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REVIEW® OF OPTOMETRY

June 15, 2016

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REVIEW OF OPTOMETRY 125 YEARS SERVING THE OPTOMETRIC PROFESSION ESTABLISHED 1891

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VOL. 153 NO. 6 ■ JUNE 15, 2016

IN THE NEWS

IOP fluctuations are more significant in patients with **pseudoexfoliation syndrome** (a known risk factor for the development of glaucoma) than in those with healthy, normal eyes, reports a study in the May 2016 *Journal of Glaucoma*. Using a **Triggerfish** (Sensimed) contact lens sensor, researchers at the **University of Toyama** in Japan monitored the IOP levels of 11 subjects with pseudoexfoliation syndrome and 11 subjects with healthy eyes. After 24 hours of continuous monitoring, the researchers found that participants with PE had significantly larger IOP fluctuations, as well as greater post-CL wear central corneal thickness, than those with healthy eyes. This larger fluctuation might be one of the reasons underlying the aggravation of **visual field loss** in patients with PE, the researchers conclude.

Google applied for a patent for what appears to be an **electronic accommodating intraocular lens device**. According to the application, filed April 28, 2016 with the US Patent Office, the device includes an electronic lens, a flexible polymeric material that fills the lens capsule, an accommodation sensor and a controller. After the device is implanted, the eye and lens capsule apply "accommodation forces" to the polymeric material, which are detected by the accommodation sensor. This prompts the controller to change the optical power of the electronic lens. The device and polymeric material "can restore a degree of accommodation to the eye" on par with natural accommodation, the patent reads. The device would also include an antenna to wirelessly send and receive updated calibration information.

Visual Loss, Blindness to Double by 2050

But the numbers will be lower if Americans get more eye exams and refractions. **By Bill Kekevian, Senior Editor**

The number of Americans with visual impairment or blindness will climb to more than eight million by the year 2050—approximately twice the current number—and an additional 16.4 million Americans are expected to have vision impairment due to uncorrected refractive error, based on a National Institutes of Health analysis of six large studies.

Several factors explain the increases, including the aging of the baby boom generation and a rise in systemic diseases (such as diabetes) that can impact patients' vision. This study also shows that refractive error is the leading cause of visual impairment in the United States, as well as worldwide.

But these predictions aren't inevitable. Optometrists and ophthalmologists can help lessen these estimated numbers by encouraging patients to get vision screenings and eye exams, according to the investigators. Vision screening and proper refractive correction could produce clinical improvements in up to 72% of Americans with vision impairment and 22% of those with blindness, they say.

"Early detection and intervention—possibly as simple as prescribing corrective lenses—could go a long way toward preventing a significant proportion of avoidable vision loss," said Paul A. Sieving,

MD, PhD, director of the National Eye Institute, which funded the study.

Among all demographic groups, non-Hispanic white women will represent the largest proportion of people affected by visual impairment and blindness, with their numbers rising to 2.15 million visually impaired and 610,000 blind. However, the highest prevalence of visual impairment among non-whites will shift from African Americans (15.2% in 2015 to 16.3% in 2050) to Hispanics (9.9% in 2015 to 20.3% in 2050).

The study even localized its predictions by state, speculating that blindness will most affect Mississippi (up to 1.25% by 2050) and Louisiana (1.2% by 2050). For visual impairment, Florida will have the highest per capita prevalence (3.98% by 2050) and Hawaii (3.93% by 2050) will closely follow.

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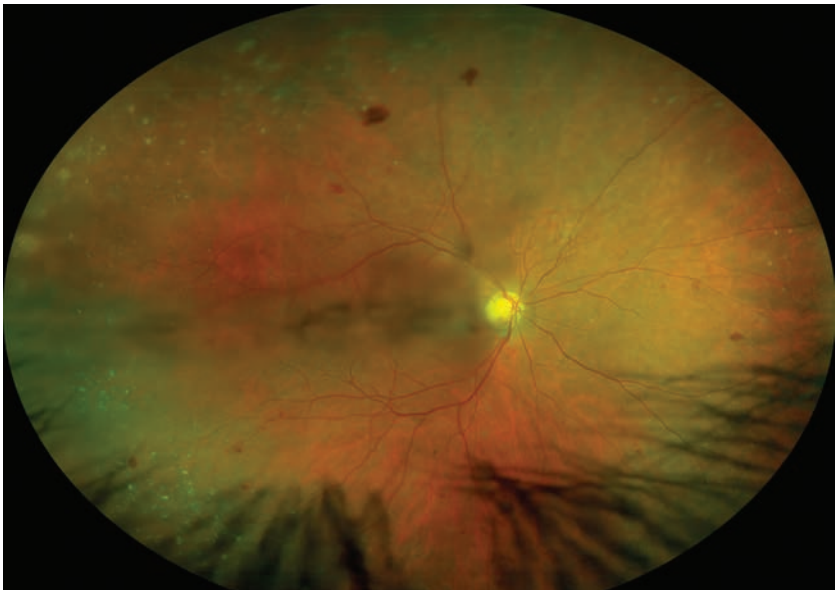
Scientists Reverse Diabetic Retinopathy in Lab Study

Researchers from Indiana are investigating a potential new intraocular treatment, based on manipulating the renin angiotensin system (RAS), that may prevent or even reverse diabetic retinopathy. In studies using mice, it seems to be working, according to *The American Journal of Pathology*.

The research is based on the hypothesis that an imbalance between two axes of the RAS leads to development of diseases like diabetic retinopathy. The team injected a therapeutic agent known as AAV-ACE2 directly into the vitreous cavity of the eye of diabetic mice to increase angiotensin converting enzyme-2 (ACE-2) expression.

The researchers' conclusion was reached after two experiments. The first saw the agent administered two weeks prior to a streptozotocin injection, which induced diabetes in the mice. The second saw it administered six months after a streptozotocin injection, after diabetic retinopathy developed.



Long believed to be irreversible, retinal damage from diabetes could one day be ameliorated by therapy to reduce proinflammatory cells.

The investigators found both strategies effectively decreased the numbers of proinflammatory cells present in the diabetic retina.

In addition, the intravitreal approach is designed to deliver the agent without interference from the blood-retinal barrier. Hypothetically, this therapy could be modified to address vascular diseases in other systems, such as the heart or kidneys.

Exercise Tires the Eyes as Well as the Body

But caffeine perks eyes up again, research shows.

Strenuous exercise can dampen the central nervous system (CNS)—an effect known as central fatigue. Research published in *Nature* now shows that this fatigue also weakens the oculomotor muscles and reduces saccadic speed. But, as one might expect, a shot of caffeine appears to be the remedy.

In this study, researchers at the University of Auckland, New Zealand, assigned 12 cyclists to three hours of stationary cycling. Immediately after the workout, the researchers tested saccadic eye movements and found that the subjects' saccade velocity decreased by 8%.

"It's remarkable that tiring the legs also slows the eyes," says co-lead investigator Nicolas Gant, PhD, MSc. "This might well be the reason the tired cyclist never saw that bus coming!"

This effect was reversed in individuals given caffeine, who experienced an increase in their saccadic velocities by up to 11% after exercise.

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Exercise Tires the Eyes as Well as the Body

(Continued from p. 6)

"The amount of caffeine we gave during exercise was the equivalent of two cups of coffee. We saw no effect [in control subjects] with a decaffeinated placebo drink," Dr. Gant says.

The researchers concluded that strenuous exercise of the locomotor system impairs the human oculomotor system, but caffeine exerts a protective effect on oculomotor control.

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But exercise had no effect on non-oculomotor perceptual tasks, such as visual attention and visual processing.

"Interestingly, the areas of the brain that process visual information are robust to fatigue," Dr. Gant says. "It's the pathways that control eye movements that seem to be our weakest link."

However, Dr. Gant adds, "there's hope for coffee drinkers because this visual impairment can be prevented by consuming caffeine."

Connell CJ, Thompson B, Kuhn G, et al. Fatigue related impairments in oculomotor control are prevented by caffeine. Sci Rep. 2016 May 25;6:26614.

Infants with Zika Virus Show Retinal Findings

Presence of the Zika virus at birth may lead to certain ophthalmologic findings in infants, reports a study in the May 2016 issue of *JAMA Ophthalmology*.

Previous research has found the virus can transmit from an infected mother to the fetus in utero and lead to microcephaly, with resultant optic nerve and macular abnormalities.

For this study, researchers conducted a cross-sectional analysis of 40 infants born with microcephaly and presumed Zika virus infection in Brazil between May and December 2015. The researchers grouped the infants into those with fundus abnormalities and those without.

The researchers found that 37 eyes in 22 infants had fundus alterations. They observed optic

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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
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Marc Ferrara

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Infants with Zika Virus

(Continued from p. 8)

nerve abnormalities in 25 eyes of 15 infants, and found macular abnormalities in 24 eyes of 17 infants.

These fundus findings were associated with infants with smaller cephalic (head) diameter at birth, and in infants whose mothers reported symptoms during the first trimester, the researchers write.

The latter finding mirrors the history of other congenital infections, the researchers note.

"No mothers reported conjunctivitis or ocular symptoms during pregnancy, which differs from the findings encountered during the Micronesia outbreak."

However, "no mothers reported conjunctivitis or ocular symptoms during pregnancy, which differs from the findings encountered during the Micronesia outbreak," they state in the *JAMA Ophthalmology* article. "Furthermore, the last country before Brazil to have a [Zika virus] outbreak was French Polynesia, and it did not report ocular abnormalities in infants." ■

Ventura CV, Maia M, Travassos SB, et al. Risk factors associated with the ophthalmoscopic findings identified in infants with presumed Zika virus congential infection. JAMA Ophthalmol. 2016 May 26. [Epub ahead of print]

For allergic conjunctivitis[1]

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INDICATION AND USAGE

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

IMPORTANT SAFETY INFORMATION

- BEPREVE® is contraindicated in patients with a history of hypersensitivity reactions to bepotastine or any of the other ingredients.
- BEPREVE® is for topical ophthalmic use only. To minimize risk of contamination, do not touch the dropper tip to the eyelids or to any surface. Keep the bottle closed when not in use.
- BEPREVE® should not be used to treat contact lens-related irritation. Remove contact lens prior to instillation of BEPREVE®. Lenses may be reinserted 10 minutes after BEPREVE® administration.
- The most common adverse reaction occurring in approximately 25% of patients was a mild taste following instillation. Other adverse reactions occurring in 2%-5% of patients were eye irritation, headache, and nasopharyngitis.

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

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

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

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.

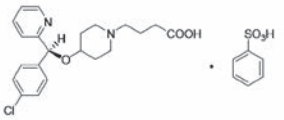
8.3 Nursing Mothers
Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 mcg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection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

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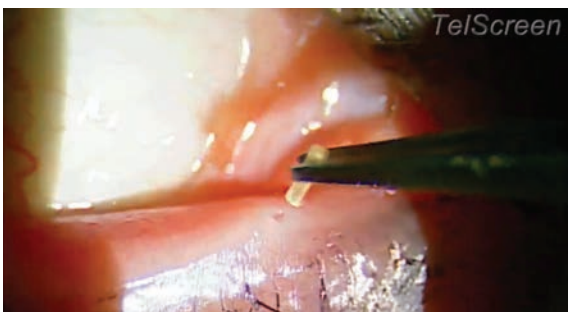

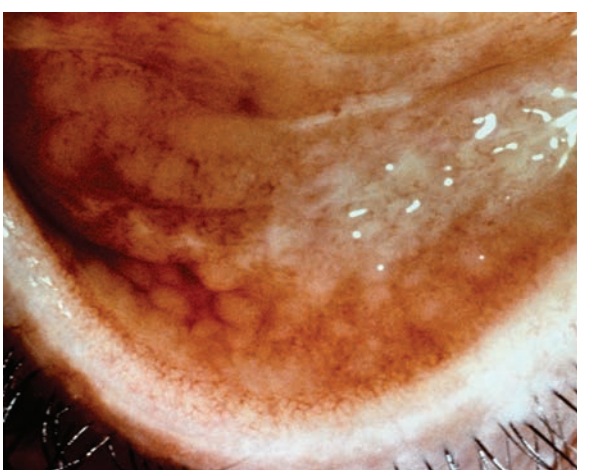

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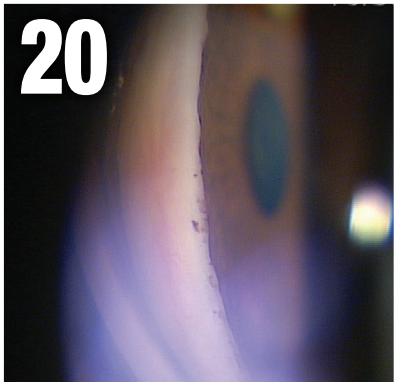

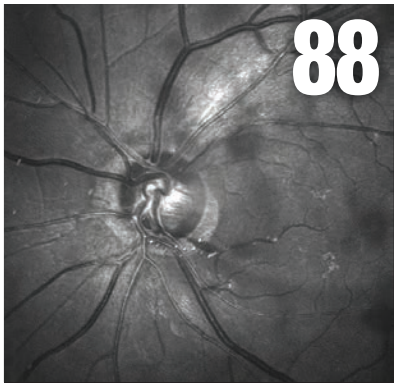

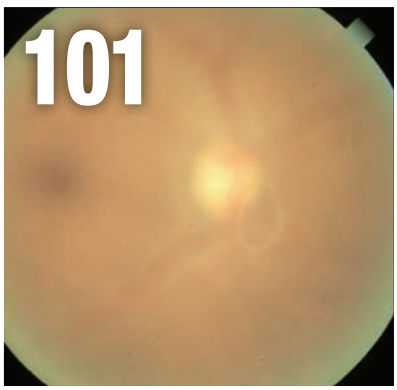

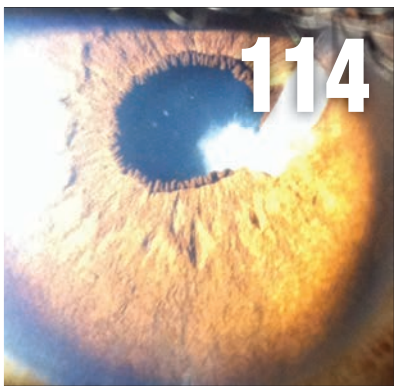

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REVIEW OF OPTOMETRY

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Outlook

By Jack Persico, Editor-in-Chief

Defeating Diabetes

Over 100 million Americans are either at risk or actively in need of care. What can you do? In a word, more.

There's a reason why the cliché "an ounce of prevention is worth a pound of cure" rings true. Health is easier to maintain than to regain. But that old adage understates just how difficult the work of prevention really is. People at risk need to be educated and motivated; most are neither.

To see one formidable challenge preventive medicine is up against, look no further than the sobering statistics in this month's cover story on diabetic retinopathy. Drs. Steven Ferrucci and Brenda Yeh do an excellent job of laying out in black and white the debilitating impact diabetes has on millions of people today and the threat that looms over millions more. "An estimated 25.6 million Americans age 20 or older have diabetes, with a third still undiagnosed," they write. "An additional 79 million people have prediabetes, and are at risk for developing diabetes."

That's over 100 million people—a third of the population—in harm's way. For those who already have diabetes, the prevalence of diabetic retinopathy among adults is 28.5%, or 4.2 million Americans, Drs. Ferrucci and Yeh write. "If the overall rate of diabetes continues to rise at the current trajectory, the projected prevalence of individuals with any diabetic retinopathy by 2020 will increase to six million, with 1.34 million having sight-threatening disease."

So, those are the stakes—in ocular health alone. And of course, the threat extends far beyond the eye. Prevention is urgently needed.

Despite decades of public outreach on the importance of lifestyle change, diabetes remains deeply entrenched in America. What's undergirding it? Girth, frankly. Americans remain overweight at unprecedented levels.

New research in the June 7 issue of *JAMA* provides an update on obesity in the US. "The news is neither good nor surprising," the authors write. "Using 2013-2014 data from 5,455 adults," they say, "35% of men were obese (BMI ≥30) and 5.5% were morbidly obese (BMI≥40); among adult women, 40.4% were obese and 9.9% were morbidly obese. These prevalences are unchanged since 2005 among men and represent a slight increase in obesity among women." In children, obesity rates decreased among those age two to five since 2003-2004, stabilized in 6- to 11-year-olds since 2007-2008, "but steadily increased among adolescents since 1988," the study finds. Childhood obesity has a prevalence of 17%; for extreme obesity, it's 5.8%.

Problems this pervasive won't get fixed any time soon. But you can help by deciding that all aspects of diabetes are appropriate for an optometrist to address. Don't limit your role to diabetic retinopathy. Get involved earlier in its course, discussing risk factors and even, delicately, how obesity sets up patients to fail.

Few professions perform as much routine care as optometry. A concerted effort to raise diabetes awareness and change behavior could be the profession's biggest opportunity and greatest gift. ■


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Supplemental Information

Of course you should Rx 'neutraceuticals.' Just pray to St. John that his Wort works.

By Montgomery Vickers, OD

Do you recommend supplements to your patients? I do and I always have. I also take supplements. Do they work? Absolutely! Sure. Maybe. Sort of. Do they? I don't know.

Seeing a Man About a Horse

My long-time doctor back in West Virginia did not really believe in vitamins or other supplements. At my last physical with him, I presented him with my typical big ol' bag-o-pills. He looked like I had just handed him a year's worth of stool samples.

Obviously disgusted, he asked, "Why are you taking all these? You are totally wasting your money!"

Me: "Is there anything in there that could hurt me?"

Dr.: "No, but you are wasting money!"

Me: "YOU OWN A HORSE!"

This guy spends more on hay than I could ever spend on my vitamins and my vitamins don't need me to shovel out a barn every morning!

We parted as friends and I truly appreciate the wonderful care he gave my family and me for almost three decades. We love you, Stephen! Oh, and ditch the horse. You're wasting a lot of money.

Something Smells Fishy

The tricky part in recommending supplements to our patients is determining how much of which ones. If you don't watch out, you will soon be recommending 10 times your patient's body weight in capsules full of sticks, twigs and strange and unusual powdery stuff.

And how much of each substance? I have an optometric friend who is very highly regarded across the country for his research on AMD and supplements. If I called him on Monday and asked how much lutein a patient should take, he might say "10mg, for certain!" If I called him on Friday, he might say "Definitely 100mg!" If this guy doesn't know, how can I?

The new trend is to actually sell supplements from your office. Having the fish burps with six different fish oils before I found out what worked for me has led me to believe that some of the high quality in-office products are indeed better choices for the patient. But you can't just buy a bunch of bottles of pills and expect smiling patients to buy them all up. They will end up expiring on your shelf, or in your own stomach.

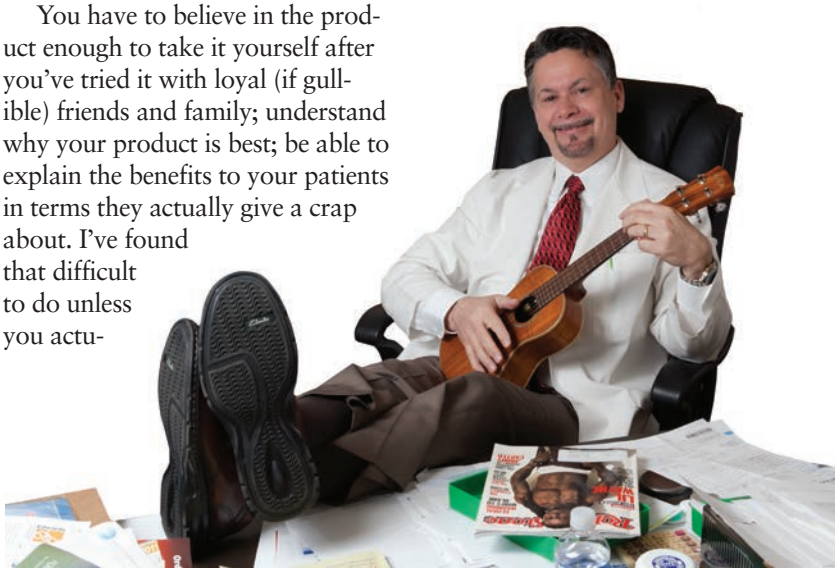
You have to believe in the product enough to take it yourself after you've tried it with loyal (if gullible) friends and family; understand why your product is best; be able to explain the benefits to your patients in terms they actually give a crap about. I've found that difficult to do unless you actually believe that your 67-year-old ocular rosacea patient will take four strokes off his golf game for every 50mg of turmeric root extract he ingests. If that were true, I'd lower my own score from 170 to 160 based upon my turmeric intake. (I just found out that in golf the LOW score wins. Better late than never.)

Crazy Pills

I've invented two new supplements:

- Emesisdine: 400IU per day makes the patient vomit unless they throw their contact lenses away at proper intervals. Note: Some will just carry a bucket and still overwear them to save money.
- Cannistaff*: Bake it into brownies and give it to your office manager every day. Trust me. Good for glaucoma suspects, too.

**Check with state optometry board before prescribing. Check with state parole board after prescribing.* ■



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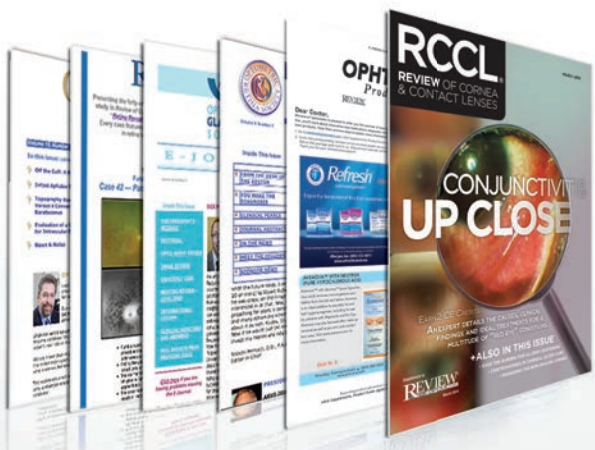

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Angle Closure: A Bad Connection

When a patient's iris and lens connect, trouble emerges.

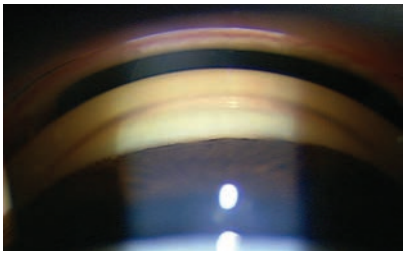
By Ian McWherter, OD, and Richard Mangan, OD

Acute primary angle closure is an ocular emergency where hours can make the difference in a patient's final visual outcome. If left untreated, primary angle closure glaucoma—a major cause of blindness worldwide—can occur and prompt intervention will be needed to preserve vision.[1-3] Primary angle closure most commonly occurs when aqueous flow from the posterior to anterior chamber is blocked at the pupil by contact between the iris and the lens, leading to an increased intraocular pressure (IOP) in the posterior chamber and a forward bowing of the peripheral iris (known as iris bombé). As the peripheral iris bows forward, it makes contact with the trabecular meshwork and blocks the outflow of aqueous from the eye, leading to an elevated IOP. As the iris continues to touch the trabecular meshwork, it can form peripheral anterior synechiae. This can occur acutely, causing an angle closure attack, or proper aqueous flow may be restored spontaneously, resulting in a subacute/intermittent or chronic disease course.

Primary angle closure can occur by non-pupil block mechanisms as well, such as angle crowding from a thickened peripheral iris stroma, or plateau iris syndrome.[1,2]

The Patient Experience

Primary angle closure is more common in people of Asian or Inuit decent and usually occurs in female patients with hyperopia, shorter axial length and a thickened crystalline lens.[1] Prolonged exposure to dim illumination or topical medications, such as tropicamide 1.0% or vasoconstrictors such as tetrahydrozoline 0.05% (found in Visine eye drops) may cause at-risk patients to develop an acute angle closure attack.



This semi-narrow angle patient is a candidate for the laser peripheral iridotomy.

Patients with an acute angle closure attack will experience blurry vision with halos around lights, nausea, vomiting, headaches and severe eye pain. Slit lamp exam findings include conjunctival hyperemia, microcystic and stromal corneal edema, a shallow anterior chamber with cells and flare, iris bombé and a classic mid-dilated pupil.

The mid-dilated pupil occurs in acute angle closure for two reasons. First, the greatest amount of iris/lens contact occurs when the pupil is mid-dilated—this is why angle closure attacks commonly occur hours after patients are dilated as the drops start to wear off and the pupil begins to return to normal size. As the IOP increases to above 40mm Hg, the iris sphincter muscle becomes ischemic and can no longer constrict the pupil. Iris pigment cells may be liberated into the anterior chamber and coat the endothelium and anterior lens capsule. Residual iris atrophy is common after acute angle closure attacks. Glaucomflecken, whitish opacities on the anterior lens capsule, may also be present. Glaucomflecken is a result of lens epithelial cell necrosis from the elevated IOP. If the IOP remains elevated long enough, glaucomatous optic neuropathy may occur, resulting in primary angle closure glaucoma.

Diagnosis

Compression gonioscopy is key to properly diagnosing an acute angle closure. On slit lamp examination, the anterior chamber will be shallow and only anterior trabecular meshwork or Schwalbe's line will be visible on gonioscopy. The corneal wedge technique, using an optic section to find the end of Descemet's membrane, can be helpful in determining your location within the angle. On compression of the cornea with a flange-less gonioscopy lens, the iris should indent, exposing at least the posterior trabecular meshwork, implying appositional angle closure. This may help to break the angle closure attack. However, if no deeper structures are seen, then peripheral anterior synechiae are present and the angle is closed. In this scenario, a laser peripheral iridotomy is contraindicated and filtration surgery or goniosynechialysis should be considered. Other possible causes of secondary angle closure should also be explored, such as neovascular or inflammatory glaucoma. Anterior segment optical coherence tomography (AS-OCT)

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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.

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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.

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

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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

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can also be useful in identifying angle structures and showing angle closure, especially if the cornea is cloudy from edema. The cornea can be cleared using glycerin, a topical hyperosmotic, to perform gonioscopy or a laser peripheiral ididotomy.

Medications

Therapeutic agents used for acute angle attacks include topical beta blockers, alpha-2 agonists, carbonic anhydrase inhibitors and prostaglandin analogs—even though their onset of action may be delayed. Topical drops are given every five minutes for 30 minutes and the pressure is rechecked in one hour. Additionally, oral carbonic anhydride inhibitors, such as 1,000mg oral acetazolamide, are given as long as the patient does not have kidney disease or a sulfa allergy. Oral acetazolamide should be given as the immediate release tabs and not the extended release version. If the pressure is still not down at the one-hour check, apply more drops and check the pressure in another hour.

Paracentesis

At this point, if the pressure is not responding and is at a sight-threatening level, it's time to consider an emergent paracentesis. This can be performed easily at the slit lamp with a lid speculum, sterile 30g needle and Betadine. First, the eye is numbed with a topical anesthetic eye drop and the lid speculum is placed. Topical Betadine drops are applied, and the patient is positioned in the slit lamp. A 30g-needle attached to a 1ml tuberculin syringe with the plunger removed is inserted tangentially into the cornea, parallel to the iris, as close to the limbus as possible. Extreme care must be taken to not hit the iris or lens during this procedure, which can be difficult due to the shallow anterior chamber. If the needle cannot be safely inserted, a paracentesis should not be performed. Once a few drops of aqueous are removed from the anterior chamber, remove the 30g-needle and apply pressure to the needle track using a sterile cotton tip applicator. Apply Betadine again after the procedure and check for a Seidel sign. If present, apply additional pressure to the needle track until the wound is sealed. A bandage contact lens may also help seal the cornea.

Iridotomy

Topical antibiotics should be started for at least three days following paracentesis. If paracentesis cannot be performed and the IOP is still at sight-threatening levels, send the patient to the emergency room for intravenous 20% mannitol 1g/kg.

Once the IOP is less than 40mm Hg, topical pilocarpine 2% can be given and a laser peripheral iridotomy should be performed as soon as possible. Giving pilocarpine when the IOP is above 40mm Hg is usually not effective as the iris sphincter is ischemic and topical pilocarpine may also exacerbate the angle closure attack by rotating the iris-lens diaphragm anteriorly.

Laser peripheral iridotomy is performed with a Nd:YAG laser (neodymium-doped yttrium aluminium garnet). The eye is numbed with topical proparacaine and an iridotomy lens is placed on the eye. The laser is set to a 0µm offset with a starting power of 3mJ to 5mJ and a single shot burst. Ideally, a crypt at 11 o'clock or 1 o'clock, hidden under the upper lid, is found and the iridotomy is placed at that location, avoiding iris blood vessels. Care should be taken to find a location with adequate space between the corneal endothelium and the iris to avoid potential damage to the cornea. The patient will feel a small snap, hear a click and see a flash of light. The laser should be applied until a patent iridotomy is made in the iris and a plume of fluid is seen rushing from the posterior chamber to the anterior chamber. This plume indicates that the pressure between the posterior and anterior chamber has equalized and the iris should fall flat. If iris debris or blood blocks the iridotomy site and no laser response is seen, it is best to pause and have the patient wait for 10 to 15 minutes, until the debris settles and additional laser shots can be applied to create a patent iridotomy. The iridotomy should be approximately 1mm x 1mm in size. Following the procedure, the patient is given a topical alpha-2 agonist and advised to continue all topical and oral IOP medication. Additionally a topical steroid QID for one week is started following the procedure to control inflammation. The IOP should be checked in an hour and again 24 hours following the LPI procedure.

Iridoplasty

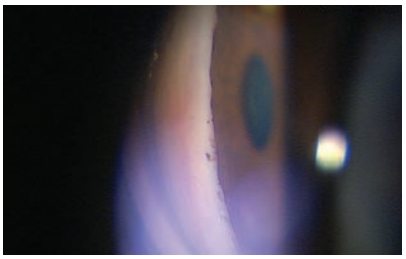
On follow-up examination, the peripheral iridotomy should be checked to confirm that it is patent and repeat goniopscopy to ensure the angle has deepened. Transillumination of the peripheral iridotomy is not sufficient to confirm its patency. Topical and oral IOP medications are stopped as needed. The fellow eye is also scheduled for a laser peripheral iridotomy as soon as possible as 50% of patients will develop an angle closure attack in the other eye within five years.[1] A dilated fundus exam, visual fields and OCT imaging should be performed following the LPI to evaluate the optic nerve for glaucomatous optic neuropathy, Cataract extraction may also be considered at this time.

If, on follow up, the angle is still narrow on gonioscopy, even in the

presence of a patent PI, and the IOP is still elevated, additional angle closure mechanisms may be involved, such as plateau iris syndrome which results when the iris inserts into the ciliary body too far anteriorly, or the ciliary body is rotated anteriorly, putting the angle in appositional closure. This is usually diagnosed only after LPI is performed. Chronic topical miotics may be needed to treat this; however, research shows LPI may reduce IOP in these patients by 32%.[4] Laser peripheral iridoplasty physically pulls the angle open and reduces appositional iris closure.[4]

To perform the laser peripheral iridoplasty, an argon laser or frequency-doubled Q-switched Nd:YAG laser is used. The patient is given topical pilocarpine 2% to constrict the iris and numbed with topical proparacaine. An iridotomy lens is then placed on the eye and the laser is set to 300mW with a 0.5 second duration. A 400µm spot size is used to contract the iris and the laser spots should be placed as far peripheral on the iris as possible, with six laser spots every 90 degrees. The lasers power can be titrated until iris constriction occurs and the angle opens. Care should be taken to avoid large iris blood vessels. Following the procedure, a topical alpha-2 agonist is given and the IOP checked in one hour. Additionally, a topical steroid should be started four times a day for one week.

Prognosis for acute angle closure is good as long as it is treated promptly and appropriately. Following an acute angle closure attack, 62% of patients do not have residual visual field loss; however, if treatment is delayed and the IOP is elevated for a prolonged period of time, vision loss can develop.[5] ■



A semi-narrow angle seen from the side.

Dr. McWherter is a consultative optometrist with Bennett & Bloom Eye Centers in Louisville, KY.

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I'd Like to Place an Order

Optometrists have the right, and often the duty, to order labs and imaging. Do so with confidence. **Edited by Paul C. Ajamian, OD**

Q I tried ordering an MRI recently, and was told that only an MD can place that order. What gives?

A "All state practice laws allow ODs to order lab and imaging studies for conditions germane to the eye and related structures," says James Fanelli, OD, of Cape Fear Eye Institute in Wilmington, NC.

Optometrists simply need to know the ins and outs of ordering, allowing them to request testing with confidence to eliminate hassle.

Lab Studies

Here, the OD has three options:

In-office. This is feasible for multidisciplinary practices, but not worth the hassle in the optometric office due to the onerous rules and regulations, Dr. Fanelli says.

