URGENT CARE: Cilioretinal Artery Occlusion, *P. 92* | **THE ESSENTIALS:** Cotton Wool Spots, *P. 98*

REVIEW® of OPTOMETRY

22nd Annual Dry Eye Report

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Leadership in clinical care

RESCUE PATIENTS FROM

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22nd Annual Dry Eye Report

RESCUE PATIENTS FROM DRY EYE

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†In SVS and toric lenses only.
‡Based on total rebate amount offered to customers ordering an annual supply of Biotrue® ONEday for 3 consecutive years. Terms and conditions apply. See full terms and conditions at www.BauschRewards.com.

REFERENCE: 1. Results of a randomized, masked evaluation of the non-invasive tear break-up time (NITBUT) measured using an Oculus Keratograph 5M after 10 hours of wear. Twelve subjects wore one pair of lenses per day on 6 individual days. Data represents the mean of measured "average" NITBUT.

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See better. Live better.

ODs in Four States Administer COVID Vaccine

CA, UT, KY and OH are among the first to include optometrists in immunization efforts.

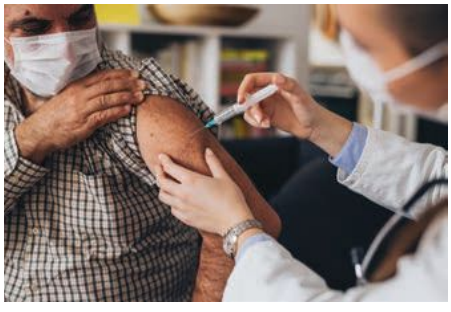
The much-anticipated COVID-19 vaccine rollout has begun, and optometrists in a handful of states have been granted the right to administer shots, while professional groups on the state and federal level continue to push for more to follow suit. Optometrists are authorized to provide vaccinations in Ohio, California, Kentucky and Utah, and similar legislation is pending in New Jersey, according to the American Optometric Association (AOA).

California Begins to Train

In a move to address the state's shortage of healthcare providers available to administer the vaccine, the California Department of Consumer Affairs recently approved a public health emergency waiver to allow doctors of optometry to give COVID-19 shots.

"Optometrists are located in almost every county in California. Often, there is no wait time for an appointment. When there are enough vaccines, patients can be asked to get a vaccine at every office visit," California Optometric Association (COA) President Jason Tu, OD, said in a statement. "Optometrists are particularly helpful in filling the vaccine gap since we care for patients who do not annually see a physician."[1]

Many CA optometrists are already trained to administer vaccines as part of a 2018 law that allows certified ODs to administer some immunizations.[1] Optometrists must undergo the same 20-hour course required for pharmacists and be certified in basic life support. The course includes 12 hours of virtual self-study, eight hours of lecture/injection technique and an online test. To qualify, ODs must also complete a COVID-19 training program developed by the California Department of Public Health.



ODs can help fill in the vaccine gap, as many can administer immunizations.

The order also allows certified optometrists to provide diphenhydramine by injection for the treatment of a severe allergic reaction.

The California Department of Public Health offers the pharmacy course on a regular basis. Ketchum will also be hosting the training course on March 21, and Western University will offer the class at some point in the next month.

Until more vaccines become available, most state optometrists are planning to volunteer at mass vaccination sites or local optometry colleges, explains COA Executive Director Kristine Shultz.

Utah Practices Prepare

Ian Whipple, OD, president of the Utah Optometric Association (UOA), looked into the possibility of administering COVID-19 shots at his practice, but says the current storage requirements for the Pfizer and Moderna vaccines are cost prohibitive.

"I expect that with the recent approval of the Johnson & Johnson vaccine, we will be able to administer these shots to our patients," he says.

Dr. Whipple's practice sees 5,000 patients a year, which means 5,000 fewer patients will need to seek out the vaccine from their medical doctors or state health departments, reducing the burden on the healthcare system.

The UOA is planning large-scale training opportunities for its member doctors, in addition to offering a vaccine training course at its annual convention in June, Dr. Whipple says.

Ohio Pushes ODs to the Frontline

An urgent call for volunteer medical professionals from Ohio's public health emergency program recruited ODs as part of the effort to support its COVID-19 vaccination campaign.[2]

Ohio pressed for optometry's inclusion even before the first vaccines became available, and ODs were bolstered in the effort since the state is one of a few that permit authorization for vaccinations in an emergency.[2]

In 2014, the Ohio Optometric Association successfully advocated for clusion in a new law that granted legal authority for the state's Department of Health to temporarily expand eligible vaccine administrators—normally prohibited by scope limitations—during a declared emergency.

(Continued on page 7)

NO PAZEO*? NO PROBLEM!

For ocular itch associated with allergic conjunctivitis

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Available by prescription only

Formulated with HYDRELLA™ for comfort.[1]
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INDICATIONS AND USAGE
ZERVIATE® (cetirizine ophthalmic solution) 0.24% is a histamine-1 (H1) receptor antagonist indicated for treatment of ocular itching associated with allergic conjunctivitis.

IMPORTANT SAFETY INFORMATION

ADVERSE REACTIONS
The most commonly reported adverse reactions occurred in approximately 1%-7% of patients treated with either ZERVIATE or vehicle. These reactions were ocular hyperemia, instillation site pain, and visual acuity reduced.

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

References: 1. ZERVIATE [package insert]. Fort Worth, TX: Eyevance Pharmaceuticals LLC; 2018. **2.** Malhotra RP, Meier E, Torkildsen G, et al. Safety of cetirizine ophthalmic solution 0.24% for the treatment of allergic conjunctivitis in adult and pediatric subjects. *Clin Ophthalmol.* 2019;13:403-413. **3.** Meier EJ, Torkildsen GL, Gomes PJ, et al. Phase III trials examining the efficacy of cetirizine ophthalmic solution 0.24% compared to vehicle for the treatment of allergic conjunctivitis in the conjunctival allergen challenge model. *Clin Ophthalmol.* 2018;12:2617-2628.

eyevance pharmaceuticals

ZERVIATE™ (cetirizine ophthalmic solution) 0.24%

Brief Summary

INDICATIONS AND USAGE

ZERVIATE (cetirizine ophthalmic solution) 0.24% is a histamine-1 (H1) receptor antagonist indicated for treatment of ocular itching associated with allergic conjunctivitis.

DOSAGE AND ADMINISTRATION

Recommended Dosing: Instill one drop of ZERVIATE in each affected eye twice daily (approximately 8 hours apart). The single-use containers are to be used immediately after opening and can be used to dose both eyes. Discard the single-use container and any remaining contents after administration. The single-use containers should be stored in the original foil pouch until ready to use.

CONTRAINDICATIONS

None.

WARNINGS AND PRECAUTIONS

Contamination of Tip and Solution: As with any eye drop, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle or tip of the single-use container to avoid injury to the eye and to prevent contaminating the tip and solution. Keep the multi-dose bottle closed when not in use. Discard the single-use container after using in each eye.

Contact Lens Wear: Patients should be advised not to wear a contact lens if their eye is red.

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

ADVERSE REACTIONS

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

In 7 clinical trials, patients with allergic conjunctivitis or those at risk of developing allergic conjunctivitis received one drop of either cetirizine (N=511) or vehicle (N=329) in one or both eyes. The most commonly reported adverse reactions occurred in approximately 1%–7% of patients treated with either ZERVIATE or vehicle. These reactions were ocular hyperemia, instillation site pain, and visual acuity reduced.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There were no adequate or well-controlled studies with ZERVIATE in pregnant women. Cetirizine should be used in pregnancy only if the potential benefit justifies the potential risk to the fetus.

Data

Animal Data

Cetirizine was not teratogenic in mice, rats, or rabbits at oral doses up to 96, 225, and 135 mg/kg, respectively (approximately 1300, 4930, and 7400 times the maximum recommended human ophthalmic dose (MRHOD), on a mg/m^2 basis).

Lactation

Risk Summary

Cetirizine has been reported to be excreted in human breast milk following oral administration. Multiple doses of oral dose cetirizine (10 mg tablets once daily for 10 days) resulted in systemic levels (Mean C_{max} = 311 ng/mL) that were 100 times higher than the observed human exposure (Mean C_{max} = 3.1 ng/mL) following twice daily administration of cetirizine ophthalmic solution 0.24% to both eyes for 1 week. Comparable bioavailability has been found between the tablet and syrup dosage forms. However, it is not known whether the systemic absorption resulting from topical ocular administration of ZERVIATE could produce detectable quantities in human breast milk.

There is no adequate information regarding the effects of cetirizine on breastfed infants, or the effects on milk production to inform risk of ZERVIATE to an infant during lactation. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for ZERVIATE and any potential adverse effects on the breastfed child from ZERVIATE.

Pediatric Use: The safety and effectiveness of ZERVIATE has been established in pediatric patients two years of age and older. Use of ZERVIATE in these pediatric patients is supported by evidence from adequate and well-controlled studies of ZERVIATE in pediatric and adult patients.

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenicity

In a 2-year carcinogenicity study in rats, orally administered cetirizine was not carcinogenic at dietary doses up to 20 mg/kg (approximately 550 times the MRHOD, on a mg/m^2 basis). In a 2-year carcinogenicity study in mice, cetirizine caused an increased incidence of benign liver tumors in males at a dietary dose of 16 mg/kg (approximately 220 times the MRHOD, on a mg/m^2 basis). No increase in the incidence of liver tumors was observed in mice at a dietary dose of 4 mg/kg (approximately 55 times the MRHOD, on a mg/m^2 basis). The clinical significance of these findings during long-term use of cetirizine is not known.

Mutagenesis

Cetirizine was not mutagenic in the Ames test or in an *in vivo* micronucleus test in rats. Cetirizine was not clastogenic in the human lymphocyte assay or the mouse lymphoma assay.

Impairment of Fertility

In a fertility and general reproductive performance study in mice, cetirizine did not impair fertility at an oral dose of 64 mg/kg (approximately 875 times the MRHOD, on a mg/m^2 basis).

PATIENT COUNSELING INFORMATION

Risk of Contamination: Advise patients not to touch dropper tip to eyelids or surrounding areas, as this may contaminate the dropper tip and ophthalmic solution. Advise patients to keep the bottle closed when not in use. Advise patients to discard single-use containers after each use.

Concomitant Use of Contact Lenses: Advise patients not to wear contact lenses if their eyes are red. Advise patients that ZERVIATE should not be used to treat contact lens–related irritation. Advise patients to remove contact lenses prior to instillation of ZERVIATE. The preservative in ZERVIATE solution, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted 10 minutes following administration of ZERVIATE.

Administration: Advise patients that the solution from one single-use container is to be used immediately after opening. Advise patients that the single-use container can be used to dose both eyes. Discard the single-use container and remaining contents immediately after administration.

Storage of Single-use Containers:
Instruct patients to store single-use containers in the original foil pouch until ready to use.

Rx Only

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ZER-04-20-MS-44

Mask Wear Leads to Clinical Concerns

Recent research has determined that wearing a mask in the past year has affected both the clinician and the patient. One study warns that poorly fitting masks worn by glaucoma patients can cause visual field (VF) artifacts, which may be interpreted as disease progression, or make the tests less reliable.[1] Face mask use during the COVID-19 pandemic has sparked an increase in reported dry eye symptoms among regular mask wearers that hasn't been described in the literature.[2]

VF Test Errors

The investigation included 127 glaucoma patients who underwent standard automated perimetry. In patients with low test reliability or VF changes, testing was repeated after repositioning and taping masks. A total of 101 patients wore surgical masks, and 26 others wore cloth masks.

The researchers found low levels of testing reliability in 23 patients (18%) and inferior VF defects in three patients (2%). The most common testing issues were increased fixation losses and false positives.

Additionally, low testing reliability was notably higher in patients who wore cloth masks compared with those in surgical masks (48% vs. 10%). Eyeglass fogging due to face masks prior to testing was a strong predictor of trial lens fogging and low testing reliability. In all repeated tests, the patients' reliability parameters improved and inferior VF artifacts disappeared.

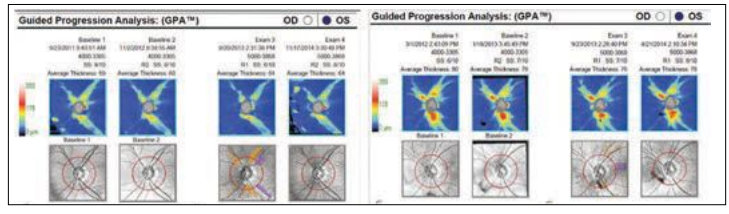

Photo: Danica J. Marrelli, OD

Poor-fitting masks can produce artifacts and improper segmentation of RNFL on macular scans, similar to that seen here in a different patient.

"Careful assessment of structure-function correlation and repeated VF tests with the taped mask are critical to differentiate between artifacts and abnormalities," the researchers wrote in their paper.[1]

Eye Discomfort Complaints

A different study looked at the patient's experience. This observational, descriptive, cross-sectional study analyzed the results of a survey that received a total of 3,605 responses. Of these, 2,447 reported symptoms, with 26.9% saying their symptoms were exacerbated by mask wearing. Of all participants, 18.3% said they experienced mask-associated dry eye.

The researcher found no significant association between perceived mask-associated dry eye, age, refractive correction and pre-existing ocular discomfort, but did find a positive association with female sex and retail work.

The author wrote in her paper that, although most participants reported no changes in ocular symptoms, those who reported exacerbated symptoms are still important to consider. "As face masks are necessary to slow down the spread of COVID-19, it's important not to underestimate all symptoms that could discourage the population from using them," she concluded. "Eye care professionals should verify the presence of clinical signs in all patients complaining about mask-induced eye discomfort, and suggest methods to mitigate this condition."

1. Bayram N, Gundogan M, Ozsaygılı C, et al. The impacts of face mask use on standard automated perimetry results in glaucoma patients. J Glaucoma. January 7, 2021. [Epub ahead of print].

2. Boccardo L. Self-reported symptoms of mask-associated dry eye: a survey study of 3,605 people. Contact Lens Ant Eye. January 20, 2021. [Epub ahead of print].

States Push for Vaccine Green Light

(Continued from page 4)

National Push for the Profession

In a recent letter to the White House, the AOA urged the new administration to amend the current COVID-19 Public Readiness and Emergency Preparedness Act declaration to recognize that all optometrists can administer vaccines.

According to the AOA, 99% of Americans live in a county with a doctor of optometry, and ODs have the necessary knowledge to provide vaccines, not to mention the fact that optometry schools teach injections. Optometrists in 19 states are already authorized to administer injections, and in an additional 20 states, optometrists can provide anaphylaxis through injection.

One month into the pandemic, ODs across the country provided urgent and emergency care to roughly 206,000 individuals, the AOA cites. Doctors of optometry also reported 60% of patients would have otherwise sought care at an emergency department or urgent care center when such facilities were taxed with COVID-19 cases. For these efforts, state administrations generally agreed to include optometry among the initial distribution phases, the AOA said in a statement.

1. COA applauds decision to allow optometrists to administer COVID-19. California Optometric Association. February 12, 2021. www.coavision.org/i4a/pages/index.cfm?pageid=3313. Accessed February 25, 2021.

2. Ohio activates eligible doctors for COVID-19 vaccine administration, AOA focuses new relief efforts. American Optometric Association. February 25, 2021. www.aoa.org/news/advocacy/federal-advocacy/ohio-activates-eligible-doctors-for-covid-19-vaccine-administration-aoa-focuses-new-relief-efforts?sso=y. Accessed February 25, 2021.

Red Wine Helps Combat Eye Disease

Resveratrol (RSV), a polyphenol compound made by plants to fight off fungal infections and other invaders, has been touted for its healing and protective qualities against conditions such as cancer and heart disease. With these restorative properties in mind, a new study in the *International Journal of Molecular Sciences* suggests RSV can also be highly effective in combating eye conditions, including age-related macular degeneration (AMD), glaucoma, cataract, diabetic retinopathy, proliferative vitreoretinopathy and corneal infection.[1]

The study, a literature review by a team of international researchers, cites RSV's ability to act on common targets such as reactive oxygen species, lipid mediators, apoptosis, pro-inflammatory mediators and angiogenesis to prevent age-related ocular diseases. Additionally, the authors report RSV has innate properties that protect eyes against environmental factors such as diabetes, hypertension, stress, UV light, acrolein found in cigarette smoke and air pollution.[1]

Found naturally in red wines, Japanese knotweed roots, black currants, grape juices, peanuts and certain berries, RSV is hailed for its healing powers, not to mention its ability to modulate various targets in numerous pathologies. "Its properties have been shown to fight inflammation or inhibit inflammation and oxidation of certain cells, and it's been found in studies to prevent cell death, or apoptosis," says Paul Karpecki, OD.

"We've had some good results with RSV and cataracts, particularly in diabetic and aging cataracts," Jeffrey Anshel, OD, adds. He explains that RSV activates the survival gene, Sirtuin 1 (SIRT1). "That's where the anti-aging part of RSV comes in. It helps to activate the survival gene," he says.

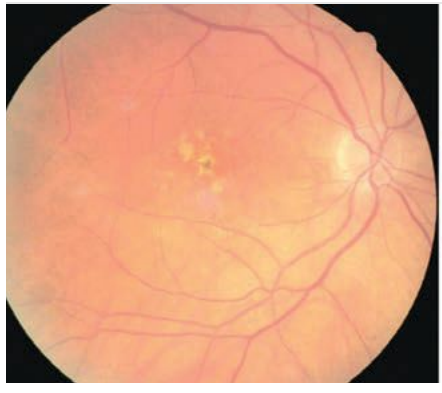

Photo: Julie Poteet, OD

RSV can battle specific AMD hallmarks, such as impaired RPE.

RSV and AMD

The research paper posits that RSV can battle specific AMD hallmarks, including oxidative damage, impaired retinal pigment epithelium (RPE), increased apoptosis, chronic inflammation and neovascularization.[1]

Various environmental factors produce free radicals, which lead to oxidative stress in ocular tissues and consequently provoke the initiation of diseases such as AMD. The investigators suggest RSV is able to scavenge free radicals (O_2-) and activate superoxide dismutase or glutathione reductase, while also inhibiting inflammation through the reduction of various pro-inflammatory cytokines and blocking the signaling pathway induced by vascular endothelial growth factor-A to promote neo-angiogenesis.[1]

One study in the literature review found treatment with 50µmol/L and 100µmol/L RSV significantly reduced proliferation of RPE cells by 10% and 25%, respectively. Additionally, RSV (100µmol/L) inhibited basal and H_2O_2-induced intracellular oxidation and protected RPE cells from H_2O_2-induced cell death.[2]

Looking at inflammation, the study cited one investigation that showed RSV reduced the production of IL-6 and IL-8 induced by glucose in retinal cells, which is significant as the latter is an important risk factor for AMD.[3]

RSV and Glaucoma

Oxidative stress is known to be an early hallmark sign of hydrostatic pressure-induced retinal ganglion cell damage in glaucoma. Several studies have shown that oxygen metabolism and, more specifically, reactive oxygen species, are crucial in the development of glaucoma. RSV has antioxidant properties that, through its hydroxyl groups, have the ability to react with reactive oxygen species in glaucoma.[1]

Trans-RSV activates sirtuin, which leads to the phosphorylation of Akt and inhibits Bax activity. RSV also activates the AMPK pathway, which leads to mitochondrial DNA transcription and replication. RSV is also able to alter Oma-1 and Yeme-1 mRNA expression, leading to the alteration of the long optical autophagy 1/short optical autophagy (L-Opa-1/S-Opa-1) ratio.[1]

In addition, RSV lowers reactive oxygen specie levels not only by activating the scavenger pathway, but also by facilitating the translocation of Nrf2 into the nucleus, thereby favoring interaction between Nfr2 and the antioxidant response element leading to HO production.[1]

RSV and Cataract

In an experimental model of naphthalene-induced age-related cataract in rats, RSV (20mg/kg and 40mg/kg per day IP) slowed lenticular opacity, restored antioxidants, Ca_2+ ATPase function and protein content and reduced lipid peroxidation in the lenses of RSV-treated rats.[4]

Another study in the review found RSV could counter posterior capsule opacification-related physiological events in two human lens model systems.[5]

Dr. Karpecki cites yet another investigation not part of the current review that also looked at the effects of RSV on cataracts in a rat model. In this investigation, the rats either received subcutaneous injection of selenite,

(Continued on page 11)

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INDICATION

Upneeq® (oxymetazoline hydrochloride ophthalmic solution), 0.1% is indicated for the treatment of acquired blepharoptosis in adults.

