepf_calendar.

■ **9-12.** *VOA Annual Convention.* Omni Homestead Resort, Hot Springs, VA. Hosted by: Virginia Optometric Association. CE hours: 20 total, 16 per OD. To register, email Bo Keeney at office@thevoa.org, call (804) 643-0309 or go to www.thevoa.org.

■ **9-12.** *Georgia Optometric Association Annual Meeting.* Omni Amelia Island Plantation Resort, Amelia Island, FL. Hosted by: Georgia Optometric Association. CE hours: 15. To register, email Vanessa Grosso at VanessaGOA@aol.com, call (770) 961-9866 x-1 or go to www.GOAeyes.com.

■ **9-12.** *New Technologies and Treatments in Vision Care.* Hamilton Princess & Beach Club, Bermuda City, Hamilton. Hosted by: *Review of Optometry.* Key faculty: Paul Karpecki (meeting chair). CE hours: 14. To register, email Lois DiDomenico at reviewmeetings@Jobson.com, call (866) 658-1772 or go to www.reviewofoptometry.com/Bermuda2016.

■ **10.** *Dual Sensory Loss.* Envision, Wichita, KS. Hosted by: Envision University. Key faculty: Walter Wittich. CE hours: 4. To register, email Michael Epp at michael.epp@envisionus.com, call (326) 440-1515 or go to www.envisionuniversity.org.

■ **10-11.** *Northwest Residents Conference.* Pacific University Campus, Forest Grove, OR. Hosted by: Pacific University College of Optometry. Key faculty: 21 residents from affiliated programs in MN, NV, OR, PA and WA. CE hours: 10.5. Registration details: www.pacificu.edu/future-graduate-professional/colleges/college-optometry/continuing-education.

■ **11.** *Clinical Update Conference.* Sheraton Omaha, Omaha, NE. Hosted by: Nebraska Optometric Association. Key faculty: Kyle Cheatham, Christopher Wolfe. CE hours: 8. To register, email David S. McBride at dmcbride@assocoffice.net, call (402) 474-7716 or go to www.noaonline.org.

To list your meeting, please send the details to:
Adrienne Taron, Associate Editor: ataron@jobson.com

Advertisers Index

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.

Merchandise Offered

Software

Practice For Sale

Merchandise Offered

Merchandise Offered

Continuing Education

Graduates of Medical Optometry Residencies

The American Board of Certification in Medical Optometry (ABCMO) is recognized by credentialing and privileging committees at Joint Commission accredited hospitals and clinics as board certification in the specialty of medical optometry. ABCMO certified optometrists are appointed and issued privileges at Joint Commission accredited organizations as specialists in medical optometry rather than general practice optometry.

The Joint Commission, the gold standard of accreditation, is utilized at over 21,000 federal (VA, Indian Health Svc., Dept. of Defense) and state-chartered hospitals and clinics (Mayo Clinics, Cleveland Clinic, Henry Ford hospitals, et al).*

To be eligible for ABCMO board certification an applicant must:

- Complete an accredited clinical residency in medical optometry that meets ABCMO standards for types and number of presenting patients.
- Pass Advanced Competence in Medical Optometry national examination administered by the National Board of Examiners in Optometry.
- Practice medical optometry in a suitable clinical setting for at least two years. #

www.abcmo.org

Visit www.abcmo.org to understand why medical facilities and teaching clinics credential optometrists certified by ABCMO as board certified specialists and how ABCMO certification enhances the careers of those completing medical optometry residencies.

For complete application procedures see Bylaws at www.abcmo.org or contact myers.kenj@gmail.com.

* www.jointcommission.org.
# Waived for two years following residency.

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

Contact Lenses

Career Opportunities

IT STILL EXISTS!

Delaware private practice with like new 3,500 square foot **free standing building**, custom designed and built to be an eye care facility. Immediate opening for an Associate or Partnership leading to purchase in a unique state with **no corporate practice** (OD's can't practice in Pearl Vision or LensCrafters per state law). Large concentration of Glaucoma and Ocular Disease. **Grossing $700K plus** with high net and phenomenal growth. **Will sell or lease building**. Extensive website with e-commerce included. Only 1/2 hour to Philadelphia or Baltimore, and 1 hour to the beach.

Call 302-994-2299 or e-mail **confidentially**
privpracticeopportunity@gmail.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.

Products and Services

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

Practice For Sale

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

Diagnostic **Quiz**

Patient Gets a Hole in One

By Andrew S. Gurwood, OD

History

A 25-year-old black female presented via the emergency room with acute eye pain. She explained that she had been putting on her makeup in the morning when she felt something fly into her right eye. Unable to get it out, she reported for care. She was in considerable distress, but did not report any altered vision. She reported no previous ocular history or allergies.