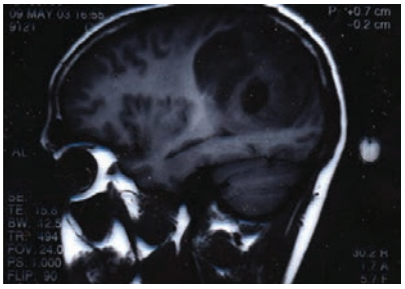
Hospital labs. This is a great option if you have hospital privileges. If not, it can be problematic in some hospitals, but not in others.

Commercial labs. The best option for ODs. "These companies are in the business of performing lab testing; they have account managers on site," says Dr. Fanelli. All you need is a license to practice and a request for specific labs. "Contact the office, tell them you're a new practice or a practice that wants to use their services for lab work, and to send you the necessary forms; then tell them to set up an account for you."

Imaging Studies

For imaging studies, the OD again has three options:

General or internal medicine practice. "If the patient in need of imaging is already plugged into a large primary care facility, that facility will probably have on-site CT imaging and some will have mobile MRI," Dr. Fanelli says.



Optometrists have the legal right to order brain scans like this one.

Order the tests by communicating with the patient's primary care provider, who can order the necessary imaging in-house. "The plus here is that the PCP usually uses his or her own imaging facilities and that can foster OD/MD relationships. The downside—if the MD doesn't know the OD, they may bypass you by sending the patient to an ophthalmologist, and you can lose the patient," Dr. Fanelli says.

Hospital. Ordering images from a hospital comes with the same issues as ordering labs from a hospital—some accept outside prescriptions and some don't. "My suggestion for imaging and lab orders is to simply act like you're a staff physician: Have your tech call the scheduler at the imaging center, and tell them you have a patient who needs *X* type of scan for *Y* condition," Dr. Fanelli says. "Don't ask—just act like it's something you do every day, and have confidence in your authority to order such a test or image."

Commercial/For-Profit Centers. Just as with labs, these are the easiest locations for ODs to obtain imaging. "They welcome the referrals because they are in the business of scaning," he says. "So, call them, set up an account with the account/office manager, and order away. It should be pretty straightforward."

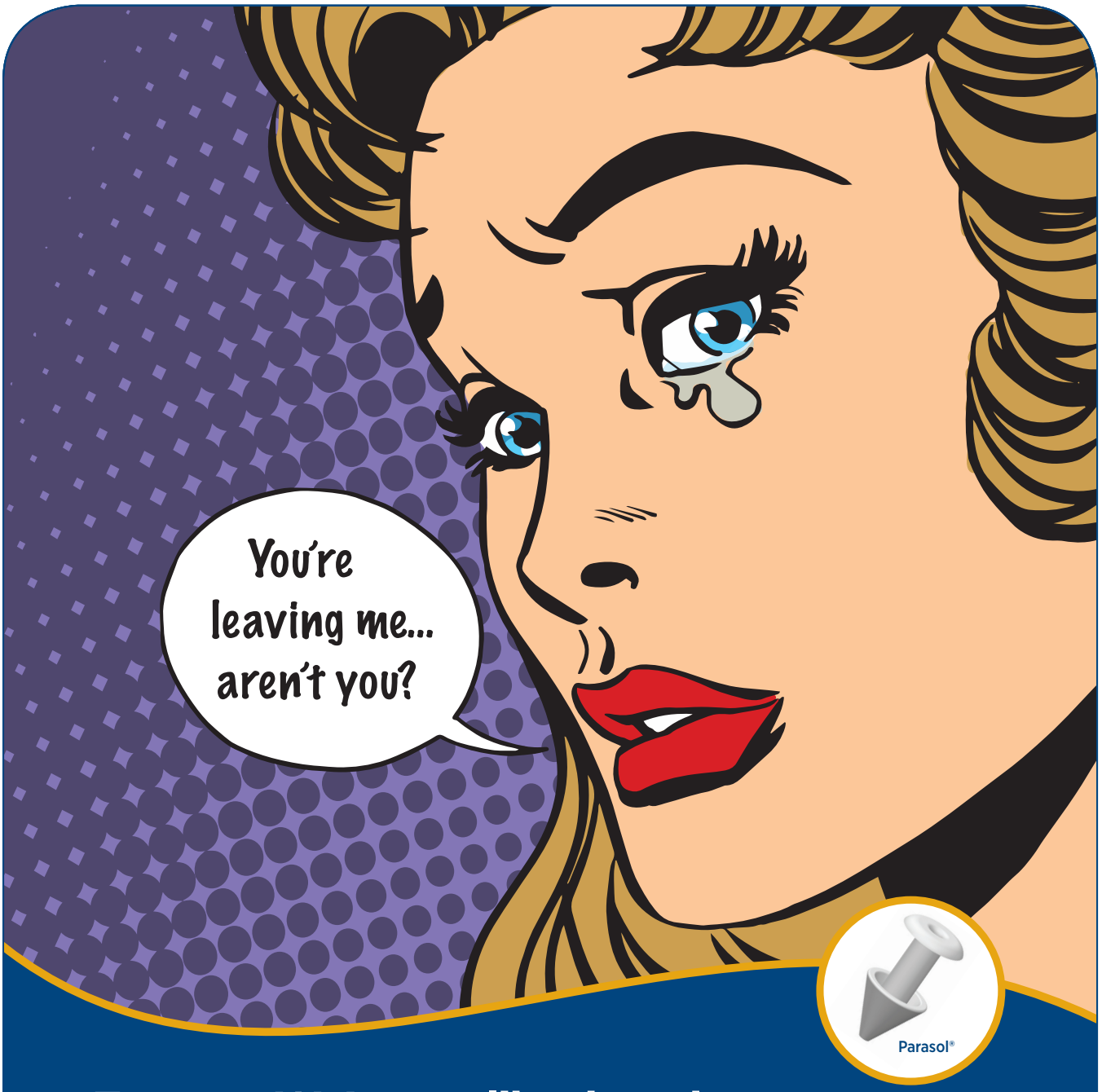
Interpreting Results

Lab studies give you hard data from the tests ordered; they provide the results, not the clinical interpretation, Dr. Fanelli explains.

"For example, the results might tell you that the patients RBC count is low, hemoglobin is low, and the red cells are larger and paler than normal. Now it's up to the ordering physician to know that this is macrocytic hypochromic anemia," he says. "What that means must be combined with the clinical presentation, and how the patient is subsequently managed is up to the ordering physician."

Imaging studies are usually read by radiologists who will typically give you the Dx. "What you do with that information is what's important. I will look over CTs and MRIs myself, but I rely on the radiologist's interpretation for more detailed information," Dr. Fanelli explains.

Optometrists have the legal right and, in many instances, a legal obligation to order tests. So, go ahead and order what your patient needs. Call lab or imaging facilities with the confidence of an expert. ■



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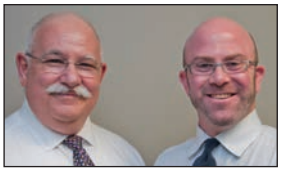

Refraction, in Retrospect

A review of old data reveals the conditional nature of prescribing.

By Marc B. Taub, OD, MS, and Paul Harris, OD

We have all had cases in which we look back and question our treatment approach. These are not second thoughts related to which antibiotic was prescribed or whether the patient should have been sent for an MRI; rather, we have all questioned our refractions—something done on a daily basis. As we practice in an academic setting, maintaining continuity of care can be a challenge. The case presented this month was seen over the course of several years by four different clinicians, and I wanted to exercise my right—as the last one to examine the patient—to play Monday morning quarterback!

Second Thoughts

Regarding the data, many questions exist, but the global question is: Looking back at the individual exams—would you have prescribed? I will be honest—every time I look at the data, I change my mind. The question in this case becomes: Should glasses have been prescribed earlier? Let's tease apart the exam data to point out some aspects of the case that are noteworthy.

Before we start, let us preface the discussion with a few facts. This child came in for routine exams and did not present with academic difficulties. If a complaint of an eye turn or poor school performance existed, prescribing most likely would have taken a different direction. The patient was a normal little girl on every level.

The Case

Looking at the first exam *(see table at right)*, we see decent adequate acuities at distance, but poorer acuities at near, which were taken with Lea symbols. The stereopsis and the NPC are acceptable, but the cover test shows a high exo posture. The retinoscopy warrants attention, since the anisometropia is at a level some might consider amblyogenic. Based on the visual acuity at distance, the retinoscopy finding did not seem to be an issue. Since acuities for a four-year-old can be variable and difficult to attain, I fall back on the stereopsis to help guide the decision making process. In this case, stereopsis was within expected values, so I would have watched closely and rechecked the patient in three months.

The exam at age five presents interesting findings to consider. While the acuities at a distance equalized at around 20/40, near acuities showed improvement. The stereopsis dropped from 50 to 100 seconds of arc, but the cover test normalized. The retinoscopy data show a small decrease in the anisometropia but an increase in the astigmatism in the right eye. To be honest, this is a tough call to make. The increase in astigmatism in one eye could signal that correction is needed; however,

	4 years old	5 years old	6 years old	8 years old
Visual Acuity (D)	20/25 20/40 20/40	20/40 20/40 20/30	20/25 20/25 20/20	20/25 20/25 20/20
Visual Acuity (N)	20100 20/60 20/60	20/30 20/30 20/30	20/25 20/20 20/20	20/30 20/30 20/30
Stereo	50 sec, + forms	100 sec, + forms	40 sec, + forms	40 sec, + forms
CT	6 XP, 10 XP	ortho, 4 XP	ortho, 4 XP	ortho, 1 XP
NPC	8/10 X 3	Hirschberg +	TTN X 3	TTN X 3
Retinoscopy	+4.00-1.00 X 180 +2.50	+3.50-2.00 X 150 +2.50-0.75 X 020 20/30 20/30 20/30	+4.00-1.50 X 160 +2.75-0.75 X 010 (Cyclo +.25 more OS) 20/25 20/25 20/20	+4.00-1.00 X 180 +3.00-1.00 X 180 BB +3.00-1.00 X 180 +3.00-1.00 X 180 20/15 OD, OS, OU @ D 20/25 OD, OS, OU @ N
Treatment	No Rx	No Rx	No Rx-6m	Rx, full time

a case could also have been made for close observation only, since the uncorrected acuity was good—20/40.

At age six, we found the uncorrected acuities to be quite good. The stereopsis, cover test and NPC were all essentially normal. The retinoscopy showed a similar level of anisometropia (1D at 5-year-old exam vs. 1.25D at 6-year-old exam) and the right eye's astigmatism dropped by 0.50D; but with this in place, the acuity did not change. Since the child was asymptomatic and had excellent acuities, the clinician decided to see the girl back in six months and did not prescribe.

Monday Morning Quarterback

My first encounter with this patient came at the final exam at age eight. The testing was fairly normal with near acuities slightly lower than distance. We performed a subjective refraction for the first time; the binocular balance was +3.00-1.00 X 180 in both eyes, and both the distance and near acuities improved in the exam room. Given the improvement and knowing that near work would be more challenging—smaller text/longer working time—I decided it was prudent to prescribe.

Lessons Learned

In such cases, the literature provides minimal guidance, but two recent studies show a possible link between uncorrected refractive error and learning. The research shows that the presence of astigmatism is negatively associated with academic readiness on the domains of the Work Sampling System as well as on the domains of the Ages and Stages Questionnaire.[1] The VIP-HIP Study Group compared the early literacy of four- and five–year-old uncorrected hyperopes (n=244) with emmetropes (n=248).[2] In comparing scores using three diagnostic metrics, hyperopes scored significantly worse. The impact was even greater if the binocular visual acuity was less than or equal to 20/40, or if the near stereo acuities were less than or equal to 240 seconds of arc.

The question, of course, is whether or not correcting astigmatism or hyperopia, as suggested by the studies, will impact the scores on the specific tests. More inductively, the impact of refractive correction on a child's social, emotional and academic development remains unanswered by the research. Until this is answered by large-scale, longitudinal studies—which can take many years—we are left with our exams and intuition. ■

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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

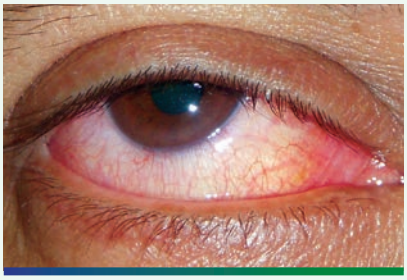

Figure 1 Allergic conjunctivitis.
(Image courtesy of Randall K. Thomas, OD, MPH, and Ron Melton, OD.)

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]

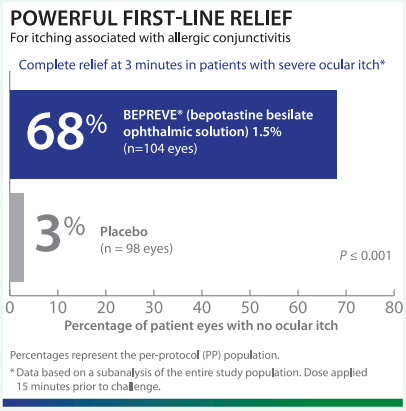

Figure 2 First-line relief. *(Meier reference 12.)*

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.

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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.

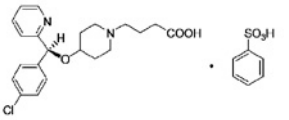
8.3 Nursing Mothers
Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 mcg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection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

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Tampa, FL 33637
Under license from:
Senju Pharmaceutical Co., Ltd.
Osaka, Japan 541-0046

Multifocal IOL in a Fuchs' Patient?

Are these devices suited for patients with compromised endothelial function? Experts weigh in. **Edited by Joseph P. Shovlin, OD**

Q A 59-year-old cataract patient with mild Fuchs' endothelial corneal dystrophy presented to the clinic with minimal stromal haze and no epithelial edema. Her cell counts were relatively good—approximately 1,700 cells/mm². She reported interest in multifocal IOL implantation. Is there an expert consensus on whether this is a safe modality for this type of patient?

A "In order to maximize our outcomes, it is important for us to match the technology to the patient and the patient to the technology," says Walter O. Whitley, OD, of Virginia Eye Consultants. Typically, once a patient with no signs of a progressive disease is implanted, they are good to go. However, Fuchs' dystrophy is a condition that can progress over time, he says, lending credence to the reasoning why he and his colleagues typically do not recommend multifocal IOLs in this population.

"We don't feel it's a match," Dr. Whitley says. "Even with mild Fuchs', the cornea can become compromised several years down the road, which can leave the patient with less than optimal vision." Instead, standard or toric IOLs would be better, he concludes.

Aaron Bronner, OD, of the Pacific Cataract and Laser Institute, also agrees that the first rule for multifocal IOL success is good patient selection.

"The current generation of lenses work using diffraction optics, which effectively split light into two simultaneous optical packets: a distance-focused packet and a near-focused packet. This allows the retina to receive an image with less contrast as compared to a monofocal system," he explains.

"This system works well in a healthy visual system, but its shortcomings are compounded by any other source of visual deterioration," Dr. Bronner says. As such, "multifocals are generally contraindicated for patients with conditions that either reduce retinal image quality (such as Fuchs' dystrophy) or those that reduce retinal image processing (such as macular degeneration or epiretinal membrane)."

Brian Den Beste, OD, of LASIK Pro Eye Consultants in Orlando concurs. He points to a study in which monovision and multifocal IOLs were compared, with the monovision IOLs scoring higher in terms of satisfaction and lower in terms of complaints and out-of-pocket costs, while visual outcomes were essentially the same.[1]

Derek Cunningham, OD, director of optometry at Dell Laser Consultants, notes that patients with Fuchs' dystrophy are generally considered high risk due to probable progression of the condition and are not usually even given the option.

Indeed, "a good deal [of the choice to move forward with implantation does] depend on the severity of the disease and transparency of Descemet's membrane," says Eric Donnenfeld, MD, of Long Island LASIK.

"Often, patients with Fuchs' dystrophy will have a beaten metal appearance to the endothelium," he says. "This opacification of Descemet's membrane degrades the quality of vision following cataract surgery with all IOLs, but is more significant with a multifocal IOL."

Given all these caveats, if the patient still insists on a presbyopia-correcting IOL, both Dr. Cunningham and Dr. Den Beste recommend the Crystalens (Bausch + Lomb) to reduce patient spectacle dependence. As an accomodating IOL, it does not use apodized diffractive optics, Dr. Den Beste adds.

On the other hand, new generations of multifocal IOLs with low adds like the Tecnis 2.75 (Abbott) and the Restor 2.5 (Alcon) might be tolerated in mild cases of Fuchs' dystrophy, Dr. Donnenfeld notes. "However, once patients start developing stromal edema and certainly epithelial edema, they are generally not good candidates for multifocal IOLs," he cautions. ■

1. Zhang F, Sugar A, Jacobsen G, Collins M. Visual function and patient satisfaction: comparison between bilateral diffractive multifocal intraocular lenses and monovision pseudophakia. J Cataract Refract Surg. 2011 Mar;37(3):446-53.

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7th Annual Retina Report

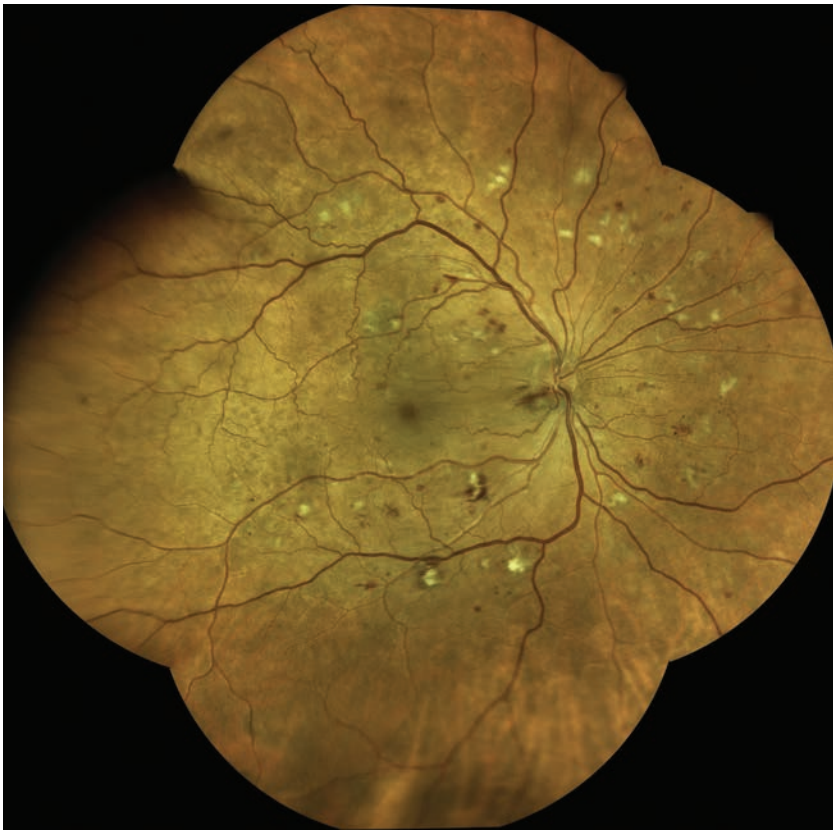
Diabetic Retinopathy By the Numbers

A guide to following and educating patients who face this sight-threatening diagnosis.

By Steven Ferrucci, OD, and Brenda Yeh, OD

Today, optometrists play a crucial role in managing diabetes, a leading—and growing—instigator of vision loss. With management of this disease now firmly in optometry's wheelhouse, the depth of research into its ocular impact has provided the ability to delineate its progression using various categories. In the case of diabetic retinopathy, these are divided, chiefly, into two: proliferative diabetic retinopathy and nonproliferative diabetic retinopathy. These categories are each further split by severity. It may seem like minutiae, but even minor distinctions can be valuable as they inform our treatment protocol and, ultimately, prevent significant visual impairment for our patients.

This article explains the care diabetes patients require and details the biological processes that indicate where to classify a patient with diabetic retinopathy, as well as what treatment should follow.

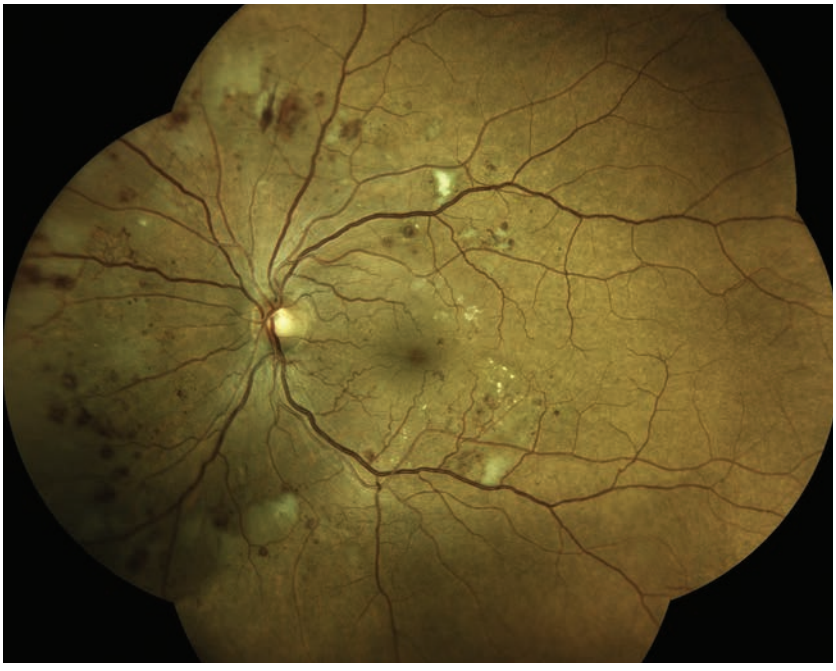


Using an Eidon True Color Confocal Scanner, this image shows moderate to severe NPDR with multiple cotton-wool spot and dot/blot hemorrhages.

Risk Factors

Two particular aspects of diabetes can put patients at risk for developing diabetic retinopathy: duration and glycemic control.

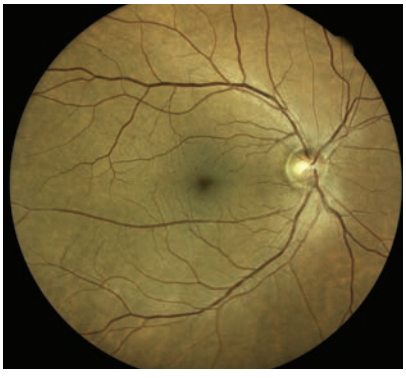
• ***Duration.*** Approximately 25% of Type 1 patients have some retinopathy after five years.[7,8] These numbers increase to almost 60% after 10 years and greater than 80% after 15 years.[7,8] In Type 2 patients older than age 30 with a known duration of diabetes of less



An Eidon True Color Confocal Scanner was used to image this PDR with an area of NVE at 10 o'clock. Below, this image shows a patient with mild nonproliferative diabetic retinopathy. Note the three dot hemorrhages superior to the macula.

than five years, 40% of patients taking insulin and 24% of those not taking insulin are found to have retinopathy. After 10 years, the numbers increase to 84% and 53%, respectively. Proliferative diabetic retinopathy is found in approximately 2% of type 2 patients who have diabetes for less than five years, and 25% who have had diabetes for 25 years or more.[9]

• *Glycemic control.* Multiple clinical studies, as well as epidemiologic studies, support this association. For example, the United Kingdom Prospective Diabetes Study revealed intensive blood sugar control in newly diagnosed patients with Type 2 diabetes had less microvascular complications, including retinopathy, compared with patients who received standard treatment.[10,11] For every 1% decrease in HbA1c, there was a corresponding 35% risk reduction in retinopathy.[10]



Once retinopathy is present, glycemic control becomes the more important factor in predicting the progression to advanced stages.[12,13] In general, a HbA1c of 7% or less is recommend for most patients with diabetes.[14] The management of hypertension, as well as lipids, has also been shown to reduce the progression of retinopathy, and delay the need for treatment.[15-17]

Patients with retinopathy should be counseled about these risk factors and encouraged to work with

Diabetes in America

An estimated 25.6 million Americans age 20 or older have diabetes, with a third still undiagnosed.[2] An additional 79 million people have prediabetes, and are at risk for developing diabetes.[2,3] Researchers estimate the prevalence rate for diabetic retinopathy among adults with diabetes older than 40 years in the United States is 28.5%—4.2 million Americans.[4]

Further, the rate of vision-threatening diabetic retinopathy in the United States is 4.4% or 0.7 million.[5] If the overall rate of diabetes continues to rise at the current trajectory, the projected prevalence of individuals with any diabetic retinopathy by 2020 will increase to 6 million, with 1.34 million having sight-threatening disease.[4,5]

Type 1 diabetes is characterized by an absolute lack of endogenous insulin. These patients must be on exogenous insulin injections to survive. Type 1 accounts for only 5% of diabetes in the United States, and is generally diagnosed in children and young adults, although it can occur at any age.[2]

Type 2 diabetes is characterized by insulin resistance or the inability of the body to use the insulin it makes effectively. This accounts for 90% to 95% of all diabetes, and develops more frequently in adults.[2] However, due to childhood obesity and other factors, the prevalence of Type 2 diabetes is increasing in children and teens.[6] Typical treatment starts with diet and exercise, then proceeds to oral medications. Some patients with Type 2 diabetes may take insulin as well, although typically do not need it for survival, like patients with Type 1.

Because of the higher proportion of patients with Type 2 diabetes, it accounts for the largest number of patients with visual loss from diabetic retinopathy, even though patients with Type 1 typically suffer from more frequent and more serious ocular complications.

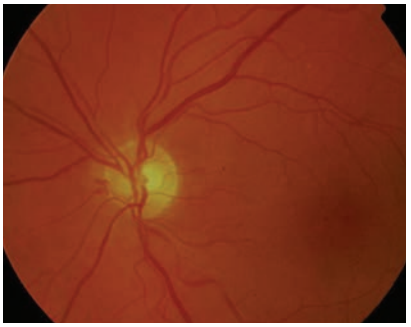
their physicians to obtain optimal control of their diabetes, as well as other associated medical issues.

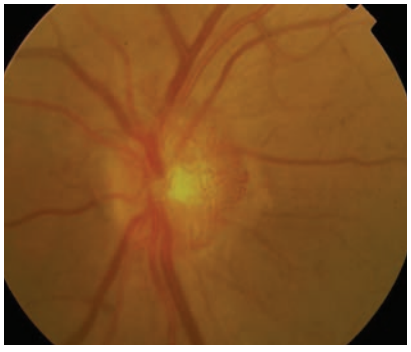
Regular Check-ups

All patients with diabetes should have regular eye examinations. Patients with Type 1 diabetes without known retinopathy should have dilated retinal examinations beginning five years after their initial diagnosis, and annually thereafter.[7,18]

Type 2 patients should be examined shortly after their initial diagnosis, as often they have had the disease for several years before diagnosis.[19] In fact, retinopathy is detected in 20% to 39% of patients upon initial diagnosis of Type 2 diabetes, and up to 3% of patients are found to have clinically significant macular edema (CSME) or high-risk retinopathy upon initial exam if their diabetes is diagnosed after age 30.[7,9,20] Patients with no retinopathy should be counseled regarding the importance of routine examinations, even those with good vision and no symptoms. Approximately 5% to 10% of patients without retinopathy will develop it within one year.[21,22] Those with retinopathy should be examined more frequently, depending upon their level and severity of involvement.

At the initial exam, as well as subsequent exams, a thorough history, including type of diabetes, duration of disease, glycemic control, current medications, current medical history (with particular attention to comorbid diseases such as hypertension, hyperlipidemia, obesity), and ocular history (including previous treatment for diabetic eye disease), should be obtained. Any retinal findings consistent with diabetic retinopathy in an undiagnosed patient warrants further investigation including lab tests, such as fasting blood sugar or glycosylated hemoglobin, and referral to primary care, as appropriate.





Above, PDR with early NVD at 9 o'clock. Below, high-risk PDR with significant NVD greater than 1/3DD.

Diabetic retinopathy can worsen during pregnancy, either due to physiologic changes in pregnancy itself or changes in overall glycemic control.[23-25] Therefore, patients with diabetes who plan to become pregnant should have a comprehensive eye exam prior to pregnancy, and be informed of the increased risk of retinopathy or its progression. A dilated retinal exam should be performed within the first trimester, with appropriate follow-up depending on presence and severity of retinopathy, if discovered. Conversely, women who develop gestational diabetes do not require an examination, as they do not appear to be at increased risk of retinopathy during their pregnancy.[26]

Physical Examination

When a diabetes patient presents to your office, perform a complete ophthalmic exam—including examination of the peripheral retina and vitreous through a dilated pupil. Pupil dilation is essential as research shows only 50% of eyes are correctly classified for the presence and severity of retinopathy through an undilated pupil.[27]

Ancillary testing methods—such as gonioscopy, optical coherence tomography (OCT) and fundus photos—should be performed when indicated, on a case-by-case basis. The presence or absence of any signs of retinopathy, such as hemorrhages, venous beading (VB), cotton-wool spots and retinal neovascularization, as well as exudates and thickening in the macula, should be documented.

Retinopathy Patients

Two major classifications of this disease exist: nonproliferative diabetic retinopathy (NPDR) and proliferative diabetic retinopathy (PDR).

NPDR is characterized by retinal vascular abnormalities, such as microaneurysms, intraretinal hemorrhages, venous dilation, and cotton-wool spots. Intrarertinal microvascular abnormalities (IRMA) may also occur at this stage. NPDR is divided into mild, moderate, severe and very severe.

As the retinopathy progresses, gradual closure of the retinal vessels may occur, leading to decreased perfusion and retinal ischemia. Proliferative diabetic retinopathy can then follow, characterized by neovascularization, either of the optic disc (NVD) or elsewhere in the retina (NVE). These neovascular vessels are weak and fragile, and can rupture or bleed, leading to preretinal or vitreous hemorrhages, and subsequent vision loss. PDR can be further divided into PDR and high risk PDR.

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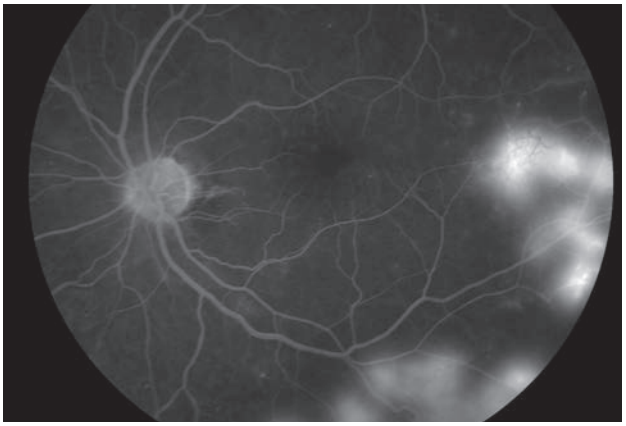
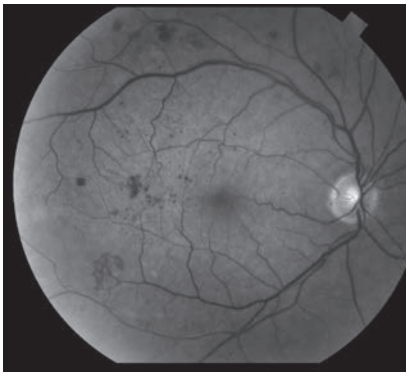
1. Kiss et al. Comparison of ultra-widefield fluorescein angiography with the Heidelberg Spectralis® \noncontact ultra-widefield module versus the Optos® optomap. Clin Ophthalmol. 2013, 389-94. 2. Silva, Cavellerano, Sun, Noble, Aiello. Nonmydriatic Ultrawide Field Retinal Imaging Compared with Dilated Standard 7-Field 35-mm Photography and Retinal Specialist Examination for Evaluation of Diabetic Retinopathy. American Journal of Ophthalmology, 2012.
3. Data on file 4. Silva, Cavellerano, Haddad, Kwak, Dyer, Omar, Shikari, Aiello, Sun, Aiello; Ophthalmology, 2015

• *Mild NPDR.* This classification is characterized by the presence of at least one retinal microaneurysm or hemorrhage. Microaneurysms are outpouchings of retinal capillary walls, caused by loss of pericytes of the cell wall—which leads to weakening. Hemorrhages result from leaking or ruptured microaneurysms deep within the retina, where the cells are compact and vertically oriented, leading to the characteristic pinpoint or dot/blot shape.

On clinical exam, a microaneurysm and hemorrhage appear quite similar and can truly only be differentiated by fluorescein angiography (FA), with microaneurysms appearing hyperfluorescent and hemorrhages appearing hypofluorescent. However, the difference between the two is clinically insignificant, as both point out the beginning stages of diabetic damage, and patients with mild NPDR should be reexamined in one year. Approximately 5% to 10% will increase to further stages of retinopathy over the course of a year.[21,22] FA and laser are not indicated, nor are color photos necessary, but are often helpful in establishing a baseline to look for future progression, and can be useful in patient education.