IMPORTANT SAFETY INFORMATION

WARNINGS AND PRECAUTIONS

- Alpha-adrenergic agonists as a class may impact blood pressure. Advise Upneeq patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to seek medical care if their condition worsens.
- Use Upneeq with caution in patients with cerebral or coronary insufficiency or Sjögren's syndrome. Advise patients to seek medical care if signs and symptoms of potentiation of vascular insufficiency develop.
- Upneeq may increase the risk of angle closure glaucoma in patients with untreated narrow-angle glaucoma. Advise patients to seek immediate medical care if signs and symptoms of acute narrow-angle glaucoma develop.
- Patients should not touch the tip of the single patient-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

ADVERSE REACTIONS

Adverse reactions that occurred in 1-5% of subjects treated with Upneeq were punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation, and headache.

DRUG INTERACTIONS

- Alpha-adrenergic agonists, as a class, may impact blood pressure. Caution in using drugs such as beta blockers, anti-hypertensives, and/or cardiac glycosides is advised. Caution should also be exercised in patients receiving alpha adrenergic receptor antagonists such as in the treatment of cardiovascular disease, or benign prostatic hypertrophy.
- Caution is advised in patients taking monoamine oxidase inhibitors which can affect the metabolism and uptake of circulating amines.

To report SUSPECTED ADVERSE REACTIONS or product complaints, contact RVL Pharmaceuticals at 1-877-482-3788. You may also report SUSPECTED ADVERSE REACTIONS to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see next page for Brief Summary of full Prescribing Information.

Reference: 1. Upneeq® (oxymetazoline hydrochloride ophthalmic solution), 0.1%. [Prescribing Information].

RVL PHARMACEUTICALS, INC.

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UPNEEQ®
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*Each mL of Upneeq contains 1 mg of oxymetazoline hydrochloride, equivalent to 0.09 mg (0.09%) of oxymetazoline free base.

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UPNEEQ® (oxymetazoline hydrochloride ophthalmic solution), 0.1%,* for topical ophthalmic use

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BRIEF SUMMARY: The following is a brief summary only; see full Prescribing Information at https://www.upneeq.com/Upneeq-PI.pdf for complete information.

1 INDICATIONS AND USAGE

UPNEEQ is indicated for the treatment of acquired blepharoptosis in adults.

2 DOSAGE AND ADMINISTRATION

Contact lenses should be removed prior to instillation of UPNEEQ and may be reinserted 15 minutes following its administration.

If more than one topical ophthalmic drug is being used, the drugs should be administered at least 15 minutes between applications.

4 CONTRAINDICATIONS

None.

5 WARNINGS AND PRECAUTIONS

5.1 Potential Impacts on Cardiovascular Disease

Alpha-adrenergic agonists may impact blood pressure. UPNEEQ should be used with caution in patients with severe or unstable cardiovascular disease, orthostatic hypotension, and uncontrolled hypertension or hypotension. Advise patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension/hypotension to seek immediate medical care if their condition worsens.

5.2 Potentiation of Vascular Insufficiency

UPNEEQ should be used with caution in patients with cerebral or coronary insufficiency, or Sjögren's syndrome. Advise patients to seek immediate medical care if signs and symptoms of potentiation of vascular insufficiency develop.

5.3 Risk of Angle Closure Glaucoma

UPNEEQ may increase the risk of angle closure glaucoma in patients with untreated narrow-angle glaucoma. Advise patients to seek immediate medical care if signs and symptoms of acute angle closure glaucoma develop.

5.4 Risk of Contamination

Patients should not touch the tip of the single patient-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

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 practice.

A total of 360 subjects with acquired blepharoptosis were treated with UPNEEQ once daily in each eye for at least 6 weeks in three controlled Phase 3 clinical trials, including 203 subjects treated with UPNEEQ for 6 weeks and 157 subjects treated with UPNEEQ for 12 weeks. Adverse reactions that occurred in 1-5% of subjects treated with UPNEEQ were punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation, and headache.

7 DRUG INTERACTIONS

7.1 Anti-hypertensives/Cardiac Glycosides

Alpha-adrenergic agonists, as a class, may impact blood pressure. Caution in using drugs such as beta-blockers, anti-hypertensives, and/or cardiac glycosides is advised.

Caution should also be exercised in patients receiving alpha adrenergic receptor antagonists such as in the treatment of cardiovascular disease, or benign prostatic hypertrophy.

7.2 Monoamine Oxidase Inhibitors

Caution is advised in patients taking MAO inhibitors which can affect the metabolism and uptake of circulating amines.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on UPNEEQ use in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. In animal reproduction studies, there were no adverse developmental effects observed after oral administration of oxymetazoline hydrochloride in pregnant rats and rabbits at systemic exposures up to 7 and 278 times the maximum recommended human ophthalmic dose (MRHOD), respectively, based on dose comparison. [see Data]. The estimated background risks of major birth defects and miscarriage for the indicated population are unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

Animal Data

Effects on embryo-fetal development were evaluated in rats and rabbits following oral administration of oxymetazoline hydrochloride during the period of organogenesis. Oxymetazoline hydrochloride did not cause adverse effects to the fetus at oral doses up to 0.2 mg/kg/day in pregnant rats during the period of organogenesis (28 times the MRHOD, on a dose comparison basis). Oxymetazoline hydrochloride did not cause adverse effects to the fetus at oral doses up to 1 mg/kg/day in pregnant rabbits during the period of organogenesis (278 times the MRHOD, on a dose comparison basis). Maternal toxicity, including decreased maternal body weight, was produced at the high dose of 1 mg/kg/day in pregnant rabbits and was associated with findings of delayed skeletal ossification.

In a rat prenatal and postnatal development study, oxymetazoline hydrochloride was orally administered to pregnant rats once daily from gestation day 6 through lactation day 20. Maternal toxicity was produced at the high dose of 0.2 mg/kg/day (28 times the MRHOD, on a dose comparison basis) in pregnant rats and was associated with an increase in pup mortality and reduced pup body weights. Delayed sexual maturation was noted at 0.1 mg/kg/day (14 times the MRHOD, on a dose comparison basis). Oxymetazoline hydrochloride did not have any adverse effects on fetal development at a dose of 0.05 mg/kg/day (7 times the MRHOD, on a dose comparison basis).

8.2 Lactation

Risk Summary

No clinical data are available to assess the effects of oxymetazoline on the quantity or rate of breast milk production, or to establish the level of oxymetazoline present in human breast milk post-dose. Oxymetazoline was detected in the milk of lactating rats. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for UPNEEQ and any potential adverse effects on the breastfed child from UPNEEQ.

8.4 Pediatric Use

Safety and effectiveness of UPNEEQ have not been established in pediatric patients under 13 years of age.

8.5 Geriatric Use

Three hundred and fifteen subjects aged 65 years and older received treatment with UPNEEQ (n = 216) or vehicle (n = 99) in clinical trials. No overall differences in safety or effectiveness were observed between subjects 65 years of age and older and younger subjects.

10 OVERDOSAGE

Accidental oral ingestion of topical intended solutions (including ophthalmic solutions and nasal sprays) containing imidazoline derivatives (e.g., oxymetazoline) in children has resulted in serious adverse events requiring hospitalization, including nausea, vomiting, lethargy, tachycardia, decreased respiration, bradycardia, hypotension, hypertension, sedation, somnolence, mydriasis, stupor, hypothermia, drooling, and coma. Keep UPNEEQ out of reach of children.

PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Instructions for Use).

RVL PHARMACEUTICALS, INC.

Manufactured for: RVL Pharmaceuticals, Inc.
Bridgewater, New Jersey 08807

PM-US-UPN-0203 01/21

RSV Gets Good Marks for Eye Health

(Continued from page 8)

which induces advanced cataract within 24 hours, saline or a combination of sodium seleneite and 40mg of RSV. As expected, the rats injected by saline had clear eyes and the ones exposed to pure selenite had higher-grade cataracts. In the rats that received the RSV/selenite combination, only nine out of the 16 developed cataracts, which were of a lower grade.[6]

RSV and Diabetic Retinopathy

The authors also suggest RSV can combat diabetic retinopathy, since RSV activates SIRT1, which leads to the phosphorylation of Akt and inhibits the mitochondrial apoptosis pathway. Additionally, RSV stimulates mitochondrial activity through the AMPK–PGC1 alpha pathway, which reduces apoptosis. RSV also lowers ROS through the iPf2 alpha, AGE/RAGE, PKC and polyol pathways and downregulates pro-inflammatory cytokines such as IL-1 beta, IL-6 and IL-8, the researchers said.[1]

Other Ocular Benefits

Dr. Karpecki cites another study that found both red wine polyphenolic compounds and green tea polyphenols were able to inhibit several key events of the angiogenic process, such as the proliferation and migration of endothelial cells and vascular smooth muscle cells and the expression of two major proangiogenic factors—vascular endothelial growth factor and matrix metalloproteinase-2—by both redox-sensitive and redox-insensitive mechanisms.[7]

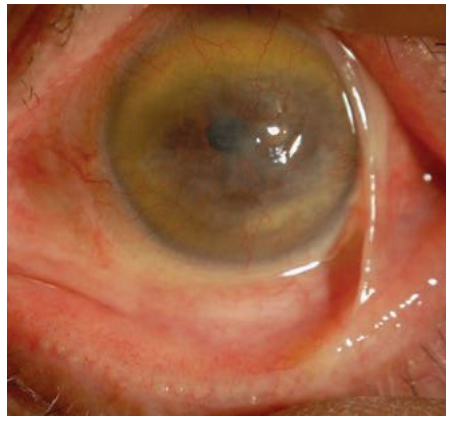

Photo: W. Munir, MD

RSV may possibly reduce corneal neovascularization due to VEGF.

Antiangiogenic properties of polyphenols have also been observed in the chick embryo chorioallantoic membrane since the local application of RWPCs and GTPs strongly inhibits the formation of new blood vessels. Moreover, intake of RSV or green tea has been shown to reduce corneal neovascularization induced by proangiogenic factors such as VEGF and fibroblast growth factor in mice.[7]

RSV in Practice

Despite RSV's good marks in the literature, this doesn't mean ODs should suggest their patients consume wine to ward off eye disease, experts caution.

While wine in moderation has proved to be beneficial in some cases, Dr. Karpecki stresses that RSV can be found in other forms, including grape seed extract, black currants and certain supplements.

"If you look at the amount of RSV in wine, it's pretty minimal. What I specifically tell people is, 'You'll only need 14 glasses of wine a day to get enough RSV,'" Dr. Anshel says with a laugh. "You're actually better off taking a supplement with RSV in it."

Dr. Anshel notes there are many supplements on the market.

One study that looked at the effects of the OTC supplement over a several-year period showed broad bilateral improvements in ocular structure and function in three AMD patients, including one with a treatment-resistant variant, which was opposite to what might be expected due to aging and the natural progression of the patient's pathophysiology.[8]

Still, other OTC products contain GLA derived from black currant seed oil, a foundation of RSV, can also combat dry eye.

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IN BRIEF

Spending less time outdoors and more time looking at screens during prolonged school closures brought on by the pandemic, school-aged **children ages six to eight are at risk of experiencing a substantial myopic shift due to home confinement** resulting from COVID-19, according to a new study published in *JAMA Ophthalmology*.

"Younger children's refractive status may be more sensitive to environmental changes than older children, given that they are in an important period for the development of myopia," the researchers wrote in their paper.

They launched a prospective, cross-sectional study of school-based photoscreenings (noncycloplegic photorefraction) that included 389,808 eyes of 123,535 children aged six to 13 from 10 elementary schools in Feicheng, China. About half of the students were boys.

The researchers noted a substantial shift in myopia prevalence in the 2020 screenings compared with preceding years for younger children. These differences were minimal in children aged nine to 13 years.

Wang J, Li Y, Musch D, et al. Progression of myopia in school-aged children after COVID-19 home confinement. JAMA Ophthalmol. January 14, 2021. [Epub ahead of print].

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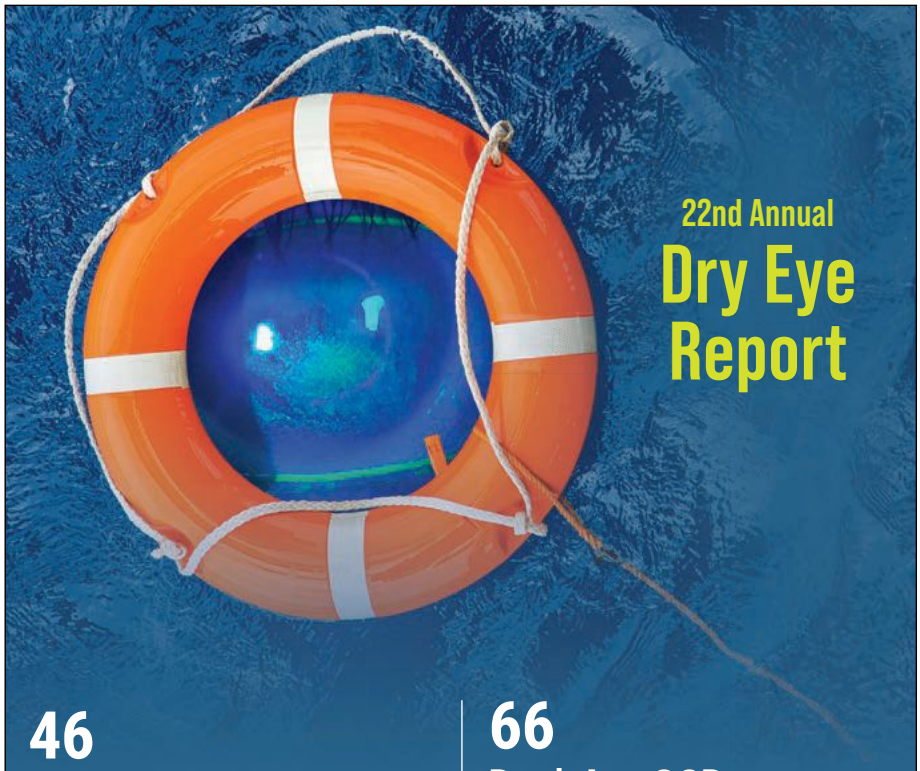

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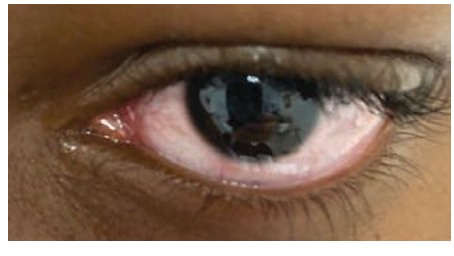

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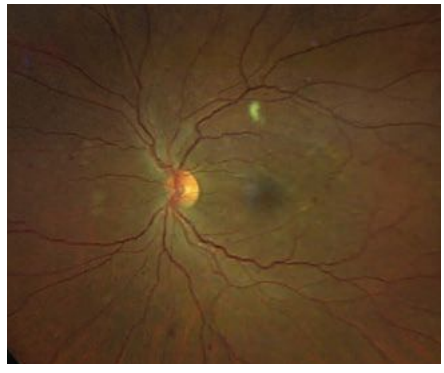

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INDICATIONS AND USAGE

PROLENSA® (bromfenac ophthalmic solution) 0.07% is a nonsteroidal anti-inflammatory drug (NSAID) indicated for the treatment of postoperative inflammation and reduction of ocular pain in patients who have undergone cataract surgery.

IMPORTANT SAFETY INFORMATION

- PROLENSA® contains sodium sulfite, a sulfite that may cause allergic type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.
- All topical nonsteroidal anti-inflammatory drugs (NSAIDs), including bromfenac, may slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.
- There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including bromfenac. Use with caution in patients who have previously exhibited sensitivities to these drugs.
- There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery. Use with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

IMPORTANT SAFETY INFORMATION (CONT.)

- Use of topical NSAIDs may result in keratitis. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs, including bromfenac, and should be closely monitored for corneal health. Patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients. Post-marketing experience with topical NSAIDs suggests that use more than 24 hours prior to surgery or use beyond 14 days post-surgery may increase patient risk for the occurrence and severity of corneal adverse events.
- PROLENSA® should not be instilled while wearing contact lenses. The preservative in PROLENSA®, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of PROLENSA®.
- The most commonly reported adverse reactions in 3%-8% of patients were anterior chamber inflammation, foreign body sensation, eye pain, photophobia, and blurred vision.

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

References: 1. PROLENSA Prescribing Information. Bausch & Lomb Incorporated. **2.** Baklayan GA, Patterson HM, Song CK, Gow JA, McNamara TR. 24-hour evaluation of the ocular distribution of (14)C-labeled bromfenac following topical instillation into the eyes of New Zealand white rabbits. *J Ocul Pharmacol Ther.* 2008;24(4):392-398. **3.** Data on file, Bausch & Lomb Incorporated.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

PROLENSA® (bromfenac ophthalmic solution) 0.07%

Rx only
Initial Rx Approval: 1997

INDICATIONS AND USAGE

PROLENSA® (bromfenac ophthalmic solution) 0.07% is indicated for the treatment of postoperative inflammation and reduction of pain in patients who have undergone cataract surgery.

DOSAGE AND ADMINISTRATION

Recommended Dosing

One drop of PROLENSA ophthalmic solution should be applied to the affected eye once daily beginning 1 day prior to cataract surgery, continued on the day of surgery, and through the first 14 days of the postoperative period.

Use with Other Topical Ophthalmic Medications

PROLENSA ophthalmic solution may be administered in conjunction with other topical ophthalmic medications such as alpha-agonists, beta-blockers, carbonic anhydrase inhibitors, cycloplegics, and mydriatics. Drops should be administered at least 5 minutes apart.

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Sulfite Allergic Reactions

Contains sodium sulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people. The overall prevalence of sulfite sensitivity in the general population is unknown and probably low. Sulfite sensitivity is seen more frequently in asthmatic than in non-asthmatic people.

Slow or Delayed Healing

All topical nonsteroidal anti-inflammatory drugs (NSAIDs), including bromfenac, may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

Potential for Cross-Sensitivity

There is the potential for cross-sensitivity to acetylsalicylic acid, phenylacetic acid derivatives, and other NSAIDs, including bromfenac. Therefore, caution should be used when treating individuals who have previously exhibited sensitivities to these drugs.

Increased Bleeding Time

With some NSAIDs, including bromfenac, there exists the potential for increased bleeding time due to interference with platelet aggregation. There have been reports that ocularly applied NSAIDs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery.

It is recommended that PROLENSA ophthalmic solution be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

Keratitis and Corneal Reactions

Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration, or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs, including bromfenac, and should be closely monitored for corneal health.

Post-marketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients.