Diagnostic Data

Her best uncorrected visual acuities were 20/20 OD and 20/20 OS at distance and near. External examination was normal with no evidence of afferent pupillary defect. The anterior segments of both eyes were normal. The pertinent finding, in the right eye, is demonstrated in the photograph (*Figure 1*). Applanation intraocular pressures measured 19mm Hg in both eyes. Her dilated fundus examination was normal.

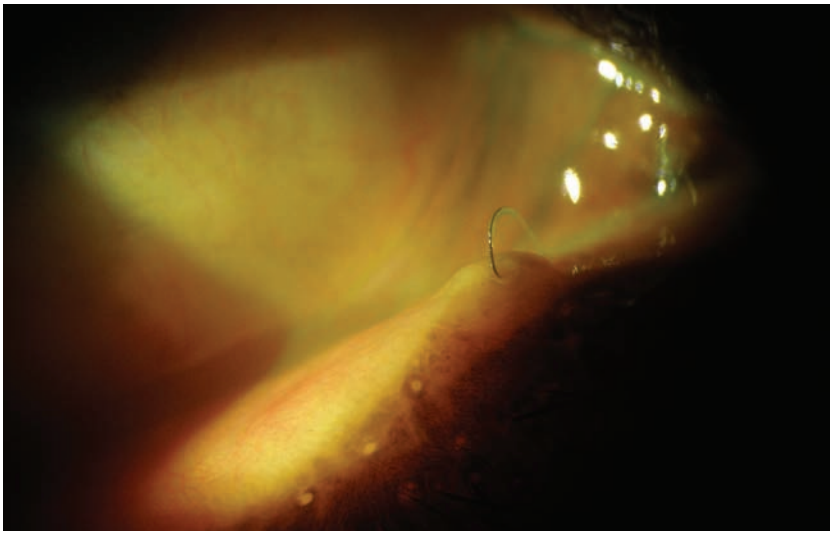


Fig. 1. Can you tell what's causing this patient's ocular pain? How would you manage this patient?

Your Diagnosis

Does this case require any additional tests? What does this patient's history and clinical findings tell you about her likely diagnosis? To find out, please visit www.reviewofoptometry.com. ■

Retina Quiz Answers *(from page 116):* 1) d; 2) d; 3) b; 4) a; 5) c.

Next Month in the Mag

In June, *Review of Optometry* will present its 7th annual retina report. Topics include:

- *How to Understand and Identify Proliferative vs. Nonproliferative Diabetic Retinopathy*
- *Nutritional Strategies to Prevent Age-Related Macular Degeneration: Consensus and Controversy*
- *Dilation Dilemmas: Why Aren't ODs Doing it Routinely?*
- *Optometric Study Center: Can You Identify These Vitreous Anomalies?* (earn 2 CE credits)

Also in this issue:

- *Essential Procedures: How to Perform Punctal Plug Insertion in Dry Eye Patients*
- *Viral Conjunctivitis Treatment Do's and Don'ts*
- *Case Report: Hypertensive Crisis*

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]
- Offers easy, predictable fitting where 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.

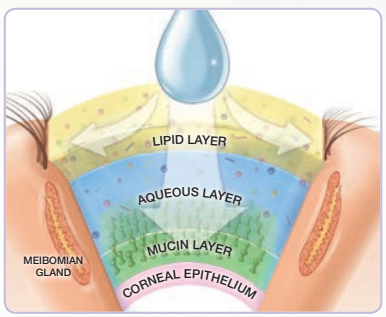
REFERENCES: 1. Data on file. Bausch & Lomb Incorporated. Rochester, NY; 2013. **2.** Data on file. Bausch & Lomb Incorporated. Rochester, NY; 2015. **3.** Thirty-nine ECPs (from 10 countries) refitted 422 existing soft contact lens wearing presbyopes into PureVision®2 Presbyopia lenses. Patients returned 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.

For the 75% of dry eye patients worldwide with evaporative dry eye (MGD) symptoms[1]...

SYSTANE® BALANCE Lubricant Eye Drops:

Protecting the Ocular Surface by Increasing Lipid Layer Thickness (LLT)



SYSTANE® BALANCE Lubricant Eye Drops forms a protective matrix that is designed to replenish the lipid layer for long-lasting relief from the symptoms associated with evaporative dry eye (MGD). This unique formulation is designed to work on all 3 layers of the tear film, specifically increasing LLT. This helps create a protective environment for the ocular surface.[2]

SYSTANE® Brand products are formulated for the temporary relief of burning and irritation due to dryness of the eye.

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

Your recommendation counts.

Make sure your patients get the lasting symptom relief they need by offering them SYSTANE® BALANCE Lubricant Eye Drops.[2]

Alcon®
a Novartis company

 05/14 SYS14005JAD-B

Systane® Family of Products

Relief that lasts