• *Moderate NPDR.* This is characterized by increasing hemorrhages and microaneurysms as well as cotton wool spots, VB or IRMA to a mild degree. IRMAs represent either new vessel growth deep within the retina, or more likely, pre-existing vessels that serve to shunt blood through areas of nonperfusion. Patients with this level of retinopathy should be re-examined in six months, due to the increased disease progression, with approximately 16% of patients with moderate NPDR progressing to PDR within four years.[21]





At left, FA image demonstrates hyperfluorescence consistent with NVE. Below, this red-free photo shows PDR with NVE at 8 o'clock.

As with mild NPDR, laser and FA are not indicated, but photos may be helpful to monitor for future progression.

• *Severe NPDR.* You can categorize this version of the condition by using the "4-2-1" rule—that is, one has severe NPDR if hemorrhages or microaneurysms, or both, appear in all four retinal quadrants; venous beading appears in two or more retinal quadrants; or prominent IRMAs are present in at least one retinal quadrant.

• *Very severe NPDR.* The most severe classification is reached when any two or more of these criteria are met. These patients should be followed extremely closely, within two to four months, due to the high risk of progression to proliferative disease. Approximately half of the patients with severe NPDR will progress to PDR within a year—and, of those, 15% will exhibit high-risk characteristics.[28] For patients with very severe NPDR, the risk for PDR is approximately 75% within a year, with 45% becoming high risk.[28]

Due to the high rate of PDR progression in these patients, it is also reasonable to consider a consult to a retinal specialist at this level of retinopathy to consider treatment. This should especially be considered if there are extenuating circumstances, such that the patient cannot or will not be followed closely, or there are other considerations, such as pregnancy or impending cataract surgery.

Analysis shows that the risk of severe vision loss or need for vitrectomy was reduced by 50% in patients with Type 2 diabetes who received panretinal photocoagulation (PRP) treatment at this stage vs. waiting until high-risk PDR developed.[29] Currently, the role of anti-VEGF treatment in the management of severe and very severe NPDR is being studied.

FA is often helpful at this stage to determine the presence of non-perfusion, peripheral ischemia or any clinically undetected areas of neovascularization, making a referral to a retinal specialist and treatment consideration even more important.

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PDR

The hallmark of PDR is neovascularization, either on or within one disc diameter (DD) of the optic disc (NVD) or elsewhere in the retina (NVE); a preretinal hemorrhage (PRH); or vitreous hemorrhage (VH).

High-risk PDR is characterized by NVD greater than one-fourth to one-third disc area in size; any NVD with a vitreous or preretinal hemorrhage; or NVE greater than one-half a disc area in size with a PRH or VH. Any patient with PDR or high-risk PDR should be referred promptly to a retinal specialist for treatment, preferably within one week for PDR and one to two days for high-risk PDR. Without appropriate treatment, approximately 50% of eyes with PDR are blind within five years.[28]

The risk of severe vision loss in patients with high-risk PDR has been shown to be reduced substantially when treated with PRP.[28,29] Therefore, most patients with PDR should receive PRP in hopes of causing regression of the retinal neovascularization. Newer studies have demonstrated that anti-VEGF agents such as Lucentis (ranibizumab, Genentech) may be a superior alternative to PRP laser, alone or when done in conjunction with conventional laser.[30] For patients who fail to have vessel regression with laser or anti-VEGF treatment, a vitrectomy may be necessary.

Macular Edema

Another issue that must be addressed in diabetes patients is diabetic macular edema (DME), or accumulation of intraretinal fluid in the macula. While it is important to assess for diabetic retinopathy, it is equally as important to look for any evidence of DME. In fact, more patients with Type 2 diabetes suffer moderate vision loss from DME than frank retinopathy. Therefore, a careful assessment of the macula for exudates or signs of thickening is crucial in all patients with diabetes, even those with seemingly good visual acuity, as macular thickening only shows moderate correlation with visual acuity.[31]

Lastly, remember that diabetic macular edema can occur at any level of retinopathy, from mild NPDR to proliferative disease.

Traditionally, diabetic macular edema was classified as CSME if any of the following criteria were met:

1. Thickening of the retina at or within 500µm (1/3DD) of the center of the macula;
2. Hard exudates at or within 500µm (1/3DD) of the center of the macula with thickening of the adjacent retina;
3. A zone or zones of retinal thickening greater than 1 disc area in size, any portion of which is within 1DD of the center of the macula.[32]

With the advancement of OCT,

Diabetic Retinopathy Level and Management

Level of Retinopathy	Retinal Findings	Additional Testing	Follow-Up/ Referral
No Retinopathy	None	None	Twelve months
Mild NPDR	≥1 MA/Heme	Fundus photo‡	Twelve months
Moderate NPDR	MAs/Hemes, CWS, VB, mild IRMA -at level < Severe NPDR	Fundus photo‡	Six months
Severe NPDR	4-2-1 Rule: MAs/hemes in 4 quadrants -or- VB in ≥ 2 quadrants -or- Prominent IRMA in ≥ 1 quadrant	Fundus photo FA‡	Two months to four months retina referral‡
Very Severe NPDR	Two or more of the above "4-2-1" Criteria		
PDR	Any NVD, NVE, PRH, VH	Fundus photo FA	Retina referral within one week
High Risk PDR	NVD >1/4 to 1/3DD -or- Any NVD with VH or PRH -or- NVE > 1/2DD with VH or PRH	Fundus photo FA	Retina referral within one day to two days
With CSME **Non CI-Macular Edema** **CI-Macular Edema**	Thickening within 500 µm (1/3DD) of the macular center -or- Hard exudates within 500µm (1/3 DD) of macular center with adjacent retinal thickening -or- Zone(s) of retinal thickening ≥1DD in size within 1DD of the macular center	Fundus photo FA macular OCT	Non center-involved macular edema: Two months to four months Center-involved macular edema: retina referral within one week to two weeks

‡=Recommended
NPDR=nonproliferative diabetic retinopathy; PDR=proliferative diabetic retinopathy; MA=microaneurysms; Hemes=hemorrhages; CWS=cotton wool spots; VB=venous beading; IRMA=intra-retinal microvascular abnormalities; NVD=neovascularization of the disc; NVE=neovascularization elsewhere; VH=vitreous hemorrhage; PRH=preretinal hemorrhage; CSME=clinically significant macular edema; CI=centrally involving; DD=disc diameter

Coding Connection

By John Rumpakis, OD, MBA, Clinical Coding Editor

The Retinal Examination

Seven commandments of coding for the posterior segment.

Ask any insurance auditor what creates the largest area of concern for any ophthalmic physician—and special testing related to the retina/posterior pole will top the list. The retina has long been pertinent in our professional clinical journals, but until recently, most ODs haven't been actively managing retinal conditions. In addition, the ICD-10 is creating areas of audit exposure due to the specificity of its codes.

1. According to the CPT, when performing any 920XX code, dilation is not mandatory, but rather, is often included "as indicated."[1]

2. According to 1997 CMS E&M Guidelines governing any 992XX code, when the retinal components of a single system eye examination are performed, they must be done through a dilated pupil unless contraindicated due to age or medical reasons.[2] Good medical record protocol dictates that the dilating agent(s) be listed.

3. Medical necessity for return office visits or for any ordered special ophthalmic procedures should be stated in your assessment and plan for the office visit. Medical necessity rules the day—any test you order or perform must relate to clinically managing the patient, not just documenting a condition.

a. A question I'm frequently asked: "Can I do a fundus photograph (CPT 92250) on a patient with a diagnosis of E11.9 (Type 2 Diabetes without Complications)?" People too often submit this combination, which tells the carrier: here's a patient "without complications" on whom you've performed a fundus photograph. Where's the medical necessity? Unless the patient has unexplained symptoms or signs of a documented visual disturbance, you shouldn't document a normal retina in a diabetes patient and bill the carrier.

4. A special ophthalmic test defined as a separate and distinct procedure by virtue of having its own CPT code is not part of any office visit, whether a 920XX or 992XX code, but can be ordered and performed on the same date as the office visit if done so in accordance with National Correct Coding Initiative Edits and it meets requirements for medical necessity.

The CPT section on special ophthalmic tests preamble describes services in which a special evaluation of the part of the visual system is made, which goes beyond the services included under general ophthalmological services or in which special treatment is given. These services may be reported in addition to the general ophthalmological service or evaluation and management services.[1]

5. All special ophthalmic tests are subject to the Multiple Procedure Payment Reduction (MPPR) of 2013, which comes into play regarding multiple procedures on the same day full payment is made for the technical component (TC) service (with the highest payment under the Medication Physician Fee Schedule). Payment is made at 75% for subsequent TC services by the same physician (or by multiple physicians in the same Group NPI) to the same patient on the same day.[3]

6. These tests require an Interpretation and Report, distinct and separate from notes contained in the office visit itself (if performed). A special ophthalmic test is not complete (or billable) until the physician has completed the I&R. Essentials of an I&R:

a. Clinical findings—pertinent findings regarding the test results

b. Reliability of the test

c. Comparative data—comparison to previous test results

d. Clinical management—how the test results will affect management of the condition/disease, (i.e.: medication changes; surgery recommendation; diagnostic testing recommendation; referral for additional treatment).

7. When performing a special ophthalmic test, you are essentially referring a patient to yourself. So you must place the name and NPI of the referring physician (even if it's yourself) into box 17 and 17B respectively of the CMS 1500 form to allow the carrier to properly process it and to avoid the claim rejection CO-16.[4]

The Medicare Access and CHIP Reauthorization Act of 2015 (MACRA) will change the economics of how you get paid to manage retinal conditions. Remember—we don't perform coding and billing; we provide clinical care and our clinical medical record is our written proof of that care. The CPT code is the translation of medical care into a five-character code. Profitability is a by-product of the standard of care, a thorough and accurate medical record, and the translation of the clinical care provided into a CPT code used in accordance with the laws we have to follow. ■

Send comments to ROcodingconnection@gmail.com.

1. CPT: Professional Edition. American Medical Association;2016:591
2. Evaluation & Management Guidelines, Centers For Medicare and Medicaid Services;1997.
3. Multiple Procedure Payment Reduction (MPPR) on the Technical Component (TC) of Diagnostic Cardiovascular and Ophthalmology Procedures. https://www.cms.gov/outreach-and-education/medicare-learning-network-mln/mlnmattersarticles/downloads/mm7848.pdf.
4. WPC. Claim Adjustment Reason Codes. Claim Adjustment Reason Codes. http://www.wpc-edi.com/reference/codelists/healthcare/claim-adjustment-reason-codes/.

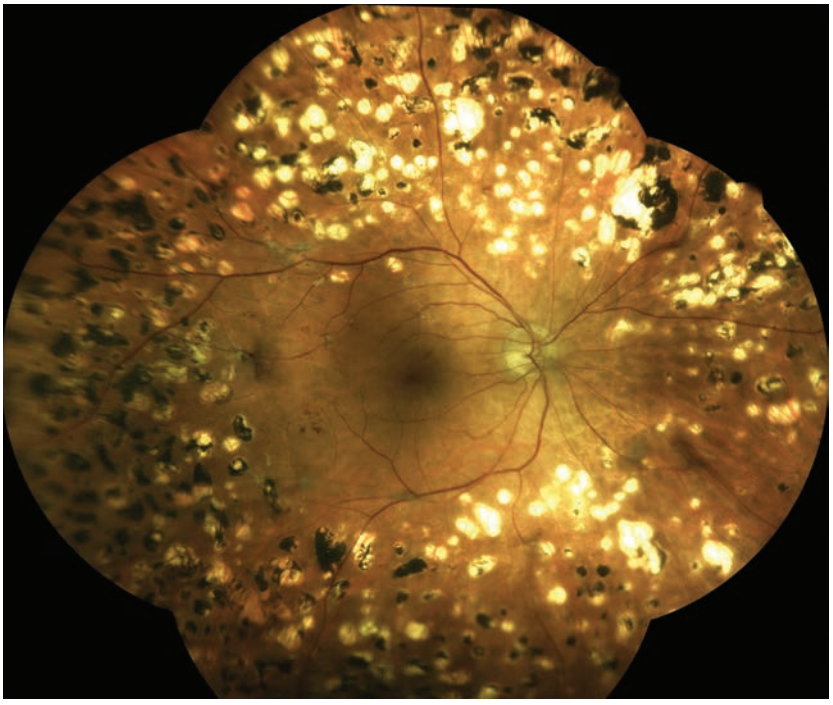
some clinicians now prefer to subdivide macular edema according to the involvement at the center of the macula—opting for the term "center-involving diabetic macula edema" when it is centrally located, and "non-center involving edema" when the center of the macula is spared. In general, the risk for vision loss and need for treatment is greater with central involvement.

The diagnosis of DME can be difficult even for experienced clinicians. It is best viewed through a dilated pupil using slit lamp biomicroscopy and appropriate lenses, or stereo photos. OCT is also particularly helpful for detecting subtle edema, as well as in following the edema after treatment for resolution. However, studies indicate that routine OCT imaging is not indicated in patients with minimal diabetic retinopathy when no retinal thickening is suspected on clinical exam.[33]

Any patient suspected of having center-involving DME should be referred to a retinal specialist for consideration of treatment within one to two weeks. FA prior to treatment is helpful to identify those lesions amenable to treatment. Also, it is useful to detect areas of capillary dropout around the macula and enlargement of the foveal avascular zone, which may be useful in deciding the most appropriate treatment.[32]

Patients with non-center involving DME should be followed closely, every two to four months, with repeat OCTs as needed, with a prompt referral when the central macula begins to become involved. Also, a referral to the patients' primary care physician to optimize glycemic control as well as other associated issues is warranted.

Traditional treatment of CSME has been laser surgery. Early studies showed that using focal laser for patients with center-involving CSME would decrease the loss of by 50% vs. observation alone.[32] Further, it was shown that patients with center-involving CSME had a ten-fold greater risk of moderate vision loss at one year compared with those patients without center involvement.

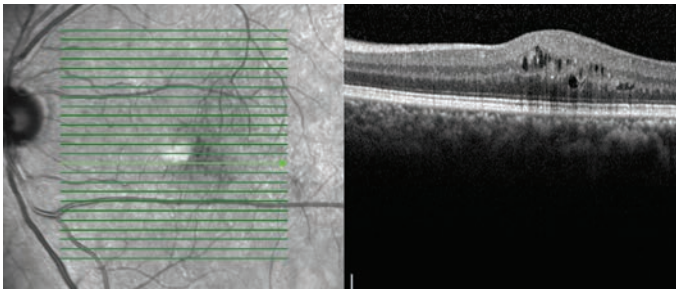


Taken with an an Eidon True Color Confocal Scanner, this image shows a patient following extensive panretinal photocoagulation for proliferative diabetic retinopathy.

However, data from several more recent, well-designed studies reveal that intravitreal anti-VEGF agents may provide more effective treatment for center-involving CSME than laser therapy alone.[34,35,36] Therefore, referral to a retinal specialist well-versed in the latest studies and protocols for treating CSME is advised.

Monitoring

Since the majority of patients with diabetes will develop some retinal involvement during the course of the disease, the importance of careful examination with a dilated retinal exam and appropriate follow-up or treatment when indicated cannot be overstated. Referral to a retinal specialist at the onset of sight threating, treatable retinopathy is crucial. Studies indicate that early detection and prompt



OCT image demonstrating mild CSME temporal to the macula, left eye.

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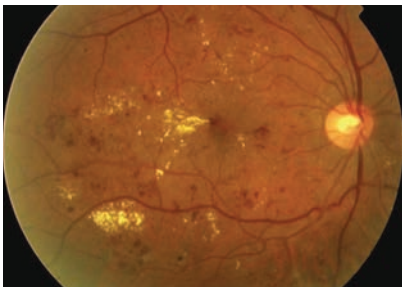

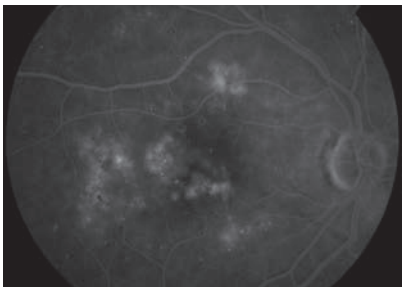

This image clearly demonstrates moderate NPDR with CSME—note extensive paramacular exudates. At right, this FA image shows areas of paramacular hyperfluorescence consistent with CSME.

treatment of diabetic retinopathy is approximately 90% successful in preventing severe vision loss (visual acuity less than 5/200). However, according to several studies, it appears that only about 50% of patients with diabetes are receiving timely dilated eye examinations.[37]

Patients with diabetes should be counseled regarding the visual side effects of their disease, and be encouraged to report any symptoms associated with progressive disease, such as decreased vision or floaters. They should be educated that retinopathy may occur even with normal vision, in the absence of any symptomatology, highlighting the need to adhere to your recommended recall and routine examinations. Patients should be encouraged to work with their other physicians to obtain good glycemic control as well as control of other associated diseases, such as hypertension, to reduce the risk of retinopathy or its progression. Lastly, those patients who suffer vision loss despite our best efforts should be referred to a provider specializing in low vision.

Hopefully, with increased vigilance and better communication, we can work with our patients with diabetes to prevent the devastating effects of this disease and help our patients lead healthy and productive lives. ■

Dr. Ferrucci is chief of optometry and residency director at the Sepulveda VA Ambulatory Care Center in North Hills, Calif. He is also a professor at Southern California College of Optometry at Marshall B. Ketchum University and a consultant to Eidon.

Dr. Yeh is a staff optometrist at the VA Sepulveda Ambulatory Care Center and an adjunct faculty member at Southern California College of Optometry at Marshall B. Ketchum University.

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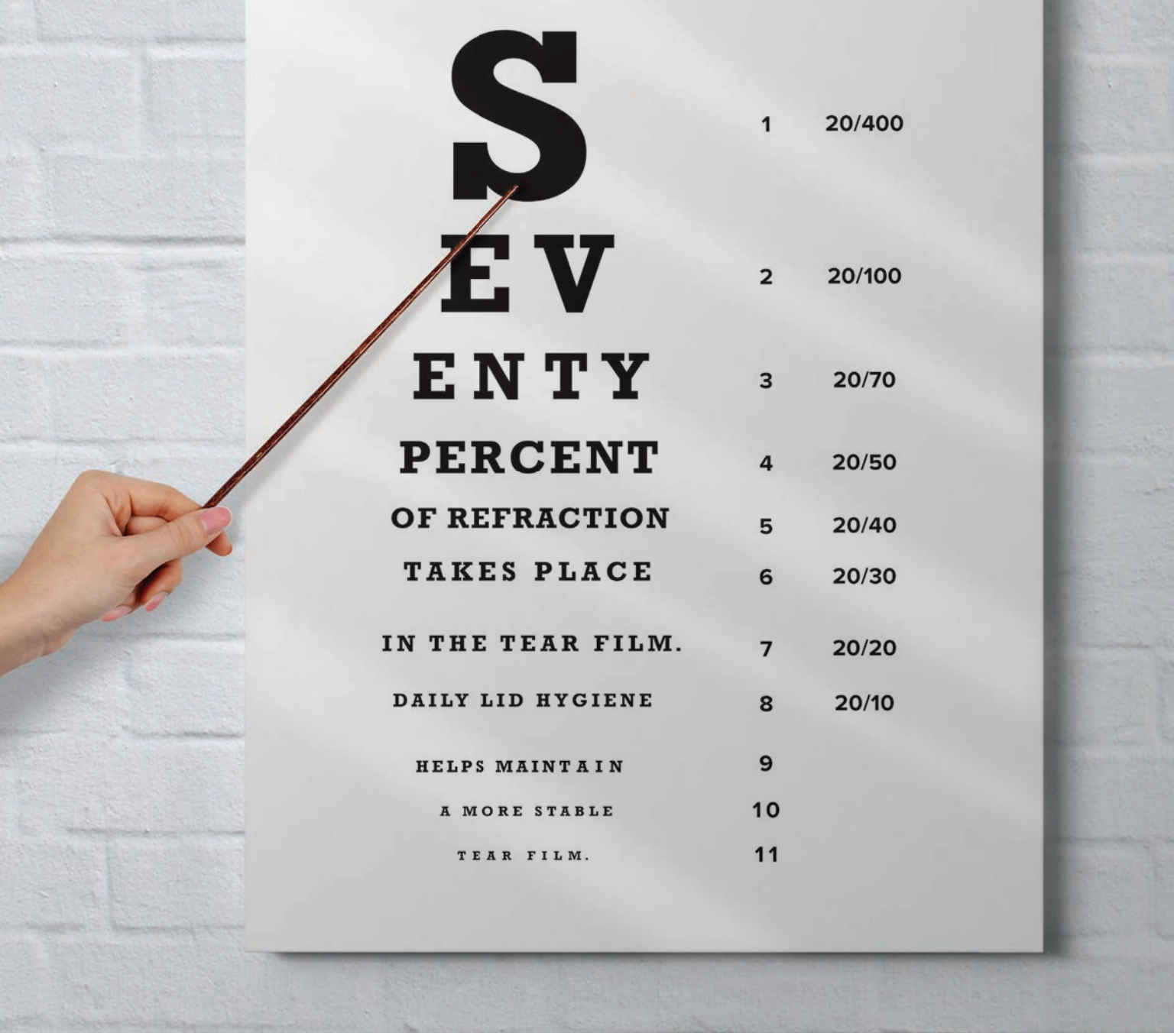

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7th Annual Retina Report

Food for Thought: Diet, Genetics and AMD

Is genetic testing prior to AMD supplementation indicated by AREDS data? A nutritionist OD takes a detailed look at this long-running debate. **By Julie Poteet, OD**

Age-related macular degeneration (AMD) remains the leading cause of irreversible visual loss among the elderly in developed nations.[1] In 2004, the prevalence of advanced AMD in the United States was estimated to be 1.47%, indicating approximately 1.75 million patients, and was projected to increase to 2.95 million by 2020.[2] Depending on one's definition of the disease, it will affect about one in three people older than 75 years of age.[3]

We are all familiar with the 2001 National Eye Institute's (NEI) Age-Related Eye Disease Study (AREDS). This double-masked randomized clinical trial (RCT) evaluated the effects of nutritional supplementation on the progression of AMD, and found that treatment with antioxidants plus zinc was associated with a statistically significant reduction in disease progression in patients with intermediate or advanced AMD—by about 25% after five years.[4] This was exciting news for anyone in the business of caring for patients with macular degeneration.

Before this trial, all we had to offer to patients were Amsler grids for home monitoring, consultations on smoking cessation, protecting the eyes from UV radiation and improvements in diet. Having a treatment that would reduce disease progression in intermediate or advanced disease by 25% transformed the way we practice and the recommendations we are obligated to make to best serve our patients and practice according to our oath. ("I will advise my patients fully and honestly of all which may serve to restore, maintain or enhance their vision and general health," from *The Optometric Oath*.)

The Age-Related Eye Disease Study 2 (AREDS2), a subsequent RCT, was then performed to determine if adding lutein plus zeaxanthin, DHA plus EPA, or both to the AREDS formula would further reduce the risk of advanced AMD. From the results of this trial, the National Eye Institute recommended replacing the beta carotene in the original formula (over concerns of increasing the risk of lung cancer in smokers) with 10mg of lutein and 2mg of zeaxanthin.[22] This substitution to the original AREDS formula resulted in an additional beneficial effect of about 20% beyond the effects of AREDS in reducing the progression to advanced AMD.

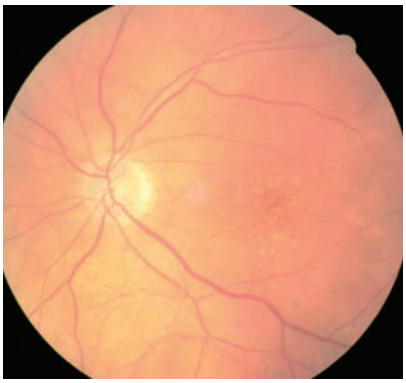
Even with AREDS2 therapy, patients vary substantially in disease progression rates, which suggests a potential pharmacogenetic component in treatment response.

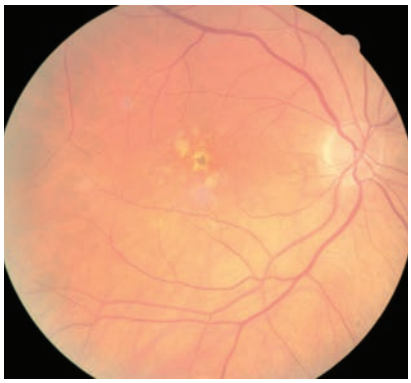
Pharmacogenetics is the study of inherited genetic differences in drug metabolic pathways, which can affect an individual's response to drugs, both in terms of therapeutic effect as well as adverse results.

The Genetics of AMD

AMD is not a Mendelian (or monogenetic) disorder like Stargardt disease or X-linked retinitis pigmentosa, in which the development of clinically detectable disease is very likely if a disease-causing genotype is present in a single gene. Rather, AMD is considered a complex genetic disease where the presence of one or more risk alleles does not necessarily result in a more affected phenotype, and the absence of risk alleles does not necessarily result in a less affected phenotype.[23,24]

In AMD, the genotypes of many





At left, this eye qualifies as intermediate AMD per the AREDS classification system. This is a patient who would benefit from supplementation per the AREDS data. In the image at right, the patient qualifies as intermediate AMD and is progressing to the advanced stage due to the pigment clumping centrally.

genes appear to interact with each other and with the environment to determine whether a patient will develop clinically significant disease.[24] However, of all the human multi-genetic diseases, AMD has been shown to have the strongest genetic contribution.[25]

The Human Genome Project catalogued and identified single nucleotide polymorphisms (SNPs), which are genetic variations that influence disease risk. Since then, SNPs involving at least 19 genes have been shown to be involved in AMD.

Of those 19 genes, two major susceptibility genes for AMD—CFH and ARMS2—have been shown to have a substantial contribution (perhaps 80%) to the heritability of AMD.[26] Complement factor H (CFH) is the main regulator of the alternate complement pathway of the immune system, and multiple independent genetic studies have shown that dysfunction of the complement system is a key factor in AMD development.[27] The age-related maculopathy susceptibility 2 (ARMS2) gene is involved with energy metabolism in the mitochondria.[26]

Despite advances in genetic research, the American Academy of Ophthalmology's Task Force on Genetic Testing currently recommends against routine testing for AMD until specific treatment or surveillance strategies are shown in prospective studies to benefit those with specific genotypes.[24,28]

Pharmacogenetics and AREDS

Recent pharmacogenetic studies using the original AREDS data have reported differences in treatment outcomes with respect to variants in genes for CFH and ARMS2.

In 2008, Michael Klein, MD, co-director of the Macular Degeneration Center at the Casey Eye Institute, and colleagues published a study using AREDS data that showed an observed interaction between CFH and antioxidants plus zinc.[29] This analysis was based on genetic data from 876 white participants of the original AREDS trial who had intermediate AMD or unilateral advanced AMD at baseline. Using multivariate analysis, and after controlling for age, sex, education, smoking and body mass index (BMI), researchers reported a greater reduction effect in AMD progression in patients with the CFH non-risk genotype compared to the CFH risk genotype. However, antioxidants

plus zinc reduced progression to advanced AMD (compared to placebo) in all six genotype subgroups tested. Neither zinc alone or antioxidants alone were superior to antioxidants plus zinc in any genotype subgroup; therefore, the researchers did not recommend genetic screening.[29]

In 2013, Carl C. Awh, MD, and colleagues at Tennessee Retina analyzed AREDS data but reached different conclusions.[30] These authors studied 989 white AREDS patients with intermediate AMD in at least one eye. They estimated AMD progression rates for nine CFH/ARMS2 genotypes. Using multivariate analysis, and after controlling for age, sex, education, smoking and BMI, the researchers reported that patients had statistically significant differences in outcomes based on CFH and ARMS2 genotypes. For 23% of patients, the original AREDS formulation was the best treatment. For 49% of patients, a formulation other than AREDS was more beneficial. For 13% of patients, the AREDS combination was harmful and accelerated vision loss significantly faster than placebo, which was thought to be due to an excess of zinc.[30]

Following this publication, the AREDS investigators (NEI's Emily Y. Chew, MD, and colleagues) reported in 2014 an "unplanned retrospective evaluation" of 1,237 white AREDS study participants (AREDS Report Number 38).[31] The AREDS investigators tested the response to the original AREDS supplement using genotypes described by Klein et al. and then by Awh et al. They dissented from the study results from Awh et al. because they found no significant interactions, and concluded that AREDS supplementation reduces the rate of progression across all genotype groups.[31]

Awh et al. responded by disputing

How Much Zinc is Enough (or Too Much)?

The concentration of zinc in the eye is higher than in most tissues of the body. Zinc is a cofactor for enzymes involved in visual function, and it plays an important role in regulating enzymes that are involved in the oxidative process.

One major problem in assessing the need for zinc in AMD is the lack of information about its biological role in the retina and surrounding structures.[5] Like other tissues, the retina can be damaged by too much or too little zinc.[6,7] At least one study has found that levels of zinc are reduced in human eyes with signs of AMD.[8] Depletion of zinc increases oxidative stress, may cause deficits in phagocytic and lysosomal functions, and may induce macro-molecule synthesis and caspase-dependent apoptosis—mechanisms that are all implicated in AMD.[5,7,9,10,11] Zinc depletion also markedly increases the vulnerability of retinal pigment epithelial cells to UV radiation through UV-induced DNA damage.[12] In addition, inflammation has been associated with AMD and we know that zinc supplementation raises plasma zinc concentration, which then boosts the immune system and provides better protection in AMD and in general aging.[5,13,14,15]

So, the role of zinc depletion and its consequences have been established—and now recent research indicates that excess zinc may be just as harmful in AMD.[5] Researchers have shown that drusen are filled with anomalous deposits of zinc, some of which are free or weakly protein bound.[5,16] This discovery led to the hypothesis that while zinc (along with antioxidants) has been shown to be protective during the intermediate to late stage of AMD (as was shown in the AREDS trial), excessive levels may contribute to the development of AMD at the early stages.[5,16,18] A 2013 paper clarified a potential molecular mechanism for zinc-induced drusen formation.[18] This study show excess zinc induces precipitation of immune factors that may contribute to the development of drusen and reduce the progression to advanced AMD in higher risk patients.[18]

Obviously, more research needs to be done to further elucidate the role of zinc regulation or dysregulation in retinal tissue and AMD. It could be possible that the pathway to drusen formation and from drusen to advanced disease could be quite different.[18]

In the AREDS2 trial, the version of AREDS2 with reduced zinc was shown to be as efficacious as the AREDS2 formula with higher zinc, and is therefore arguably the safer choice in a well-nourished population. The recommended dietary allowance (RDA) for zinc in adults is 12mg to 15mg/day. However, some elderly people appear to require zinc intakes above the RDA in order to maintain positive zinc balance.[19] Elderly people below the poverty line or people with certain food preferences (vegetarians or people who only eat fish or chicken) are likely to be zinc deficient.[5] Therefore, the AREDS2 formulation with the original zinc dosage would be a better choice in this population.

Of note, copper is necessary with long-term high zinc supplementation above the RDA to avoid a copper/zinc imbalance. Supplementation with quantities of zinc above the suggested upper limit can result in copper deficiency, suppress the immune system, increase the risk for metastatic prostate cancer and impair behavior.[5,20] Interestingly, the original AREDS formulation provides copper in the form of cupric oxide. However, animal studies have shown that the bioavailability of this form of copper "is not significantly different from zero."[21]

Practitioners who are still recommending the original AREDS formula or AREDS2 with the higher zinc levels (80mg vs. 25mg) to all patients with AMD without taking into consideration the stage of the disease, or the nutritional status of the patient, could potentially be doing more harm than good.

My recommendation as an optometrist as well as a certified nutrition consultant: Consider the nutritional status of the patient and opt for an AREDS2 formulation with lower zinc and a form of copper other than cupric oxide when indicated.

AREDS Report Number 38, claiming that the 27 comparisons made by Chew et al., many with small sample sizes, were not clinically interpretable.[31,32]

Awh et al. subsequently analyzed 989 white participants from the same AREDS trial and defined four categories of risk variants based on alleles at CFH and ARMS2. Their findings showed that patients with a high CFH risk and no ARMS2 risk treated with the AREDS formula had a 135% increased AMD progression compared to those treated with placebo. Also, patients with a low CFH risk allele and a high ARMS2 risk allele had a 37% decreased AMD progression if treated with the AREDS formula compared to placebo.

They presented their research at the American Society of Retinal Specialists annual meeting in September 2014 and then later published their findings in 2015.[32] They recommended using genotype-directed nutritional supplementation for high-risk patients, specifically to identify the highest risk patients—those homozygous for CFH without ARMS2 risk alleles.