Post-marketing experience with topical NSAIDs also suggests that use more than 24 hours prior to surgery or use beyond 14 days post-surgery may increase patient risk for the occurrence and severity of corneal adverse events.

Contact Lens Wear

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

ADVERSE REACTIONS

Clinical Trial 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 commonly reported adverse reactions following use of PROLENSA ophthalmic solution following cataract surgery include: anterior chamber inflammation, foreign body sensation, eye pain, photophobia and vision blurred. These reactions were reported in 3 to 8% of patients.

USE IN SPECIFIC POPULATIONS

Pregnancy

Treatment of rats at oral doses up to 0.9 mg/kg/day (systemic exposure 90 times the systemic exposure predicted from the recommended human ophthalmic dose [RHOD] assuming the human systemic concentration is at the limit of quantification) and rabbits at oral doses up to 7.5 mg/kg/day (150 times the predicted human systemic exposure) produced no treatment-related malformations in reproduction studies. However, embryo-fetal lethality and maternal toxicity were produced in rats and rabbits at 0.9 mg/kg/day and 7.5 mg/kg/day, respectively. In rats, bromfenac treatment caused delayed parturition at 0.3 mg/kg/day (30 times the predicted human exposure), and caused dystocia, increased neonatal mortality, and reduced postnatal growth at 0.9 mg/kg/day.

There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Because of the known effects of prostaglandin biosynthesis-inhibiting drugs on the fetal cardiovascular system (closure of ductus arteriosus), the use of PROLENSA ophthalmic solution during late pregnancy should be avoided.

Nursing Mothers

Caution should be exercised when PROLENSA is administered to a nursing woman.

Pediatric Use

Safety and efficacy in pediatric patients below the age of 18 have not been established.

Geriatric Use

There is no evidence that the efficacy or safety profiles for PROLENSA differ in patients 70 years of age and older compared to younger adult patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis and Impairment of Fertility

Long-term carcinogenicity studies in rats and mice given oral doses of bromfenac up to 0.6 mg/kg/day (systemic exposure 30 times the systemic exposure predicted from the recommended human ophthalmic dose [RHOD] assuming the human systemic concentration is at the limit of quantification) and 5 mg/kg/day (340 times the predicted human systemic exposure), respectively, revealed no significant increases in tumor incidence.

Bromfenac did not show mutagenic potential in various mutagenicity studies, including the reverse mutation, chromosomal aberration, and micronucleus tests. Bromfenac did not impair fertility when administered orally to male and female rats at doses up to 0.9 mg/kg/day and 0.3 mg/kg/day, respectively (systemic exposure 90 and 30 times the predicted human exposure, respectively).

PATIENT COUNSELING INFORMATION

Slowed or Delayed Healing

Advise patients of the possibility that slow or delayed healing may occur while using NSAIDs.

Sterility of Dropper Tip

Advise patients to replace bottle cap after using and to not touch dropper tip to any surface, as this may contaminate the contents. Advise patients that a single bottle of PROLENSA be used to treat only one eye.

Concomitant Use of Contact Lenses

Advise patients to remove contact lenses prior to instillation of PROLENSA. The preservative in PROLENSA, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of PROLENSA.

Concomitant Topical Ocular Therapy

If more than one topical ophthalmic medication is being used, the medicines should be administered at least 5 minutes apart.

Rx Only

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BY JACK PERSICO
EDITOR-IN-CHIEF
OUTLOOK

Changing the Culture

OD-MD cooperation succeeds when there's mutual trust and respect. Expect it—but earn it, too.

Comanagement used to be the sort of thing a niche group of ODs would do if they had the inclination and legal authority to get involved in some elements of medical care. When *optometry* was still synonymous with *glasses and contact lenses*, comanagement was a choice. More often than not, optometrists would refer out their medical cases and just concentrate on taking care of the patient's optical needs—if they even returned to the practice at all.

Not any more. The profession, and the public's expectations of it, have advanced. Trouble is, ophthalmologists aren't always supportive, to put it mildly. Too often, they still see optometric advancement as a competitive threat encroaching on their domain rather than as a resource that can help them. Increasingly, optometrists have the clinical skills to practice full-scope care, but not a willing partner on the MD side who sees it as mutually beneficial. That needs to change.

This month, we begin a six-part series that delves into the tricky business of making these relationships work better, called Comanagement Connections to reflect the primacy of the person-to-person interactions at the heart of a successful partnership. ODs, MDs and, to some extent, patients all have to be on the same wavelength about what they expect of each other.

"Comanagement represents cooperation," observes Paul Ajamian, OD, at the outset of the first installment of the series. Dr. Ajamian, of course, was a member of the optometric vanguard that made comanagement a reality, beginning in the 1980s with the creation of the Omni Eye Centers.

Among the virtues Dr. Ajamian credits Omni's success to was the modeling of good behavior. "The practice was predicated on not doing anything that would compete with the referring OD: no optical, no contact lenses and no primary care. Add to that the automatic return of each patient, a meaningful letter back and ongoing continuing education to move the profession forward, and a transformative model was born," he explained to us a few years back in a retrospective on comanagement's impact.

That sense of mutual respect and trust is what to strive for as you strengthen your relationships with ophthalmology. I think we'd all agree that cooperation and reconciliation are needed in many spheres of life right now, eye care included.

"No man is an island," wrote the English poet John Donne nearly 400 years ago. No optometrist is either these days. And the same goes for the ophthalmologists who, in a prior era, neither wanted nor needed any help serving their patients. We wish you the best of luck in strengthening these all-important bonds.

This month, we're also pleased to welcome Danica Marrelli, OD, to our editorial board. Dr. Marrelli is a glaucoma expert who works hard to advance optometric skills in this area, both among the students she teaches at the University of Houston College of Optometry and the wider field of practicing optometrists who attend her lectures or read her articles. We're excited to showcase her expertise in these pages. ■

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BY PAUL M. KARPECKI, OD
CHIEF CLINICAL EDITOR

THROUGH MY EYES

Go Deep on DED

With new tools and techniques flourishing, now's the time to expand your skill set and offerings.

Although it's hard for me to believe how time passes, I started my first dedicated dry eye disease (DED) clinic in 1998. Things were limited back then—we had crude diagnostics, a poor understanding of the disease, a large unserved patient population and no on-label therapeutic agents. There were times when more than half the patients I saw were dissatisfied with their treatment. What a terrible scenario.

Fast forward 23 years and we have four approved dry eye disease therapies, numerous effective in-office treatment options, advanced DED diagnostics, easy-to-follow protocols and a greater understanding of the disease. Today, over 95% of the patients that come into my dry eye clinic are satisfied with their treatment.

I'll share what I feel are the keys to that transformation.

Where to Start?

Many doctors serve their dry eye patients well even without advanced technology, but for those looking for more control over the experience, the first piece of equipment I'd recommend would be a slit lamp imaging system (*e.g.*, Haag-Streit, TelScreen, Firefly). This helps with patient education and lets you reference the baseline pathology from a previous visit. Another consideration for education is providing dedicated video assets from Rendia (formerly Eyemaginations) that explain the complexities of DED in a straightforward way without tying up staff time. If you want to offer in-office procedures, you'll need a tool for expressing meibomian glands (*e.g.*, Mastrota Paddle or Meibomian Gland Evaluator) and an eyelid debrider. For evaluation, NaFl dye and a yellow filter are standard. If you want to have a dedicated dry eye center, you'll also need osmolarity, meibography or a tear diagnostic system.

DED Screening Questions

- How do your eyes feel (*e.g.*, dry, gritty, burning)?
- How do they look (red or irritated)?
- Do you experience fluctuating vision?
- Do you use or have the urge to use artificial tears?
- How much time do you spend on digital devices per day?

Next, you need to identify patients who may have DED. My favorite triaging questions came from the Optometric Dry Eye Summit in 2014 and I still use them today (see table above). These quick and easy questions could even be asked by your front office staff with each patient.

Find a good diagnostic protocol such as the Tear Film and Ocular Surface Society's DEWS II diagnostic methodology algorithm. Be sure to differentiate the types of dry eye (lipid/evaporative, mucin or aqueous-deficient), as each has slightly different treatment approaches, although inflammation may be the one consistent component across all forms.

Management Methods

In-office procedures to mitigate dry eye symptoms have become increasingly relevant during this pandemic as patients have spent far more time on digital devices, which exacerbates pre-existing dry eye. Consider the merits of procedures that may include BlephEx, thermal pulsation, intense pulsed light and/or low-level light therapy. Products such as omega fatty acids, hydrating compresses, nighttime lid seals and lid cleansers also provide patients with much-needed convenience when offered and explained in the practice, rather than expecting them to fend for themselves with nothing but Google to guide them.

The eyelids are the most important component of DED and you have to be a keen observer to differentiate *Demodex* from staphylococcal and seborrheic blepharitis. You must then treat each condition appropriately. Meibomian gland dysfunction (MGD) is a greater opportunity than DED. This requires early identification and treatment, but patients will remain in contact lenses longer. Look for reasons why MGD is present, such as non-sealing lids, with the Korb-Blackie light test.

In addition to immunomodulatory drugs, steroids are a necessity when managing DED, but keep them to short-term therapy and flare-ups. Consider extended-duration punctal plugs for appropriate patients and be open to the role of biologics (e.g., amniotic membrane, autologous serum, cytokine extract) and ultimately scleral lenses.

Managing dry eye disease is an enormous opportunity that, with a sound protocol, is exciting to treat and extremely rewarding for both you and your patients. ■

About Dr. Karpecki

Dr. Karpecki is medical director for Keplr Vision and the Dry Eye Institutes of Kentucky and Indiana. He is the Chief Clinical Editor for *Review of Optometry* and chair of the New Technologies & Treatments conferences. A fixture in optometric clinical education, he consults for a wide array of ophthalmic clients, including ones discussed in this article. Dr. Karpecki's full disclosure list can be found in the online version of this article at www.reviewofoptometry.com.

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BY MONTGOMERY VICKERS, OD

CHAIRSIDE

New Year, New Me

COVID-19 has spared me thus far, so I guess it's time I start living my best life.

I might be a little late to the game with my New Year's resolutions, but that's not unusual for me. Happens all the time actually. The last entry in my "daily" personal journal is dated September 12. At least it was from 2020. I'm pretty sure it was, anyway.

But not a whole lot has happened since then, so I don't feel too bad about it. I wake up, put on my scrubs, pull on my mask, solve the world's eye problems and start all over again the next day. No biggie.

It's a new year, though. We have a new government. We have new vaccines. I recently had my first dose of what I hope was the COVID-19 vaccine. I haven't experienced any side effects, other than the fact that I am now a foot taller and have been signed by the Dallas Mavs. Don't worry; I'll still be practicing optometry on the side. In fact, it's time for my optometric New Year's resolutions. So, in no particular order, this year I pledge to:

1. Quit griping about the state board of optometry. These people work tirelessly to keep you and me gainfully employed. It's not easy. They have to deal with politicians and, even worse, silly optometrists who think the board should solve all the problems in the universe of eye care and spend all year emailing board members dumb questions. Maybe that's just me. But, barring another pandemic, I trust the board will take good care of us. If there's another pandemic, however, all bets are off.

2. Focus all my energy on what's really important to optometry in the year 2021, *i.e.*, taking more time off to not do optometry. I advise you to do the same.

3. Figure out all the words that rhyme with optometry. Aberrometry? Deuteronomy? Never mind, that's hard. I'll just stick with haikus, where making no sense makes sense and rhymes are nonexistent.

4. Take a moment each day to individually thank each of my wonderful staff members who works tirelessly around the clock. After I'm done with that, I'll fire the rest of them and sleep like a baby.

5. Listen, with pure intent, to the ideas presented by all of our many, many wise colleagues who stand to educate me on optometry's potential. I'll consider what they have to say and, as always, decide to ignore their advice.

6. Take my wife on the trips of a lifetime: Paris (in Texas), Dublin (in Texas), Stockholm (in Texas), Italy (in Texas) and anywhere that sounds like Europe but is in Texas. She's already been to London (in West Virginia).

7. Try to understand why a young, highly educated doctor of optometry would want to work until nine o'clock every night and every Saturday instead of having the unfettered joys and miserable sleepless nights that come with owning a practice.

8. Make sure all the patients who never, ever support my practice receive only the finest in eye care by referring them to ophthalmologists who tell state legislators that optometrists are horrible but send Christmas boxes of chocolates anyway to show appreciation for the referrals we mindlessly continue to send along.

9. Work day and night for peace. Sorry, I mean pizza.

10. Spread the word that *all* people need a yearly eye examination, excluding those who just waste my time, aka my kids.

11. Spend my time passing my 41 years of accumulated optometric wisdom on to the next generation of fine young doctors. I know they are really busy, but this should only take one 10-minute Zoom meeting.

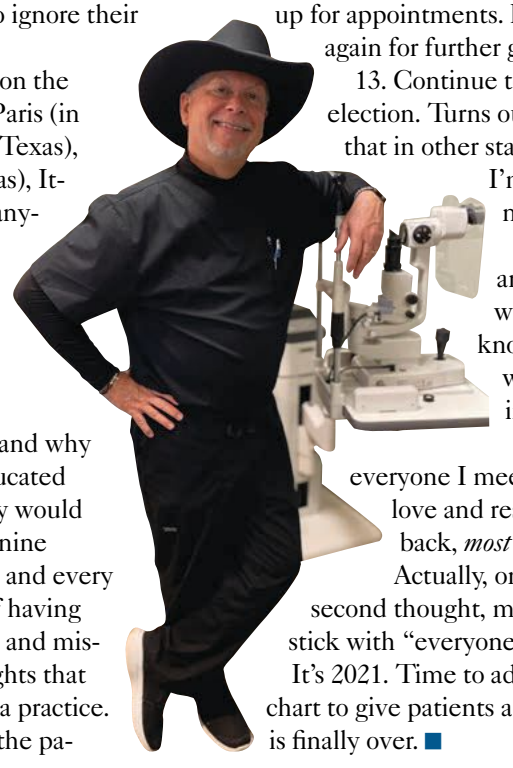
12. Give up trying to solve the no-show problem. I've been obsessing about no-shows my whole career. All I have been able to deduce is that no-shows are people who don't show up for appointments. Please refer to #8 again for further guidance.

13. Continue to vote in every election. Turns out I can even do that in other states and when I'm dead, so why not?

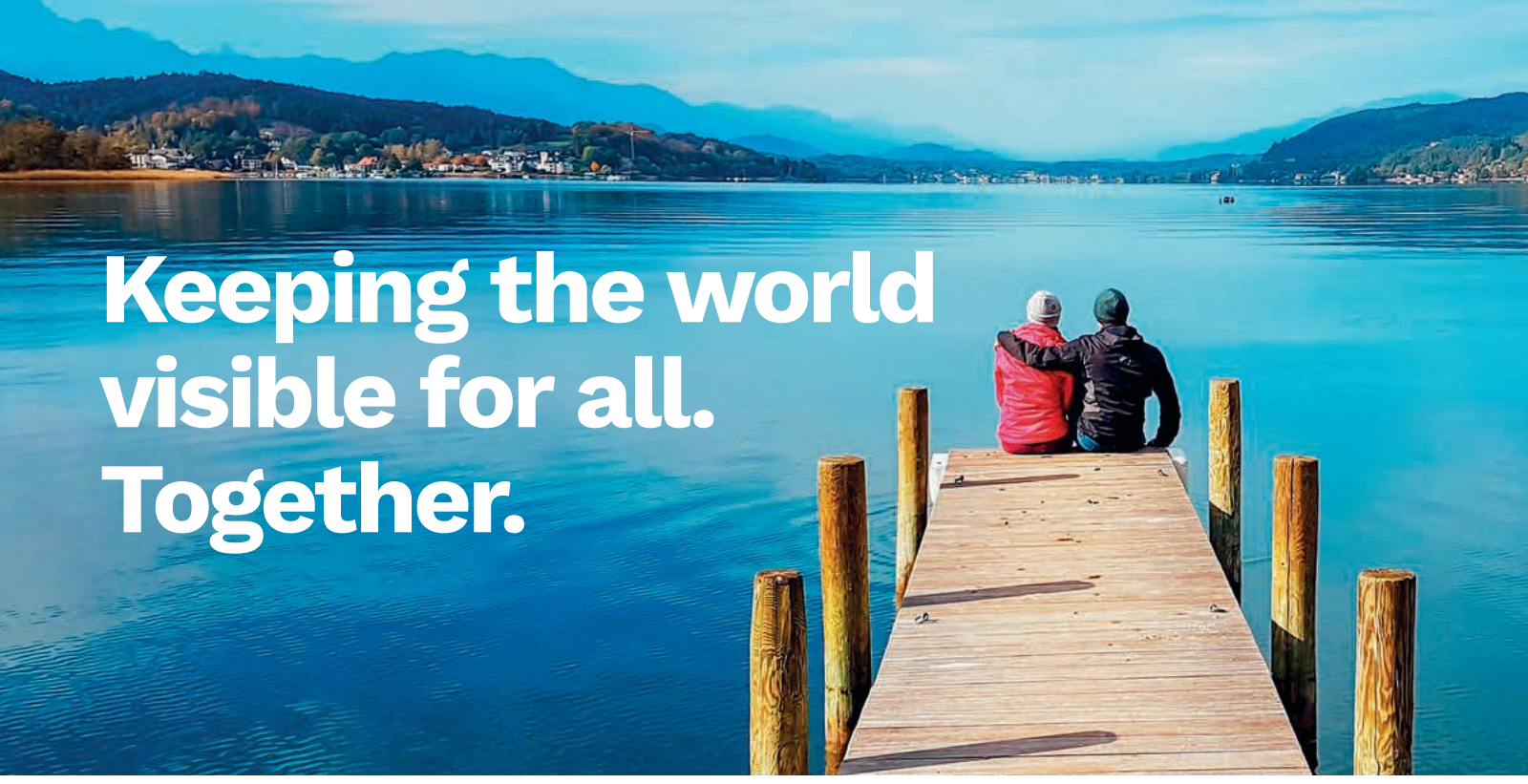
14. Face each and every day with Joy. You know, Joy. The lady who does our insurance billing.

15. Assume everyone I meet is worthy of love and respect. I take that back, *most* of them are. Actually, only a few. On second thought, maybe I should stick with "everyone."

It's 2021. Time to adjust the Snellen chart to give patients a lift. At last, 2020 is finally over. ■



About Dr. Vickers **Dr. Vickers** received his optometry degree from the Pennsylvania College of Optometry in 1979 and was clinical director at Vision Associates in St. Albans, WV, for 36 years. He is now in private practice in Dallas, where he continues to practice full-scope optometry. He has no financial interests to disclose.



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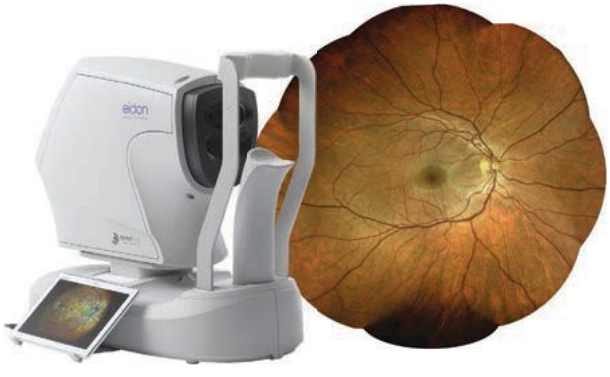

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Stymied

A bacterial infection or retained punctal plug could be the cause of this patient's epiphora.