Dueling Statisticians

Most recently, Chew et al. have responded, criticizing Awh et al. for presenting results that they characterize as biased, and therefore difficult to interpret.[33] Awh et al. had acknowledged the following in their conclusions: "Validation by an independent data set would be helpful, but no such data set exists, and a replication trial would take years."[30,32] However, a data set was recently made available to the NEI AREDS researchers. Chew et al. had access to an additional 526 patients from the AREDS trial with the same qualifications used by Awh et al., a residual cohort whose DNA had recently become available. The demographics from the Awh et al. test data and Chew et al. validation sets are almost the same. If Awh et al. were correct in their conclusions, the findings from the residual cohort would serve to validate them.

Chew et al. analyzed the 526 patients in the residual cohort using the same four genetic groupings developed and used by Awh et al., and their findings did not, in fact, validate the findings by Awh et al. They reported that the combination of antioxidants plus zinc was beneficial in all genetic subtypes described by Awh et al.[33]

Based on the latest findings by Chew et al., the NEI concluded that because the findings by Awh et al. were not verified by the results of the residual cohort, genetic testing prior to treatment with AREDS supplements is not recommended.[33]

This debate between Awh et al. and Chew et al., which has played out in meetings and journals for several years, has caused much confusion and frustration for clinicians. Beyond the disagreements over data, claims of potential conflict of interest have been made on both sides.[34] Such allegations—whether warranted or unwarranted—further muddle the arguments being made by introducing another dimension to the debate.

Clinical Applications

Both sides of the debate are quick to point out flaws in the other side's data analysis hinging on such esoteric issues as "Bonferroni corrections for multiple comparisons."

So, how should clinicians—who are not experts in trial design, genetics, or statistical analysis—interpret these conflicting results? Information from three credible resources may provide assistance in answering this question.

The first source, a 2015 review from Bascom Palmer Eye Institute, concluded that the balance of available evidence does not support the use of genetic screening to guide clinical decisions in AMD patients at this time.[35] The Bascom Palmer doctors pointed out that many of the subgroups analyzed on both sides of the debate were too small for statistical significance. They also noted that retrospective subgroup analysis is not the same thing as a prospective RCT, such as the AREDS trial. The likelihood of inadvertent selection bias, resulting in statistically significant but clinically meaningless associations, increases with the number of subgroups. They further pointed out that it was the original AREDS formula and not AREDS2 that was used in the studies.

The second source is an article by Edwin Stone, MD, PhD, a researcher and professor at the University of Iowa Carver College of Medicine with over 25 years' experience in studying the interplay between genes and eye disease. Dr. Stone is the director of the University's Center for Macular Degeneration and the Nonprofit Genetic Testing Laboratory. He also headed the AAO's task force on genetic testing.

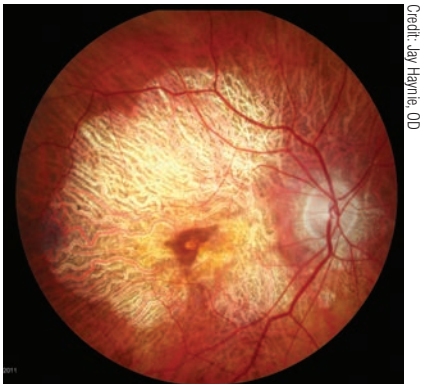
In a May 2015 article in *JAMA Ophthalmology* ("Genetic Testing for Age-related Macular Degeneration Not Indicated Now"), he wrote, "I think that it is very important for all ophthalmologists (and optometrists) to recognize that the burden of proof of this hypothesis (that specific genotypes are associated with different responses to antioxidants plus zinc) lies with Awh and his colleagues; there is no burden of disproof for the AREDS investigators or, for that matter, anyone else in the scientific community. I continue to recommend AREDS vitamin supplementation to my patients with AMD, regardless of their genotype. I believe that all hypotheses about the clinical utility of genetic testing for AMD should be tested in a prospective fashion, with participants randomly assigned to groups that receive either conventional care or genotype-guided care. If, in such a prospective study, the clinical outcomes of the genotype-guided groups are significantly better than the clinical outcomes of the conventionally managed groups, this, and only this, will be meaningful evidence in favor of using genetic testing to help care for patients with AMD."[24]

Dr. Stone reported no financial conflicts of interest. He does have a personal interest in AMD because both of his maternal grandparents lost substantial vision to the disease.

Recently, a report by University of Toronto biostatistician Rafal Kustra, PhD, in a Canadian online journal, concluded that the raw data in the NEI's AREDS Report Number 38 actually supported the contention that 19% of patients had the genotypes that appear to fare worse on the supplement than placebo.[34] In a personal communication, Dr. Stone noted that this study did not prompt a rethinking of his conclusions in the *JAMA Ophthalmology* article.[36]

The third source to illuminate the genetic testing and AMD supplementation question is a lecture given at the American Academy of Optometry's annual meeting in October 2015 by Stuart Richer, OD, PhD, which presented slides from both Dr. Awh and Dr. Chew that contradicted each other's research.[37]

Dr. Richer then summarized options for doctors. One point concerned the dose of zinc in the original AREDS formula and the negative associations for lack of efficacy for the homozygous CFH/null ARMS2 subgroup, noted by Dr. Awh and several other researchers and biostatisticians. Dr. Richer explained that, from the AREDS2 conclusions, lowering the zinc dosage did not statistically diminish the efficacy of the formula, albeit in an older and sicker group of patients compared to AREDS. Therefore, using a lower zinc formula is one option for doctors to consider. Another option, he noted, was to offer a one-time genetic test to monocular patients "to [possibly] avoid a zinc hyperimmune response in one-seventh of all high-risk AMD patients."



Credit: Jay Haynie, OD

Dry AMD patients require ongoing education about nutrition and other influences on their ocular status.

All three sources pointed out the importance of pharmacogenetics and that more research needs to be done to further elucidate the very important role it will likely have in AMD.

As a clinician on the front lines caring for patients with AMD, the following considerations come to mind when deciding treatment:

- The original AREDS study was a prospective RCT that showed a benefit for patients with intermediate to advanced AMD.
- The AREDS2 formula with lutein and zeaxanthin was shown to have an additional beneficial effect beyond that of the original AREDS.
- The studies by Awh et al. and Chew et al. were conducted on the original AREDS formula with higher zinc levels.

• Lowering the zinc dosage in the AREDS2 formula did not decrease efficacy for the "average" patient.

Last but not least, consider your patient's eye health in relation to their total well-being. Although some practitioners use genetic testing to guide follow-ups with their AMD patients, this should not be offered without counseling and consideration of the psychological risks. For example, fear or unfamiliarity of genetic testing could cause some patients with very low-risk genotypes to defer appointments, which could increase their risk of vision loss. Meanwhile, other patients with high-risk genotypes may worry for 20 years yet never go on to develop clinically significant vision loss. ■

Dr. Poteet holds an MS in human nutrition, is a certified nutrition consultant and a fellow of the Ocular Nutrition Society. She currently practices in Atlanta, Ga.

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The Dilation Dilemma

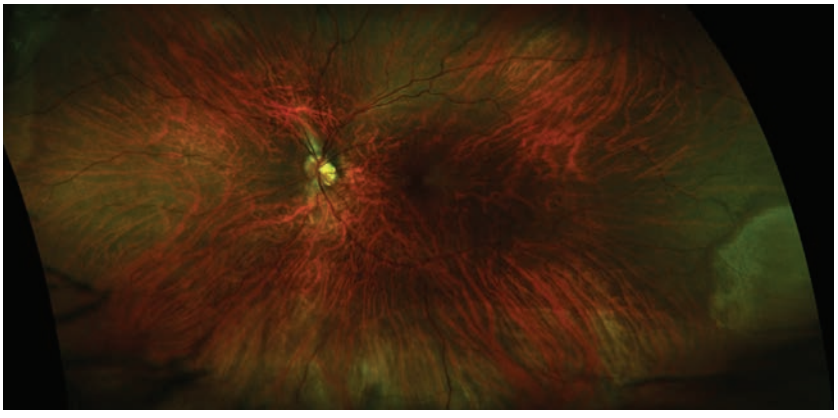
Advances in imaging have allowed for greater patient convenience and satisfaction. But are they a substitute for the tried-and-true practice of dilation?

By Jessica Steen, OD

No one would dispute that dilation is indicated for a patient who presents with acute-onset photopsia in the presence of floaters—but would you dilate a healthy, asymptomatic 25-year-old female optometrist with best-corrected visual acuity of 20/15 in each eye who presents solely for an updated glasses prescription?[1] Would your recommendation change if she had refractive error of -7.00D in each eye, and her last normal peripheral retinal examination was performed one year prior?

Advances in technology have given optometrists the ability to better view the posterior segment without subjecting patients to dilation. In particular, the development of ultra-widefield imaging (UWFI) by companies such as Optos, Centervue and Heidelberg Engineering provides optometrists with an adjunctive tool of objective retinal documentation. For asymptomatic patients undergoing routine eye examination, we may ask ourselves if dilation is really necessary. Are ancillary procedures such as UWFI appropriate substitutes for dilation in low-risk patients?

Pupillary dilation is essential for the thorough stereoscopic assessment of ocular health, including peripheral fundus examination.[2] In the state of Florida, pupillary dilation is required by law for all patients undergoing an initial comprehensive eye examination.[3]



Ultra-widefield image of clinically diagnosed inferior retinal break with shallow retinal detachment not apparent in image.

Given that malpractice litigation against optometrists is frequently based on the misdiagnosis of retinal pathology due to failure to dilate, and that eye care professionals have had access to diagnostic topical agents in some states since the early 1970s, it is striking that such significant dialogue in eye care still exists regarding the pertinence and frequency of routine dilation.[4,5]

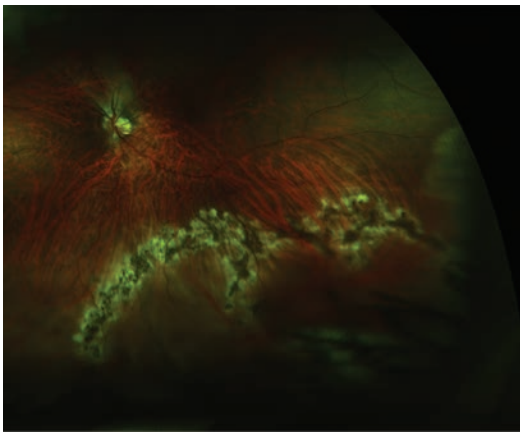
How Frequent is Enough?

Evidence-based clinical practice guidelines on the frequency of dilated fundus examinations have been well established in patients with concomitant systemic disease (e.g., diabetes mellitus) and ocular disease risk factors such as primary open angle glaucoma, lattice degeneration and posterior vitreous detachment.[1,6]

The American Optometric Association's 2015 evidence-based clinical practice guideline states that pharmacological dilation is generally required for the thorough evaluation of ocular structures.[2] For patients between the ages of 18 and 39, a comprehensive eye examination including ocular health evaluation is recommended at least every two years.[2] For patients age 65 and older, comprehensive eye examinations are recommended annually in the absence of a diagnosed ocular condition.[2] More frequent monitoring with dilation is indicated in a patient with a previous diagnosis of ocular pathology, or if the patient

is at risk for developing ocular disease, and if there is a change in patient symptomatology such as new onset photopsia, floaters or vision loss[1,2,7,8]

Although the presence of symptoms—including visual changes, flashes of light or floaters—may affect the frequency of dilation, it should not be the only indication for dilation of a patient otherwise considered to be at "low risk" for retinal pathology.[1,2]



Post-treatment UWFI of the same patient.

In a population-based analysis of patients age 40 or older, 2.39% of patients with normal baseline eye examination experienced vision loss (visual acuity less than 20/40 or visual field loss) over a five-year period without follow-up examination that included dilation during that time period.[7] Researchers recently determined that only 4% of adult patients who presented for routine eye exam had peripheral retinal pathology requiring treatment that would have gone undiagnosed without pupillary dilation.[8] As such, the clinical utility and cost effectiveness of routine dilation, in the absence of a known pathology, is sometimes brought into question.[7,8] It is increasingly common for some practitioners to offer UWFI as an alternative to a dilated exam. Doing so must include a full explanation of the trade-offs, and this does not absolve you of responsibility to arrive at a diagnosis even in the absence of evidence of pathology on UWFI.

Keep in mind that, although helpful, guidelines are just that. Clinical acumen will guide the practitioner when more frequent dilation is necessary. However, if in doubt, the most appropriate course of action is to dilate for all of your fundus examinations.

UWFI vs. Peripheral Exam?

Ultra-widefield imaging devices have the capacity to document peripheral retinal pathology, providing up to a 200-degree temporal and nasal imaging field and the ability to image up to 82% of the retina.[9] However, retinal lesions located anterior to the equator are likely to be missed by doctors using UWFI alone.[10] Researchers have determined this technology to have reduced sensitivity (36%) for the detection of the lesions compared with binocular indirect ophthalmoscopy using scleral indentation (76%), and concluded that ultra-widefield imaging alone is not sufficient for making a clinical diagnosis.[10]

Advantages of UFWI

Applications of ultra-widefield imaging have been expanded and applied to fluorescein angiography (FA), indocyanine green angiography, and fundus autofluorescence (FAF).[9] In patients with diabetes, UWFI in fluorescein angiography has been proven to be advantageous over the seven standard mydriatic stereoscopic 30-degree images that were used by the Early Treatment Diabetic Retinopathy Study (ETDRS).[11,12] Research comparing ultra-widefield and standard techniques identified retinal non-perfusion and neovascularization in an additional 10% of eyes, which would have otherwise been missed with standard imaging techniques alone.[11]

Research also shows that non-mydriatic ultra-widefield imaging correlates well with the ETDRS seven standard 30-degree field fundus photography for the identification of diabetic retinopathy.[13] Additionally, diabetic retinopathy was identified 17% more frequently in non-mydriatric ultra-widefield imaging as compared with the ETDRS standard.[14,15]

Limitations of UWFI

UWFI possesses its own set of drawbacks relative to traditional fundus photography methods. The lack of "true-color" images, due to the use of red and green scanning lasers, may limit interpretation compared with traditional fundus photography.[9]

The technology's most clinically significant limitation is its inability to image the entire retina.[9] Recall that 18% of the retinal area cannot be imaged through a dilated pupil with current ultra-widefield technology.[9] Additionally, the lack of sensitivity to retinal lesions anterior to the equator compared with clinical examination means that UWFI is not apt to detect retinal holes and breaks, especially anterior to the equator in the superior and inferior quadrants, and is therefore recommended only as an adjunct to a dilated fundus exam that includes careful peripheral retinal examination.[9,10,16]

The Role of Ancillary Testing

To patients and professionals alike, new technology is often equated with better quality of care.[17] However, the cost of new devices may create financial pressure for practitioners to incorporate their use into routine evaluation.[18] Performing ancillary tests for screening purposes without regard to a patient's individual clinical presentation or clinical history without reasonably expected benefit can be construed as unnecessary and unethical.[19] This may be particularly concerning when practitioners profit from performing such tests.[18-20]

Ancillary procedures that lack a medical indication are not covered by most insurance plans, including Medicare, requiring the overall cost to be borne by the patient. If done under circumstances that do not offer a patient benefit, such testing runs the risk of been called exploitative.[18-20] Of course, on an individual basis, the same test may indeed be necessary or justifiable. For instance, UWFI screening may reveal pathology or raise suspicion that warrants additional clinical investigation, or the patient may prefer the convenience of avoiding a dilated exam and be willing to accept it when properly educated about the different testing methods available. Regardless, the determination of necessity of ancillary testing cannot occur without a complete clinical evaluation.[20,21]

The standard of care in medical practice evolves from the behavior of physicians.[22] Choosing to perform ancillary tests for screening purposes should not supplant a thorough clinical exam and full patient history; otherwise, the result could influence one's diagnosis or management and can establish incomplete medical decision-making protocols.[19,20,22]

Case Outcome

Our optometry colleague-turned-patient agreed with her OD's recommendation for routine dilation. Stereoscopic evaluation of the far inferior periphery of the left eye revealed pinpoint vitreous hemorrhage with associated retinal tear, and shallow retinal detachment. Documentation of the lesion with UFWI was unsuccessful because the pathology was located outside the field of view. She was promptly treated with laser photocoagulation and maintained visual acuities of 20/15 in each eye.

In this case, not only was treatable pathology uncovered in a healthy, asymptomatic patient that would have gone undiagnosed without routine dilation, but the lesion was not visible with UWFI—a close-to-home example of the technology's limitations as a primary diagnostic modality. Although cases of treatable, vision-threatening peripheral retinal pathology in asymptomatic patients are uncommon, this particular one—involving an OD—allows us to address the debate from a distinct perspective: If it were *your* eye, would you dilate? Therein lies the critical importance that education and consent play. Many low-risk patients do elect to choose UWFI as a time-saving alternative to a dilated exam without incident, after giving their informed consent, while more risk-averse patients may decline.

UWFI, including its application to fluorescein angiography and other diagnostic modalities, has provided optometrists with an expanded, objective way to document posterior segment findings as well as to better understand the role of peripheral pathology in retinal disease.[9] UWFI should augment, not replace, your own clinical acumen. Like any other diagnostic test, it should be used as a tool—not a crutch. ■

Dr. Steen is an attending optometrist and instructor of ocular pharmacology at Nova Southeastern University's College of Optometry.

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7th Annual Retina Report

Managing Patients With Hypertensive Crisis

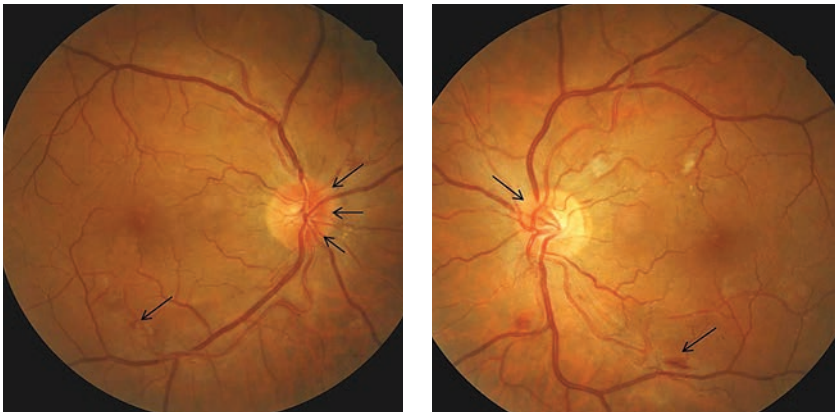
Uncontrolled blood pressure can cause visual disturbances as well as headaches. Here's how to recognize the signs. By Gurpinderjeet Kaur, OD

Hypertension is one of the most common chronic medical conditions that affects millions of Americans.[1] It is a risk factor for premature cardiovascular, renal and cerebrovascular disease, and is responsible for up to seven million deaths a year.[1,2] It is estimated that 1% to 2% of individuals with hypertension will present with acute and severe elevations in blood pressure termed "hypertensive crisis."[2] Hypertensive crisis is defined as a systolic blood pressure greater than 179mm Hg or a diastolic blood pressure greater than 109mm Hg.

This case report describes a patient who presented from the emergency department with bilateral disc edema with visual field loss secondary to uncontrolled blood pressure.

History

A 44-year-old white male was referred for a visual field deficit from the local emergency department, where he presented with complaints of visual disturbances, dizziness and a headache. His blood pressure was 195/139mm Hg. The



Figs. 1a and 1b. These fundus photos display our patient's disc edema (as shown with the black arrows) more prominent nasally and in the right eye than in the left.

Table 1. End Organ Damage in Arterial Hypertension[1]

Vasculopathy	**Cerebrovascular Damage**
• Endothelial dysfunction	• Acute hypertensive encephalopathy
• Remodeling	• Stroke
• Generalized atherosclerosis	• Intracerebral hemorrhage
• Arteriosclerotic stenosis	• Lacunar Infarction
• Aortic aneurysm	• Vascular dementia
Heart Disease	**Nephropathy**
• Left ventricular hypertrophy	• Albuminuria
• Atrial fibrillation	• Proteinuria
• Coronary microangiopathy	• Chronic renal insuffiency
• CHD, myocardial infarction	• Renal failure
• Heart failure	

1. Schmieder RE. End Organ Damage In Hypertension. Deutsches Ärzteblatt International. 2010;107(49):866-873.

patient was started on 10mg IV hydralazine to lower blood pressure over the course of several hours. CT scan of the brain showed an old, right basal ganglia lacunar infarct. The patient had a history of hypertension, but was noncompliant with his medication (due to cost).

During this examination, he reported that the right half of his vision was "missing" in both eyes—this started three days prior. Corrected visual acuities were 20/40^{-2} OD and 20/25^{-3} OS, but he missed letters on the right half of the chart. Extraocular muscles were full and smooth without restriction. Confrontation fields revealed constricted right superior quadrant in both eyes. Pupils were round and reactive to light with no relative afferent pupillary defect (RAPD). Slit lamp examination was unremarkable. Intraocular pressure was 14mm Hg OD and 15mm Hg OS. His blood pressure was 157/126mm Hg. Dilated fundus examination of the right eye showed cup-to-disc ratio of 0.25 with blurred and elevated disc margins nasally.

We discovered evidence of scattered blot hemorrhages with macular edema, narrowing of arterioles and increased arterial light reflex (*Figure 1a*). Dilated fundus examination of the left eye showed cup-to-disc ratio of 0.3 with blurred disc margins nasally as well. There was evidence of scattered cotton-wool spots, blot and flame hemorrhages, macular edema, narrowing of arterioles and increased arterial light reflex (*Figure 1b*).

Diagnosis

Based on these findings, the patient was diagnosed with bilateral disc edema secondary to hypertensive crisis. He was referred back to his primary care provider for blood pressure control and was asked to return in one week for Humphrey 24-2 visual fields. A referral to a retina specialist was recommended due to presence of macular edema. However, the patient declined due to lack of insurance.

At the one-week visit, his visual acuities improved to 20/25^{-2} OD and 20/20^{-2} OS. His blood pressure measured 120/80mm Hg. A 24-2

Table 2. Clinical Findings

Signs[3]	Pathogenesis
Arteriolar narrowing/straightening	Due to vasospasm and increased vascular tone
Copper or silver-wire arteriole changes	Results from intimal thickening, media-wall hyperplasia and hyaline degeneration of the arterioles
Arteriovenous crossing changes	Thickened arterioles compress venules.
Exudates (*Figure 2a*)	Break in inner blood-retina barrier.
Hemorrhages (*Figure 2b*)	Break in inner blood-retina barrier.
Cotton wool spots (*Figure 2b*)	Ischemia of the nerve fiber layer due to the damaged retinal microvasculature.
Elsching spots	Infarction of segments of the choriocapillaris due to severe hypertension.[4]
Siegrist streak	Linear RPE hyperplasia over infarcted choroidal arterioles.[5]
Disc edema	Elevated intracranial pressure, obstruction of axoplasmic flow.

1. Hayreh SS. Hypertensive fundus changes. In: Guyer DR, ed. Retina- Vitreous-Macula. Philadelphia: Sanders;1999:354-71.
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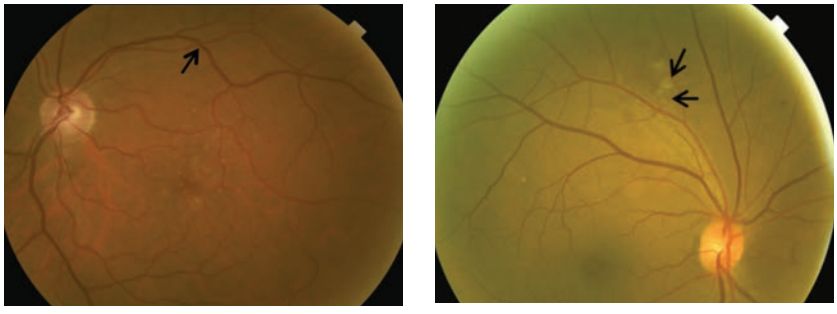
Table 2 illustrates possible clinical findings in patients with hypertensive retinopathy and their pathogenesis. The patient in this case had narrowing of arteries, hemorrhages, cotton-wool spots and bilateral disc edema. The disruption of blood-retinal barrier with degeneration of vascular smooth muscle and endothelial cell necrosis results in blood and exudation in the retina.[1,2] Hypertensive choroidopathy can occur in cases of moderate and severe hypertensive retinopathy.



Figs. 2a. and 2b. At left, this fundus image shows arteriovenous crossing changes along superior temporal arcades. At right, this fundus images shows hypertensive retinopathy with retinal hemorrhages and cotton-wool spots.

visual field showed right homonymous hemianopia (*Figure 3a*).

It was unclear if the visual field defect was new or secondary to the pre-existing basal ganglia infarct.

The patient was asked to return in three weeks to repeat the visual field test and dilated fundus examination. The patient reported an improvement in the vision in his left eye. His visual acuities improved to $20/25^{+1}$ OD and $20/20^{-2}$ OS. Visual fields showed improvement in the field defect in the right eye with a stable defect in the left (*Figure 3b*). A dilated fundus examination showed improvement in hemorrhages and cotton-wool spots.

He was advised to continue seeing his primary care provider to maintain control of his blood pressure. We asked him to return in six weeks for a follow-up. He was also referred for a low vision consult due to visual field defects.

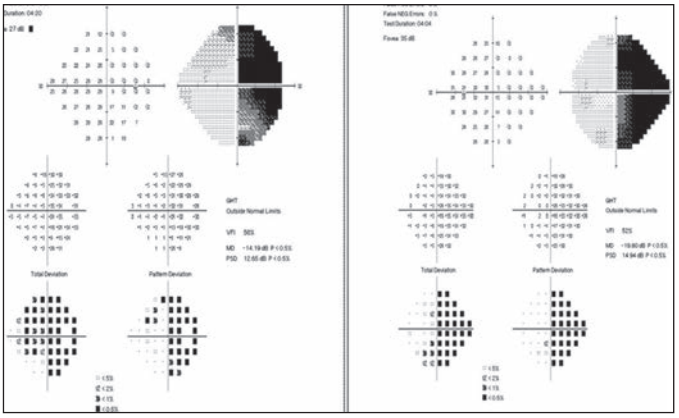


Fig. 3a. 24-2 Humphrey visual field revealed right homonymous hemianopia.

Discussion

Chronic and acute hypertension are established risk factors for cardiovascular, cerebrovascular, renal disease, organ damage and significant morbidity.[1] According to researchers, patients with a systolic blood pressure greater than 179mm Hg or a diastolic blood pressure greater than 109mm Hg are considered to have a "hypertensive crisis." The term "malignant hypertension" has been removed from national and international blood pressure control guidelines and the status is best referred to as a hypertensive crisis.[1]

Hypertensive crises can be further classified as either "hypertensive emergency" or "hypertensive urgency."[2,3] Hypertensive emergency is characterized by severe elevations in blood pressure with acute end-organ damage.[3] Hypertensive urgency does not have associated end-organ damage.[4]

Major end-organ damage can include aortic aneurysm, myocardial infarction, stroke and renal failure (*Table 1*).

Ocular Complications and Pathogenesis

Retinopathy is the most common sign of hypertension in the eye. The Beaver Dam Eye Study estimated that 10.7% of hypertensive patients older than age 40 have hypertensive retinopathy and, over a five-year follow-up period, 6% of those who had normal retinal exams developed hypertensive retinopathy.

A 2001 study suggested a more recent, three-grade classification of hypertensive retinopathy.[8,9] In this approach, "mild" hypertensive retinopathy includes generalized and focal arteriolar narrowing, arteriovenous nicking and arteriolar wall opacification. "Moderate" includes mild retinopathy signs plus flame or blot hemorrhages, cotton-wool spots, hard exudates or microaneurysms. "Severe" hypertensive retinopathy includes the signs of moderate retinopathy associated with optic disc swelling.

Table 2 on page 59 illustrates possible clinical findings in patients with hypertensive retinopathy and their pathogenesis. The patient described in this case report had narrowing of arteries, hemorrhages, cotton-wool spots and bilateral disc edema. The disruption of blood-retinal barrier with degeneration of vascular smooth muscle and endothelial cell necrosis results in blood and exudation in the retina.[7,8] Hypertensive choroidopathy can occur in cases of moderate and severe hypertensive retinopathy.

Management

More than 65 million Americans have hypertension, and half of those don't have it under control.[9] Patients with hypertensive retinopathy need to be properly counseled on the underlying condition. Patients with blood pressure of 180/110mm Hg or higher should be referred to the local emergency department.

It is yet unknown if patients can progress from hypertensive urgency to hypertensive emergency.[3,10] The latter requires immediate blood pressure control in an inpatient setting, whereas blood pressure elevation in hypertensive urgency can be reduced more slowly, and inpatient treatment is not necessarily required.[15] In hypertensive emergency, blood pressure is titrated by 10% to 25% within the first four hours of intravenous therapy. The goal is to decrease the diastolic blood pressure to between 100mm Hg and 110mm Hg.[3]

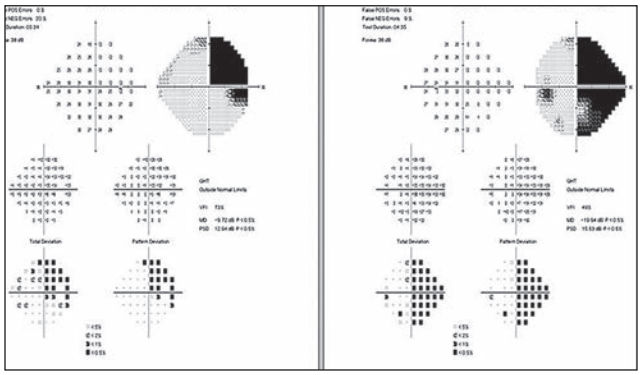


Fig. 3b. Visual field three weeks after initial visit. Visual field in the right eye had improved, but the left remained unchanged.

Mild hypertensive retinopathy will typically regress over six to 12 months with strict control of blood pressure under the care of a primary care practitioner. Poor control of blood pressure will delay the regression of retinopathy. A series of case studies show progressive reduction in retinal hemorrhages, exudates, cotton-wool spots and macular star in patients with persistent retinopathy secondary to hypertensive crises with intravitreal bevacizumab injection.[12,13]

As primary eye care physicians, optometrists may be the first to see hypertensive changes in patients who are undiagnosed with this condition. Routinely checking blood pressure in the optometric practice will assist the clinician to make an appropriate diagnosis and referral in a timely manner. ■

Dr. Kaur is on staff at Louis Stokes VA Medical Center in Cleveland, Ohio.

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Can You Identify These Vitreous Anomalies?

The vitreous is critical to ocular diseases and their prognoses. Learn the techniques to make examination a breeze, and better identify and manage common aberrations.

By Bisant A. Labib, OD

The vitreous gel composes 80% of the total volume of the eye, making it the largest ocular structure.[1] It serves many important functions, such as acting as a shock absorber, maintaining the retina and choroid in direct apposition, storing and transferring nutrients to the posterior segment of the eye, and finally in transmitting and refracting light to aid in focus on the retina.[2]

Recent emphasis has been placed on the role of the vitreous in the prognosis of retinal disorders such as macular degeneration, making its examination of great clinical value. With its high concentration of water and its transparency, this important structure is often under examined and thus the identification of its various pathologies may be overlooked.

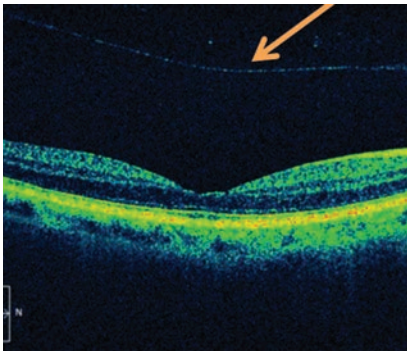

Fig. 1. OCT image displaying a posterior vitreous detachment (denoted with arrow).