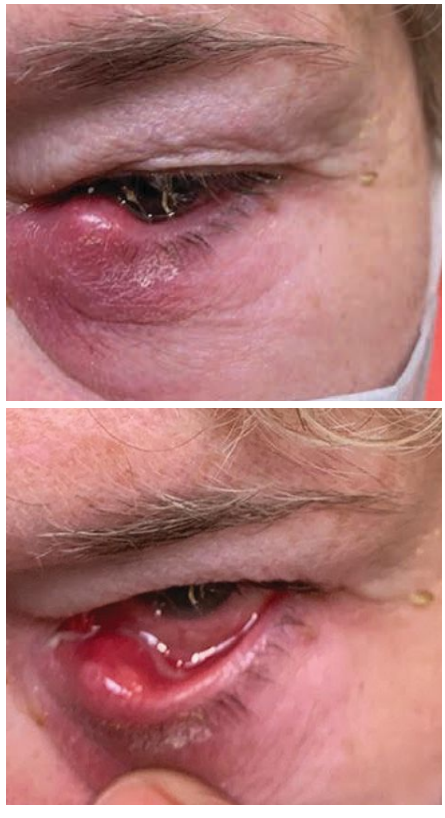
Q A 57-year-old female presented with a painful stye and tears running down her face for several days. Where do you go from here?

A "When a patient presents with a painful, red eye with epiphora, there are a multitude of differential diagnoses that come to mind," says Shundale Mixon, OD, a staff doctor at the North Georgia Eye Clinic in Clayton, GA. "Put on your detective hat and dig deep for information," she advises. Ask if this has happened before and inquire about any history of previous eye infections, surgeries or procedures, as well as the time course of the redness, pain and tearing.

Bumps in the Road

A chalazion or hordeolum from meibomian gland disease is often the culprit when you see a lump or bump. But don't label everything a stye without thinking it through, Dr. Mixon warns. If the lesion is near the punctum, your differential should include two additional disorders, dacryocystitis and canaliculitis, she points out.

Dacryocystitis is inflammation of the nasolacrimal sac that may be caused by a nasolacrimal duct obstruction. Symptoms include a painful, red and swollen tear sac that may produce a pus-like material that seeps out of the punctum when pressure is applied. When discharge is present, there may be an associated conjunctivitis observed. The underlying bacteria that may be responsible for dacryocystitis include *Staphylococcus aureus*, *Staphylococcus epidermidis* and *Pseudomonas aeruginosa*.



While initial presentation mimicked a chalazion, examination uncovered canaliculitis (bottom).

Canaliculitis is inflammation of the canaliculus and is associated with redness, tearing and tenderness upon touch. Some common causes include infection or a retained punctal plug. Symptoms appear very similar to dacryocystitis except that in canaliculitis the punctum and canaliculus are red and swollen, whereas the punctum and canaliculus are normal in dacryocystitis and the tear sac is red and tender. Those signs help differentiate these two conditions. The most common bacterial culprit responsible for canaliculitis is *Actinomyces israelii*.

Dr. Mixon emphasizes that, in this case, it was the repeated questioning about the dry eye history that revealed the fact that punctal plugs had been placed in the inferior punctum of both eyes about a year ago. The punctal plug of the patient's left eye had lodged down in her canaliculus, which resulted in an eventual external lid infection known as canaliculitis.

Treatment Protocols

Dacryocystitis and canaliculitis management includes an oral and topical antibiotic, warm compresses over the affected site and dacryocystorhinostomy to remove the foreign material. Beta-lactam agents are the first choice for systemic medications due to their ability to inhibit the synthesis of the peptidoglycan layer of bacterial cell walls.

This patient was given amoxicillin-clavulanate 875mg/125mg TID for 10 days and a topical fourth-generation fluoroquinolone, 0.6% besifloxacin ophthalmic solution, QID OS to cover the associated bacterial conjunctivitis. She was referred to an oculoplastics specialist for a dacryocystorhinostomy procedure, and the punctal plug was removed.

When you have a red eye, always obtain a good case history to help narrow down your list of differentials. It can save you valuable time and visits. Not all stye-like lesions are really styes, so make sure that your diagnosis makes sense. "If tearing is the chief complaint, ask if the tears run down the face or just 'well up' in the eye," Dr. Mixon says. "If the former, think about a drainage problem and evaluate the punctal openings, lid apposition to the globe and canalicular and nasolacrimal duct system." ■

About Dr. Ajamian **Dr. Ajamian** is the center director of Omni Eye Services of Atlanta. He currently serves as general chairman of the education committee for SECO International. He has no financial interests to disclose.

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BY JOHN RUMPAKIS, OD, MBA
CLINICAL CODING EDITOR

Keep Order in Your Sights

Maintaining your process and sequence is important for peace of mind.

This month's issue covers a number of dry eye and corneal topics, so I thought it would be valuable to relate those with our discussion here since the process of medical record documentation and coding are so intertwined. Whether we are talking about the diagnosis and treatment of meibomian gland dysfunction, corneal neuropathy or contact lens intolerance due to dry eye, or how to conduct a proper dry eye assessment, it is critical that the physician and their care team develop a process that does two things simultaneously: creates an accurate medical record from which you can properly code and prevents audit triggers with the carrier during the claim submission or post-payment review process.

When a Patient Comes in

Let's start with a proper assessment of the patient. Keep in mind that this actually starts with the patient contacting the office, whether by phone or through your online portal. The most important question to ask the patient is why they need to see the doctor. We need to obtain the chief complaint as early as possible in the care sequence so that we can allocate the necessary and appropriate resources to that encounter (*e.g.*, time, staff, facilities) as well as allow the office to properly inform the patient about the status of any third-party benefits.

Once you establish the reason for the visit, the new E/M definitions and coding rules now allow you to perform a medically appropriate history and physical examination. Determine just how much information and what type of information that you require.

> **"All special ophthalmic testing may be done on the same date and the same session as any examination services provided."**

For example, you may find it important to provide every patient with a qualified questionnaire that allows you to assess whether they have a clinically relevant sign or symptom of dry eye. If they fill it out, this allows you to have standing orders for your staff to perform CLIA-waived tests like osmolarity (83861) and InflammaDry (Quidel; 83516) before you see the patient—just like your physician often does by having labs done before the encounter.

Test the Same Day

Once you have conducted your history and examination, you must diagnose the patient, order additional tests (if necessary) and recommend a treatment program. The key, again, is the sequence. Other than CLIA-waived tests with standing orders based upon the patient's responses to a qualified questionnaire, all special ophthalmic testing must be done after you have seen the patient, established appropriate medical necessity for the test(s) and properly ordered them. This prevents an audit trigger in your medical record by ensuring that you have examined the patient, established the necessity for the test and ordered the test—in that order.

Many are under the misconception that you have to bring the patient back to do additional special ophthalmic testing; that is simply incorrect. All special ophthalmic testing may be done on the same date and the same session as any examination services provided, irrespective of who is paying for them.

If you are providing treatment on the same day as the examination, particularly surgical treatment, such as the placement of an amniotic membrane, please be aware of the CCI rules and regulations specific to the particular code pair being performed and appropriate use of modifiers, if necessary.

Another audit trigger is the inappropriate or excessive use of modifiers, particularly modifiers -25 and -59. Ensure that your use of the modifier is not only correct but that you also fully understand and comply with the definition of the modifier. Keep in mind coding rules surrounding performing minor surgical procedures (those with a global period of less than 90 days) and office visits on the same date of service.

Other procedures performed may not yet have rules or reimbursements established, such as BlephEx (92499) and TearCare (Sight Sciences; 0653T), because they would use the unlisted ophthalmic procedure code or have a Category III code.

In diagnosing and treating conditions associated with dry eye, MGD or more advanced conditions such as corneal neuropathy, it is comforting to know that you only have one set of rules to follow—but the sequencing of those rules is critical to your coding, reimbursement and audit prevention success. ■

Send your coding questions to rocodingconnection@gmail.com.

About Dr. Rumpakis

Dr. Rumpakis is president and CEO of Practice Resource Management, a firm that provides consulting, appraisal and management services for health care professionals and industry partners. As a full-time consultant, he provides services to a wide array of ophthalmic clients. Dr. Rumpakis's full disclosure list can be found in the online version of this article at www.reviewofoptometry.com.

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CATARACT COMANAGEMENT: RELATIONSHIPS GET RESULTS

Learn to cultivate the interprofessional bonds that are at the heart of a productive pairing of OD-MD colleagues.

BY CATLIN NALLEY
CONTRIBUTING WRITER

Comanagement is a crucial component of day-to-day optometric practice, with a significant impact on both patients and providers. However, the referral relationship can be complicated, and the best approach may not always be clear.

"Comanagement represents cooperation and, in the case of optometry, that means medical eye care in collaboration with our surgical counterparts—ophthalmologists," notes Paul C. Ajamian, OD, center director of Omni Eye Services of Atlanta. "What it *doesn't* mean is referring to the ophthalmologist and losing control of your patient's care." That instinct runs deep, though, ingrained through decades of practice in which that was just about all an OD could do.

Not any more. "We should be the general practitioners of eye care," Dr. Ajamian argues, "and as such it is our responsibility to make the patient feel confident in the fact that they are in the hands of an expert who is going to identify and treat anything they can, and consult with a trusted specialist when something is beyond their scope."

When comanagement is effective, the entire field will reap the benefits. "Comanagement is critical to the growth of the profession. It improves our clinical and critical thinking skills as well as our ability to deal with medical pathology," says Aaron Bronner, OD, who practices at a large OD-MD multidisciplinary practice in the Pacific Northwest. Dr. Bronner's practice literally bears the slogan, "Serving optometric physicians in the spirit of comanagement." Their doctors seem to have figured out what makes these relationships tick.

To help those ODs who may still find it a struggle, this new six-part series will delve into various areas of optometric practice where comanagement is essential, beginning with cataract care. Each article will take a closer look at the referral relationship, structural challenges and knowledge gaps while offering day-to-day pearls to help ODs elevate their practice.

Fostering Mutual Respect

The comanagement process is only as strong as the relationship between providers. To collaborate effectively, both parties have to recognize the unique skills each bring to the table. For an optometrist, this starts with finding skilled ophthalmologists who respect the profession and align with the practice's clinical methods and overall philosophies of care.

The first consideration should always be patient outcomes. "Optometrists should limit their relationship building to those individuals who provide optimal results," notes James Fanelli, OD, a private practitioner from Wilmington, NC. "Then you have to hone that down even further and identify those surgeons who not only provide good surgical outcomes, but also understand and respect the skills of an optometrist."

It is also important to work with someone who understands your philosophy, says Dr. Fanelli. "Optometrists must convey their comanagement approach to the surgeon and ask them, 'Are you willing to comanage cataract patients this way?'"

The services offered by an ophthalmologist should also factor into an OD's decision. Do they offer the newer premium IOLs like trifocals or light-adjusting lenses? Is dropless cataract surgery an option at their practice? Do they perform MIGS procedures? If so, what's their protocol for selecting prospective candidates? These are some of the questions to

ask when considering a comanagement relationship, according to Paul Karpecki, OD, of Lexington, KY.

"A surgeon with a variety of tools at their disposal is a good indicator that they are dedicated to ensuring the best possible outcomes for your patients," he says, suggesting that optometrists should make the time to shadow an ophthalmologist before referring a patient. This gives you the opportunity to gain first-hand knowledge of not only their surgical skills, but also how they treat and interact with patients. ODs should also get to know ophthalmologists outside of their practice. In a post-COVID world, this could include a lunch or dinner, Dr. Karpecki advises.

Optometrists are in the driver's seat and have a responsibility to facilitate the best possible care for their patients. "If the right surgeon isn't nearby, optometrists shouldn't hesitate to refer their patients to someone further away," says Dr. Ajamian. "Explain your reasoning to your patients and emphasize your commitment to providing optimal care. And then, take it a step further and schedule the appointment for them before they even leave your office." That sort of hands-on approach will signal to the patient that you're their primary eye care doctor and the surgeon, while valued and respected, is only being called in for a limited encounter.

Successful comanagement does not end when an optometrist finds a skilled ophthalmologist. It is a two-way street that requires a commitment from everyone involved. "There's a burden on both sides to develop a strong relationship," explains Dr. Ajamian. "Just as optometrists must get to know a surgeon and how they practice, ophthalmologists must also make the effort to get to know us and what we do."

When comanaging, ODs should not just be content with an MD who has the courtesy to send their patient back. "A comanagement relationship is more than this and it should not be the only basis for continued referrals," notes Dr. Fanelli. "I'm sending over patients they otherwise would not have had, and they should do the same when the opportunity presents itself."

Dr. Fanelli offers the example of a glaucoma patient who had yet to find an optometrist. "This is a chance for the ophthalmologist to refer a patient to the OD," he said. "That's what it means to have mutual respect between providers. That is a two-way street and true comanagement."

Building a robust comanagement relationship takes time and dedication. There will be a learning curve, but with continued communication, clear expectations and mutual respect, optometrists and ophthalmologists can create a collaborative environment that benefits everyone, particularly their patients.

Optimizing Cataract Care

With the number of people in the US who develop cataracts expected to double from 24 million to approximately 50 million by 2050, the need for surgical intervention will only continue to grow.[1] At the same time, an impending shortage of ophthalmologists will make the role of optometrists even more critical.

"Working with cataract patients, in my opinion, is one of the pillars of medical optometric practice," notes Dr. Bronner. "This is not something the profession can escape, nor should we try. We should lean into it and take the opportunity to be leaders in the care of these patients."

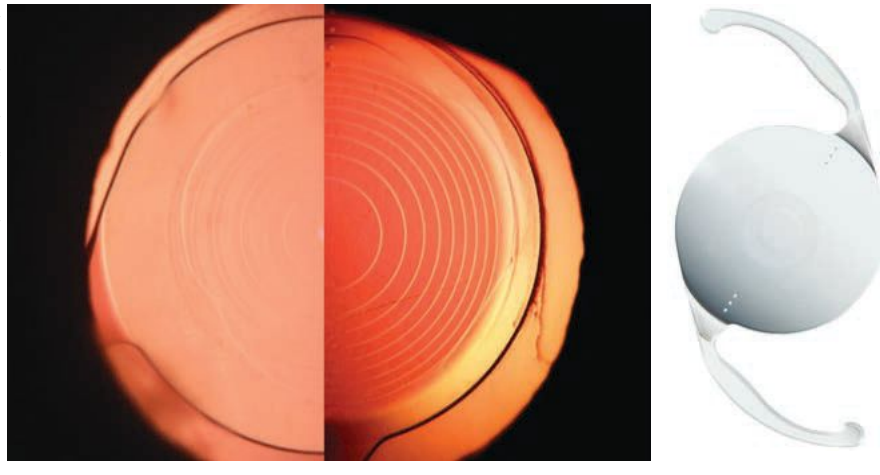
Proper cataract care should include a good assessment, patient education, referral for surgery, and the necessary follow-up eye and vision care. Successful comanagement occurs when both the optometrist and ophthalmologist are on the same page, which can only happen with effective communication from the very beginning of the process.

Preoperative care. As with any condition, effective treatment begins with a thorough exam. In the case of cataracts, optometrists must rule out any other causes of the reduced vision as well any potential complications.

"These are all things we're called to do every day," notes Dr. Ajamian. "It is then our responsibility to thoroughly educate a patient on available treatments and what the best approach is for their specific case."

While you know your patients very well, be mindful not to make assumptions. It is imperative to educate them on all options, including premium IOLs that come with a substantial out-of-pocket cost. "It is incumbent on the OD to carefully describe all

Photos: Oliver Kuhn-Wilken, OD, Alcon



A successful comanagement relationship is one where ODs and MDs are able to rely on each other so that they're splitting rather than duplicating the work. For instance, the optometrist should understand and be able to articulate the differences between newer IOLs to lead the patient discussion about options. Left to right: PanOptix (Alcon), Symfony (Johnson & Johnson Vision) and Vivity (Alcon) lenses.

lens implant options," emphasizes Dr. Ajamian. "Patients have every reason to be upset if they find out about a potentially beneficial treatment option after the fact."

Thorough education is also important because it strengthens your relationship with the patient and positions you as their primary resource. "If a patient receives information from the ophthalmologist instead of from their OD, it can undermine their faith in you as a provider," warns Dr. Ajamian.

Once the optometrist has discussed the different treatment approaches with their patient and determined the best course of action, it is their responsibility to communicate this to the surgeon. Sharing as much information as possible with the surgery center sets the stage for smooth handoffs and positive outcomes.

"When a case involves more than one provider, balls can be dropped," says Dr. Bronner. "Clear and consistent communication can help avoid this. Everyone needs to be on the same page and using similar verbiage when speaking with patients to eliminate any mixed messages."

Oftentimes, the OD has worked with this patient for years, making them experts on not only their visual status, but also their personality and individual needs. This is why the referral letter is one of the most important components of cataract comanagement.

> **"I have received referral letters from ODs who have treated a patient for 30 years and yet only include minimal details for the cataract surgeon."**

"I have received referral letters from ODs who have treated a patient for 30 years, and yet include only minimal details for the cataract surgeon," Dr. Ajamian says. "Others offer a comprehensive treatment plan that outlines what has been discussed with a patient and how they want to proceed. This is very valuable for the ophthalmologist and also ensures that the optometrist is guiding the surgical process and the desired refractive outcomes."

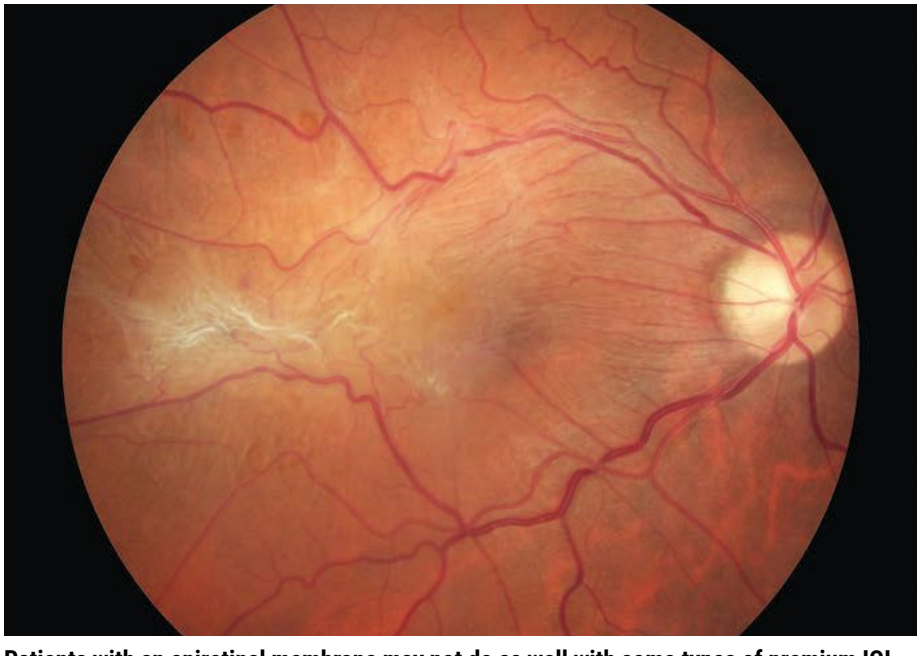


Photo: Diana Shechtman, OD, Jay Haynie, OD

Patients with an epiretinal membrane may not do as well with some types of premium IOL. The comanaging OD needs to have pre-op ocular health assessment and the anticipation of visual outcomes in their skill set. Doing so will elevate the relationship from simple referral to true collaboration.

Postoperative care. Just as optometrists should be leaders preoperatively, they must continue guiding a patient's care after cataract surgery. "All postoperative care can be handled by the OD," says Dr. Fanelli, noting that there are very few cataract complications that require a return to the operating room. "As optometrists, we are the ones driving the bus, before and after cataract surgery."

Why is it important for optometrists to take charge postoperatively? There are a number of benefits for all parties involved, according to Dr. Fanelli. "If an optometrist has a practice where they are generating revenue based on office visits and medical care, it makes sense from a fiscal perspective," he explains. It's also a more efficient use of everyone's time and talents.

"Importantly, it also ensures the patient doesn't lose their bond with the OD," he continues. "You have been their primary eye care provider for years, and when someone they know needs a cataract referral, they will share your name rather than the surgeon's."

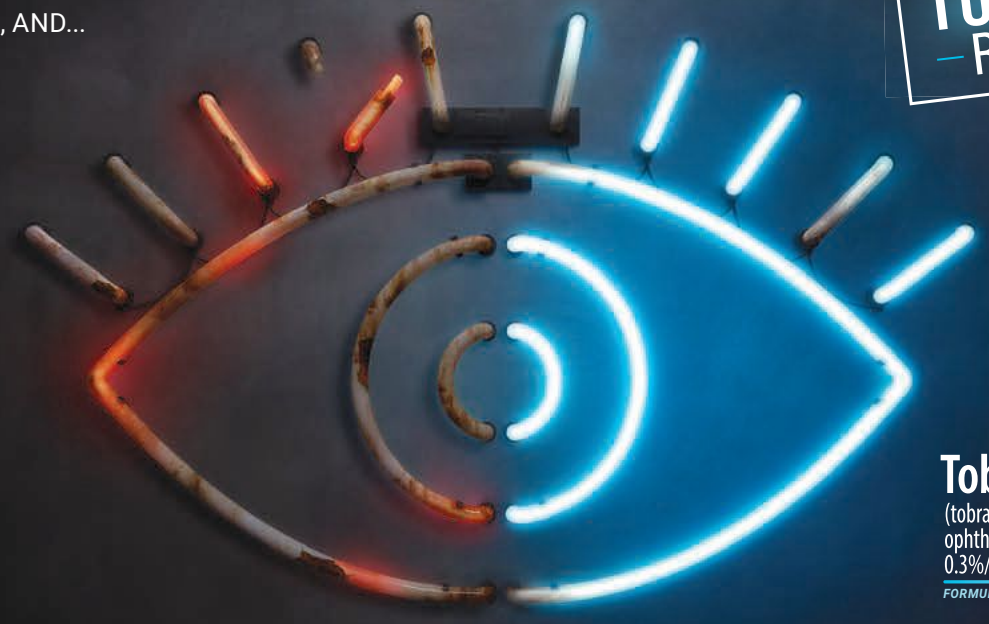
Day one post-surgery is critical, notes Dr. Karpecki. "The optometrist loses a valuable opportunity by not comanaging that early," he warns. Post-op care contributes to the optometrist's growth, allowing them to hone their skills and strengthen their relationship with the patient.

It's also reassuring for patients. "On day one a patient may be anxious, and their familiar optometrist should be the one to ease their concerns," Dr. Karpecki adds. "There is also a lot of excitement immediately following surgery and ODs should be there to celebrate that moment with their patients."

As with any aspect of comanagement, post-op communication is a two-way street. If an optometrist observes a postoperative complication, they need to share that with the surgeon, especially if it is happening more than once, Dr. Bronner advises.

"ODs need to make the ophthal-

TREAT OCULAR INFLAMMATION
AND INFECTION, AND...



TobraDex® ST
(tobramycin/dexamethasone ophthalmic suspension) 0.3%/0.05%
FORMULATED WITH XanGen™

PRESCRIBE TOBRADEX® ST to control ocular inflammation with risk of bacterial infection

- Rapid relief from blepharitis/blepharoconjunctivitis symptoms[1,a]
- XanGen™ suspension technology provides increased viscosity for improved ocular bioavailability of drug and consistent delivery[2]
- TOBRADEX ST contains half the dexamethasone as TobraDex®, yet similar ocular tissue exposure[2,b]

Eligible patients could pay as little as $45 for TOBRADEX ST
LEARN MORE AT MYTOBRADEXST.COM

Indications and Usage

For steroid responsive inflammatory ocular conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the globe and chronic anterior uveitis, corneal injury from chemical, radiation or thermal burns, or penetration of foreign bodies for which a corticosteroid is indicated and where the risk of superficial bacterial ocular infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye.

Important Safety Information

CONTRAINDICATIONS:
Most viral disease 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 disease of ocular structures. Hypersensitivity to any components of the medication.

WARNINGS & PRECAUTIONS:
- **IOP increase** – Prolonged use may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. IOP should be monitored.
- **Aminoglycoside sensitivity** – Sensitivity to topically applied aminoglycosides may occur.
- **Cataracts** – Posterior subcapsular cataract formation may occur.
- **Delayed healing** – May delay healing and increase the incidence of bleb formation. Perforations of the cornea or sclera have occurred. Slit lamp biomicroscopy, and fluorescein staining should be conducted.
- **Bacterial infections** – May suppress host response and increase secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
- **Viral infections** – Use with history of herpes simplex requires great caution. The course and severity of many viral infections of the eye (including herpes simplex) may be exacerbated.
- **Fungal infections** – Fungal infections of the cornea may occur and should be considered in any persistent corneal ulceration.
- **Use with systemic aminoglycosides** – Total serum concentration of tobramycin should be monitored.

ADVERSE REACTIONS:
The most frequent adverse reactions (<4%) to topical ocular tobramycin are hypersensitivity and localized ocular toxicity, including eye pain, eyelid pruritus, eyelid edema, and conjunctival hyperemia.

The reactions due to the steroid component are increased intraocular pressure with possible development of glaucoma, and infrequent optic nerve disorder; subcapsular cataract; and impaired healing.

The development of secondary infection has occurred. Fungal infections of the cornea may occur. Secondary bacterial ocular infection following suppression of host responses also occurs.

Non-ocular adverse events (0.5% to 1%) included headache and increased blood pressure.

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

[a]Randomized, investigator-masked, active-controlled, parallel-group trial conducted at 7 private practice clinical sites in the United States with 122 adult patients who had moderate to severe blepharitis/blepharoconjunctivitis.[1]

[b]Multicenter, double-blind, parallel-group, single-dose study of 987 patients receiving a single dose of TOBRADEX ST or TobraDex ophthalmic suspension.[2]

References: 1. Torkildsen GL, Cockrum P, Meier E, et al. *Curr Med Res Opin.* 2011;27(1):171-178. **2.** Scoper SV, Kabat AG, Owen GR, et al. *Adv Ther.* 2008;25(2):77-88.

eyevance pharmaceuticals

TOBRADEX® ST (tobramycin/dexamethasone ophthalmic suspension) 0.3%/0.05%

Brief Summary

This Brief Summary does not include all the information needed to use TOBRADEX ST safely and effectively. Please see Full Prescribing Information for TOBRADEX ST at MyTobraDexST.com.

INDICATIONS AND USAGE

TOBRADEX ST is a topical antibiotic and corticosteroid combination for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists.

Ocular steroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe where the inherent risk of steroid use in certain infective conjunctivitides is accepted to obtain a diminution in edema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns, or penetration of foreign bodies.

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

DOSAGE AND ADMINISTRATION

Recommended Dosing: Instill one drop into the conjunctival sac(s) every four to six hours. During the initial 24 to 48 hours, dosage may be increased to one drop every 2 hours. Frequency should be decreased gradually as warranted by improvement in clinical signs. Care should be taken not to discontinue therapy prematurely.

CONTRAINDICATIONS

Nonbacterial Etiology: TOBRADEX ST 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.

Hypersensitivity: Hypersensitivity to any component of the medication.

WARNINGS AND PRECAUTIONS

IOP increase: Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. IOP should be monitored.

Aminoglycoside sensitivity: Sensitivity to topically applied aminoglycosides may occur.

Cataracts: May result in posterior subcapsular cataract formation.

Delayed healing: May delay healing and increase the incidence of bleb formation after cataract surgery. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids.

Bacterial infections: May suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

Viral infections: Treatment in 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 with long-term use. Fungal invasion must be considered in any persistent corneal ulceration.

Use with systemic aminoglycosides: Use with systemic aminoglycoside antibiotics requires monitoring for total serum concentration of tobramycin.

ADVERSE REACTIONS

The most frequent adverse reactions to topical ocular tobramycin (TOBREX®) are hypersensitivity and localized ocular toxicity, including eye pain, eyelids pruritis, eyelid edema, and conjunctival hyperemia. These reactions occur in less than 4% of patients. Similar reactions may occur with the topical use of other aminoglycoside antibiotics.

Non-ocular adverse events occurring at an incidence of 0.5% to 1% included headache and increased blood pressure.

The reactions due to the steroid component are: increased intraocular pressure (IOP) with possible development of glaucoma, and infrequent optic nerve disorder; subcapsular cataract; and impaired healing.

Secondary Infection.
The development of secondary infection has occurred. Fungal infections of the cornea are particularly prone to develop with long-term use. Fungal invasion must be considered in any persistent corneal ulceration. Secondary bacterial ocular infection following suppression of host responses also occurs.

USE IN SPECIFIC POPULATIONS

Pregnancy and Nursing Mothers

There are no adequate and well controlled studies in pregnant women. TOBRADEX® ST ophthalmic suspension should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus. Caution should be exercised when TOBRADEX® ST is administered to a nursing woman.

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

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

Rx Only

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eyevance® pharmaceuticals

TST-01-20-MS-05

mologist aware of any issues—no matter how small—so they can minimize these complications in the future," he elaborated. "Surgery centers also have a responsibility to tell ODs about any complications that occurred during surgery so the patients can receive the necessary care and support."

Effective postoperative communication goes hand-in-hand with a strong relationship that recognizes the contributions and expertise of each provider. "If it is purely a referral relationship, you lose a lot of what you—and your patients—potentially could gain," reiterates Dr. Bronner.

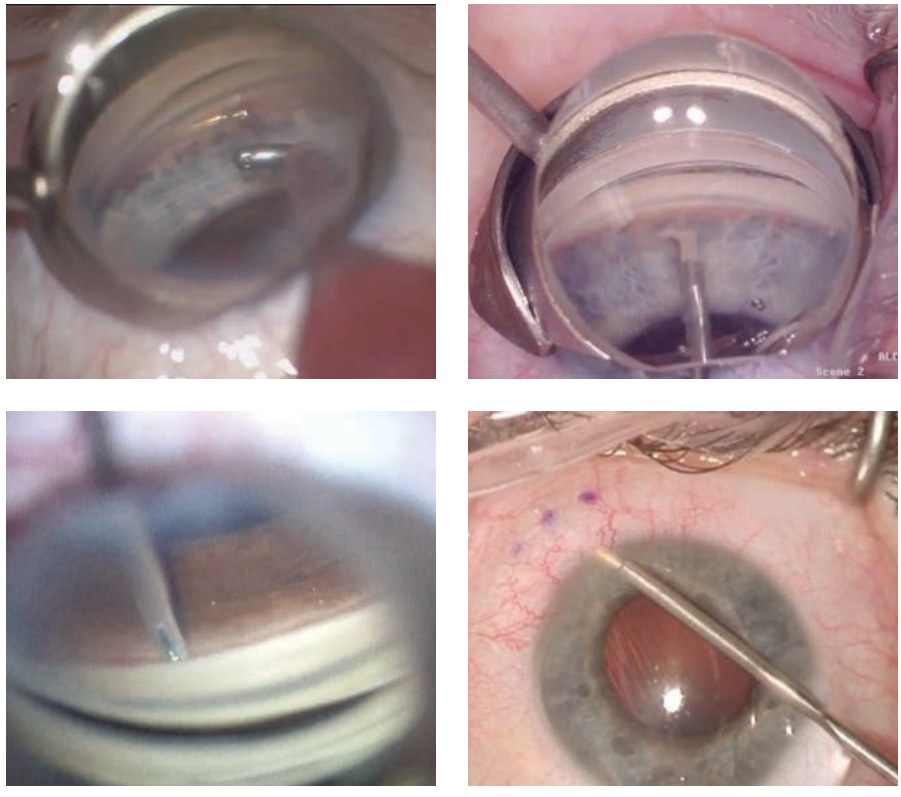
Addressing Gaps in Care

As a patient's primary eye care provider, it is the optometrist's responsibility to be both an educator and facilitator of treatment. While comanagement opens the door for a comprehensive, team-driven approach, ODs must take the lead and address any potential gaps in care.

An example of this in the cataract realm is the use of minimally invasive glaucoma surgery (MIGS) at the time of cataract surgery. A notable advancement in the management of glaucoma, MIGS offers an opportunity for patients to reduce their dependence on IOP-lowering medications.

In one study, four years after a MIGS procedure with the Hydrus implant on glaucoma patients taking one topical medication, over 70% of patients had IOPs low enough to remain medication free. There was a 25% to 30% advantage over patients who only had cataract surgery alone and a 65% reduction in the number of patients requiring invasive surgical procedures such as trabs and shunts.[2] However, less than half of MIGS candidates actually receive these procedures, according to Dr. Karpecki.[3]

There are a number of factors that could contribute to the underutilization of MIGS, Dr. Karpecki notes, including a lack of awareness among providers. "As a relatively recent advance, education until now has been limited," he explains. "Newer technologies have vastly improved patient outcomes, and it is imperative that optometrists are aware of the benefits."



Photos: Brooke Mathie, OD, Justin Schweitzer, OD, Rachel Caywood, OD

The development of minimally invasive glaucoma surgeries for use at the time of cataract surgery has increased the capabilities of surgeons—and the expectations placed on comanaging optometrists, who need to be able to sort out the many proceudres and make well-informed recommendations to the ophthalmologist. Clockwise from upper left: Hydrus Microstent (Ivantis), Kahook Dual Blade (New World Medical), Xen implant (Allergan), iStent (Glaukos).

Given that MIGS procedures are not approved after cataract surgery in the US, there is only one opportunity for patients to take advantage of these procedures, emphasizes Dr. Karpecki. Optometrists must educate eligible patients on their options while also communicating effectively with the cataract surgeon.

"Our intake forms include a question on glaucoma; however, the comanaging doctor's office doesn't always include this information," Dr. Karpecki says. "And, if a case of glaucoma is mild or missed during the exam at the surgical practice, the patient loses the opportunity for a potentially life-changing procedure." This, he says, highlights the importance of comanagement as well as the leadership role optometrists must take in educating patients and communicating their needs to the ophthalmologist.

A deeper understanding of available procedures is important not just to ensure patients receive the care they need, but to also stop them from undergoing a treatment that isn't right for them. "Problems arise when the optometrist does not communicate the needs of their patent to the surgeon," notes Dr. Fanelli. "For instance, an OD should be well aware of the nuances of an individual's glaucoma and whether or not a MIGS device is indicated. That information needs to be shared with the surgeon to ensure a patient is not given an unnecessary intervention."

Another area where optometrists

can better serve their patients is how they explain options from a refractive cataract perspective, according to Dr. Karpecki. "A lot of people come in at age 55 for LASIK and truthfully, in most cases, they'd be better served with a lens-based procedure," he explains. "Otherwise, they're doing a corneal procedure now and then turning around within a decade or two and having cataract surgery," which, as a result, will be more difficult. Furthermore, a cornea-based surgery won't help with presbyopia the way a refractive lens surgery can.

"Many times we say, 'Let's wait until you're 65 and insurance covers it.' The truth is, insurance still doesn't cover the premium lens, so you might as well consider doing it sooner, if it is beneficial and a patient is inclined to do so," he continues. "At the very least, having this discussion with our patients is important so we can help them make the decision that is best for them."

KEY TAKEAWAYS

- Find an ophthalmologist that aligns with your practice values.
- Build a referral relationship based on mutual trust and respect.
- Signal to patients that you remain their primary doctor, with the surgeon called in at your behest for a limited encounter.
- Counsel patients on available treatment options, including premium IOLs and MIGS.
- Provide a comprehensive referral letter outlining your thoughts on the best treatment approach.
- Take charge of post-op management.

An Opportunity for Growth

Comanagement is a crucial part of medicine, with benefits well beyond a single specialty. For ODs, a partnership built on mutual give-and-take helps their practice grow while providing a higher level of care.

"I believe strongly that comanagement is the most effective way to provide care, especially among the cataract population," says Dr. Bronner. "It has been well-established that centers with higher volumes of surgery, up to a point, have a lower risk of complications and, on average, best corrected visual acuity outcomes."

By focusing more of their time on surgery, ophthalmologists become better at this aspect of their work. Delegating non-surgical matters to optometry facilitates this growth, according to Dr. Bronner. "Sharing care with optometry, a profession that's well-trained to take on non-surgical responsibilities, is going to make both surgeons and optometrists better at their respective roles while increasing access to care," he concludes. "Arguments against comanagement just don't hold water, given its many benefits." ■

1. National Eye Institute. Cataract Data and Statistics. nei.nih.gov/eyedata/cataract.
2. Rhee DJ. 4-year findings from the HORIZON trial AGS 2020, Washington, DC.
3. MarketScope. Q1 Glaucoma Quarterly Update 2020. www.market-scope.com.

Part 1 of 2

A GLAUCOMA STARTER KIT: GEAR UP FOR CLINICAL CARE

Learn the steps needed to elevate the management of these patients.

BY JACK PHU, OD, PhD, AND HENRIETTA WANG, BOptom, BSc
KENSINGTON, NSW, AUSTRALIA

Glaucoma is a significant public health issue, and optometrists, as primary eye care clinicians, play an integral role in the diagnosis and management of the condition. As glaucoma is a chronic disease that has a nebulous definition, a successful glaucoma clinic requires the doctor to be proficient in a range of clinical skills and maintain continuing education in an evolving field; it also requires the doctor to have an efficient practice system in place. The successful clinic is rewarding, with many long-term patients, and the ability to prevent irreversible blindness. In this primer, we will be outlining some of the considerations for the early-career doctor who wants to develop their glaucoma clinic.

Why Should We Care?

Glaucoma is one of the leading causes of irreversible blindness worldwide.[1] With age being one of the primary risk factors for development of glaucoma, the aging and increasingly longevous populations in many countries creates a cumulative public health issue.[1] As a chronic disease that requires close eye care, glaucoma can potentially occupy a lot of a clinician's time and office space, and its treatment presents a significant cost to the health care system (*Figure 1*).[2,3]

Despite glaucoma's prevalence and its dubious distinction as the most common optic neuropathy, diagnosing the disease is complex in some patients. The diagnosis of glaucoma requires careful examination of many clinical features: the optic nerve head, visual fields (VFs), intraocular pressure (IOP), anterior chamber angles and corneal thickness.[4,5] Alongside these typical measurements, comprehensive history-taking can assess a patient's risk profile. Cross-sectional data from a single examination, such as of the optic nerve head, IOP and VF, especially in the earliest stages of glaucoma, can provide only suspicious or borderline signs for glaucoma and can be inconclusive. Therefore, longitudinal information is often required, necessitating frequent reviews of these patients. As a result, it is unsurprising that over half of all cases of glaucoma are undiagnosed—and many are over- or misdiagnosed. This further confounds the problem posed by the disease.[6-8]

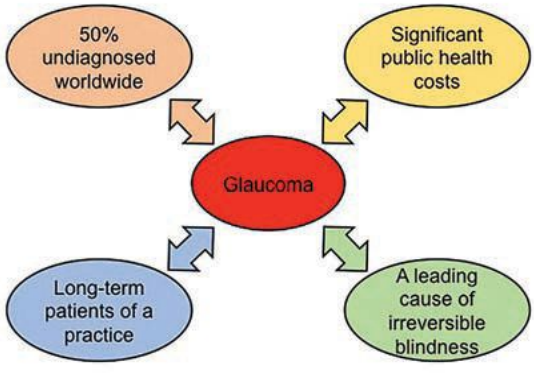


Fig. 1. Glaucoma in the context of the current health care system.