The Aging Vitreous

At birth, vitreous composition is made up of a rigid, hydrophilic and homogenous gel containing more than 98% water, as well as a matrix of collagen fibrils, hyaluronic acid (HA), proteoglycans (PGs) and glycoproteins (GPs).[1,7] It is the precise spacing of the collagen and HA network that creates the structure of the gel, allowing for its transparency and strong adherence to the underlying retina.[8]

Liquefaction of the vitreous (synchysis) occurs as we age, and

Release Date: June 2016
Expiration Date: June 15, 2019
Goal Statement: Although the vitreous humor comprises the largest ocular cavity, it is an optically clear structure, which makes it difficult to routinely examine. This course provides an overview on examination techniques as well as the identification and management of common vitreous anomalies. It also emphasizes the importance of careful examination of the vitreous, as this structure plays an integral role in the pathogenesis and prognosis of many retinal disorders.
Faculty/Editorial Board: Bisant A. Labib, OD
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Disclosure Statement: The authors have no relationships to disclose.

may begin as early as age four as evidenced through ultrasonographic studies; more than 50% of the vitreous liquefies by 80 years of age.[9,10] The process of liquefaction is multifactorial and not well understood. Several of these mechanisms include damage wrought by oxidative stress through free radical formation, mechanical stress from ocular movementsand enzymatic breakdown of the collagen meshwork.[1,11-13]

Vitreous syneresis (condensing or collapsing of the gel) concurrently occurs with age, and is what ultimately causes weakening of vitreoretinal adhesion at multiple sites. These processes occur over several years to decades.[4]

Age-Related Posterior Vitreous Detachment

The most common age-related vitreous change is the formation of a posterior vitreous detachment (PVD). This results from two insidious processes occurring at the vitreoretinal interface. The first is synchysis (as described above; an increase in gel liquefaction), which appears as collagen-free zones of fluid-filled pockets.[7,9,11,14] The second is syneresis (the breakdown of the collagen arrangement), which manifests as optically dense areas within the vitreous chamber.[7,14]

The combination of liquefaction with the aggregation of collagen fibrils results in weakening of the adhesion between the posterior vitreous cortex (PVC) and internal limiting membrane (ILM) of the retina at the posterior pole.[9] This then allows liquefied vitreous to enter the retrohyaloid space through either microbreaks in the thin perifoveal layer of vitreous cortex or through the prepapillary hole in the vitreous cortex.[9,15] Detachment begins first in the perifoveal region, and progresses to the superior and temporal midperiphery through gravitational effects. It then continues into the fovea, inferior midperiphery and finally to the level of the optic disc.[9] Once this process is complete, a PVD is evident clinically in the form of a visible Weiss ring.

Several classifications or stages of PVD exist, depending mainly on the method of examination, which differentiate between a complete or partial PVD, depending on degree of attachment of the cortex to the retina. In general, the first stage is an incomplete perifoveal PVD in up to three quadrants. Stage two is the progression of perifoveal PVD in all quadrants with residual attachment to the fovea, optic nerve and midperipheral retina. Stage three consists of an incomplete PVD over the posterior pole with residual attachment to the optic nerve and midperipheral retina. Finally, stage four is identified as a complete detachment.[14,16,17]

Techniques to Examine the Vitreous

Eye doctors of the past used to look right through the nearly transparent vitreous with hardly a second thought. Now, advances in imaging technology show us that the vitreous is an important ocular structure that has an integral role in a number of retinal diseases. These technologies include:

- ***Slit lamp biomicroscopy.*** Routine slit lamp examination of the anterior vitreous includes static and dynamic observation to visualize the changes in the posterior cavity. Dynamic observation allows examination of the vitreous when the cortex is displaced and before it returns to its original position, which is important in the detection of pigment in the vitreous (Schaeffer's sign), suggestive of a retinal break.[3] Static vitreous examination is reliant on the Tyndall effect, which requires maximum pupil dilation and dark adaptation.[4] To examine the posterior vitreous, use of a +90D lens increases the field of view to allow examination of the peripheral retina.
- ***Indirect ophthalmoscopy.*** This method allows for an extended field of view as well as stereopsis, but due to the reduced image size, only significant alterations in the vitreous are readily visible. It is also sometimes difficult to retain binocularity when viewing the far retinal periphery.[3]
- ***Contact lens biomicroscopy.*** A three-mirror Goldmann lens allows the examiner to view the entire vitreous cavity. A narrowed beam aids in minimizing the amount of glow from the underlying choroidal vasculature.[3]
- ***B-scan ultrasonography.*** In the presence of ocular media opacifications, this method uses echography to detect vitreous opacities, membranes, and areas of adhesion and traction.[3] In cases where vitreous abnormalities obscure the posterior segment of the eye, B-scan is useful in the timing and visualization of vitreoretinal surgeries.[5]
- ***Optical coherence tomography.*** While OCT is commonly used for macular disease and glaucoma progression, it also offers clinicians much information on areas of vitreous attachment, traction and detachment. This is most beneficial in the detection of abnormalities at the vitreoretinal interface, such as both vitreomacular and vitreopapillary adhesion and traction. With more advanced spectral domain imaging and the use of radial scans, the stages of posterior vitreous detachment are more readily understood.[6]
- ***Magnetic resonance imaging.*** MRI is often used in eye care for identification of neurological disorders, but may also assist in diagnosis of vitreous abnormalities especially in patients with hazy ocular media. MRI is useful in developmental anomalies, such as persistent hyperplastic primary vitreous, as well as vitreous hemorrhage and liquefaction.[4]

Asteroid Hyalosis

Asteroid hyalosis (AH) is the most common clinically observed degenerative opacification of the vitreous.[47] It manifests as small, cream-colored or white spherical bodies suspended in the vitreous cavity in either a random arrangement or deposited along the collagen fibrils.[48-51] Under diffuse illumination, these asteroid bodies appear gold and are located predominantly in the inferior quadrant, oscillating with eye movement.[51]

The prevalence of AH is 1.0% to 1.2% of the population, predominantly in males, with a well-established link to increasing age.[47,50-52] AH presents unilaterally in 90% of cases and rarely impacts visual acuity.[48,50,53]

The correlation between AH and systemic conditions remains controversial. Earlier reports claimed an association between AH and diabetes, hypertension, hyperlipidemia, hyperopia, gout and increased serum calcium.[50,52] However, the Beaver Dam Eye Study did not substantiate these claims.[50] One report speculated that bilateral cases of AH have a statistically significant association in the diabetic population.[47]

While systemic associations remain inconclusive, anatomical analysis revealed a decrease in vitreous gel liquefaction and lower prevalence of complete PVD in patients with AH.[54] Additionally, AH patients who do experience PVD will have a spontaneous, anomalous PVD and associated vitreoschisis. This is due to the presence of abnormal, firm vitreoretinal adhesion.[54]

AH rarely impacts vision and patients remain relatively asymptomatic. In severe cases, the opacification may obscure the underlying retinal detail, warranting the use of additional testing, including OCT, fluorescein angiography and B-scan ultrasonography.[48] Caution should be exercised with the use of A- and B-scan ultrasonography in measuring axial length, as it has been shown to be artificially lower and may lead to significant error in calculating intraocular lens power prior to cataract extraction.[53] In the rare cases that AH does result in visual deficit, pars plana vitrectomy with phacoemulsification is an effective treatment option.[51]

The incidence of PVD increases with age and myopia.[18-20] Some 63% of patients have a PVD by their eighth decade, with an estimated onset of 10 years earlier in myopes. Other factors accelerating this process include the presence of collagen vascular diseases (e.g., Marfan syndrome or Stickler syndrome), retinal vascular disease, trauma and inflammation.[9]

Recent studies establish a link between early onset PVD in postmenopausal women due to the potential effect of decreased estrogen and subsequent decrease in hyaluronic acid synthesis.[9] PVDs are also sometimes induced following intravitreal injections, regardless of the injected agent, with a high incidence of PVD following cataract extraction.[21]

Floaters are the most commonly reported symptom of an age-related, non-pathologic PVD and result from either the aggregation of collagen into visible fibers, blood in the vitreous cavity or the glial remnant (Weiss ring) following detachment around the optic disc.[20,22] The onset of a large amount of floaters with or without associated flashes indicate a concurrent retinal break from vitreous traction at the time of detachment.[23] Flashes are reported in 50% of cases, occurring in mesopic conditions and mainly restricted to the temporal field.[16] The occurrence of flashes is less understood, but they are likely due to the vitreous traction, and the separation of vitreous and retina induced by eye movements.[20]

Although the development of a non-pathologic, age-related PVD is a benign condition, symptomatic floaters have been associated with a marked decrease in contrast sensitivity and quality of life, giving rise to the investigation of treatment modalities for symptomatic patients.[10,22] Nd:YAG laser has been used to treat the dense collagen fibers and large vitreous opacities that interfere with the visual axis, although studies reporting efficacy are inconclusive due to small sample sizes.[10] Surgical vitrectomy has also been evaluated in these symptomatic patients, resulting in small improvements in visual acuity and symptomatology.[10,22] Although minimal improvement is possible, surgical intervention is not without risk of complications, such as cataract development.[22]

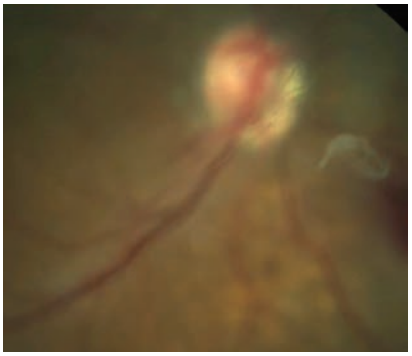

Fig. 2. Fundus photograph of posterior vitreous detachment.

Anomalous PVD

An anomalous PVD occurs when a portion of the posterior vitreous cortex remains attached to the internal limiting membrane of the retina.[16,17] The most common site of partial detachment, before progressing further and detaching fully, is the superior retina.[17] While complete PVDs commonly result from the age-related processes discussed above, an anomalous PVD may arise in cases where there is vitreous liquefaction without simultaneous dehiscence of the vitreoretinal interface.[8,9,15] This causes traction at the interface, resulting in increased risk for developing retinal breaks and detachments, epimacular membrane formation,

macular holes and vitreomacular traction.[9]

Complications vary depending on the location of the remaining area of adhesion. If liquefaction occurs with firm retinal adhesion in the periphery, a greater likelihood exists for retinal tears and detachments to develop. Remaining areas of adherence to the optic disc are more likely to promote vitreous hemorrhage or stimulate neovascularization.[14] Finally, if attachment remains in the macular region, vitreomacular traction leading to macular hole and epimacular membrane formation is more likely to arise.[14]

Anomalous posterior retinal detachment occurs in approximately 26% of cases of vitreous detachment. The incidence is even greater in patients with lattice degeneration due to the strong adherence of vitreoretinal forces at the border of lattice lesions.[8] As such, these patients should be followed for up to two years after initial diagnosis of incomplete and symptomatic PVD to assess vitreoretinal status.[20]

Other risk factors leading to anomalous posterior vitreous detachment include increased myopia (greater than -6.00D), history of trauma or surgery, other peripheral retinal degenerations (e.g., retinoschisis), and a personal or family history of retinal detachments.[9,23]

A higher frequency of complications also exists in pseudophakes or aphakes, those who experience subjective visual loss, and those with certain posterior segment findings such as retinal or vitreous hemorrhage, lattice degeneration, and the presence of "tobacco dust" in the anterior vitreous.[23] The incidence of retinal break formation following posterior vitreous detachment is estimated to be 8% to 15%, and as high as 92% in the presence of pigment within the vitreous cavity.[18]

While detachments of the posterior vireous have the potential to cause serious and sight-threatening complications, they can be protective in some cases. Without the vitreous attachment to the underlying retina, the development of neovascularization in proliferative disease, such as diabetic retinopathy, is limited.[16] Studies have also reported the efficacy of surgical PVD in the reduction of macular edema due to diabetes, vein occlusion and macular degeneration.[21] Also, the presence of complete PVD allows rhegmatogenous retinal detachments to progress much more slowly than in patients with intact vitreous.[16]

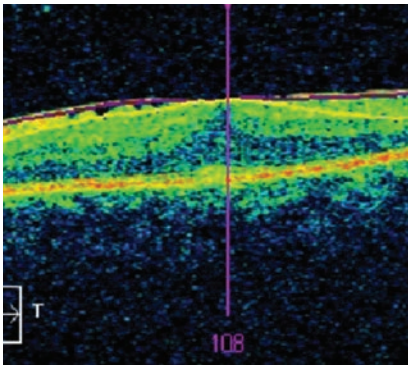

Fig. 3. OCT of an epiretinal membrane, a complication of anomalous PVD.

Vitreoschisis

Because of the remaining firm vitreoretinal attachments present in anomalous PVD, a splitting of the PVC may occur during syneresis; this is known as vitreoschisis, where the vitreous collapses forward and leaves the outermost layers adherent to the macula.[14]

In one study, 57% of patients with anomalous PVD exhibited concurrent vitreoschisis as evidenced through ultrasonographic and histopathologic studies.[24] This is possible because of the anatomy of the vitreoretinal interface. It is now well recognized that several adhesion molecules, known as the "five-substance glue," are responsible for the direct apposition of the vitreous to the retina. This matrix consists of fibronectin, laminin, opticin, chondroitin sulfate and heparin sulfate, all of which are located between the PVC and ILM and are responsible for holding the collagen fibrils in place.[14,25]

Also keep in mind the anatomy of the PVC, which is a multi-lamellar structure containing a single layer of hyalocytes. Due to the PVC's multi-lamellar composition, a vitreoschisis may occur at any level, and causing different degrees

Chemical Vitrectomy

The vitreous is bound to the retina by a matrix of collagen and proteins, including laminin and fibronectin.[40] Ocriplasmin, an injectable form of human plasmin with proteolytic activity, works on these proteins to release adhesion. It has two main mechanisms: to induce vitreous liquefaction and subsequent separation.[44] It is FDA approved for patients with symptomatic VMT and with small full-thickness macular holes (less than 400µm).[38]

Studies show resolution in 26.5% of patients with vitreomacular adhesion, and closure in 40.6% of patients with macular holes after a single injection.[44,46] It was found to be most effective in younger, female populations who are phakic.[46]

Though much less invasive than surgical pars plana vitrectomy, ocriplasmin intravitreal injections are not without side effects. The most common reported side effects are vitreous floaters, eye pain, photopsia, decreased vision or acute vision loss, dyschromatopsia or worsening of macular hole. Most of these side effects are transient and resolve within two weeks of onset; they likely affect the retinal photoreceptors as evidenced by OCT findings of transient damage to outer retinal layers, with all cases resolving.[38]

of complications.[25]

Vitreoschisis is a well-known finding in the development of proliferative diabetic retinopathy (PDR), occurring in 80% of cases.[14,24] Vitreoschisis is also prevalent in macular disease, specifically 53% of macular holes and 43% of macular pucker.[14,24-26] The occurrence of the schisis in reference to the layer of hyalocytes is presumed to play an integral role in macular hole formation in comparison with macular pucker. If the schisis occurs posterior to hyalocyte layer in the PVC, the anterior surface of the cortex will detach along with the detachment of hyalocytes, forming a macular hole. In contrast, schisis that occurs anterior to the hyalocyte layer will leave remnant hyalocytes adhering to the macula, forming a macular pucker.[26]

Besides anomalous posterior vitreous detachment, vitreoschisis may also be induced by vitreoretinal surgery, leading the surgeon to take extra care to search for membranes during peels. If removal of the PVC is incomplete following surgical intervention, it may give rise to cases of tractional retinal re-detachment and epiretinal membrane reformation.[14] As such, alterations of vitreoretinal surgical techniques are currently being evaluated.

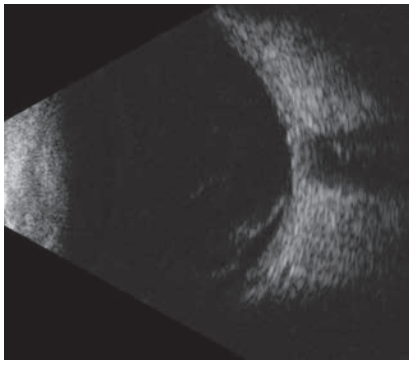

Fig. 4. B-scan image of a vitreous hemorrhage.

Vitreous Hemorrhage

Proliferative disease, notably proliferative diabetic retinopathy (PDR), is the main cause of blood in the vitreous cavity, known as vitreous hemorrhage (VH). Other identifiable causes of VH include trauma, age-related macular degeneration (AMD), vein occlusion, sickle cell retinopathy and PVD. In an estimated 8.3% of cases, the underlying cause remains unidentifiable, even following surgical vitrectomy.[27] The prevalence of acute onset VH is seven cases for every 100,000 people.[27]

The etiology of VH is important to ascertain as it often dictates the visual prognosis and management. Most patients younger than 60 have a VH secondary to a retinal tear, which releases blood into the vitreous cavity. Because the sites of vitreous attachments include retinal blood vessels, traction in this region can also release blood into the vitreous cavity. Patients with this etiology have good visual resolution and outcome without the need for surgical intervention.[27] In contrast, patients older than 60 years of age most commonly present with acute VH secondary to proliferative disease, such as PDR, AMD, sickle cell retinopathy and venous occlusion.[27]

Retinal ischemia results in hypoxia, which leads to the development of neovascularization that invades the space between the retinal and posterior vitreous, leading to traction and subsequent VH.[28] Patients with this known cause of VH have poorer visual outcome. Laser photocoagulation in conjunction with an anti-VEGF agent is recommended, and early pars plana vitrectomy in some cases is also warranted.[27,28]

Other, less common causes of VH include use of oral anticoagulants, radiation retinopathy, Terson's syndrome, anomalous PVD and carbon monoxide poisoning.[29-33] Rarely, VH can occur secondary to Ozurdex implant, iridocilliary cyst and from optocilliary vessels following chronic papilledema.[34-36]

In children with bilateral VH, it is important to first consider shaken baby syndrome, as trauma is the leading cause of the presentation in pediatric patients. Vasculitis secondary to systemic disease such as tuberculosis may also result in VH formation. Other conditions to consider are hematologic disorders, including leukemia, sickle cell anemia and thrombocytopenia. Less commonly, VH may arise from the presence and leakage of a persistent hyaloid artery. Better visual outcomes in children are found in cases of closed-globe injuries and vascular and hematologic causes.[37]

Vitreomacular Traction

When the vitreous begins to detach without subsequent separation from the macula, these vitreomacular adhesions may progress and cause morphological disturbances to the underlying retinal surface, known as vitreomacular traction (VMT). This manifests as a symptomatic vision decrease or metamorphopsia.[38,39] VMT may give rise to complications such as cystoid macular edema (CME), macular pucker, tractional macular detachment, epiretinal membrane or macular hole formation.[40]

The prevalence of VMT is 0.35% to 1.6% of the population and has been implicated in multiple disease processes, including diabetic macular edema, AMD, venous occlusion and myopic traction maculopathy.[38,41]

VMT is classified in two main categories, broad or focal, depending on the width of vitreous attachment to the retina. Broad areas of

attachment can lead to generalized macular thickness, vascular leakage on fluorescein angiography, macular schisis and cystoid macular edema. Focal attachments may elevate the foveal floor or cause pseudocysts in the central macula.[42]

Anatomical configuration and clinical course of VMT vary greatly among individuals, making it difficult to establish a treatment standard.[41] Diagnosis is made through structural changes on OCT in three stages: evidence of perifoveal vitreous cortex detachment from the retinal surface; macular attachment of the vitreous cortex within a 3mm radius of the fovea; and finally, association of attachment with distortion of the foveal surface, intraretinal structural changes, elevation of the fovea above the RPE, or a combination of these. No full-thickness interruption of the retinal layers exists.[41]

For patients with symptomatic VMT, pars plana vitrectomy is a well-documented surgical treatment. While effective, this form of intervention is invasive and has the ability to cause serious complications like cataracts, retinal detachment or endophthalmitis.[43] In 2012, ocriplasmin injection (Jetrea, ThromboGenics) was approved for the treatment of symptomatic VMT and small, full-thickness macular holes. This serine protease enzyme induces vitreous liquefaction by lysing molecular substrates connecting the vitreous to the retina, and releasing adhesion at the macula and peripapillary retina, with fewer side effects than more invasive techniques.[38,40,44] (See "Chemical Vitrectomy," page 65.)

Another study has suggested the potential use of a single intravitreal injection of C3F3 gas in patients with symptomatic and persistent VMT. Release occurred in 40% of patients within one month, and in up to 60% of cases at six-month follow up.[45]

Research has also shown that patients receiving intravitreal anti-VEGF injections can have spontaneous resolution of VMT, especially when retinal distortion is limited to the inner retinal layers. As such, it is best to watch these patients not only because of the higher rate of spontaneous resolution, but because removing the vitreous using pars plana vitrectomy will make the injected agents less effective.[41]

Although formerly known as the "vitreous humor"—one of several bodily fluids or "humors"—there's nothing humorous about the important involvement of the vitreous in a plethora of serious retinal diseases. Advanced research and improved instrumentation have now given us a clearer view of this easy-to-overlook but very important structure. ■

Dr. Labib is a full-time assistant professor at the Pennsylvania College of Optometry at Salus University, in Elkins Park, Pa., working in both the traditional optometry program as well as the accelerated scholars program.

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1. Functions of the vitreous include:
a. Transmission and storage of nutrients.
b. Shock absorbency.
c. Focusing light onto the retina.
d. All of the above.

2. What examination method is used in presence of ocular media opacities?
a. B-scan ultrasonography.
b. Optical coherence tomography.
c. Magnetic resonance imaging.
d. Both a and c.

3. Vitreous liquefaction has been documented to begin to occur at which age?
a. Four years old.
b. 20 years old.
c. 50 years old.
d. 65 years old.

4. _____ is the breakdown of the vitreous collagen arrangement and _____ is the process of gel liquefaction.
a. Synchisis, syneresis.
b. Syneresis, synchisis.
c. Vitreoschisis, synchisis.
d. Syneresis, vitreoschisis.

5. Which factor accelerates PVD formation?
a. Trauma.
b. Inflammatory conditions.
c. Collagen vascular disease.
d. All of the above.

6. The most commonly reported symptom of PVD is:
a. Flashes.
b. Floaters.
c. Orbital pain.
d. Vision loss.

7. The incidence of retinal break following PVD is approximately:
a. 1% to 2%.
b. 8% to 15%.
c. 18% to 27%.
d. 35% to 38%.

8. Remaining areas of adherence to the optic disc in an anomalous PVD promotes which condition?
a. Macular hole.
b. Peripheral retinal break.
c. Neovascularization.
d. Vitritis.

9. Attachments that remain to the macula in an anomalous PVD promotes which condition?
a. Vitreomacular traction.
b. Neovascularization.
c. Vitreous hemorrhage.
d. None of the above.

10. Which is NOT a treatment option for PVD?
a. Intravitreal injection.
b. Nd:YAG laser.
c. Observation.
d. Vitrectomy.

11. A PVD is protective in which condition?
a. Artery occlusion.
b. Ocular melanoma.
c. Asteroid hyalosis.
d. Macular edema.

12. Splitting of the posterior vitreous cortex is called?
a. Syneresis.
b. Vitreoschisis.
c. Synchisis senilis.
d. Synchisis scintillans.

13. Vitreoschisis is reported to occur in what percentage of eyes with proliferative diabetic retinopathy?
a. 60%
b. 70%
c. 80%
d. 90%

14. The leading cause of vitreous hemorrhage in patients older than 60 years of age is:
a. Age-related macular degeneration.
b. Vein occlusion.
c. Proliferative diabetic retinopathy.
d. Posterior vitreous detachment.

OSC QUIZ

15. In patients under 60 years of age, the most common cause of vitreous hemorrhage is:
a. Retinal tears.
b. Vein occlusion.
c. Leukemia.
d. Anemia.

16. Complications of vitreomacular traction include:
a. Cystoid macular edema.
b. Macular pucker.
c. Macular hole.
d. All of the above.

17. The two stages of vitreomacular traction are:
a. Small and large.
b. Focal and broad.
c. Complete and incomplete.
d. None of the above.

18. The rate of resolution of macular holes following a single injection of ocriplasmin is approximately:
a. 26.5%.
b. 34.9%.
c. 40.6%.
d. 51.2%.

19. The rate of resolution of vitreomacular adhesion following a single injection of ocriplasmin injection is approximately:
a. 40.6%.
b. 26.5%.
c. 34.9%.
d. 51.2%.

20. Asteroid hyalosis has an association with:
a. Increasing age.
b. Myopia.
c. Posterior vitreous detachment.
d. Age-related macular degeneration.

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18.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
19.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
20.	Ⓐ	Ⓑ	Ⓒ	Ⓓ

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Plug the Drain with Lacrimal Occlusion

Keep dry eye patients flowing into your office with this time-honored technique.

By Nicole Stout, OD, Abby Gillogly Harsch, OD, and Nate Lighthizer, OD

Optometry's dry eye armamentarium has increased significantly in recent years to include condition-specific artificial tears, anti-inflammatories, better lid disease treatments, amniotic membranes and autologous serum. These have all come about in an effort to treat the growing dry eye epidemic.

With all of these new treatment options available, it's easy to forget that lacrimal occlusion is a tried-and-true—and often effective—treatment for dry eye. In fact, punctal plugs have been on the market since the 1970s and have become one of the most popular minor procedures in optometry today. One of the many reasons for this is that approximately 25% of tears are lost to evaporation, while the remaining tears drain from the eyes through the minute orifices on the upper and lower eyelids known

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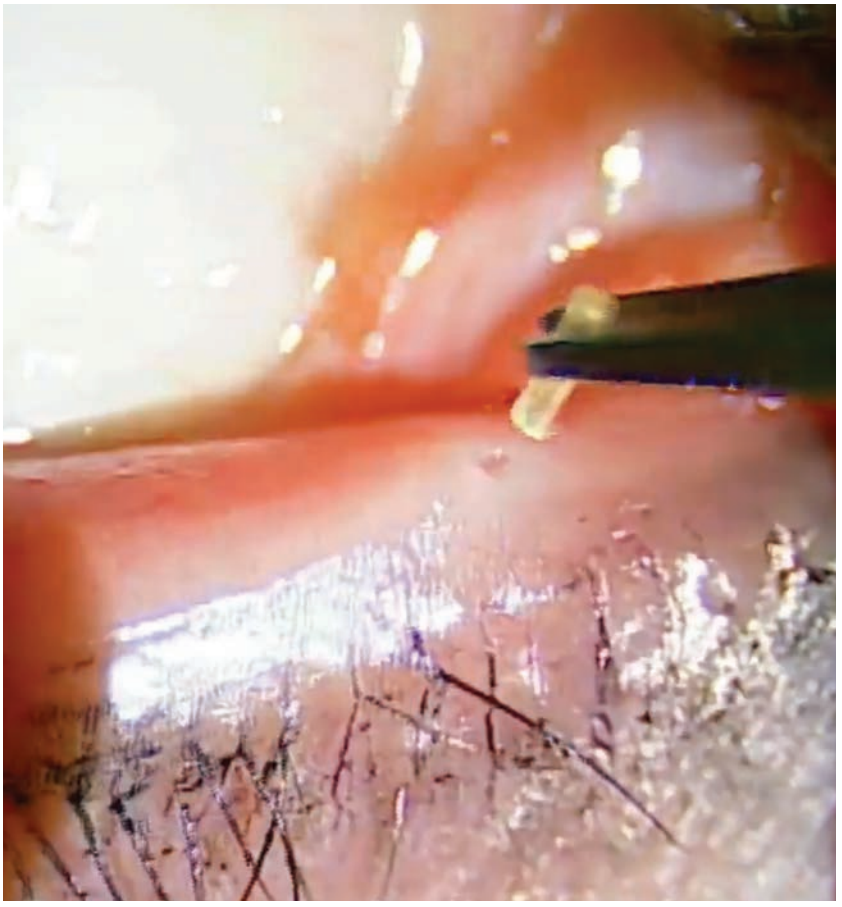

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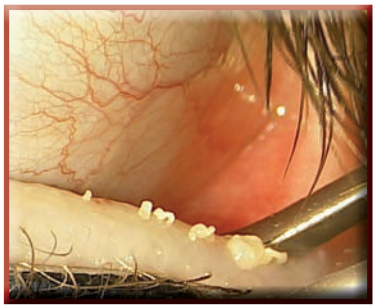

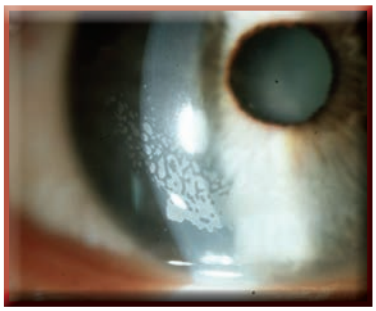

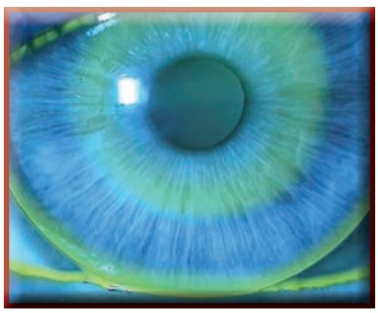

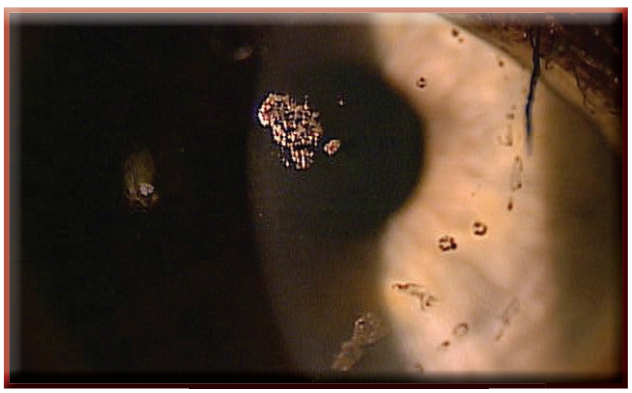

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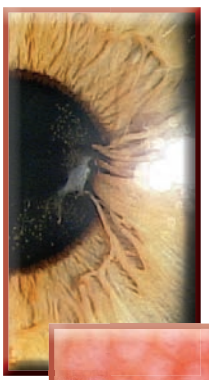

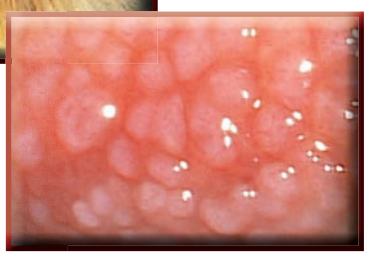

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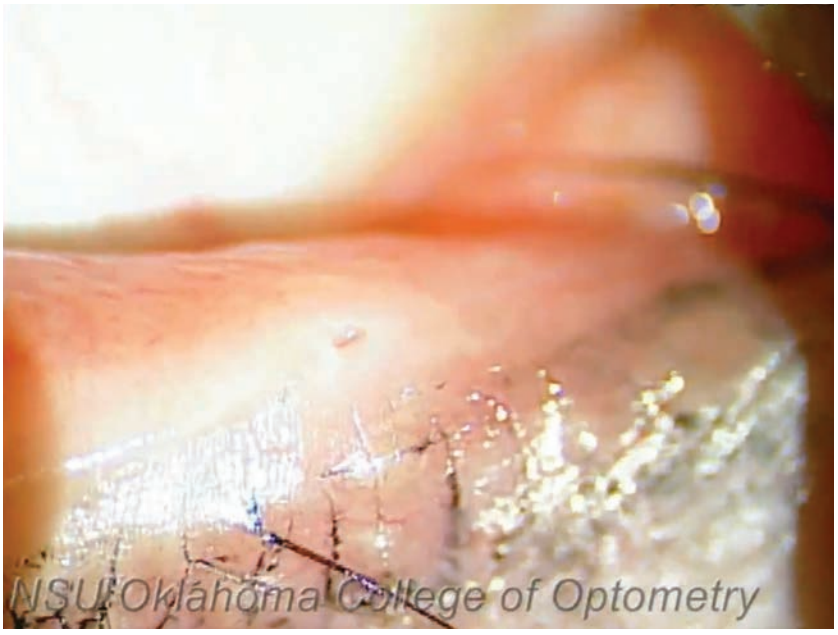
as the lacrimal puncta.

Maintaining a higher level of moisture on the eye is often achieved through temporary remedies such as artificial tears. But a more permanent method of symptom management can be achieved with the insertion of punctal plugs. The punctal ducts can be occluded with these plugs to help reduce tear drainage and thus retain moisture on the eye, bringing lasting relief to the dry eye sufferer. The growing popularity of this treatment has given way to a large variance of plug sizes, shapes and compositions.

This article examines the process of lacrimal occlusion with both intracanalicular and punctal plugs.



Here you can see the patient's punctum prior to occlusion.

Lacrimal Occlusion

The procedure is a non-pharmacological therapy used to increase the retention of the patient's own tears. It is primarily used for dry eye syndrome when relief of symptoms is not achieved with first-line treatments, such as ocular lubricants. The inhibition of tear drainage results in increased tear volume and increased contact time of natural tears on the ocular surface. The latter is why lacrimal occlusion may also be used to retain topical medications on the ocular surface.

Lacrimal occlusion may be temporary, semi-permanent or permanent and can be achieved with the use of intracanalicular plugs, punctal plugs or punctal cautery. Temporary plugs are most commonly intracanalicular and made of collagen. These plugs dissolve and are typically used diagnostically to determine if semi-permanent or permanent lacrimal occlusion should be pursued. Semi-permanent plugs tend to be made of silicone and are considered semi-permanent because they don't dissolve; however, they can be removed if necessary. Semi-permanent plugs can be punctal or intracanalicular. Permanent lacrimal occlusion is achieved via surgical intervention.