Unfortunately, despite advances in the field of glaucoma

About the authors

Dr. Phu is a clinician-scientist with academic and clinical positions at the Centre for Eye Health in Kensington, New South Wales, Australia, and the School of Optometry and Vision Science, University of New South Wales. He is a Fellow of the American Academy of Optometry and a Diplomate in glaucoma. **Dr. Wang** is a research and clinical staff optometrist at the Centre for Eye Health. She is a Fellow of the AAO. They have no financial interests to disclose.

diagnostics, around half of all cases of initially diagnosed glaucoma are at the moderate stage or worse.[9,10] This means, sadly, that many patients already have established, significant and often irreversible vision loss.

Despite these issues, glaucoma is a condition that, if managed correctly, can be professionally rewarding. In the sections below, we outline some of the essential tools and considerations for the eye doctor, especially those in the early stages of their career, to build their own glaucoma practice.

Clinical pearl: Glaucoma is a significant public health problem, but represents an opportunity for doctors to make an impact in patient care.

Tools of the Trade

The advancement of imaging in this field has altered the optometrist's approach to the diagnosis of glaucoma. In addition to taking history and symptoms, comprehensive glaucoma examination can be broken down into four key elements:

1. IOP measurement and characterization of diurnal profile (including fluctuations)
2. Assessment of visual function
3. Examination of anterior eye structures
4. Examination of posterior eye structures

IOP measurement and profiling. The current standard for measurement of IOP in the management of glaucoma is Goldmann applanation tonometry (GAT).[4,5] Other measurement techniques include non-contact tonometry, rebound tonometry and the Tono-pen (*Table 1*). Although these are also often deployed as mainstream clinical tools, they are often not directly comparable to Goldmann measurements, and their accuracy may also be affected by corneal parameters such as central corneal thickness. As such, these techniques should not be used interchangeably with GAT.[11,12] Newer technologies such as methods accounting for corneal hysteresis may be available in some clinics, but this method's role in the comanagement process is still evolving and the lack of agreement in corneal correction factors remain an issue.[13,14]

TABLE 1. COMPARISON OF TECHNIQUES FOR MEASURING IOP

TONOMETRY MEASUREMENT TECHNIQUE	FEATURES
Applanation tonometry (GAT or hand-held Perkins)	- Considered the current "gold standard" for IOP measurement - For GAT, conveniently situated on the slit lamp, which may assist workflow
Non-contact tonometry	- Tends to overestimate IOP - No anesthetic required
Tono-pen tonometry	- Topical anesthetic required - Poorer level of agreement with GAT compared with other techniques - Direction of bias unclear (*i.e.*, both over- and underestimation has been reported)
Rebound tonometry	- Good agreement with GAT (usually within 3mm Hg), usually underestimation - No anesthetic required - More affected by central corneal thickness

In recent years, there has been a shift away from single IOP measurements to instead characterization of the diurnal curve or fluctuations. Higher diurnal fluctuations are thought to be associated with an increased likelihood of disease progression.[15,16] As many patients experience peak IOPs outside of typical office hours, 24-hour monitoring of IOP allows for detection of these peaks. Prior to the introduction of home-based monitoring devices such as the iCare Home, a patient-operated rebound tonometer, measurement of diurnal fluctuations would otherwise need to be performed in a setting requiring an overnight stay. These newer modalities allow for a more practical approach to implementation.[17-19]

In practices without access to patient-driven measurement devices, the water drinking test may be an alternative.[20] This test measures the change in IOP following osmotic stress induced by the rapid ingestion of a defined quantity of water, usually 10mL per 1kg of body weight or a set amount of 800mL. Peak IOP measured during this test is thought to be representative of the eye's aqueous outflow ability, whereby a higher peak pressure suggests a higher resistance to aqueous outflow.

Clinical pearl: Obtain IOP profiles for patients to assess baseline risk and treatment targets for future progression analysis.

Assessment of visual function. This step serves three key purposes in glaucoma care:

1. Determining structure-function concordance. This relationship is a hallmark feature of glaucoma, and confirming it is important in the diagnostic step.[21]
2. Disease staging and monitoring of progression. Most current glaucoma staging systems are based on VF parameters such as the mean deviation and the presence of central VF defects.[22-24]
3. Assessing impact on quality of life. For example, central VF loss primarily affects near activities and social functioning while inferior peripheral VF loss affects distance activities and a patient's sense of dependency more than superior peripheral VF loss.[25,26]

(Continued on page 41)

Help your patients with **DIABETIC RETINOPATHY (DR)**, and

HELP DRIVE PATIENT OUTCOMES

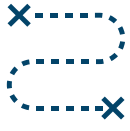
Through early detection, monitoring, and timely referral, you can play a pivotal role in managing your DR patients' vision[1-3]

IF YOU SEE OR SUSPECT DR:

Educate your patients about living with DR and potential treatment options[2,3]

Refer DR patients for timely intervention

- According to the AOA, you should refer patients with[2,3]
  - Severe nonproliferative DR (NPDR) within 2 to 4 weeks
  - Proliferative DR (PDR) within 1 week



Follow up to ensure they have visited a retina specialist

INDICATIONS AND IMPORTANT SAFETY INFORMATION

EYLEA® (aflibercept) Injection 2 mg (0.05 mL) is indicated for the treatment of patients with Neovascular (Wet) Age-related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).

CONTRAINDICATIONS

- EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.

References: 1. Early Treatment Diabetic Retinopathy Study Research Group. Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report number 12. *Ophthalmology*. 1991;98(5 suppl):823-833. **2.** Care of the Patient With Diabetes Mellitus: Quick Reference Guide. American Optometric Association website. http://bit.ly/2M22OUJ. Accessed August 7, 2019. **3.** Ferrucci S, Yeh B. Diabetic retinopathy by the numbers. *Rev Optom*. June 15, 2016. http://bit.ly/2KNNJ4E. Accessed August 7, 2019.

REGENERON

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EYLEA®
(aflibercept) Injection
For Intravitreal Injection

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Visit **diabeticretinaldisease.com** for additional information and useful patient resources

Continue to monitor your patients with DR[2,3]

- The AOA recommends frequent monitoring of patients[2]
  - At least every 6 to 8 months in patients with moderate NPDR and more frequently for patients with greater disease severity[2]

The more you know about emerging clinical science about anti-VEGF and other potential therapies for DR, the better you can help inform your patients about how treatment may be able to help

Refer patients to a retina specialist who can treat DR[2,3]

WARNINGS AND PRECAUTIONS (cont'd)

- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.
- There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

ADVERSE REACTIONS

- Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.
- The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

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

anti-VEGF = anti–vascular endothelial growth factor; AOA = American Optometric Association.

03/2020
EYL.20.02.0082

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

BRIEF SUMMARY—Please see the EYLEA full Prescribing Information available on HCP.EYLEA.US for additional product information.

1 INDICATIONS AND USAGE
EYLEA is a vascular endothelial growth factor (VEGF) inhibitor indicated for the treatment of:

Neovascular (Wet) Age-Related Macular Degeneration (AMD); Macular Edema Following Retinal Vein Occlusion (RVO); Diabetic Macular Edema (DME); Diabetic Retinopathy (DR).

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections
EYLEA is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation
EYLEA is contraindicated in patients with active intraocular inflammation.

4.3 Hypersensitivity
EYLEA is contraindicated in patients with known hypersensitivity to aflibercept or any of the excipients in EYLEA. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, severe anaphylactic/anaphylactoid reactions, or severe intraocular inflammation.

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments.
Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments [*see Adverse Reactions (6.1)*]. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately [*see Patient Counseling Information (17)*].

5.2 Increase in Intraocular Pressure.
Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA [*see Adverse Reactions (6.1)*]. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with vascular endothelial growth factor (VEGF) inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

5.3 Thromboembolic Events.
There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

6 ADVERSE REACTIONS
The following potentially serious adverse reactions are described elsewhere in the labeling:
- Hypersensitivity [*see Contraindications (4.3)*]
- Endophthalmitis and retinal detachments [*see Warnings and Precautions (5.1)*]
- Increase in intraocular pressure [*see Warnings and Precautions (5.2)*]
- Thromboembolic events [*see Warnings and Precautions (5.3)*]

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 other clinical trials of the same or another drug and may not reflect the rates observed in practice.
A total of 2980 patients treated with EYLEA constituted the safety population in eight phase 3 studies. Among those, 2379 patients were treated with the recommended dose of 2 mg. Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment. The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

Neovascular (Wet) Age-Related Macular Degeneration (AMD). The data described below reflect exposure to EYLEA in 1824 patients with wet AMD, including 1223 patients treated with the 2-mg dose, in 2 double-masked, controlled clinical studies (VIEW1 and VIEW2) for 24 months (with active control in year 1).
Safety data observed in the EYLEA group in a 52-week, double-masked, Phase 2 study were consistent with these results.

Table 1: Most Common Adverse Reactions (≥1%) in Wet AMD Studies

	Baseline to Week 52		Baseline to Week 96	
Adverse Reactions	**EYLEA (N=1824)**	**Active Control (ranibizumab) (N=595)**	**EYLEA (N=1824)**	**Control (ranibizumab) (N=595)**
Conjunctival hemorrhage	25%	28%	27%	30%
Eye pain	9%	9%	10%	10%
Cataract	7%	7%	13%	10%
Vitreous detachment	6%	6%	8%	8%
Vitreous floaters	6%	7%	8%	10%
Intraocular pressure increased	5%	7%	7%	11%
Ocular hyperemia	4%	8%	5%	10%
Corneal epithelium defect	4%	5%	5%	6%
Detachment of the retinal pigment epithelium	3%	3%	5%	5%
Injection site pain	3%	3%	3%	4%
Foreign body sensation in eyes	3%	4%	4%	4%
Lacrimation increased	3%	1%	4%	2%
Vision blurred	2%	2%	4%	3%
Intraocular inflammation	2%	3%	3%	4%
Retinal pigment epithelium tear	2%	1%	2%	2%
Injection site hemorrhage	1%	2%	2%	2%
Eyelid edema	1%	2%	2%	3%
Corneal edema	1%	1%	1%	1%
Retinal detachment	<1%	<1%	1%	1%

Less common serious adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal tear, and endophthalmitis.

Macular Edema Following Retinal Vein Occlusion (RVO). The data described below reflect 6 months exposure to EYLEA with a monthly 2 mg dose in 218 patients following CRVO in 2 clinical studies (COPERNICUS and GALILEO) and 91 patients following BRVO in one clinical study (VIBRANT).

Table 2: Most Common Adverse Reactions (≥1%) in RVO Studies

	CRVO		BRVO	
Adverse Reactions	**EYLEA (N=218)**	**Control (N=142)**	**EYLEA (N=91)**	**Control (N=92)**
Eye pain	13%	5%	4%	5%
Conjunctival hemorrhage	12%	11%	20%	4%
Intraocular pressure increased	8%	6%	2%	0%
Corneal epithelium defect	5%	4%	2%	0%
Vitreous floaters	5%	1%	1%	0%
Ocular hyperemia	5%	3%	2%	2%
Foreign body sensation in eyes	3%	5%	3%	0%
Vitreous detachment	3%	4%	2%	0%
Lacrimation increased	3%	4%	3%	0%
Injection site pain	3%	1%	1%	0%
Vision blurred	1%	<1%	1%	1%
Intraocular inflammation	1%	1%	0%	0%
Cataract	<1%	1%	5%	0%
Eyelid edema	<1%	1%	1%	0%

Less common adverse reactions reported in <1% of the patients treated with EYLEA in the CRVO studies were corneal edema, retinal tear, hypersensitivity, and endophthalmitis.

Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR). The data described below reflect exposure to EYLEA in 578 patients with DME treated with the 2-mg dose in 2 double-masked, controlled clinical studies (VIVID and VISTA) from baseline to week 52 and from baseline to week 100.

Table 3: Most Common Adverse Reactions (≥1%) in DME Studies

	Baseline to Week 52		Baseline to Week 100	
Adverse Reactions	**EYLEA (N=578)**	**Control (N=287)**	**EYLEA (N=578)**	**Control (N=287)**
Conjunctival hemorrhage	28%	17%	31%	21%
Eye pain	9%	6%	11%	9%
Cataract	8%	9%	19%	17%
Vitreous floaters	6%	3%	8%	6%
Corneal epithelium defect	5%	3%	7%	5%
Intraocular pressure increased	5%	3%	9%	5%
Ocular hyperemia	5%	6%	5%	6%
Vitreous detachment	3%	3%	8%	6%
Foreign body sensation in eyes	3%	3%	3%	3%
Lacrimation increased	3%	2%	4%	2%
Vision blurred	2%	2%	3%	4%
Intraocular inflammation	2%	<1%	3%	1%
Injection site pain	2%	<1%	2%	<1%
Eyelid edema	<1%	1%	2%	1%

Less common adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal detachment, retinal tear, corneal edema, and injection site hemorrhage.
Safety data observed in 269 patients with nonproliferative diabetic retinopathy (NPDR) through week 52 in the PANORAMA trial were consistent with those seen in the phase 3 VIVID and VISTA trials (see Table 3 above).

6.2 Immunogenicity.
As with all therapeutic proteins, there is a potential for an immune response in patients treated with EYLEA. The immunogenicity of EYLEA was evaluated in serum samples. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to EYLEA in immunoassays. The detection of an immune response is highly dependent on the sensitivity and specificity of the assays used, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to EYLEA with the incidence of antibodies to other products may be misleading.
In the wet AMD, RVO, and DME studies, the pre-treatment incidence of immunoreactivity to EYLEA was approximately 1% to 3% across treatment groups. After dosing with EYLEA for 24-100 weeks, antibodies to EYLEA were detected in a similar percentage range of patients. There were no differences in efficacy or safety between patients with or without immunoreactivity.

8 USE IN SPECIFIC POPULATIONS.

8.1 Pregnancy
Risk Summary
Adequate and well-controlled studies with EYLEA have not been conducted in pregnant women. Aflibercept produced adverse embryofetal effects in rabbits, including external, visceral, and skeletal malformations. A fetal No Observed Adverse Effect Level (NOAEL) was not identified. At the lowest dose shown to produce adverse embryofetal effects, systemic exposures (based on AUC for free aflibercept) were approximately 6 times higher than AUC values observed in humans after a single intravitreal treatment at the recommended clinical dose [*see Animal Data*].
Animal reproduction studies are not always predictive of human response, and it is not known whether EYLEA can cause fetal harm when administered to a pregnant woman. Based on the anti-VEGF mechanism of action for aflibercept, treatment with EYLEA may pose a risk to human embryofetal development. EYLEA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data
Animal Data
In two embryofetal development studies, aflibercept produced adverse embryofetal effects when administered every three days during organogenesis to pregnant rabbits at intravenous doses ≥3 mg per kg, or every six days during organogenesis at subcutaneous doses ≥0.1 mg per kg.
Adverse embryofetal effects included increased incidences of postimplantation loss and fetal malformations, including anasarca, umbilical hernia, diaphragmatic hernia, gastroschisis, cleft palate, ectrodactyly, intestinal atresia, spina bifida, encephalomeningocele, heart and major vessel defects, and skeletal malformations (fused vertebrae, sternebrae, and ribs; supernumerary vertebral arches and ribs; and incomplete ossification). The maternal No Observed Adverse Effect Level (NOAEL) in these studies was 3 mg per kg. Aflibercept produced fetal malformations at all doses assessed in rabbits and the fetal NOAEL was not identified. At the lowest dose shown to produce adverse embryofetal effects in rabbits (0.1 mg per kg), systemic exposure (AUC) of free aflibercept was approximately 6 times higher than systemic exposure (AUC) observed in humans after a single intravitreal dose of 2 mg.

8.2 Lactation
Risk Summary
There is no information regarding the presence of aflibercept in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production/excretion. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, EYLEA is not recommended during breastfeeding.
The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EYLEA and any potential adverse effects on the breastfed child from EYLEA.

8.3 Females and Males of Reproductive Potential
Contraception
Females of reproductive potential are advised to use effective contraception prior to the initial dose, during treatment, and for at least 3 months after the last intravitreal injection of EYLEA.

Infertility
There are no data regarding the effects of EYLEA on human fertility. Aflibercept adversely affected female and male reproductive systems in cynomolgus monkeys when administered by intravenous injection at a dose approximately 1500 times higher than the systemic level observed humans with an intravitreal dose of 2 mg. A No Observed Adverse Effect Level (NOAEL) was not identified. These findings were reversible within 20 weeks after cessation of treatment.

8.4 Pediatric Use.
The safety and effectiveness of EYLEA in pediatric patients have not been established.

8.5 Geriatric Use.
In the clinical studies, approximately 76% (2049/2701) of patients randomized to treatment with EYLEA were ≥65 years of age and approximately 46% (1250/2701) were ≥75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies.

17 PATIENT COUNSELING INFORMATION
In the days following EYLEA administration, patients are at risk of developing endophthalmitis or retinal detachment. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise patients to seek immediate care from an ophthalmologist [*see Warnings and Precautions (5.1)*].
Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations [*see Adverse Reactions (6)*]. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

REGENERON

Manufactured by:
Regeneron Pharmaceuticals, Inc.
777 Old Saw Mill River Road
Tarrytown, NY 10591

Issue Date: 08/2019
Initial U.S. Approval: 2011

Based on the August 2019
EYLEA® (aflibercept) Injection full
Prescribing Information.

EYL.19.07.0306

(Continued from page 37)

Aside from standard automated perimetry, alternative forms of perimetry are available. These include frequency-doubling technology, short-wavelength automated perimetry ("blue-on-yellow," SWAP), flicker perimetry and edge perimetry.

The current recommendations from the American Academy of Ophthalmology state that white-on-white perimetry remains the preferred form of testing in glaucoma patients or suspects and do not advocate for the use of alternative perimetric methods.[27,28] For initial examinations, the 24-2 is preferred for a comprehensive overview of common locations affected in the peripheral and central VF. The 10-2 is important for mapping central VF loss that may be missed by the 24-2.[29,30] Clinicians need to use their judgment on which is most suitable for the individual patient.[31,32]

While some have advocated for obtaining at least six VF results in the first two years, in combining these pieces of evidence clinicians could consider performing more VF tests per visit to increase diagnostic confidence.[33,34]

More recently, a fast-test algorithm, SITA Faster, has become commercially available. This facilitates a paradigm shift towards more testing per visit, which would have been historically impractical with slower methods. However, clinicians need to remain vigilant of low test reliability results arising due to faster testing methods.[35,36]

Clinical pearl: White-on-white standard automated perimetry, performed preferably three or more times at each visit, is recommended for glaucoma assessment.