The advantage of intracanalicular plugs is that they may be less irritating to the patient after insertion than punctal plugs; however, it is not easy to confirm their presence after insertion and they can only be removed with lacrimal irrigation. Conversely, punctal plugs remain visible at the surface of the puncta, making it easy to confirm their presence after insertion and making them easy to remove with forceps if needed; however, they can fall out and they may cause minor ocular discomfort.

Patient Selection

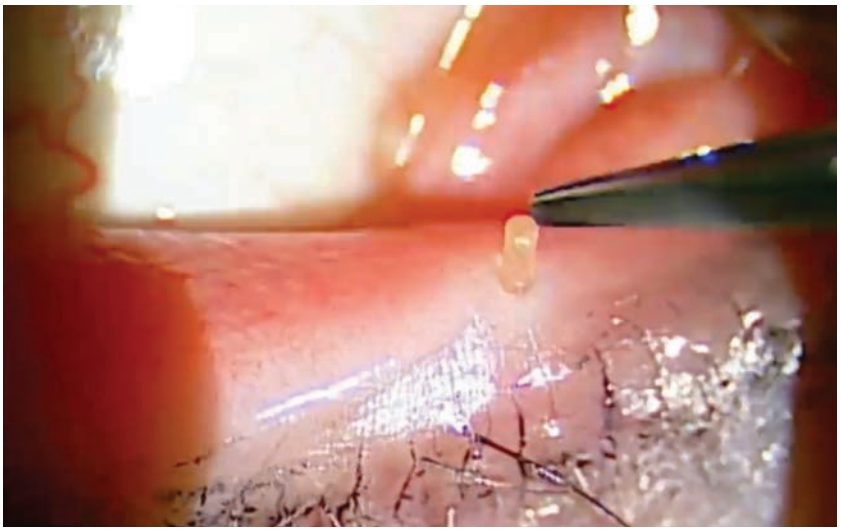
Contraindications to lacrimal occlusion include significant inflammation of the ocular surface, inflammation of the eyelids, active infection of the lacrimal system (dacryocystitis), epiphora and silicone allergy (for silicone plugs), or allergy to bovine collagen (for temporary collagen plugs).[1,2] It is advisable to ensure there is no abnormal discharge indicative of infection associated with the lacrimal drainage system by applying slight manual pressure to the area.

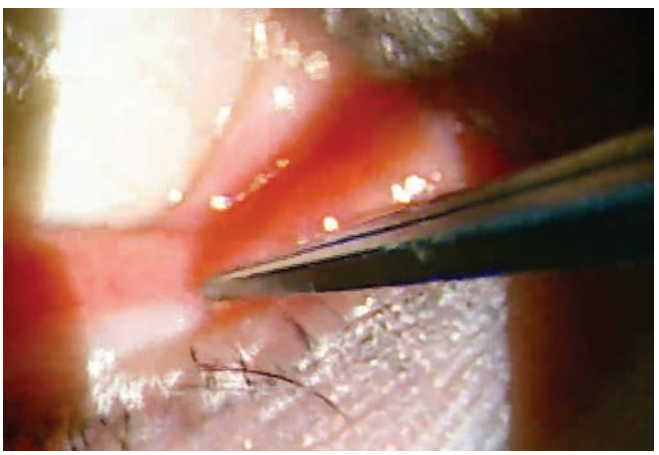
Punctal occlusion is commonly considered and highly indicated in patients with symptoms of dryness such as ocular irritation/burning sensation, redness and reflex tearing.[1,2]

Many studies report success improving patient-reported symptoms of dry eye and the procedure is considered both safe and effective when compared to artificial tear use alone.[4-6]

Young age does not contraindicate the use of punctal plugs. In fact, a study reports that punctal occlusion is safe and effective even for children with symptoms of dry eye—particularly since compliance with other treatment options such as ocular lubricants is difficult in this age group.[7]

Other indications for punctal occlusion include treatment of





Once the plug is inserted into the punctum, tap it down using the forceps. It should only take a little pressure for it to fit into place.

assorted ocular surface conditions such as pterygium, pingueculitis, blepharitis, keratitis, corneal ulcers, conjunctivitis, recurrent corneal erosions and other external ocular diseases.[1,2] The wound-healing aspect of punctal occlusion is associated with decreased frictional forces against the ocular surface.[3]

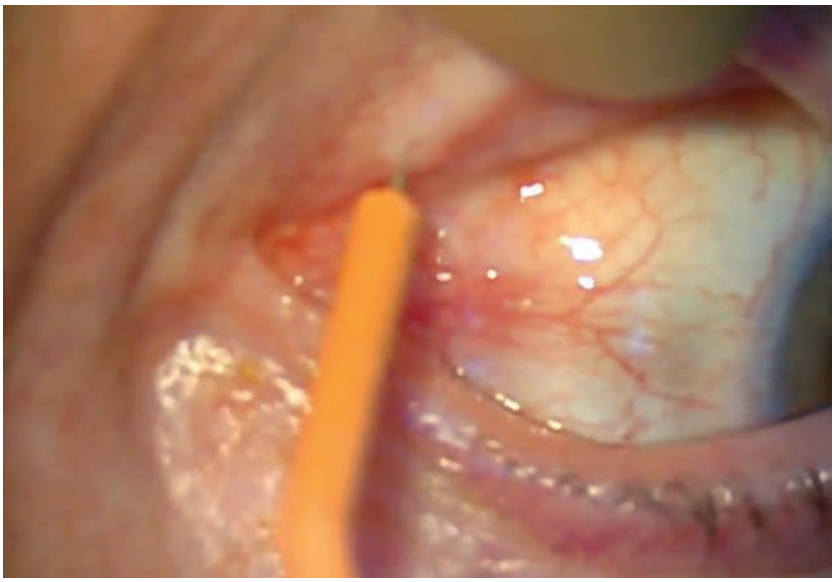
In cases of active ocular inflammation, consider the clinical picture. For example, the increased tear volume attainable through punctal occlusion may not be an acceptable treatment option in many cases of allergic conjunctivitis, as stasis of the offending allergen in the tears may increase a patient's symptoms.

Procedural Steps

Use of a topical anesthetic agent prior to punctal plug insertion is not necessary, though it can be used if desired. Two suggested methods are to either instill a drop into the conjunctival sac or to hold a cotton-tipped applicator soaked in anesthetic against the punctum for approximately 30 seconds.[2]

The following steps are common to the insertion of both intracanalicular and punctal plugs (steps are listed assuming the inferior punctum has been chosen to occlude first):

1. Instruct the patient to look up and temporally (away from the inferior punctum).



If the plugs fall out, you may consider permanently occluding the puncta. Using an Ellman unit we performed a little punctal cautery to occlude the puncta. This isn't an option in all states, but it is a procedure that takes only a matter of seconds.

2. Pull the lower lid down to expose the punctum.

3. Determine the appropriate size plug needed, either by using a punctal gauge or by careful examination, the former being preferred. The punctal gauge can determine the appropriate size (diameter) of plug. If the gauge is too small, there will be no resistance when inserting it; however, if the gauge is too large there will be a significant amount of resistance upon insertion.

4. Dilate the punctum with a punctal dilator if needed.[1-2]

Following punctal dilation, the following steps are involved in inserting intracanalicular plugs:

1. Using forceps, insert the plug partially into the punctum vertically, then pull laterally, straightening the lacrimal canal, and insert the plug the rest of the way, tilting it towards the nose.

2. Often, the plug can be released from the forceps once it is partially inserted. The tip of the forceps can then be used to push the plug the rest of the way into the punctal opening and into the canaliculus.

3. After insertion, ask the patient to blink a few times to ensure that the plug is in the correct position.

4. Repeat the procedure on the superior punctum if desired. The patient should be instructed to look down and temporally for ease of access to the superior punctum and so the patient is always looking away from where the plug is going to be inserted. To expose the superior punctum, pull the upper lid up.[1]

If inserting punctal plugs following punctal dilation:

1. Using the applicator that comes with the punctal plug, insert the plug into the punctum until the top of the plug is flush with the lid margin.

2. After insertion, ask the patient to blink a few times to ensure that the plug is in the correct position.

3. Repeat the procedure on superior punctum if desired.

a) The patient should be instructed to look down and temporally.

b) To expose the superior punctum, pull the upper lid up.[2]

Plugging In

Both collagen and silicone plugs come in a range of diameters. A common error with plug insertion is failing to use adequately sized plugs or over-dilating the punctum resulting in plug extrusion, or both. A small amount of ocular lubricant can be used on the intracanalicular or punctum plug to aid in insertion through the punctal opening.

Possible complications of lacrimal occlusion include discomfort and irritation at the site of the plug, epiphora, infection, plug migration into the lacrimal drainage system, spontaneous plug extrusion, punctal stenosis, canalicular stenosis, canaliculitis, dacryocystitis and pyogenic granuloma formation.[3]

The risk of these complications is minimal, but you'll still want to inform patients of them and advise them to return to the clinic immediately if they experience any symptoms of pain, redness or swelling.

Following plug insertion, follow up in a week or two to reassess the patient's symptoms and evaluate for side effects. Following punctal occlusion, a patient may continue using ocular lubricants and other medications.

As previously mentioned, lacrimal occlusion may increase the contact time of topical medications on the ocular surface; this may be beneficial in some cases, but you may also consider reducing the dosage of such medications when appropriate.

In the event that collagen plug removal is necessary before the plug dissolves, the intracanalicular plug can be removed by lacrimal saline irrigation—pushing the collagen plug through to the nose or throat.[1] A punctal plug can be removed by grasping it with forceps below the exposed plug head and pulling it out of the punctum.

The most common reasons to remove a plug include local discom-

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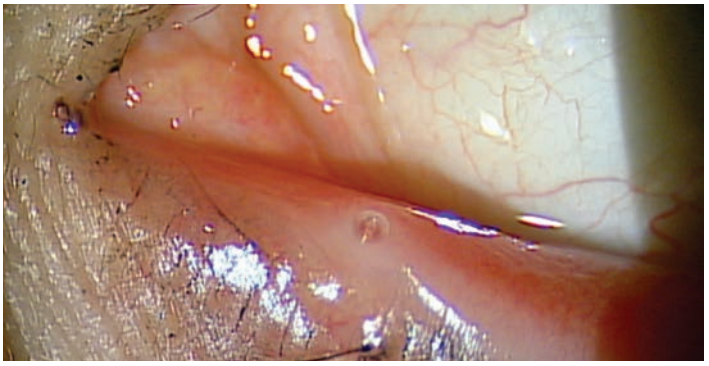

Here you can see the patient's punctum after occlusion with permanent silicone plugs.

fort and epiphora. If the lacrimal occlusion improved overall dry eye without epiphora but was irritating to the patient or spontaneously dislodged, consider punctal occlusion by cautery as an alternative (and permanent) solution. If epiphora is experienced by the patient, a plug that only partially reduces tear drainage may be considered.[2]

Lacrimal Occlusion in the Literature

Research published in *Cornea* demonstrates the effectiveness of lacrimal occlusion in a prospective double-masked study, the results of which demonstrated a 94.2% reduction in dry eye symptoms (dryness, watery eyes, itching, burning, sandy/foreign body sensation, fluctuating vision, light sensitivity) and a 93.0% reduction in conjunctival sign/symptoms (redness, discharge) at the eight-week follow-up after progressive occlusion with collagen and silicone plugs.

In contrast, the dry eye and conjunctival symptoms for the control group remained unchanged throughout the eight-week follow-up period. This study also found that eight weeks after progressive lacrimal occlusion, 76.7% of patients were relatively symptom free and 100% of patients were no longer dependent on the daily use of moisturizing agents.[8]

A 2016 study looked at symptomatic change and fluorescein staining, as well as tear cytokine levels in 29 dry eye patients prospectively. They found significant symptomatic improvement in patient-reported dryness and a decrease in staining on the ocular surface, except inferiorly. They found no decrease in the composition percentage of pro-inflammatory cytokines or MMP-9 by punctal occlusion. Due to the inflammatory nature of ocular surface disease, consider initiating anti-inflammatory therapy at the time of punctal occlusion, as opposed to delaying this treatment.[4]

In a retrospective literature review, the overall success rate of silicone punctal plug treatment was 76.8% at four weeks and the mean retention time for a silicone punctal plug was 85.1 weeks.[9]

An observational punctal plug retention and complication study shows an 84.2% three-month retention of silicone plugs, decreasing to 55.8% at two years. It also shows that canalicular stenosis was the most common complication following spontaneous plug extrusion (34.2% at two years); however, patients were asymptomatic to the clinical finding. It is presumed that mechanical stress and accumulation of debris are to blame for the stenosis. Granulomatous proliferation occurred in 3.2% of cases; their review reports that this formation is most likely to occur two to three months after plug insertion. The cause is not completely known, though mechanical injury has been suggested. Two patients in this study experienced plug intrusion as a result of the granuloma, removed under local anesthesia.[10]

With all this evidence, it is important to keep this simple procedure near the top of your list when treating dry eye patients. Don't be afraid to reach for the plugs, either canilicular or punctal. Your patients will thank you and tell their friends how you plugged their drain, improved their dry eye, and the dry eye patients will start flowing in. ■

Dr. Stout is currently completing a family practice residency with an emphasis in ocular disease at Northeastern State University Oklahoma College of Optometry.

Dr. Gillogly is currently completing a cornea and contact lens residency at Northeastern State University 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.

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2. Oasis Soft Plug Punctum Plug package insert.
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Claim Victory Over Viral Conjunctivitis

Adenovirus and herpes virus are highly contagious pathogens, but you can put a stop to them if you diagnose them quickly and manage them appropriately.

By David P. Sendrowski, OD, and John Maher, MD

Despite the widespread prevalence of herpes virus and adenovirus, their diagnosis can sometimes be deceptive and their treatment can be tricky. This article covers the basics on these vexing viruses, as well as their diagnosis and treatment—and a discussion of the do's and don'ts of using steroids.

Viral Conjunctivitis Basics

• ***HSV keratitis.*** Keratitis caused by herpes simplex virus (HSV) is the most common cause of cornea-derived blindness in developed nations.[1] There are approximately 20,000 new HSV keratitis cases and 48,000 recurrences reported annually in the United States, with a national prevalence of 400,000.[2]

Humans are the only natural host of herpes. These viruses are ubiquitous—in most parts of the world human exposure to HSV-1 is almost universal by late adulthood with a high percentage of exposure occurring in childhood.[1]

HSVs have an affinity for the sensory ganglion cells and are referred to as "neurotropic" viruses. HSV is commonly divided into Types I and II; Type I typically occurs in the orolabial area and Type II typically in the genital area. Recent studies suggest that this difference is decreasing with time.[3]

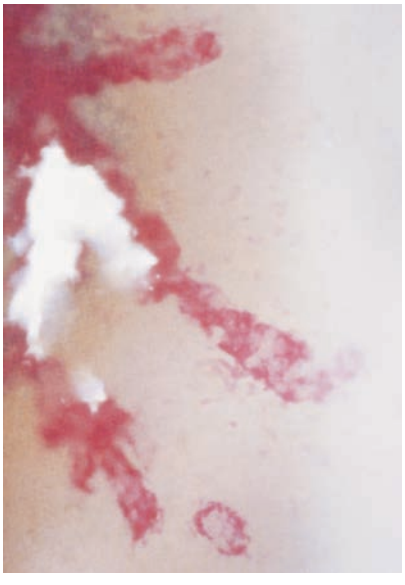

Fig. 1. Rose bengal stain of herpes simplex ulcer shows peripheral infected cells which pick up greater stain.

The source of infection is typically through direct contact with infected lesions, salivary droplets from children or adults with active disease (i.e., cold sores), or from asymptomatic virus-shedding carriers.[4]

Iatrogenic sources of patient infection occur from doctors' unwashed hands and contaminated applanation tonometer heads. HSV is viable up to two hours on a dry tonometer head and eight hours on one that is moist.[5] Swabbing the tonometer head with 70% isopropyl alcohol is almost 100% effective at killing the virus; this should be done between patients along with hand washing with a soapy solution.[6]

• ***Adenoviral conjunctivitis.*** Adenoviral infections are the most common cause for red eye visits to the doctor's office. Approximately 70% of all cases of acute conjunctivitis present to either primary care or urgent care centers. Optometry and ophthalmology practices see only about 20% of these types of cases.[7]

The spectrum of disease severity varies with the serotypes: 1 to 11

and 19 are commonly restricted to the eye and cause follicular conjunctivitis, whereas serotypes 3 to 5 and 7 cause pharyngoconjunctival fever. Serotypes 8, 9 and 37 commonly cause the classic epidemic keratoconjunctivitis (EKC).[8]

Adenoviral infections consist of a biphasic process during which the infectious phase is followed by a variable inflammatory phase. The inflammatory phase tends to begin approximately seven to 10 days post-infection. In the later inflammatory phase, it becomes harder to halt the viral production and shedding.[9,10] The virus can be shed for approximately two to three weeks following the infection.[1]

Adenovirus is a hardy and easily transmissible virus, spreading commonly through hand to eye contact, respiratory droplets and contact with contaminated surfaces or persons involved in primary eye care with other patients.[10] Intrafamilial attack rates may vary between 10% to 50%.[10]

Diagnosis of Viral Eye Disease

The diagnosis of HSV and adenoviral infections manifest in patients with early biomicroscopic signs in the conjunctiva.

• ***HSV diagnosis.*** HSV keratitis patients commonly complain of a recent onset foreign body sensation with associated photophobia, variable pain/irritation, burning, lacrimation and ocular hyperemia. Questioning the patient about recurrent eye infections is helpful when differentiating HSV early on from other acute red eyes.

Herpetic keratitis usually manifests only in one eye, but bilateral infection can happen. This should bring into question whether the patient is immunocompromised or whether the diagnosis of HSV is the underlying disorder.[11]

Do's and Don'ts of Using Steroids for Viral Eye Infections

Steroids have been known to prolong the persistence of viral infection in the cornea, enhance adenoviral replication, prolong viral shedding and lead to a long lasting dry eye.[17,18]

Then again, steroids are often used for comfort and symptomatic ocular relief by addressing pain and suppressing conjunctival and corneal inflammation. Here's how to use steroids effectively and safely for viral presentations:

Because adenoviral conjunctivitis and keratoconjunctivitis are self-limiting entities, supportive therapy is a reasonable approach. One study showed 36% of surveyed practitioners will always use corticosteroid drops while others never use them. The remaining doctors will use them under certain criteria: central infiltrates that decrease vision, intractable pain or the presence of a pseudomembrane.[19] A judicious case-by-case approach seems warranted. Many patients with only moderate discomfort appreciate the relief of steroids. If inflammation persists for four or more weeks on the corticosteroids, then their use may be tapered off with the admonition that the disease will "just have to run its course."

In a patient who is still contagious, the use of topical corticosteroids can inhibit cell shedding, leading to a prolonged clinical course.[20,21] Research suggests that normal adenovirus clearance is inhibited by the strong anti-inflammatory and anti-immune effects of the corticosteroid.

Steroids are typically avoided with herpetic epithelial keratoconjunctivitis or with an epitheliopathy suggestive of *Acanthamoeba*. The clinical signs of this infection are subtle, although the symptoms of discomfort are more severe and out of proportion. *Acanthamoeba* keratitis is slow growing and if steroids are mistakenly used, they can be discontinued before extensive damage has been done, as long as the clinician is aware of the possibility. The severe cases of *Acanthamoeba* have usually occurred after prolonged treatment and where the possibility of this organism was discounted or not considered.

Finally, steroids should not be used with presumed fungal keratoconjunctivitis, although these are rare and the clinical picture is usually unambiguous.

Side effects of corticosteroids include cataracts and glaucoma. The former problem may take many months to occur; however, as the use of the drops continues in middle-aged or older patients, the clinician runs the risk that a normal age-related cataract may be mistaken for an iatrogenic cataract. Corticosteroid use for longer than four to six weeks is unwise. Usually, the discomfort during the chronic phase is not so severe as to need steroid drops.

A steroid-related intraocular pressure rise usually takes weeks and can be easily monitored.[16] Cessation of the medication almost always results in pressure returning to baseline. Four to six weeks of drops may be used in most situations, with the steroids then tapered and pressure-reducing drops used if the pressure elevation becomes a concern.

Clinical signs may include dermal eruptions of vesicles around the orolabial area. Ipsilateral preauricular involvement is also common with HSV keratitis. Biomicroscope examination of conjunctiva usually reveals acute or recurrent follicular conjunctivitis, with a pseudomembrane rare in most cases. Dendritic, dendrogeographic or geographic ulcerations on the cornea epithelium are caused by live HSV replication in these cells. The disease may initially appear as a punctate keratitis evolving later into the classic dendrite form.

Use of the AdenoPlus point-of-care test (Rapid Pathogen Screening) may be effective in the punctate stage of HSV keratitis to help confirm the lack of an adenoviral etiology or negative test result.

Standard rose bengal staining will highlight not only the areas of epithelial absence but also the

swollen infected epithelial cells surrounding the ulcerated area. (*Figure 1*) Conversely, the center of the lesion is devoid of cells and stains with sodium fluorescein, while fluorescein may negatively stain the surrounding damaged epithelium. (*Figure 2*) Under the dendrite, it is not uncommon for the clinician to note a faint stromal infiltrate in the shape of the epithelial lesion. The anterior chamber and corneal endothelium show varying degrees of cellular activity and type.

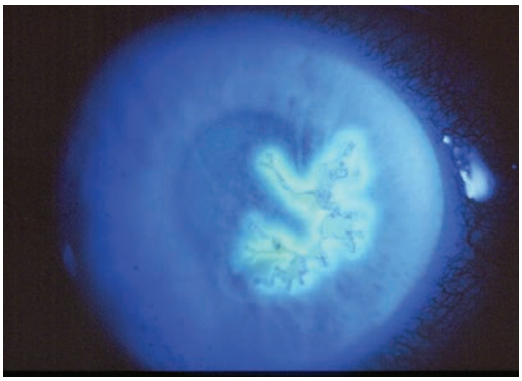

Fig. 2. Herpes simplex dendritic ulcer with sodium fluorescein stain shows a central absence of epithelial cells.

• ***Adenoviral diagnosis.*** Adenoviral ocular disease presents with marked foreign body sensation, photophobia, lacrimation to varying degrees and burning sensation. This occurs in the infected eye with the second eye becoming involved, usually less severely, after the first eye.

Further investigation may reveal an association with outside individuals (family/coworkers) with acute red eyes as significant for patients with EKC—as would be a recent upper respiratory infection or exposure to a community pool or spa in a young/adolescent patient with pharyngoconjunctival fever (PCF).

Clinical findings with the biomicroscope include hyperemia of the lids, caruncle and plica with follicles (*Figure 3*) mainly located in the inferior palpebral conjunctiva. Pseudomembranes (*Figure 4*) can be present in one-third to one-half of the cases making the patient more symptomatic. Subconjunctival hemorrhages are common and may obscure the examiner's view of the follicles in some cases.

The cornea stains with sodium fluorescein and rose bengal to reveal a diffuse, fine, punctate type of stain but without evidence of dendrites or dendritic variations.

AdenoPlus testing is most helpful in these cases as it makes for efficient, specific and sensitive diagnosis of an adenoviral infection. It can easily be performed in-office without special equipment. The test targets the hexon protein, which allows the detection of all of the adenoviral serotypes. The test has a reported sensitivity of approximately 89% and specificity of 94%.[12] Making a rapid assessment of the viral etiology (HSV vs. adenoviral) can help establish treatment plans to more quickly eradicate the infection or reduce the symptomology of the patient.

Treatment for Adenoviral Infection

When a presumptive diagnosis of adenoviral conjunctivitis is made, topical antibiotics are commonly but improperly prescribed. This is done even though more than half of the cases are viral.[13] Antibiotics are prescribed often as a result of:

• Misdiagnosis—the patient actually has a bacterial infection.

• Superinfection—the patient has both types of microorganisms.

• Patient comfort—the drops themselves are often soothing and additionally dilute out the organisms and toxins.

• Patient expectations—the patient seeks therapy that has a reasonable chance of working.

While it may not be the patient's top concern, the trend in medicine is to avoid topical antibiotics absent the certainty of a bacterial infection because of the public health risk of antibiotic microbial resistance.[14,15] They are ineffective against viral conjunctivitis and have little therapeutic impact. They may delay the proper treatment and can cause antibiotic resistance, toxicity and allergy.

Currently, no approved topical antiviral drug exists for adenoviral conjunctivitis. Treatment is typically supported with the use of cool compresses and/or artificial tears for comfort several times a day. Cycloplegic agents may be used for severe photophobia.

Because the virus is so contagious, prevention of its spread to family, coworkers and fellow students is a must. Mainstays are frequent handwashing and avoidance of touching the infected eye, as well as sanitizing instruments and surfaces in the eye care office. During active infection, recommend patients (whether students or workers) to stay at home to avoid infecting others.

Zirgan (ganciclovir 0.15%, Bausch + Lomb) has been investigated as a topical treatment for adenoviral keratoconjunctivitis. In one study, topical Zirgan resulted in a quicker cessation of signs and symptoms; however, this was not statistically significant.[14]

For patients with acute, painful adenoviral infection, consider a one-time instillation of Betadine 5% solution. (See "Can Betadine Blast Out Acute Viral Conjunctivitis?" page 86.) Pseudomembranes can be manually peeled in office every few days.

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- 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

Treatment for Herpes Virus Infection

Treatment for herpetic eye disease depends on the presentation and the location of the infection, and may include oral antivirals, topical antivirals and topical corticosteroids. Here are the recommended treatments for the following forms of ocular herpetic infection:

• ***Herpes zoster ophthalmicus (shingles).*** Initial treatment of herpes zoster ophthalmicus is almost always with an oral antiviral agent so as to lessen the severity and duration of the dermatologic disease. The least expensive treatment also requires the most doses: Zovirax (acyclovir, GlaxoSmithKline) 800-1,200mg PO five times per day. Other treatments are Valtrex (valacyclovir, GlaxoSmithKline) 1,000mg PO TID or Famvir (famciclovir, Novartis) 500mg TID. All are prescribed for seven to 10 days for patients with good renal function.

Without treatment, and usually even with it, skin lesions will erupt in the dermatome of the affected nerve(s). Early treatment lessens the severity and duration of the infection. The keratitis that can occur with zoster is usually much milder than that with simplex. The micro dendrites or pseudodendrites that occur are generally not a significant problem beyond irritation to the patient. They often have overlying mucus and may form mucus filaments or plaques.

Bacterial superinfection is usually prevented with an antibiotic such as Vigamox (moxifloxacin 0.5%, Alcon) TID. If there is a secondary sterile anterior chamber reaction, a cycloplegic such as Atropen (atropine 1%, Meridian) or Cyclogyl (cyclopentolate 1%, Alcon) may be used several times a day. Pred Forte (prednisolone acetate 1%, Allergan) may be used QID for secondary iritis and photophobia. The use of topical steroids for zoster are not contraindicated as they are for simplex. (See "Do's and Don'ts of Using Steroids for Viral Eye Infections," page 79.) Microdendrites/pseudodendrites have been shown to respond to Zirgan five times per day.[15]

A small minority of cases of zoster keratitis can lead to persistent keratitis, progressing into the stroma without a subsequent epithelial defect (disciform keratitis) or with absence of epithelium (necrotizing keratitis). Supportive therapy with steroids and cycloplegics is administered with the former case. With necrotizing keratitis, conjunctival flaps or even corneal transplants must be done (though this is uncommon in most cases). Intraocular inflammation may persist leading to glaucoma, cataracts and anterior or posterior synechiae and treatment must be directed at these problems.

• ***Herpes simplex keratitis.*** Early herpes simplex ocular infection may not initially show a dendrite. Occasionally the dendrite may present on the conjunctiva. A search with fluorescein or another stain (rose bengal or lissamine green) must be done to ensure detection of conjunctival epithelial defect in a moderately red eye. If the conjunctivitis is unilateral, then the treatment for bacterial conjunctivitis may be implemented while acknowledging the possibility of early presentation HSV. Steroids are contraindicated. If no dendrite appears in four to seven days, then steroids could be used in what is more likely bacterial blepharoconjunctivitis. If the patient develops dendrites or initially presents with them, then antivirals are indicated.

For more than 50 years, topical antiherpetic medications have been the first line of treatment. The mainstay of antiviral medication has been Viroptic (trifluridine 1%, Monarch) used usually nine times per day on initial presentation. As the dendrites begin to heal, the medication is tapered to five times per day and

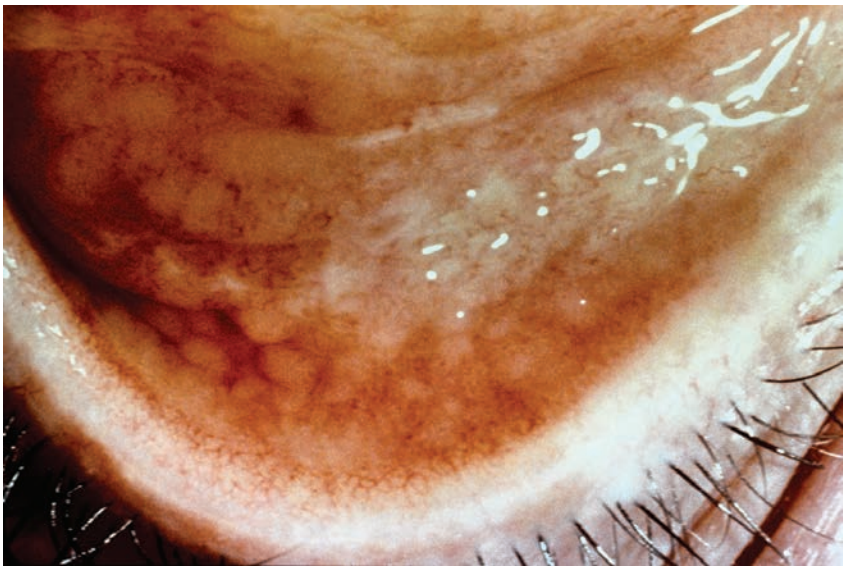

Fig. 3. Palpebral conjunctival follicles are a classic sign in a patient with epidemic keratoconjunctivitis. Note the early subconjunctival hemorrhage on the temporal conjunctiva.

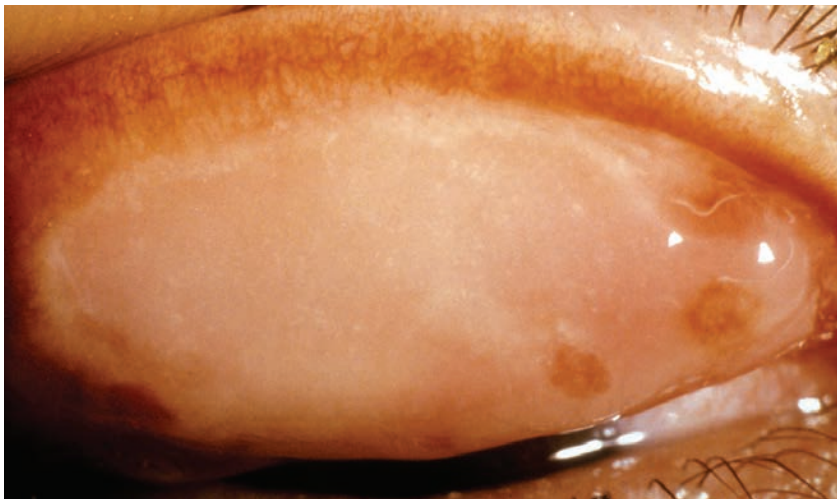

Fig. 4. Pseudomembrane of the superior palpebral conjunctiva occurs uncommonly in a patient with epidemic keratoconjunctivitis.

then discontinued. Because toxicity may occur, treatment is rarely continued longer than two to three weeks—except with a corneal transplant patient in need of prolonged treatment.

Recently, Zirgan five times per day has been used to treat epithelial keratitis; this can be used as a primary treatment or when the patient is resistant to Viroptic. The go-to topical ointment Vira-A (vidarabine, Abcam) is no longer available. Initial therapy now often consists of oral treatment: acyclovir 400mg five times per day, valacyclovir 500mg BID or famciclovir 250mg BID—any of which are to be taken for seven to 10 days.

Orals aren't often used as first line therapy for HSV except when:

1. There is a high risk of corneal toxicity.
2. The patient is immunocompromised.
3. The patient is a child in whom it is difficult to instill drops.

Treatment of superficial epithelial corneal disease occurs because of supratherapeutic levels of the antiviral in the precorneal tear film. Failure of epithelial lesions to resolve after two weeks suggests either epithelial toxicity, neurotrophic keratopathy or drug resistance.

An additional treatment at the initial presentation of a patient with HSV dendrites is to perform manual epithelial debridement with a cotton-tipped applicator. Removing infected and injured epithelial cells decreases the viral load on the cornea and can hasten the healing process.

• ***HSV geographic ulcer.*** Geographic ulcers are dendrites that widen and spread out while still remaining largely epithelial. The topical dose of either Viroptic or Zirgan is unchanged. If oral therapy is chosen, the dosage is increased to that for the treatment of herpes zoster: acyclovir 800mg five times per day, valacyclovir 1,000mg TID or famciclovir 500mg BID.

As with all purely epithelial herpes infections, avoid steroids unless there is a good reason, such as the presence of a corneal graft. Be aware that when epithelial herpes is severe enough, as in a geographic ulcer, the doctor may imagine that there is stromal involvement when there is not. Bowman's membrane can become hazy, but the disease is still limited to the epithelium.

• ***HSV disciform (stromal) keratitis.*** In this case, the stroma is swollen, usually in the central cornea. The stroma appears hazy and/or Descemet's membrane is wrinkled, indicating thickening. The overlying epithelium is intact and dendrites have usually resolved.

In this case—usually a sterile autoimmune process—steroids are added at four to eight times per day while maintaining topical Viroptic coverage five times per day, Zirgan TID, or oral antivirals given in the lower-dose regimen, such as with dendritic keratitis.

With prolonged treatment, more than three weeks of topical Viroptic may lead to ocular surface disease. Treatment is then switched to prophylactic doses of oral agents such as acyclovir 400mg BID while maintaining the steroid drops and monitoring the intraocular pressure.[16]

• ***Necrotizing (stromal with epithelial defect) keratitis.*** Here, the epithelium is gone and there is a stromal ulcer. Because of the infectious inflammation and the viral neurotropic nerve damage, it is difficult to induce the epithelium to cover and stabilize the dehydrating and thinning surface.

There is insufficient clinical trial data to support type and length of treatment. Steroids are often used, albeit cautiously. Pred Forte is used BID along with topical or oral antivirals. these agents are gaining prevalence due to the lack of toxicity. Oral antivirals are used in the higher doses for seven to 10 days, and the low-dose steroid is tapered. Ocular surface protection with a conjunctival flap or amniotic membrane must be considered. Topical antivirals are usually avoided because epithelial healing is so

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Can Betadine Blast Out Acute Viral Conjunctivitis?

One time application of topical Betadine 5% solution (povidone-iodine, Alcon) is used off label by some practitioners for acute viral conjunctivitis, such as a painful case of EKC. Although there are no controlled studies for this therapy, some anecdotes exist for sterilizing the eye using this common preoperative antiseptic in office.

For this treatment, topical anesthetic and a drop of NSAID are applied, after which one drop of Betadine is instilled and the patient is instructed to close their eyes for one to two minutes. After this, the eye(s) is irrigated to remove all the Betadine, and NSAIDs are used for a few days.[14]

problematic and topical medications would likely only worsen the healing.

• ***Endothelial keratitis.*** Some patients who have a limited anterior chamber reaction, with fine keratic precipitates on the endothelial surface. This inflammatory, primarily autoimmune reaction should be treated with Pred Forte six to eight times per day along with a low-dose oral antivirals. The Pred Forte may then be tapered and the orals reduced to the prophylactic dose.

The eye remains the premier testing ground for many drugs under evaluation in experimental human clinical trials. With the development of more specific and systemic antiviral agents and the multiple viral infections manifested in ocular disease, the prospects for new and effective therapies remain highly promising in the near and distant future. ■

Dr. Sendrowski is a professor at the Southern California College of Optometry, and the Chief of the Ophthalmology Consultation and Special Testing Service at the Marshall B. Ketchum University Eye Center, in Fullerton, Calif.

Dr. Maher is a general ophthalmologist with fellowship training in cornea and external disease in private practice in Torrance, Calif.

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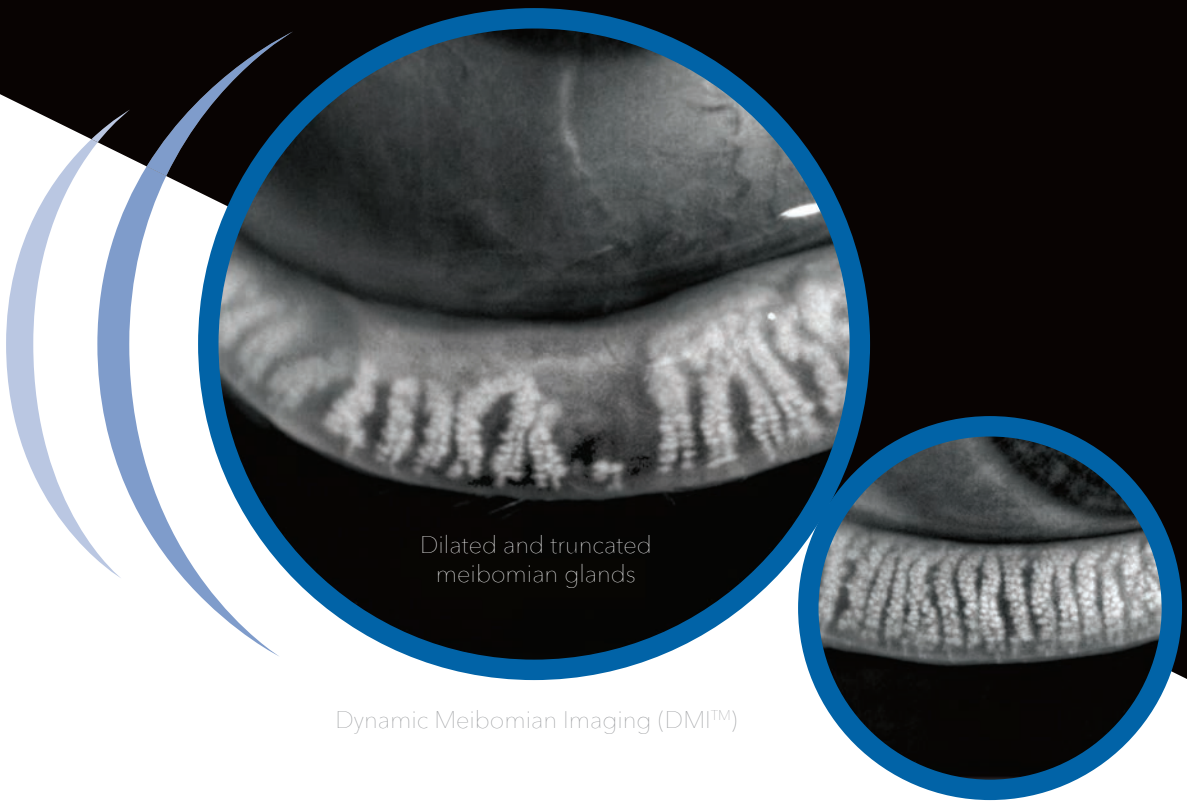

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To Solve a Puzzle, Use Every Piece

A patient with a dense asteroid hyalosis was confused about her medication schedule.

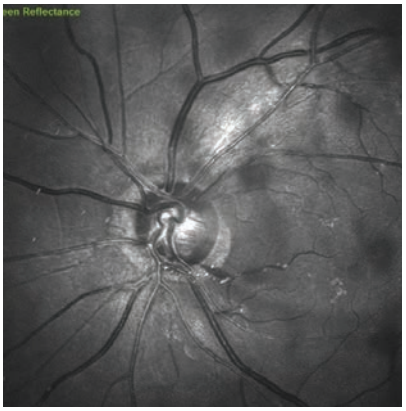
By James L. Fanelli, OD

Dense asteroid hyalosis makes for difficult viewing of optic nerve details with normal funduscopy techniques in many cases. Evaluation of the optic nerve is critical for glaucoma patients. Here is where we can use some of the other tools in our diagnostic tool box to evaluate stability or progression of the disease.

Diagnostic Data

A 78-year-old Caucasian female presented in April for a glaucoma follow up. She had been a long-time patient who was initially observed as a glaucoma suspect, but converted to frank glaucoma about 12 years ago. At this visit, she was scheduled for threshold visual field studies and optic nerve imaging with multicolor imaging technology, as her dense asteroid hyalosis in her left eye rendered standard fundus photography useless.

In the past 12 years, she's undergone slight changes to her medication regimen to facilitate stabilization. For the past four years, her glaucoma medications were pretty straightforward: generic latanoprost hs OU and 0.5% timolol Qam OU. Always a compliant patient, at this visit she asked an unusual question: "Why do I have to take the timolol since I've already had cataract surgery?" Interesting question from a long-standing glaucoma patient and one that got me thinking about medication confusion. I explained that the medication was for glaucoma, but I also asked her to tell me how and when she was administering her medications. She reported that upon awakening each morning, she would put a drop of the timolol into each eye, and then after about 15 minutes, she would put a drop of the latanoprost in each eye. Again, interesting evidence of dosing confusion.



Above, green laser image of the left optic nerve, demonstrating a disc hemorrhage at 4 o'clock and an adjacent wedge defect at 5 o'clock.

At this visit, entering visual acuities were 20/30- OD, OS and OU through hyperopic, astigmatic and presbyopic correction. These acuities were similar to her best corrected visual acuities obtained at the previous visit with minimal change in her refractive status. Pupils were ERRLA with no afferent pupillary defect noted.

Her anterior segments were essentially unremarkable, save for some mild endothelial guttatae in both eyes. Angles were open, and at the previous visit, gonioscopy demonstrated grade 4 open angles, with minimal trabecular pigmentation, and normal angle anatomy. Predilation intraocular pressures (IOP) were 12mm Hg OD and OS via Goldmann and central corneal thicknesses were previously measured to be 532µm OD and 518µm OS. Threshold visual fields were obtained. The patient was dilated prior to optic nerve imaging. Postdilation, adequate optic nerve images were obtained in her right eye, but not her left. When I looked at the blurred images of her left optic nerve, I remembered that she had dense asteroid. I proceeded to examine her and planned on obtaining her multicolor images.

Through dilated pupils, her posterior chamber IOLs were centered in the capsular bag, and the posterior capsules were open. She had long-standing bilateral PVDs. Her macular evaluations were stable with fine retinal pigment epithelium mottling in both eyes and minimal perifoveal drusen. Her retinal vascular status was stable with mild hypertensive and arteriosclerotic retinopathy OU.

Previously, her optic nerves were characterized by cupping of 0.55 x 0.70 OD and 0.55 x 0.65 OS. Examination of her left optic nerve was complicated by the asteroid, but with movement of the eye as well as the condensing lens at the slit lamp, I was able to obtain an adequate view of the left optic nerve. I noted a disc hemorrhage in the inferotemporal sector.

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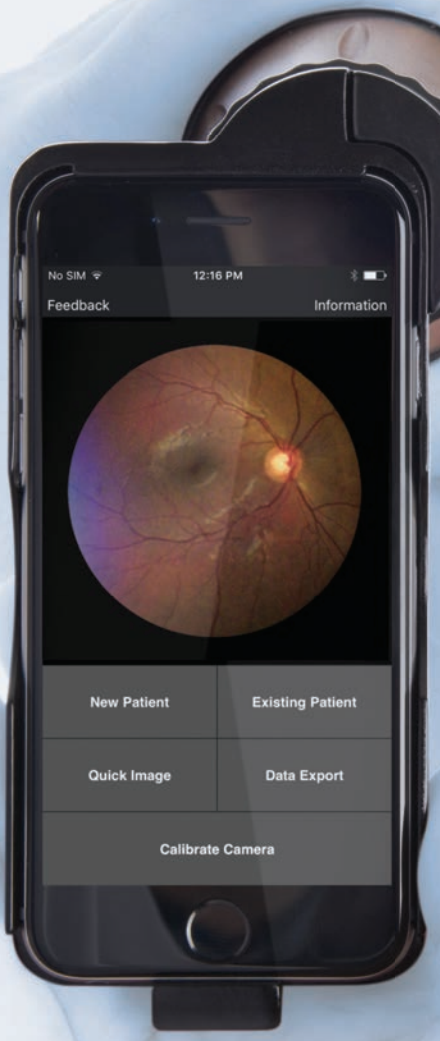

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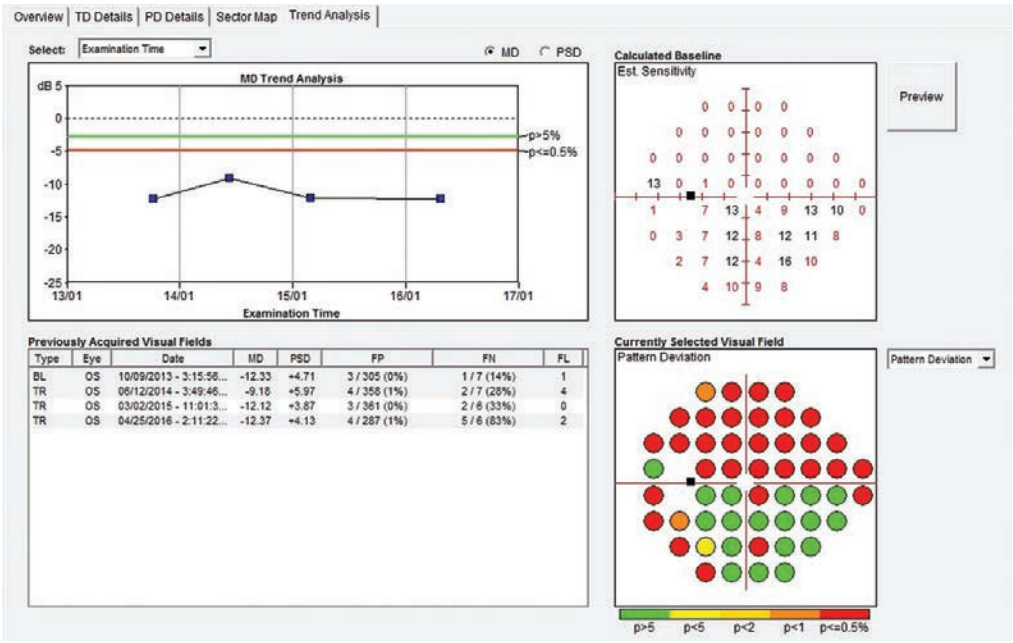


The mean deviation trend analysis of the left visual field over 4 studies. Note MD is below statistical normal (~12db), given the density of her field defects, but appears to be stable over time.

Discussion

The presence of the disc hemorrhage in the left eye, being a new finding, called into question the overall stability of her optic nerve structure and function. In reviewing her medical record, I had noted two previous episodes of disc hemorrhages in previous years. But previous visual field studies and optic nerve imaging with both HRT 3 and OCT technologies demonstrated stable optic nerve appearances (at least in the past four years). The disc hemorrhage, along with the earlier discussion with the patient about her medication dosing, genuinely had me questioning the overall stability of her glaucoma, as the appropriate medication dosing would involve the timolol in the morning, and the latanoprost in the evening. Global trend analysis of the visual field in the left eye was stable.

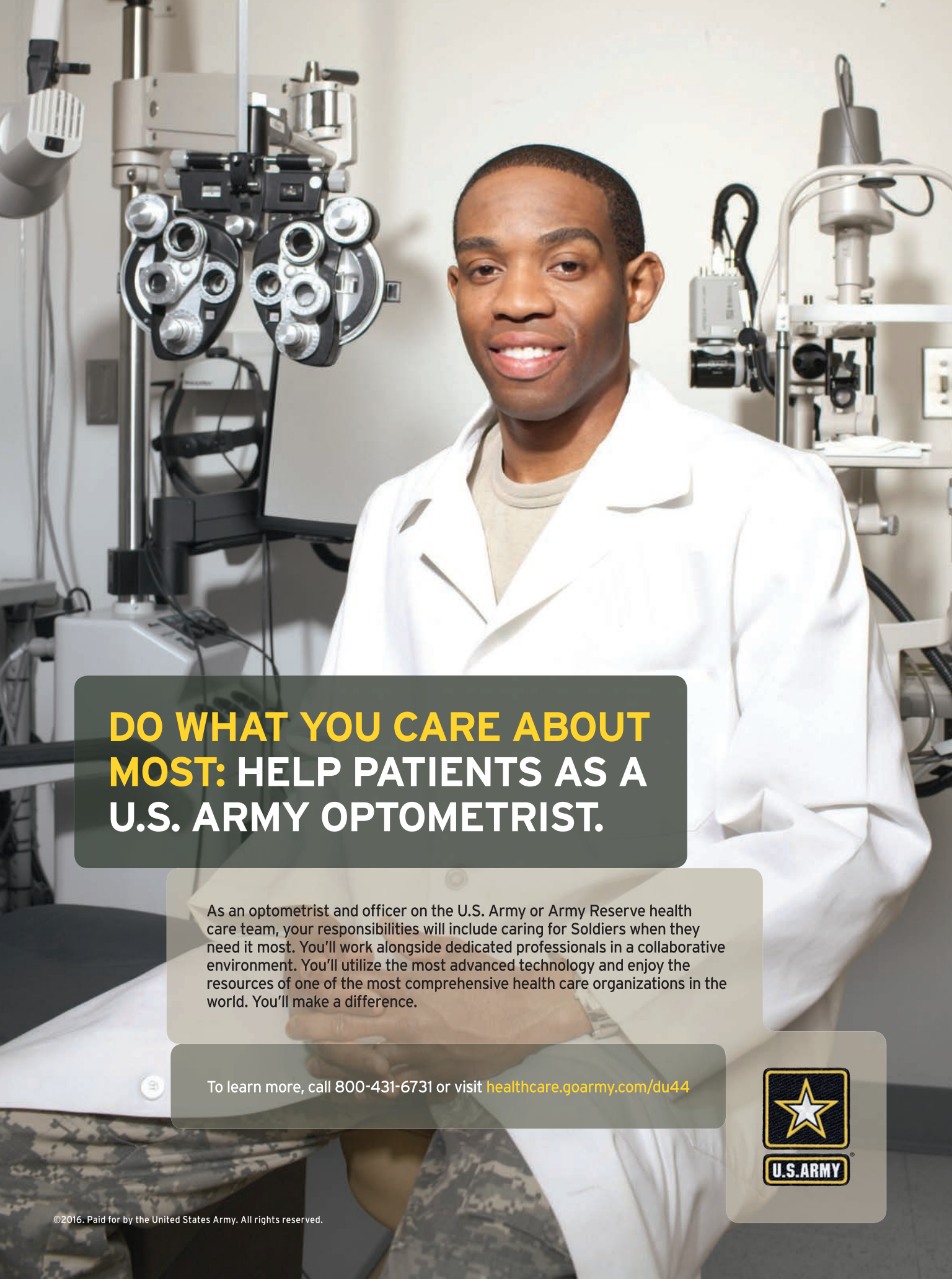
At this point, I had one of my techs take the patient back to the OCT room and obtain the multicolor images, as well as an updated optic nerve glaucoma imaging protocol (which in my office includes three scans: a standard RNFL circle scan, an optic nerve radial scan, and a macular retinal scan with segmentation of all retinal layers), and asked the patient to be placed back in one of the examination rooms upon completion of the testing.

When I reviewed the new images and her visual fields, there was evidence that she had progressed. First, we obtained a decent multicolor image of her left optic nerve, clearly showing the disc hemorrhage. This will be helpful at the next visit to give me the sense of how quickly this hemorrhage resolves. OCT RNFL scanning demonstrated a significant focal reduction in the inferotemporal RNFL OS adjacent to the disc hemorrhage. This was also seen extending into the macular scan, in particular on the ganglion cell later segmentation.

An initial look at her visual field studies seemed to show no deterioration. Visual field interpretation is one of the most variable test results to interpret because so many factors are involved in obtaining accurate and reliable visual field studies. Quickly looking at an isolated field test can show how well preserved the visual field actually is, but it is only reflective of what is happening at that particular point in time. Where the real information lies is in the trend analysis that essentially looks at several field indices over time and statistically analyzes those data points, looking for an overall or a sectoral decline overtime.

Being able to isolate individual sectors of the optic nerve in RNFL analysis (correlated to the Garway-Heath optic nerve sectors) is invaluable in dissecting out progressive structural damage in only one sector of the optic nerve, rather than a global deterioration of the RNFL.

Remember, in this particular case, there is an isolated RNFL defect that has worsened. Is that isolated defect big enough to affect global RNFL indices? Or is it small enough where a subtle change in the RNFL would be statistically unnoticed when looking at global indices? As you can guess, the



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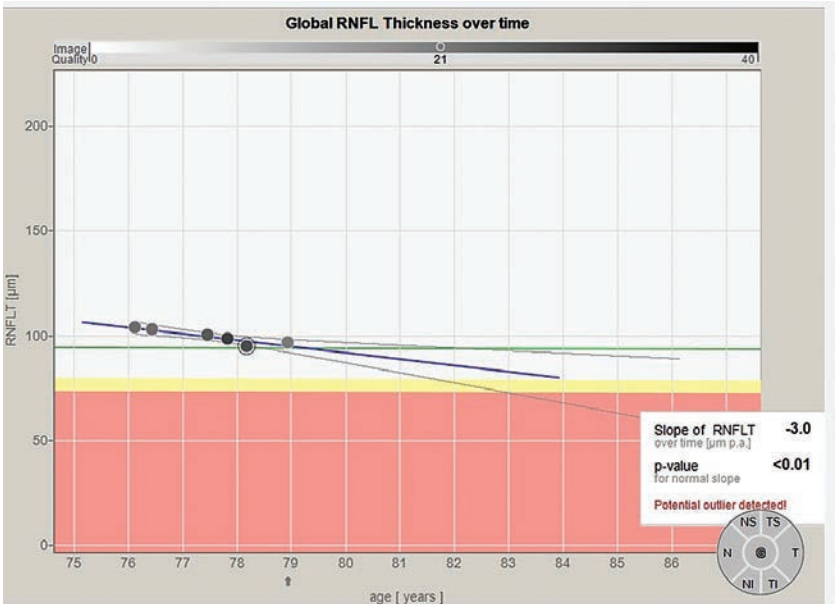
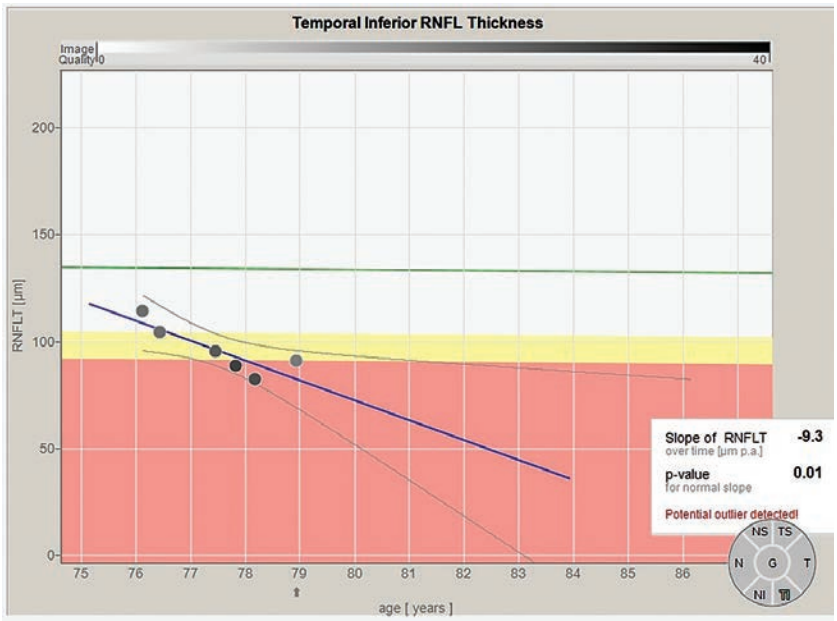
answer will vary, depending on the particular case, by how much damage has occurred structurally and where that damage has occurred. Similar to trend analyses in visual field interpretation, looking at RNFL data over time can give a clearer picture of how stable, or not, a patient remains.

This case represents progression of the disease. In this instance, the progression is manifest as a focal RNFL defect, progressive RNFL and ganglion cell layer loss in the same area, with no significant change in her visual fields. The fact that her fields have remained relatively stable is certainly a good thing. But it is only a matter of time before the structural change will manifest as a field change.

Clearly, somewhere along the line, the patient began using both glaucoma medications in the morning, whereas they were initially prescribed to be dosed in the morning (timolol) and at bedtime (latanoprost). Many studies show IOP variability plays a role in progressive damage, and stabilizing IOP over a 24-hour period is important in preserving both structure and function. Did she begin using both medications in the morning two months ago, or two years ago? She really didn't know, and neither do I. Did that play a role in the development of the RNFL defect? Possibly, and my guess is: probably. Will spreading the medication dosages out in the morning and the evening prevent further deterioration? Possibly, but only time will tell. Will she remain compliant, or will the gradual effects of aging make self-medication compliance more difficult? Possibly, but only time will tell.

Educate. Communicate.





Above, global optic nerve RNFL data over time. Note the slight decline in global RNFL thickness over time, implying slow progression. Below, inferotemporal Garway-Heath optic nerve sector RNFL data over time. Note the significant decline in the RNFL thickness in this one optic nerve sector, implying a rather significant progression.

Maintain a healthy follow-up schedule. Monitor. Treat accordingly. Know that if things change in glaucoma, they only get worse, not better. Intervene early when needed. Monitor. And take solace in the fact that in most cases of glaucoma, time is on your side. ■

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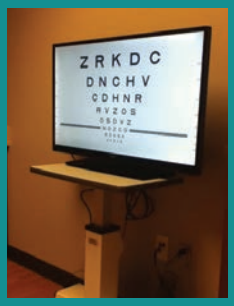

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Well, Folks, That's a RAP

Just because a patient reports no symptoms, that doesn't mean they have no problems.

By Alison Bozung, OD and Mark Dunbar, OD

An 81-year-old Caucasian male presented for a six-month follow up for dry age-related macular degeneration (AMD). He had been monitored every six months with a dilated eye examination and ocular coherence tomography (OCT) starting two years prior. There were no visual complaints and he had not noted any changes with Amsler grid testing once a week at home.

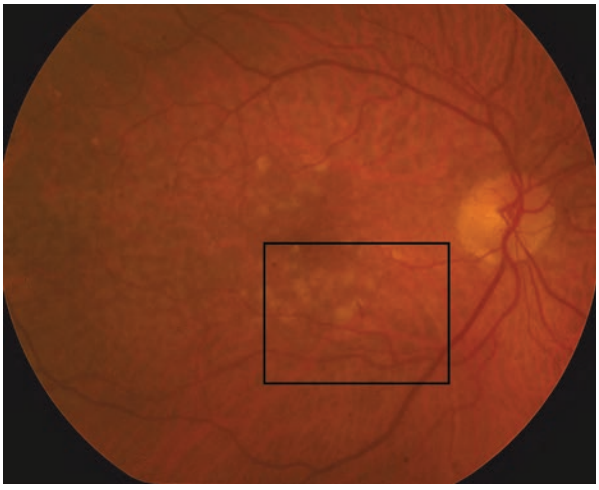
History

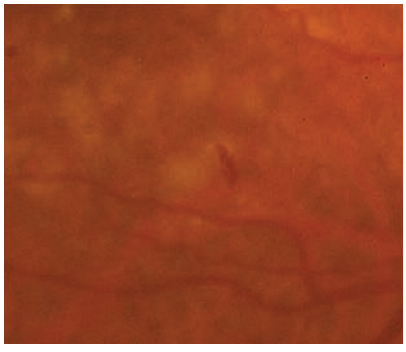
His overall medical history was unremarkable except for a history of osteoporosis. He was taking 50,000 units vitamin D, aspirin 81mg, omega-3 1200mg, and Preservision AREDS twice daily. He had no known drug allergies. He did not smoke at the time of presentation, but had previously been a smoker starting in his late teenage years for about five years.

Examination

His distance visual acuity in both eyes was 20/30 best corrected with no improvement using pinhole. His pupillary function, confrontation visual fields and extraocular motilities were normal in each eye. His intraocular pressure was 12mm Hg OU.

Anterior segment evaluation was significant for mild meibomian gland dysfunction, dry eyes and 2 to 3+ nuclear sclerotic cataracts. Posteriorly, he did have a vitreous detachment in each eye. Optic nerves were healthy in both eyes, with small cup-to-disc ratios and peripapillary atrophy OS. The macula of the left eye had many large, soft drusen with retinal pigment epithelial (RPE) changes sans fluid or elevation. In the macula of the right eye, similar large drusen and RPE changes were noted, but there was also a small intraretinal hemorrhage present inferior to the fovea (*Figure 1a and 1b*).





Figs. 1a and 1b. At left, fundus photo of the patient's right eye. Below, a close-up shot of the above fundus photo shows a small, juxtafoveal intraretinal hemorrhage of the right eye.

OCT angiography (OCTA) (*Figures 2 and 3*) and intravenous fluorescein angiography (IVFA) (*Figure 4*) were obtained and are available for review.

Take the Quiz

1. Based on the number and size of drusen, what is the classification of AMD in the left eye?
a. Early dry.
b. Intermediate dry.
c. Advanced dry.
d. Exudative.

2. What do you see in the right eye's fluorescein angiography?
a. Dark choroid.
b. Two microaneurysms inferior to fovea.
c. Hyperfluorescing drusen only.
d. Two hyperfluorescing lesions with mild late leakage inferior to fovea.

3. What is the likely diagnosis?
a. Retinal angiomatous proliferation with AMD.
b. Dry AMD alone.

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c. Retinal macroaneurysms with AMD.
d. Central serous chorioretinopathy with AMD.

4. What does the OCTA reveal?
a. Leakage of vessels.
b. Subretinal abnormal vascular proliferation.
c. Outer retinal abnormal vascular proliferation.
d. Intraretinal abnormal vascular proliferation.

5. What should our management strategy be?
a. Monitor q6mo with dilated exam, continue AREDS and Amsler.
b. Monitor q3mo with dilated exam, continue AREDS and Amsler.
c. Refer to retina specialist.
d. Refer to retina specialist, but only once vision is decreased.

For answers, see page 114.

Discussion

Our patient was being followed on a regular schedule for his AMD. Historically, it had been dry in both eyes, so he was taking appropriate AREDS2 formula supplements and self-monitoring with an Amsler grid between visits. On a routine visit, an intraretinal hemorrhage noted in the right eye prompted additional testing.

The OCTs of the fovea of each eye revealed drusen without associated subretinal fluid. When the scan pattern was aligned atop the area of retinal thickening inferior to the fovea OD, there was what appeared to be a small serous pigment epithelial detachment (PED) with disruption of overlying inner retinal architecture. The OCTA revealed vessel proliferation within the sensory retina extending to the outer retina in the area of macular thickening and hemorrhage (*Figure 2*).

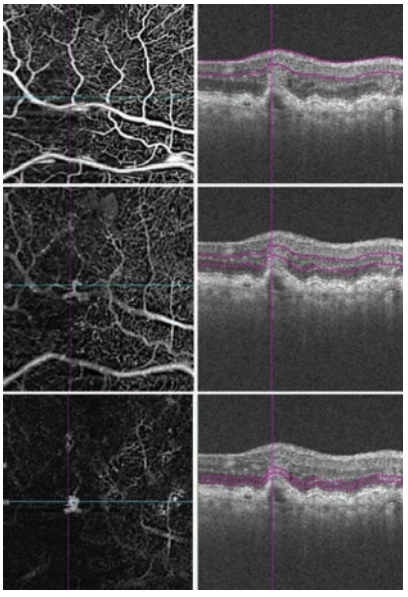

Fig. 2. OCT angiography images segmenting the retinal layers from anterior to posterior.

Though on OCT, the space underlying the PED appeared transparent and not fibrous or drusenoid, an IVFA was done to rule out a choroidal neovascular membrane (CNVM). The IVFA was consistent with hyperfluorescence staining of drusen in both eyes and mild late leakage of two focal areas inferior to the fovea in the right eye. There was no occult leakage seen, and it was not suggestive of any CNVMs.

Our patient had a focal serous PED that correlated with OCTA findings of abnormal vasculature in the outer retina, which should be avascular (*Figure 2*, bottom image). The OCTA colored depth-encoded map (*Figure 3*) signifies vessel depth by a variation in the color spectrum; reds and oranges denote inner vasculature whereas blues and purples denote deeper vessels. Note, OCTA does not image leakage itself, but rather captures serial B-scans in a given location to map volumetric flow changes. These flow changes represent erythrocyte movement through blood vessels and vascular nets.