Examination of the anterior eye structures. Conditions affecting the anterior segment may contribute to the development of glaucoma. Secondary conditions such as pigment dispersion syndrome, pseudoexfoliative syndrome, anterior segment inflammation and angle recession can result in elevation of IOP and subsequently

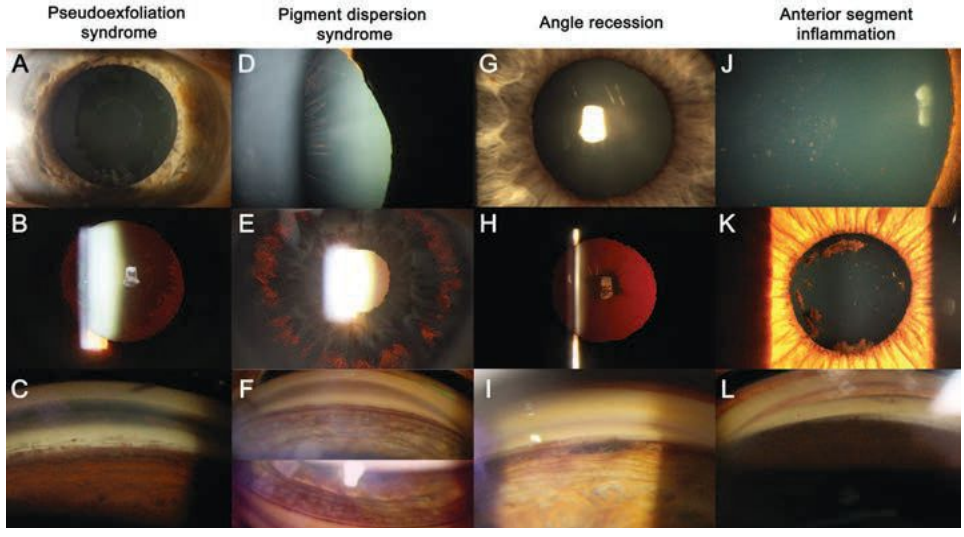

Fig. 2. The slit lamp biomicroscopic and gonioscopic findings of psuedoexfoliation syndrome (A-C), pigment dispersion syndrome (D-F), angle recession (G-I) and anterior segment inflammation (J-L). (A) Extracellular material deposition in a double concentric bull's eye pattern. (B) Transillumination view of the bull's eye pattern. (C) Increased but patchy pigmentation of trabecular meshwork on gonioscopy. (D) Radial anterior lens surface pigment deposition. (E) Mid-peripheral iris transillumination defects. (F) Homogenous increased hyperpigmentation of the trabecular meshwork on gonioscopy. (G) Loss of the pupillary ruff. (H) Transillumination view of a traumatic cataract. (I) Angle recession on gonioscopy. (J) Pigmentation on the anterior surface of the lens capsule associated with a history of anterior uveitis. (K) Larger agglomerates of pigment on the anterior lens capsule surface suggestive of broken posterior synechiae. (L) Peripheral anterior synechiae with focal narrowing of the angle.

TABLE 2. CLINICAL FEATURES OF COMMON SECONDARY CONDITIONS ASSOCIATED WITH GLAUCOMA

CONDITION	SLIT LAMP FEATURES	GONIOSCOPIC FEATURES
Pigment dispersion syndrome	- Pigment deposition on anterior segment structures (*e.g.*, anterior lens surface and corneal endothelium)	- Active stage: dense homogenous pigmentation of the anterior angle - Inactive stage: pigment reversal sign (superior angle appears more pigmented than the inferior angle)
Pseudoexfoliative syndrome	- Extracellular fibril material deposition on anterior segment structures (*e.g.*, anterior lens surface, in a double-concentric pattern, and corneal endothelium) - Peripupillary iris transillumination defects - Phacodonesis	- Deposition of exfoliative material in anterior chamber angle - Increased but patchy pigmentation of the trabecular meshwork
Anterior segment inflammation	- Anterior chamber cells or flare - Endothelial keratic precipitates - Posterior synechiae	- Peripheral anterior synechiae
Angle recession	- Acute trauma: hyphema and/or acute inflammation - Iris sphincter tears, mydriasis, phacodonesis/subluxated lens, iridodialysis or cylcodialysis	- Widening of the ciliary body band - Iridodialysis or cyclodialysis - Irregular hyperpigmentation of the angle - Whitening of the scleral spur (broken iris processes)
Neovascularization	- Iris rubeosis	- Neovascularization within the angle

glaucomatous damage to the optic nerve head (*Figure 2*).

A summary of the slit lamp findings of common secondary conditions is shown in *Table 2*. These conditions also have the potential to influence treatment selection. For example, clinicians may elect for topical treatment rather than selective laser trabeculoplasty first-line therapy in cases of angle recession glaucoma, while a patient with primary open-angle glaucoma may be a more suitable candidate for laser treatment.

Corneal endothelial dystrophies may lead to clinicians being more cautious with carbonic anhydrase inhibitors. Patients with iris or skin configurations that may be more susceptible to cosmetic changes arising from prostaglandin therapy should be carefully warned. Thus, detailed assessment of the anterior segment using slit lamp biomicroscopy, both prior to and following pupil dilation, forms an essential component of the glaucoma assessment.

Clinical pearl: Assess the anterior segment for secondary causes of glaucoma.

Assessment of the anterior chamber angle. Gonioscopy remains the gold standard for anterior angle assessment.[37] Unlike van Herick angle estimation or anterior segment optical coherence tomography (OCT), gonioscopy is not affected by ocular surface diseases such as pterygia or other limbal opacities.

To maximize the direct and dynamic visualization offered by gonioscopy, perform both primary gaze and off-axis evaluations. This allows for distinction between true narrow angles vs. open angles that appear narrow in primary gaze due to a steep iris configuration. In cases where the angle appears narrow despite off-axis viewing, perform indentation, which allows for differentiation between appositional closure (*i.e.*, widens with indentation) and mechanical closure due to the presence of synechiae or neovascularization (*i.e.*, no deepening despite indentation). It is also useful for differentiating between iris processes and synechiae. Gonioscopy also provides an *in vivo* view of the angle important for identifying secondary causes of glaucoma like pigment dispersion syndrome and angle recession.

Anterior segment OCT is an emerging technology for assessing the anterior chamber angle. While it offers a noninvasive method of visualizing the angle structures such as Schwable's line, Schlemm's canal, the scleral spur and the ciliary body, it is not able to distinguish between the pigmented and non-pigmented aspects of the trabecular meshwork. There are no widely accepted cut-offs with acceptable sensitivity and specificity to differentiate between disease and normal.[38] Other anterior segment imaging modalities include Scheimpflug imaging and ultrasound biomicroscopy, which have their own specific advantages.[39]

Clinical pearl: Gonioscopy is critical for comprehensive assessment of the anterior chamber angle.

Examination of the posterior eye structures. The current clinical standard for visualizing characteristic optic nerve head features of glaucoma is using stereoscopic funduscopy. Adding a red-free filter during funduscopic assessment or through retinal camera software allows for improved assessment of the retinal nerve fiber layer (RNFL) integrity, highlighting regions of diffuse or focal structural loss. Pharmacologic mydriasis can enhance

TABLE 3. MODIFICATIONS AND CONSIDERATIONS FOR SETTING UP A GLAUCOMA PRACTICE

	RECOMMENDATIONS
Reception	- Inform patients that they will require eye drops in their eyes (anesthesia and/or dilation) and make appropriate preparations. - Inform patients that their appointment time may be prolonged in the event that additional testing is required. - Inform patients there may be additional fees associated with extra glaucoma testing. - Create "welcome packs" for patients providing the above information to create an extra layer of redundancy.
Pre-testing or equipment room	- Instruments should be strategically placed to minimize foot traffic and disruptions. - VF testing should be conducted in a suitably dark room. - Instructions for technicians should be clear and standardized; training by a qualified professional on relevant testing equipment (*e.g.*, VF, OCT) needs to be provided and maintained. - Consider methods for direct communications with doctor for troubleshooting challenging patients.
Consulting room	- Adequately stocked lens kit (*e.g.*, Superfield, 60D/78D, gonioscope) and microscope as described above. - Suite of diagnostic drugs (anesthesia, mydriatic) in a suitable drug fridge. - Emergency ocular hypotensive drugs (*e.g.*, parasympathomimetic, beta-blocker, oral diuretic) in case of acutely elevated pressures. - Set up a practice management system that includes pertinent glaucoma-related findings (history, vision, anterior and posterior segment, IOP profiling data, corneal thickness, gonioscopy, VF and imaging results). - Have both physical and digital methods for recording data in case electronic systems go down.
Post-consultation	- Redundancy in the review process: consider direct messaging system, physical letters and phone calls to promote follow-up. - Create information pamphlets on glaucoma to promote the practice and patient health literacy.

visualization of the optic nerve by improving assessment of the cup size and depth, which is best appreciated stereoscopically. Retinal photography allows for serial documentation of the disc and peripapillary appearance, useful for detecting change through flicker stereophotography of the nerve.[40,41] Unlike some imaging modalities, fundus photography can be largely agnostic to the hardware and software and so is highly conducive to long-term monitoring of the disc appearance.

Clinical pearl: The current clinical standard is stereoscopic examination of the optic nerve head and adjacent retinal structures. Pharmacologic mydriasis is also recommended.

Ancillary imaging in the optic nerve head and retinal examination. OCT has become a practice staple for the diagnosis and management of glaucoma.[42] It offers a quantitative method for assessing glaucomatous changes such as changes to the physiological cup, neuroretinal rim loss or thinning of the neural layers. Of note, OCT is useful for early detection of glaucomatous progression that may not be appreciable based on funduscopic information alone. In addition to this, it allows for visualization of features previously thought to be "invisible" such as the anatomical disc margin (the termination of the scleral canal) and the lamina cribrosa.

As well as imaging of the optic nerve head and the adjacent structures, imaging of the macula in glaucoma is important to identify structural losses occurring in glaucoma. Significantly, approximately half of the ganglion cell bodies are located within the macula, and imaging in this region highlights relevant pathological changes across the spectrum of glaucoma stages. It is important to note for clinicians that structure-function correlations need to be made with the appropriate regions in visual space, *i.e.*, that structural loss in the macula needs to be assessed in conjunction with a suitable central VF testing grid.

Despite these advantages, use of OCT in glaucoma is not without its limitations. When starting out, it is easy for clinicians to rely on the red and green coding from instrument printouts as a guide to differentiating between normal and abnormal findings.[43] Clinicians must carefully interpret and scrutinize the data and place it in the context of the other clinical results. In some cases, the raw data (*i.e.*, heat map, TSNIT curves) may be more useful than relying on normative comparisons alone.

Another limitation of OCT is the "measurement floor" encountered in advanced stages of disease whereby the extent of structural loss such as the RNFL thickness, exceeds the lowest measurable thickness and the remaining "thickness" is due to non-neuronal structures, such as glial tissue or the retinal vasculature.[44] As such, OCT may have limited utility in later stages of disease.

Finally, the OCT features of glaucoma overlap significantly with those

of other optic nerve conditions such as ischemic or compressive optic neuropathies. Subsequently, OCT alone cannot be used to diagnose or screen for glaucoma and must be used in conjunction with other tests.

Clinical pearl: Ancillary imaging of the optic nerve head, such as OCT, can reveal additional, important details for cross-sectional diagnosis and progression analysis. The tools of the trade in a glaucoma practice are rarely used in isolation and are best maximized when applied as using a complementary approach.

Set Up Your Glaucoma Practice

So, as a doctor interested in setting up a practice to manage glaucoma, what kinds of preparations do you need? This question can be examined from the front of the practice all the way to the back in the clinician's office. Some of these considerations are shown in *Table 3*.

Doctors will find that while there can be big changes to the way a practice operates to meet the demands of glaucoma patients—such as a robust recall system, patient information handouts and separate testing rooms—many such modifications can be easily translatable to other conditions of the eye, aiding the practice as a whole. The workflow can be individualized to the doctor's clinic but should ultimately complete the loop for excellent patient care.

It is important to create layers within the practice that will promote the practice and improve patient health literacy. Many patients will be unaware that you offer comprehensive glaucoma (or other specialized) services. Strategies to change this will help the doctor build their practice and present an impression of professionalism.

Takeaways

There are a lot of considerations when setting up a clinic to provide glaucoma care. However, given the breadth of the public health issue, it is very rewarding to be able to serve a population of patients who require ongoing eye care.

Now that we have set up a glaucoma clinic, the next step is to consider processes for providing glaucoma care in the consulting room. In part two of this series, to be published next month, we will outline the process of glaucoma care by the OD, including diagnosis, identification of progression and management. ■

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PEER REVIEWED

COMPREHENDING, CATCHING AND CORRECTING MGD

Keep up with the continual advancements in treatment to better serve your patients.

BY KATHERINE SANFORD, OD
MEMPHIS

Our understanding of the multifactorial nature of meibomian gland dysfunction (MGD) has evolved significantly since the early 1980s when the term "MGD" was first coined.[1] There is now a wealth of in-office interventions practitioners can implement in addition to at-home maintenance therapies.[2,3] Despite advancements in MGD treatment, however, these procedures are not fully covered by insurance and can pose a significant cost to the patient. By developing our comprehensive knowledge of MGD therapies, we as practitioners can more effectively identify which procedures will benefit the greatest number of patients, balance improvement in quality of life with cost and build patient loyalty within our practices.

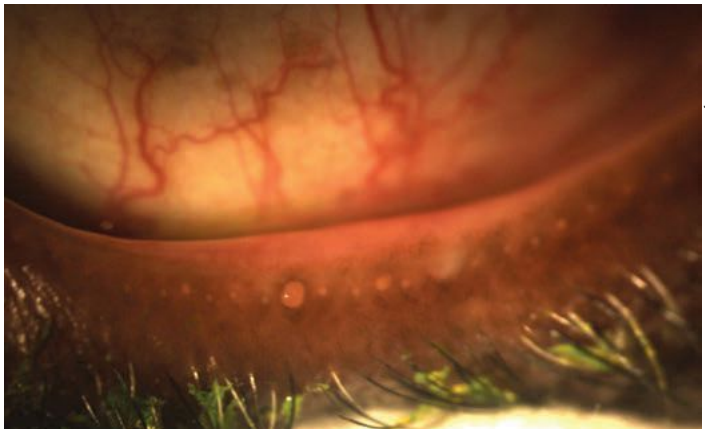

Photo: Doan Huynh Kwak, OD

Obstructed meibomian glands respond to digital pressure by releasing thickened, cloudy meibum.

Exploring MGD

The meibomian glands are sebaceous glands located within the tarsal plate of the upper and lower eyelids that produce and secrete meibum, a clear oil in non-diseased states, from orifices anterior to the mucocutaneous junction.[4] The muscle force of the orbicularis and Riolan's muscles contracting during blinking results in dispersal of the meibum from the glands.[5] It is this outermost meibum layer of the multilayer tear film that prevents evaporation of the underlying aqueous components.

Activities that lead to a decreased basal blink rate, such as computer use, can contribute to the development of MGD. Patients with MGD have decreased unsaturated fatty acids and non-polar lipids, resulting in an increased melting point of the secretions. The more severe the meibomian disease, the higher the melting point.[6] The melting point of meibum in a non-obstructed gland is 32°C (89.6°F) but can increase up to 45°C (113°F) in severely obstructed glands; this is why therapeutic warming devices should reach temperatures close to 45°C.[7]

The most common cause of MGD is non-cicatricial obstruction, during which the glands are in their normal anatomic location, but the ducts are obstructed by thickened meibum and keratinized ductal epithelium.[1,8] Meibum accumulates in the ducts, causing gland dilatation and distortion. Meibum in the tear film is thus reduced, causing evaporation, increased osmolarity, increased bacterial growth on the lid and inflammation of the ocular surface, followed by atrophic degeneration of the gland in

About the author **Dr. Sanford** is an attending optometrist at the Memphis VA Medical Center. She has no financial interests to disclose.

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response to increased ductal pressure.[4,9] Studies show that obstructive MGD contributes to dry eye in 64% to 87% of cases.[5,10]

Diagnosing MGD

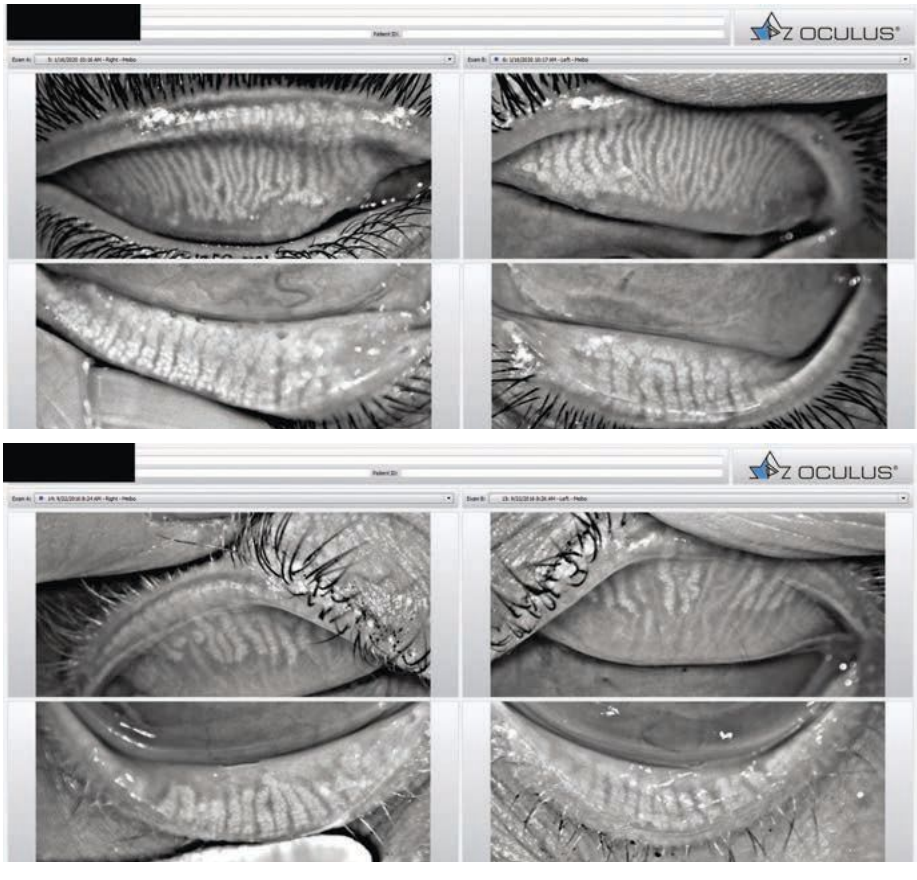
Accurately diagnosing obstructive MGD requires a combination of patient history, slit lamp exam and use of vital stains. While conducting your slit lamp exam, use your fingers or a cotton tip applicator to perform diagnostic expression of the central to nasal glands of the inferior lid. Press and hold for several seconds, noting the presence or absence of secretions and their quality.

The clinical signs of MGD include meibomian gland dilatation or dropout visible on meiboscopy with lid transillumination, altered gland secretions ranging from cloudy, viscous fluid to a dense, toothpaste-like material, plugging of meibomian orifices, notching and increased vascularity of the lid margin.[8,9,11] Infrared meibography can also aid in assessing the distortion and dilatation of glands, areas of atrophy and noninvasive keratographic breakup time of the tear film.[12]

Treating MGD

For years, the mainstays of MGD treatment have been lipid-based artificial tears, oral tetracyclines, and lid hygiene with warm compresses and lid massage for mild to moderate MGD, and short-term topical steroids for more severe disease.[13] Unfortunately, a substantial number of patients remain symptomatic and suffer further blows to their quality of life despite these therapies. Luckily, there are numerous other tools at our disposal to provide patients the ocular relief and improved quality of life they deserve.

What follows is an overview of several interventions for MGD, including a rough estimate of the out-of-pocket price to patients for each (on a scale of 0-4 dollar signs), though practices will naturally vary in what they charge.



Meibography images taken with the Oculus Keratograph. Healthy glands are columnar and relatively straight (top). Meibomian gland atrophy associated with MGD (bottom).

Therapeutic gland expression (0 to $). Gland expression is key in the diagnosis of MGD, but therapeutic expression has equal value. This is a more comprehensive procedure where the goal is to express all the content within the meibomian glands.