Diagnosis

Our patient was diagnosed with retinal angiomatous proliferation (RAP). RAP lesions—initially described in 1992, but updated in 2001—are defined as intraretinal vascular abnormalities which form and then dive deeper to form anastomoses with choroidal vasculature.[1,2] They tend to leak and may cause subretinal fluid in the form of serous PEDs, which one study found present in 22% of RAP patients.[3] Some controversy still exists as to the exact pathogenesis of these lesions.[4]

Retinal angiomatous proliferation lesions are commonly associated with AMD and represent progression of disease. One study shows 7.3% of patients with AMD had RAP lesions, but this

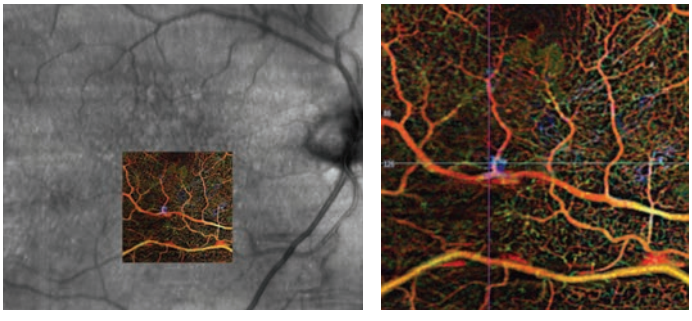

Fig. 3. OCT angiography en face photo with color-coded map representing vessel depth.

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number is likely even higher.[1] The lesions are typically found bilaterally and juxtafoveally, and since they represent conversion to neovascular AMD, they require referral to a retinal specialist for treatment.[5]

Treatment and management of this specific subset of AMD is varied, but may include laser photocoagulation, photodynamic therapy, intravitreal steroid or intravitreal anti-VEGF. Individual therapies may also be combined in some cases. There has yet to be a prospective, comparative study for treatment, but RAP lesions in AMD are typically more refractory to treatment and often require more injections.[6]

Our patient was promptly referred to a retinal specialist, and he received an intravitreal injection of Avastin (bevacizumab, Genentech). Upon his one month follow up, the intraretinal hemorrhage had absorbed and he was given another shot of Avastin as part of a treat-and-extend protocol. ■

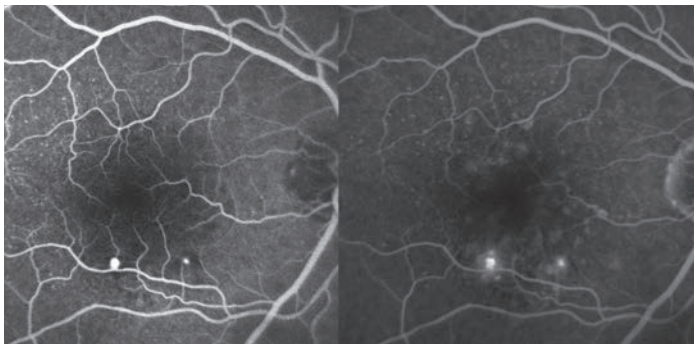

Fig. 4. IVFA in early and late phases show two focal areas of staining and late leakage.

This case was contributed by Alison Bozung, OD, optometric resident at Bascom Palmer Eye Institute.

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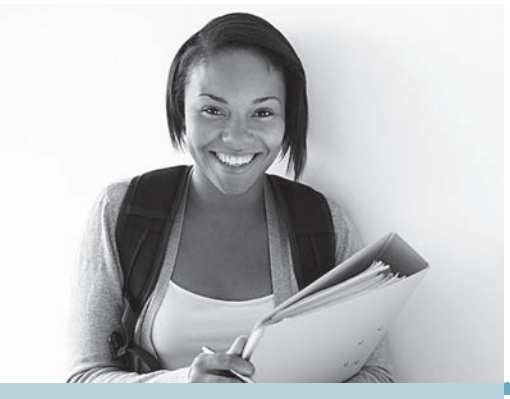

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Those Pesky Flies

What are your options for managing ubiquitous vitreous floaters?

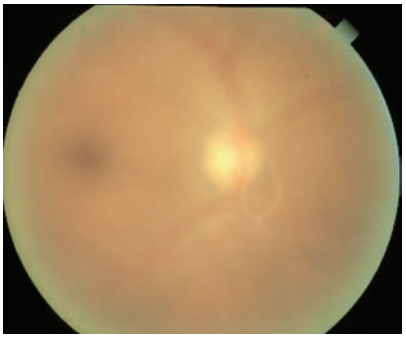
By Joseph W. Sowka, OD, and Alan G. Kabat, OD

When floaters begin to interfere with patients' work, they are going to begin looking for any solution. Such was the recent case of a physician—a friend of a friend—who felt his floaters were beginning to interfere with his ability to practice within his specialty. He had consulted an ophthalmologist who promoted a laser treatment designed to rid patients of floaters altogether. The patient was hesitant and contacted me. Although floaters are a common nuisance, their causes and treatment options are poorly understood by patients—even some who are physicians themselves.

This column provides a quick breakdown of what to tell patients experiencing this often worrying, but rarely dangerous, issue.

What are Floaters?

The vitreous is a hydrated and acellular gel constituting the bulk of the globe contents. It consists of 98% water with the remainder collagen and hyaluronan forming a clear gel. At birth, the vitreous gel is quite firm, but with aging (and myopic vitreopathy), this firm gel liquefies, forming pockets of liquid vitreous known as lacunae. This liquefaction occurs from the dissociation of hyaluronan from the collagen fibrils forming the supportive network of the vitreous gel. This allows for the aggregation of the smaller collagen fibrils into macroscopic fibers, which subsequently diffract light. The accumulation of lacunae transforms the vitreous gel into a liquid consistency. This facilitates collapse of the vitreous and the development of a posterior vitreous detachment (PVD), occurring as a separation of the posterior vitreous cortex from the internal limiting membrane of the retina. This process begins posteriorly and progresses anteriorly to the vitreous base. Additionally, lacunae increase vitreous heterogeneity and scattering of light at the gel-liquid interface.[1]



Weiss ring in an acute PVD causing a complaint of floaters.

Floaters, or symptomatic vitreous opacifications (SVO), are packed bundles of collagen fibrils that first appear in the central vitreous where they often have a linear configuration, becoming more numerous, thickened and irregular with increasing age and axial myopia.[1] The walls of the liquefied lacunae interfere with photon transmission to the retina, contributing to the common symptom of floating spots. They are more visible when viewed against a bright source such as a sunny sky or a white background. They are even more noticeable when situated in the visual axis. The onset of PVD increases the scatter of light and an increase in symptoms as more collagen aggregates are directed toward the visual axis. Many patients undergoing PVD ultimately adapt to the SVOs, most likely due to the fact that the Weiss ring eventually settles inferiorly and anteriorly, affecting the penumbra cast upon the retina in a less symptomatic form.[2]

Get Used to It?

SVOs are among the most common, and most dismissed, complaints you'll encounter. Most practitioners, upon confirming there is no tractional retinal pathology, explain to the patient that adaptation will occur and there is nothing to worry about. In most cases, patients either adapt or accept and pursue the issue no further. Indeed, as the opacifications move out of the visual axis or locate more anteriorly with forward rotation of the collapsed vitreous, the symptoms will greatly decrease, usually to an acceptable level. However, there is a small subset of patients who do not adapt and have a greatly reduced quality of life from SVOs despite excellent Snellen acuity. This makes determination of the most effective and appropriate treatments difficult to scientifically assess. Thus, virtually all interventions are patient driven.

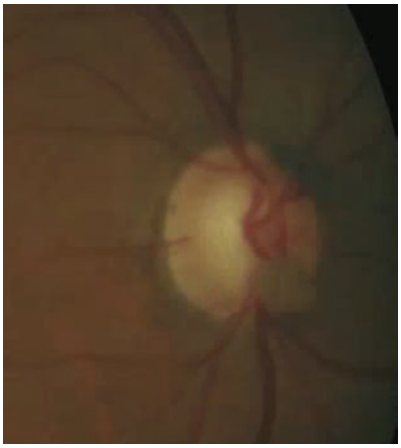
However, decreased quality of life comes from reduced contrast

sensitivity, decreased driving ability and impaired facial recognition.[1] Up to two thirds of patients with SVOs have moderate to extreme difficulty in reading small print or driving at night.[3] In patients younger than 55 years old, these effects are so deleterious that they were willing to undergo a procedure that carried a risk of 7% blindness to be cured of SVOs.[4]

Currently, two non-observational management options for SVOs exist. These are Nd:YAG laser vitreolysis and vitrectomy.

Vitreolysis

The least invasive option to combat floaters is laser vitreolysis, but the procedure may have complications and limitations. Nd:YAG vitreolysis is performed by focusing the laser onto vitreal opacities visible at the biomicroscope. The aim is to reduce the volume of the individual floaters by disintegrating them down to smaller fragments, by cutting longer strands into shorter strands or by cutting strands that suspend larger floaters, allowing them to dislodge from the visual axis.[2] Nothing is actually removed from the vitreous. The large floaters are reduced to smaller floaters or laser induced incisions in collagen strands may allow large opacities to move elsewhere. There is no guarantee that the patient won't still have SVOs after the procedure. Indeed, they may just have different floaters that are hopefully not as bothersome. Also, due to the risk of laser-induced damage, only SVOs greater than 4mm away from the retina and lens are typically treated. Hence, Nd:YAG laser vitreolysis may not be able to treat the most symptomatic floaters.[2] It is difficult to gauge outcomes from this procedure, but subjective success rate of laser vitreolysis appears to be relatively low.[1,5]



Symptomatic posterior pole floater.

While laser vitreolysis is the lesser invasive option, it is not without risk. Complications of Nd:YAG laser treatment for other conditions include induction of retinal breaks and detachment as well as cystoid macular edema. One study reported on a refractory glaucoma occurring after laser vitreolysis for SVOs requiring surgical intervention to lower IOP.[6]

Vitrectomy

Pars plana vitrectomy (PPV) is a more invasive, but possibly more effective option.[2] Smaller gauge instruments have allowed for self-sealing sutureless sclerotomies with a faster recovery and reduced rate of complications.[2]

Sutureless 25-gauge pars plana vitrectomy for symptomatic vitreous floaters improves visual acuity, resulting in a high patient satisfaction quality-of-life survey, with a low rate of postoperative complications.[1] Sutureless pars plana vitrectomy should be considered as a viable means of managing patients with symptomatic vitreous floaters. Additionally, because the SVOs are actually being removed, PPV reported success rates are very high.[7-9] In one series, the patient-reported success rate was 85%. Tellingly, 87% of patients said that they would recommend PPV to friends with similar complaints.[3]

Of course, PPV carries a greater risk of serious complications, such as induction of retinal tears and detachment, choroidal hemorrhage, proliferative vitreoretinopathy, endophthalmitis and, most commonly, cataracts, occurring in 50% to 75% of cases postoperatively.[1,10] Retinal tears and detachment are often associated with simultaneous induction of PVD during PPV. Use of small gauge instruments and not inducing PVD during the procedure greatly reduces these risks.

While Nd:YAG vitreolysis is a less invasive option, it is not without risks and the success rate is suspect. The use of smaller gauge instrumentation and sutureless PPV, combined with a highly successful, definitive outcome, appears to have lowered the threshold for performing this procedure on patients with SVOs who have reduced quality of life and function. Ultimately, it rests with the patient to decide if the benefits of an invasive surgery outweigh the risks. ■

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Surgical Minute

If At First You Don't Succeed…

New retinal surgical techniques are breaking boundaries in the fight for vision.

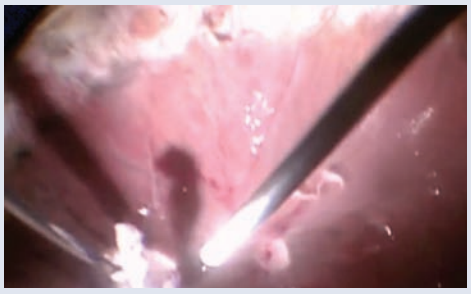
By Derek N. Cunningham, OD, and Walter O. Whitley, OD

The retina is among the most delicate and unforgiving tissues to operate on in the human body. It does not regenerate and is surrounded by a dense vascular supply, which carries constant risk for scarring and inflammation. The slightest disruption of only several microns of retinal tissue can produce devastating and permanent vision loss. These inherent limitations have laid the foundation for how we understand and, in turn, counsel our patients on retinal trauma, disease and surgical repair.

With the advent of new surgical techniques, we now have second chances to repair complex retinal surgical issues that may not respond to a single surgery. Traditionally, if a retinal surgery resulted in suboptimal results, the heavily invasive and blunt nature of subsequent retinal surgeries did not justify the risk of additional repairs. Now, microincisional techniques and high-speed vitrectomies enable surgeons to attempt repairs in even the most challenging cases.

The patient in this video had retinal trauma from a firework explosion to the eye. The retina was initially reattached with silicone oil tamponade and peripheral laser. Subsequent recurrent epiretinal membrane formation occurred, leading to decreased vision and further retinal traction.

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



What's a Retinotomy?

A retinotomy is an advanced technique in which the surgeon removes nonessential or peripheral retinal tissue. It is typically done to relieve retinal traction or limit intractable retinal foreshortening in post-traumatic proliferative vitreoretinopathy.

Until recently, the prognosis at this point would have been bleak. Further surgical intervention would have been extensive and invasive, with higher risk and potentially minimal benefit.

But in the past five to 10 years, we've adopted a minimally invasive approach that uses microincision technology within the silicone oil-filled eye to perform the tissue dissection and retinal reattachment. This technique bypasses lengthy and invasive steps traditionally performed, such as oil removal and subsequent re-replacement or scleral buckling procedures. The reattachment rate with the minimally invasive approach is between 80% to 90%, compared with 50% reported for the more invasive, traditional approach.

In the accompanying video, the tenacious epiretinal membranes are removed underneath the silicone oil. Keep in mind that without the obstruction of silicone oil, epiretinal membrane removal is incredibly difficult and delicate in an otherwise healthy eye. However, the oil tamponade assists in gently holding the retina in position while overlying or underlying scar tissue is removed.

The video also shows removal of excess fibrosis near the previous retinotomy site. Then, laser applied around the previous retinotomy site reduces the risk of detachment. The vitreous cavity is then topped up with silicone oil to provide an effective tamponade, achieving long-term functional and anatomical success.

This patient will require close follow-up care by the retinal specialist. Eventually, an optometrist will provide vision correction. The optometrist and retinal specialist then often share responsibility for monitoring the retina. They'll watch for long-term complications such as retinal detachments, subretinal neovascular membranes, band keratopathy, high or low intraocular pressure, and cataracts in phakic patients.

As surgical innovation continues to push the boundaries of retinal intervention, be sure to consult your retina specialist on patients who have had previous retinal surgery and may not have achieved an optimal visual result—yet. ■

Meetings + Conferences

June 2016

■ **17-19.** *OAL Annual Convention.* Crowne Plaza Hotel, Baton Rouge, LA. Hosted by: Optometry Association of Louisiana. CE hours: 16. To register, email Jim Sandefur at optla@bellsouth.net or go to www.optla.org.

■ **17-19.** *CE in Italy.* Victoria Hotel, Turin, Italy. Hosted by: James Fanelli. Key faculty: James Fanelli, Joseph Pizzimenti. CE hours: 12. To register, email James Fanelli at jamesfanelli@ceinitaly.com or go to www.ceinitaly.com.

■ **21-23.** *CE in Italy.* Palazzo Righini, Piedmont, Italy. Hosted by: James Fanelli. Key faculty: Joseph Pizzimenti. CE hours: 12. To register, email James Fanelli at jamesfanelli@ceinitaly.com or go to www.ceinitaly.com.

■ **25-26.** *The Optometrist's Guide to Strabismus.* Burlington, Ontario, Canada. Hosted by: Patricia Fink and OEP Foundation. Key faculty: Samantha Slotnick. CE hours: TBD. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org/oepf_calendar.

■ **29-July 3.** *AOA, Optometry's Meeting.* Boston Convention and Exhibition Center, Boston. Hosted by: American Optometric Association and the American Optometric Student Association. CE hours: 180 total, 36 per OD. To register, email Stacy Harris at saharris@aoa.org, call (314) 983-4254 or go to www.optometrys-meeting.org.

■ **29-July 6.** *AEA Cruises Alaska Optometric Cruise Seminar.* Aboard Island Princess, Anchorage to Vancouver. Hosted by: AEA Cruises. CE hours: 10. To register, email Marge McGrath at aeacruises@aol.com, call (888) 638-6009 or go to www.optometriccruiseseminars.com.

July 2016

■ **2-7.** *POA/PAFP Seminar at Sea.* Royal Caribbean's Grandeur of the Seas, departs from Baltimore for Bermuda. Hosted by: Pennsylvania Optometric Association, Pennsylvania Academy of Family Physicians. CE hours: 12. To register, email Ilene K. Sauertieg at ilene@poaeyes.org, call (717) 233-6455 or go to www.poaeyes.org.

■ **3-10.** *AEA Cruises Western Mediterranean Cruise Seminar.* Aboard NCL Epic, Barcelona. Hosted by: AEA Cruises. CE hours: 10. To register, email Marge McGrath at aeacruises@aol.com, call (888) 638-6009 or go to www.optometriccruiseseminars.com.

■ **3-10.** *A Clinical Compendium.* Royal Caribbean's Harmony of the Seas, Western Mediterranean Cruise from Barcelona. Hosted by: Dr. Travel Seminars. Key faculty: Leo Semes. CE hours: 12. To register, email Robert Pascal at DrTravel@aol.com, call (800) 436-1028 or go to www.DrTravel.com.

■ **3-10.** *Tropical CE - Disney 2016.* Disney's Yacht Club Resort, Orlando. Hosted by: Tropical CE. Key faculty: Mark Dunbar, Jill Autry. CE hours: 20. To register, email Stuart Autry at sautry@tropicalce.com, call (281) 808-5763 or go to www.TropicalCE.com.

■ **7-10.** *Oklahoma College of Optometry Advanced Procedures Course.* Tahlequah, OK. Hosted by: Northeastern State University, Oklahoma College of Optometry. CE hours: 32. Key faculty: Rich Castillo, Nathan Lighthizer. To register, email Callie McAtee at mcateec@nsuok.edu.

■ **9-10.** *Ocular Disease: Part II.* Marshall B. Ketchum University, Fullerton, CA. Hosted by: Marshall B. Ketchum University. Key faculty: George Comer, David Sendrowski. CE hours: 16. To register, email Antoinette Smith at ce@ketchum.edu, call (714) 449-7495 or go to www.ketchum.edu/index.php/ce.

■ **9-10**. *CE on the Beach.* South Padre Island, TX. Hosted by: Rosenberg School of Optometry. CE hours: 16. To register, email Sandra Fortenberry at rsoce@uiwtx.edu, call (210) 283-6856 or go to www.uiw.edu/optometry/continuing-education.

■ **9-21**. *AEA Cruises Stockholm to London Optometric Cruise Seminar.* Aboard Silversea Silverwind, Stockholm to London. Hosted by: AEA Cruises. CE hours: 12. To register, email Marge McGrath at aeacruises@aol.com, call (888) 638-6009 or go to www.optometriccruiseseminars.com.

■ **13.** *IOA Summer Seminar.* Ritz Charles, Carmel, IN. Hosted by: Indiana Optometric Association. CE hours: 7. To register, email Bridget Sims at blsims@ioa.org, call (317) 237-3560 or go to www.ioa.org.

■ **14-17.** *Colorado Vision Summit.* Steamboat Grand and Steamboat Sheraton, Steamboat Springs, CO. Hosted by: Colorado Optometric Association/Mountain States Congress of Optometry. Key faculty: Eric Schmidt, Gregory Schultz, Catherine McDaniel, William Townsend, Michelle Buckland. CE hours: 54 total, 18 per OD. To register, email Tara Weghorst at tweghorst@visioncare.org, call (303) 863-9268 or go to visioncare.org.

■ **14-17.** *2016 FOA Annual Convention.* The Breakers Palm Beach, Palm Beach, FL. Hosted by: Florida Optometric Association. CE hours: 30 total, 22 per OD. To register, email Jessica Brewton at jessica@floridaeyes.org, call (850) 877-4697 or visit www.floridaeyes.org/events.

■ **17-21.** *Argentina Premier Duck Hunting Conference.* Buenos Aires and Duck Hunters Paradise, Buenos Aires, Argentina. Hosted by: James Fanelli, CE in Italy. Key faculty: James Fanelli. CE hours: 12. To register, email James Fanelli at jamesfanelli@ceinitaly.com, call (910) 452-7225 or go to www.ceinitaly.com.

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CHRISTOPHER QUINN, O.D.
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11:00 am - 1:00 pm
CHRISTOPHER QUINN, O.D.
"Favorite Cases, Anterior and Posterior Segment "

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8:00 am - 10:00 am
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"Anterior Segment Grand Rounds"
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Product Review

Ophthalmic Lenses

New Photochromic Lens Technology

With summer almost here, optometrists can look forward to offering Super Optical's just-released line of Conversion photochromic lenses. Conversion offers a fast and seamless shift between tinted and clear, while blocking harmful UV light, according to Super Optical.

According to the company, patients can see Conversion with the company's FastGrind ADDvantage HD Plus progressives, Single Vision, and Finished Single Vision lenses. FT 28 Conversion lenses will also soon be available. Conversion's photochromic properties are in-mass, which provide truly longer performance, according to Super Optical. Additionally, their monomer will not yellow over time, and the use of a monomer solution retains the shift-speed, according to the company.

Visit www.superoptical.com.

Diagnostic Technology

New MGD Imaging Device

TearScience has released LipiScan, a dedicated high definition gland imager that allows optometrists to efficiently evaluate meibomian glands in busy practices, according to the company.

The new rapid imager was created with end users in mind, according to TearScience.

The introduction of LipiScan will allow busy practices to efficiently integrate assessment of meibomian glands and do so at an affordable price, according to the company.

Visit tearscience.com.

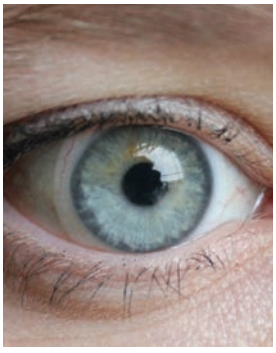
Retinal Blood Flow Imaging

Optovue has given optometrists a new imaging option to view blood flow in the retina. The AngioVue Retina is configured with OCTA and OCT features designed to allow retinal practices to adopt OCT and OCTA into the clinical workflow with minimal disruption, according to the company. Optovue's AngioVue Retina provides retinal specialists with the ability to quickly visualize the presence or absence of retinal vessels and assess new information about the microvasculature with extraordinary detail, according to the company.

Visit optovue.com.

Contact Lenses

Better Trial Lens Fitting for Sclerals



Blanchard Contact Lenses has added a new feature, called XLC, to its Onefit Scleral Lens Platform. XLC, which stands for "extra limbal clearance," is a new option that will make the existing trial set of standard 14.9mm lenses even easier to work with, by providing a simple solution for obtaining the extra limbal clearance needed, without increasing the lens diameter.

Blanchard developed the XLC option so that the lens diameter, central clearance, power and the landing on the sclera do not change, while offering more limbal clearance due to steeper mid-peripheral curves or reverse curves.

The decision will be simple, according to the company. If the diameter of the lens is ideal (3.0mm larger than HVID), while limbal clearance is not, the XLC will help to create more limbal clearance.

Visit www.blanchardlab.com. ■

Surgical Comanagement

New Cataract Drug Option

Imprimis has launched a new product that may be of interest to comanaging optometrists. The company's anti-inflammatory combination drug was launched at the ASCRS Congress in New Orleans.

The Pred-Moxi-Nepafenac (prednisolone acetate, moxifloxacin hydrocholoride and nepafenac) formulation eliminates the need for multiple postoperative eye drops, according to Imprimis.

The company also introduced a sublingual sedative, as an alternative to the IV administration route, during this year's conference.

For more information, visit www.godropless.com and www.imprimispharma.com.

TRAVATAN Z®
(travoprost ophthalmic solution) 0.004%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

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

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

TRAVATAN Z® Solution may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

CONTRAINDICATIONS
None

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

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with TRAVATAN Z® (travoprost ophthalmic solution) 0.004% can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

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

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

Macular Edema
Macular edema, including cystoid macular edema, has been reported during treatment with travoprost ophthalmic solution. TRAVATAN Z® Solution should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

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

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

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

ADVERSE REACTIONS
Clinical Studies Experience
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of a drug cannot be directly compared to rates in the clinical studies of another drug and may not reflect the rates observed in practice. The most common adverse reaction observed in controlled clinical studies with TRAVATAN® (travoprost ophthalmic solution) 0.004% and TRAVATAN Z® (travoprost ophthalmic solution) 0.004% was ocular hyperemia which was reported in 30 to 50% of patients. Up to 3% of patients discontinued therapy due to conjunctival hyperemia. Ocular adverse reactions reported at an incidence of 5 to 10% in these clinical studies included decreased visual acuity, eye discomfort, foreign body sensation, pain and pruritus. Ocular adverse reactions reported at an incidence of 1 to 4% in clinical studies with TRAVATAN® or TRAVATAN Z® Solutions included abnormal vision, blepharitis, blurred vision, cataract, conjunctivitis, corneal staining, dry eye, iris discoloration, keratitis, lid margin crusting, ocular inflammation, photophobia, subconjunctival hemorrhage and tearing.

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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Diagnostic **Quiz**

When the Good Eye Goes Bad

By Andrew S. Gurwood, OD

History

A 38-year-old black male reported to the office with a chief complaint of blurred vision, greater in the right eye than the left, of a year's duration. His systemic history was non-contributory. His ocular history was remarkable for a retinal detachment in the left eye, secondary to blunt trauma sustained during a basketball game more than five years earlier with resultant traumatic open angle glaucoma in the left eye, medicated status post seton implantation with brimonidine BID. The patient also reported having a laser treatment in 2012 but was not able to remember what for.

Diagnostic Data

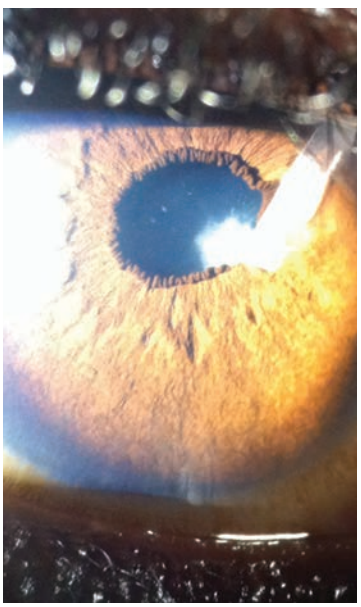
His best corrected entering visual acuities were 20/400 OD and 20/40 OS at distance and near with no improvement upon pinhole or refraction. His external examination revealed a trace afferent pupillary defect in the right eye, peripheral visual field constriction in the right eye with confrontational visual fields and a superior nasal field defect in the left eye. The biomicroscopic examination of the anterior segment of the right eye was normal.

The pertinent anterior segment findings of the left eye are demonstrated in the photograph (Figure 1). Goldmann applanation tonometry measured 11mm Hg OD and 20mm Hg OS. A dilated fundus examination of the right eye is demonstrated in a photograph (*Figure 2*). Undilated 90D fundus examination of the left eye demonstrated cup-disc ratios of 0.5/0.5 with diffuse pallor.

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. ■



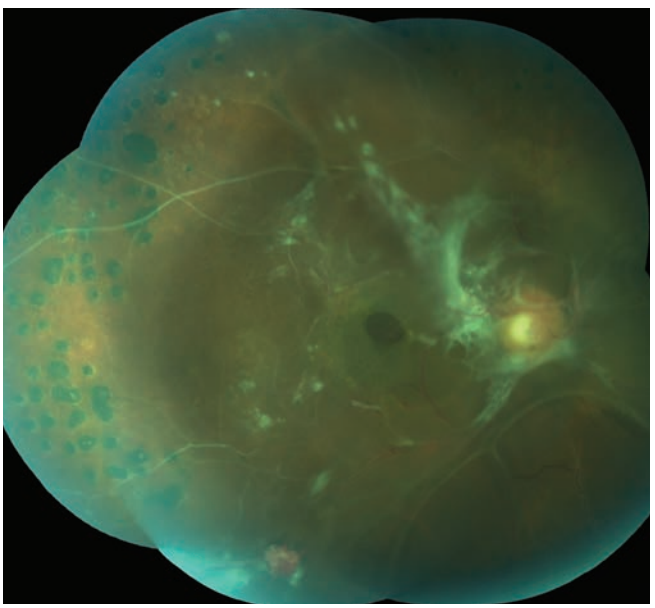


Fig. 1 (left). This patient has had a number of ocular pathologies in the past, but can you tell what's causing his blurred vision from this photograph? Fig. 2 (right). What can be learned from this fundus image of the patient's left eye?

Retina Quiz Answers *(from page 94):* 1) b; 2) d; 3) a; 4) d; 5) c.

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*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.

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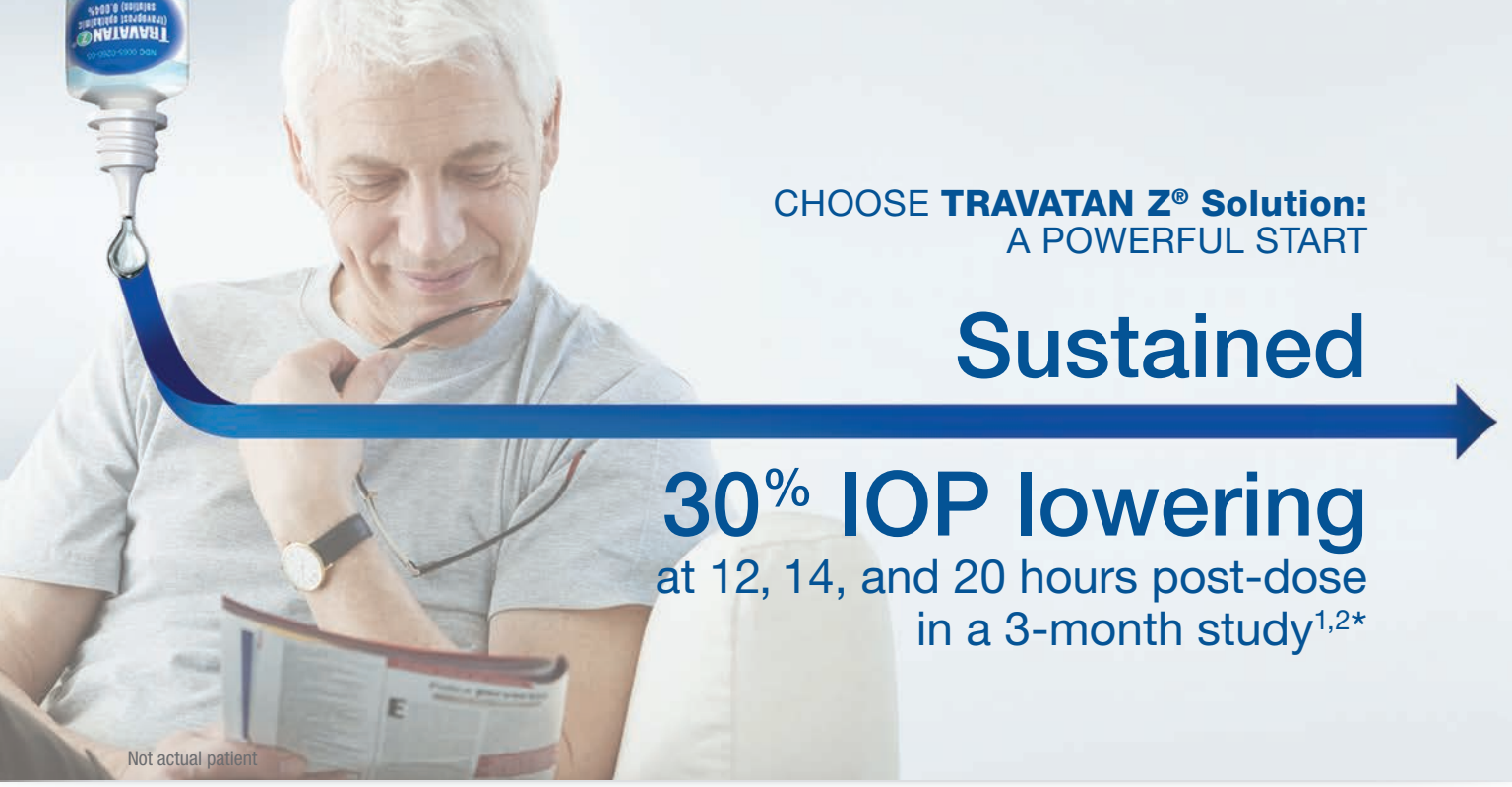

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INDICATIONS AND USAGE

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

Dosage and Administration

The recommended dosage is 1 drop in the affected eye(s) once daily in the evening. TRAVATAN Z® Solution should not be administered more than once daily since it has been shown that more frequent administration of prostaglandin analogs may decrease the IOP-lowering effect.

TRAVATAN Z® Solution may be used concomitantly with other topical ophthalmic drug products to lower IOP. If more than 1 topical ophthalmic drug is being used, the drugs should be administered at least 5 minutes apart.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

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

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

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

Adverse Reactions

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

Use in Specific Populations

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

For additional information about TRAVATAN Z® Solution, please see the brief summary of Prescribing Information on the adjacent page.

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

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

TRAVATAN Z®
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