Therapeutic expression can be performed with your fingers or cotton tip applicators, but instruments such as a Mastrota Paddle (Ocusoft) and the Maskin Meibum Expressor (Katena) can ensure a more effective and efficient procedure. For maximum efficacy, the following three-phase approach is recommended: compress, debride, express. Starting with a compress or heating device will significantly liquefy the meibum, making it possible to express the gland content by applying less force to the eyelid.

Next, instill lissamine green in the eye, wait 60 seconds for dispersal and allow the thin mucocutaneous junction (line of Marx) to stain. A stainless-steel golf club spud may be used to apply mild pressure while moving the spud in a lateral motion along this line. No anesthetic is indicated, as only mild pressure is required for debridement. When successfully completed, meibomian orifices should be exposed and there should be little to no oily sheen on the lid margin.[14]

To express the inferior glands, pull the lower eyelid down to expose the palpebral conjunctiva and apply an expressor paddle to the nasal palpebral conjunctiva midway between the fornix and lash line while the patient gazes superiorly. Release the lower lid and apply a second expressor instrument to the outer nasal lid. While holding the first device stable, apply force while rocking or moving the external expressor from the base of the glands toward the gland orifices. Several attempts or additional pressure may be necessary if the meibum is turbid. Note areas with no secretions, as this suggests gland atrophy.

Move both expressors temporal on the lid and repeat the process until you reach the outer corner of the eye. For the upper glands, have the patient

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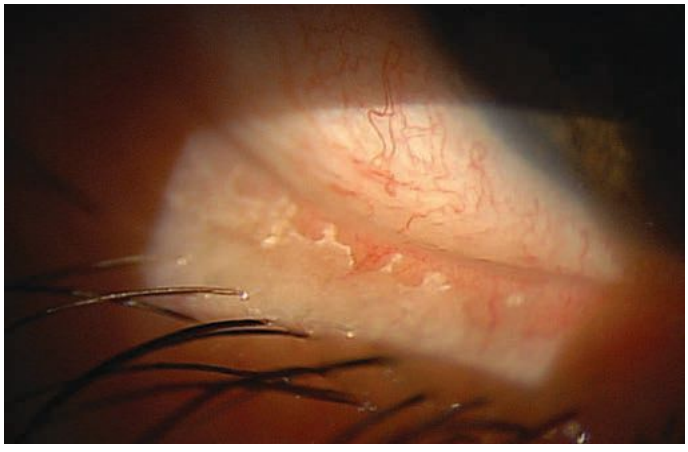


Photo: Doan Huynh Kwak, OD

Removing biofilm from the lid margin via BlephEx reduces the risk of blepharitis and dry eye.

look inferiorly and gently pull the superior lid away from the globe. Place the expressor paddle underneath the nasal lid midway between the fornix and the lash line and release the lid. Apply the second expressor to the outer nasal lid and repeat the process. Consider topical anesthetic drops and/or a bandage contact lens, depending on practitioner preference and patient cooperation.

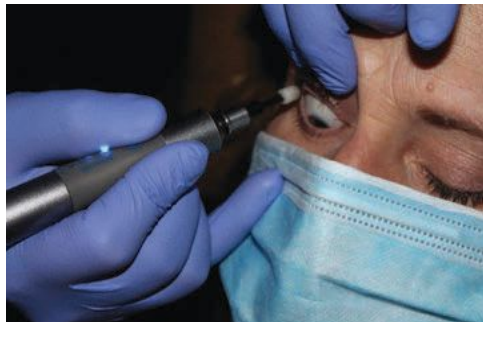
Intraductal probing, Katena ($). In 2010, Maskin described a probing technique where stainless steel probes up to 6mm in size are inserted directly into the meibomian gland orifices to unblock meibum or fibrous obstructions within the orifice and duct.[15] The procedure uses topical anesthetic in the eye and on the lid while a bandage contact lens protects the cornea.[16]

The majority of one study's participants experienced immediate relief in lid tenderness following treatment, with improvements persisting for four weeks, with only 16% of patients requiring additional treatment.[17] Subsequent studies additionally showed relative growth of the meibomian glands via infrared meibography. Comparison of pre- and post-treatment images showed reversal of proximal atrophy with lengthening of shortened glands, increased density, partial restoration of glands and the appearance of new glands.[18] Growth was consistent for all degrees of gland atrophy.[18] While repeated probing is typically necessary, annual retreatment was adequate in these cases.[18]

LipiFlow, Johnson & Johnson Vision ($$$$). Heat and gland expression are mainstays in the treatment of MGD; however, many of the conventional warming devices apply heat to the outer eyelid surface, limiting the degree and duration of heat that reaches the glands. LipiFlow is an in-office device that takes a different approach by applying heat between 41°C and 43°C to the palpebral conjunctiva while simultaneously applying pulsatile pressure to the outer eyelid surface to express the glands. By directing heat to the palpebral conjunctiva, lower temperatures are sufficient, reducing the risk of thermal injuries.[19,20]

A study assessed patients who underwent one 12-minute session of LipiFlow and found that at two and four weeks post-treatment, all participants demonstrated clinically significant improvements in meibomian gland secretion and tear breakup time (TBUT).[19] At two weeks, 76% reported an improvement in dry eye symptoms, which persisted through the four-week mark.[19] Post-treatment improvement in ocular symptoms was sustained for three to nine months in other studies.[16,20]

LipiFlow has an excellent safety profile, and a single treatment can more effectively improve the symptoms of MGD than a three-month daily course of oral doxycycline without the 40% risk of side effects



The BlephEx device for in-office removal of eyelid scurf and bacterial debris, which can cause inflammatory lid disease. The rotating pad buffs away the biofilm and other lid debris to prevent blepharitis.

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The iLux uses an LED-based heat source to warm the inner and outer lids, then applies gentle pressure to express meibum.

that doxycycline carries.[21,22] The most common findings post-treatment are mild conjunctival injection and mild petechial conjunctival or skin hemorrhages, which tend to resolve within a few weeks of LipiFlow use.

LipiFlow was the first pulsed heat device approved by the FDA and is commonly considered the standard to which others are compared, but it may be cost-prohibitive for some patients, as each session costs $900.

TearCare, Sight Sciences ($$$). TearCare is another in-office warming device but a bit more affordable than LipiFlow, at $600 to $700 per session. Four disposable electrothermal plates adhere to the outer lid and allow the patient to keep their eyes open and blink normally. By allowing the lids to move freely, this device takes advantage of natural meibomian dispersal through blinking. No portion of the device contacts the palpebral conjunctiva or ocular surface.

Connected to the TearCare controller, the plates deliver consistent therapeutic temperatures of 41°C to 45°C for 12 minutes. Following heating, most practitioners perform therapeutic expression to thoroughly evacuate the glands. One study found a statistically significant improvement in signs and symptoms of dry eye at four weeks with TearCare, which continued to six months when the device was combined with therapeutic expression.[23]

The Olympia study compared the safety and efficacy of TearCare with that of LipiFlow. The initial results indicated that TBUT and meibomian secretion scores saw similar improvements with both treatments, but 90% of patients in the TearCare cohort had a clinically significant decrease in Ocular Surface Disease Index (OSDI) score vs. 79% in the LipiFlow arm. TearCare participants also used 22% fewer lubricant drops post-treatment.[24]

iLux, Alcon ($$). Relatively new to the market, the iLux is a handheld thermal pulsation device with a disposable patient interface that uses an LED-based heat source to warm the inner and outer lids to the appropriate therapeutic range of 38°C to 42°C. Sensors continuously measure the temperature of the inner and outer lid and turn off the LED if temperatures reach 44°C or 45°C, respectively, to prevent thermal burns.

In a trial comparing iLux and LipiFlow, both treatments significantly improved signs and symptoms of MGD over four weeks with no clinically meaningful difference between the two.[25] Treatments typically take less than 10 minutes, and the built-in 15x magnifier on the device allows it to be used anywhere. With results similar to LipiFlow and costing less than it or TearCare, at roughly $300 to $500 per session, this device is an effective, more affordable option.

MiBo Thermoflo, MiBo Medical Group ($$). This device consists of a handheld probe that uses thermoelectric heat to liquefy the meibum within the glands. Ultrasound gel is applied to the probe and used to massage the outer skin of the upper and lower lids for eight to 12 minutes per eye, after which therapeutic expression is performed.[26]

The Thermoflo II has a dual handpiece, allowing both eyes to be treated simultaneously or separately. Three treatments, each two weeks apart, are recommended initially, and further treatment is determined based on patient response. All portions of the device are reusable, so treatment costs are lower, at $450 for three treatments or $100 to $300 per session.[16]

There is a relative scarcity of clinical data regarding the MiBo Thermoflo; additional investigation is needed to determine the efficacy and safety profile of this treatment.

eyeXpress Eye Hydration System, Holbar Medical Products ($$$). Using a goggle-based system, eyeXpress has soft gel inserts that uniformly distribute heat to the upper and lower lids of both eyes simultaneously, all while minimizing the need for pressure on the eye. The goggles are placed over the patient's eyes for 15 minutes, and therapeutic expression is performed after removal. Typical protocol is four treatments performed three to four weeks apart costing $450 to $750 per session.

BlephEx ($) This is an in-office treatment for exfoliating accumulated debris and biofilm from the lid margin, similar but superior to debridement. The product and the company both use the name 'BlephEx.'

The dry eye blepharitis syndrome theory asserts that a biofilm comprised of diverse microbes accumulates year after year on the lid margin and is so self-adherent that no home scrub regimen can remove it. As the biofilm thickens over time, bacteria within it proliferate and release inflammatory proteins, leading to blepharitis, hence the correlation between blepharitis

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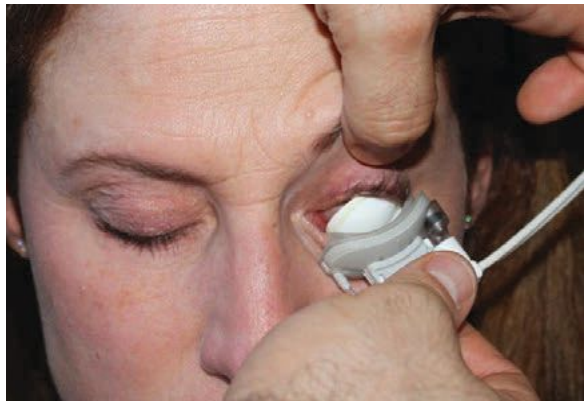
incidence and older age. Collarettes, meibomian capping and scurf are all evidence of this layer of biofilm along the lid surface. BlephEx uses a disposable medical-grade micro-sponge that spins on a handheld device to buff away the biofilm in addition to other lid debris, such as *Demodex*.

BlephEx is often used in conjunction with other procedures but can be used as a standalone treatment. Treatment for all four lids takes seven to eight minutes and is well tolerated by patients. Use of topical anesthetic drops is optional.[27] Treatments may be needed as often as three to four times per year; this varies between patients. Each session costs $150. Patients from early studies reported significant improvement in symptoms four weeks post-treatment. All participants exhibited MMP-9 inflammatory markers prior to treatment but tested MMP-9 negative post-BlephEx.[28]



LipiFlow uses a combination of heat and lid massage to liquefy meibum and clear obstructed meibomian glands.

NuLids, NuSight Medical ($$). While BlephEx achieves a thorough exfoliation of the lid margins in-office, NuLids allows patients to perform lid margin cleanings at home. A drop of gel lubricant or cleaner is placed on the soft silicone tip, which then vibrates when held against the lid. Patients should use NuLids once daily for 15 seconds per lid.

For a list price of around $320, patients can purchase a handheld NuLids from a participating practitioner. Each kit comes with an initial supply of 30 tips. The tips should be disposed of daily, and additional tips can be purchased for $1 apiece.

Intense pulsed light ($$). IPL uses a xenon flashlamp coupled with a filter that emits a wavelength of light within the visible spectrum. Blood cells in abnormal telangectasias absorb this light and coagulate, thrombosing the blood vessel and reducing the release of inflammatory mediators.

This technology has been used for years in dermatology to treat rosacea and acne and has been said to improve MGD and dry eye symptoms in patients treated with IPL for dermatologic disorders.[29] Once IPL was more widely implemented for MGD, it was additionally noted that performing meibomian gland expression post-IPL is easier due to the liquefaction of the abnormal meibum and gland dilation.

One commercial application of IPL in eye care is the Optima device from Lumenis, which applies up to 20J/cm^2 of energy to the lids and uses a water-cooled tip for patient comfort.

Studies show that even patients with severe MGD demonstrate objective as well as subjective improvement post-treatment. TBUT measurements responded more positively as the number of treatments increased.[29,30] Clinical signs improved in 87% of patients, and symptomatology improved in 93%.[29,30]

Patients can undergo treatments every four to six weeks indefinitely, at a cost of $400 per session. Maintenance IPL treatments are typically required once to twice a year.[16] One side effect of IPL is hypopigmentation; therefore, it is important to consider the degree of skin pigmentation a patient has, as lightly pigmented skin is least likely to demonstrate this side effect. Only lower lids are treated to reduce the risk of light absorption by the pigmented structures of the eye, such as the iris.

Low-level light therapy ($$). Like IPL, LLLT also originated in dermatology and has since shown efficacy in managing MGD. Specifically, this therapy can improve TBUT and OSDI scores, especially when combined with IPL.[31,32] Unlike IPL, LLLT is athermal, with photoactivation as its presumed mechanism of action, and can safely be applied to the upper lid. Three to four sessions runs about $500.

The Equinox (Marco) is an example of ocular LLLT. The procedure does not involve the use of gel and treats upper and lower lids simultaneously using direct and indirect photobiomodulation during the 15-minute application. The device uses LED lights to deliver focused wavelengths that target the mitochondria, stimulating production of the energy that powers the cell.[33]

Eye-Light (Topcon), which combines IPL and LLLT, allows for adjusted energy levels based on the patient's degree of MGD and pigmentation and also does not require gel thanks to a built-in cooling system that maintains an appropriate temperature.[31]

Warm compresses ($). There are many commercial warm compresses for at-home or in-office use that implement a variety of heating methods. MediBeads (Bruder Healthcare), TheraPearl (Bausch + Lomb) and MGDRx EyeBag (EyeBag Co.) are microwaved to produce dry heat. TranquilEyes XL (EyeEco) uses microwave energy similar to a hot towel compress to produce wet heat. Blephasteam (Thea Pharmaceuticals) and EyeGiene (Eyedetec Medical) use electrical and chemical heat, respectively.

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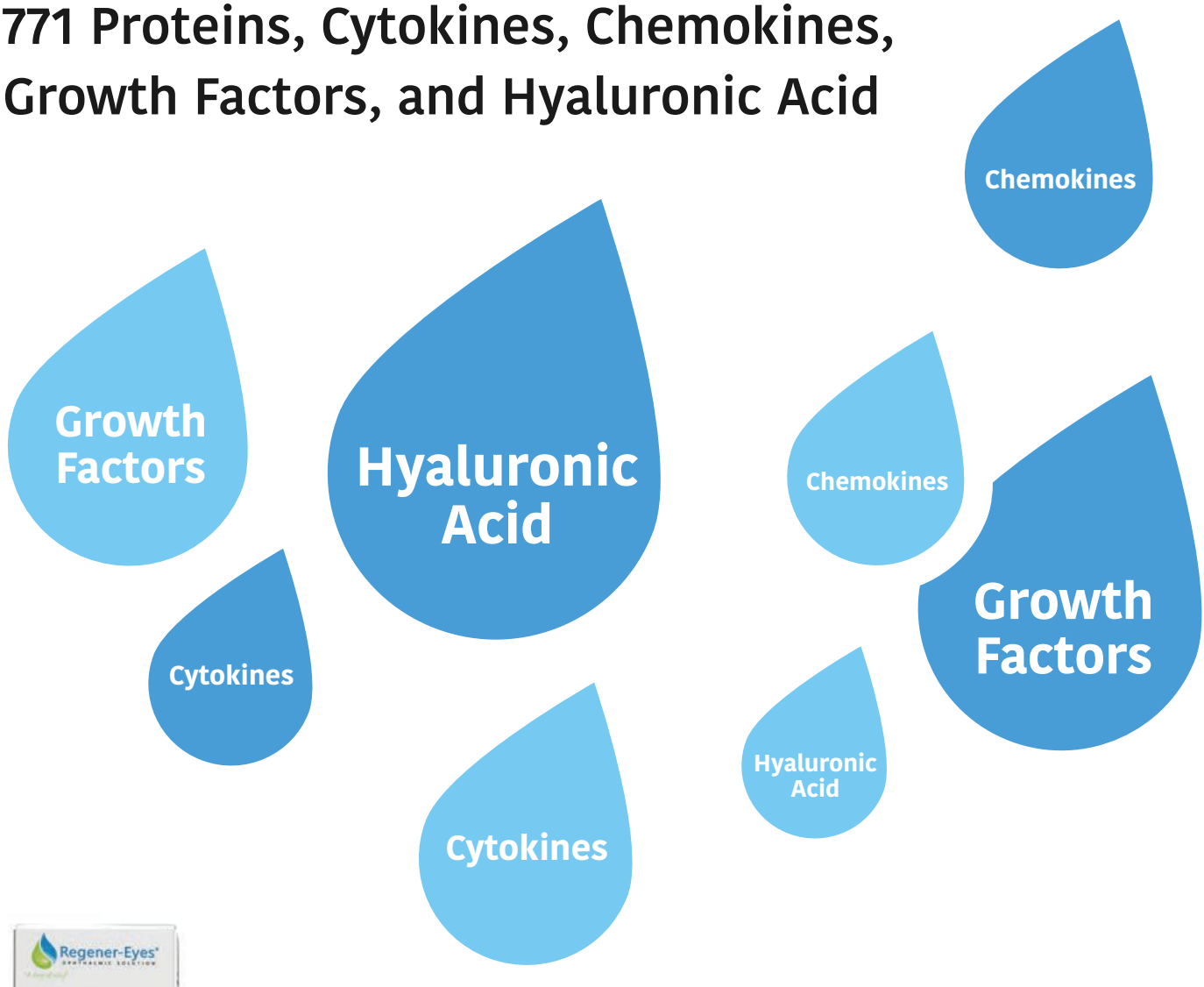

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LipiFlow established the concept of combining heat and pressure for gland expression, and the system offers practitioners useful feedback during the procedure.

While there is a general lack of agreement on the efficacy of various compresses, there's definitive consensus that applying 45°C heat for a minimum of five minutes in cases of mild MGD and up to 20 minutes for severe MGD is necessary for adequate therapeutic effect. Patients should not exceed 20 minutes of continuous 45°C heat, as burns can occur.[34,35]

At-home gland expression (0). For maintenance, patients may perform manual gland expression at home. While looking down, the patient should apply mild force on the nasal upper lid in a downward motion toward the lash line, progressing laterally across the lid to express all glands. The bottom lid should be expressed similarly with the patient looking up. Appropriate supraduction or infraduction during massage prevents direct mechanical force to the cornea, which could lead to corneal deformation. Alternatively, patients may squeeze sections of the upper and lower lids between their index finger and thumb.[36]

Take-home Message

Currently, in-office MGD therapies are not fully covered by insurance, leaving patients with a large portion of the financial burden. Patient education regarding the benefits of in-office treatment in addition to home therapy is critical in establishing buy-in when it comes to cost and compliance. As practitioners, we must stay abreast of the latest technology and look to clinical data to determine which procedures to implement in our practices for the betterment of our patients' lives. ■

Thank you to the TearWell Advance Dry Eye Treatment Center at the FocalPoint Crosstown in Memphis for performing several procedures on me free of charge to help me obtain photos for article use.

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NO PAIN, ALL GAIN: NEUROPATHIC PAIN IN PRACTICE

Bridging the difficulty in diagnosing a condition that is felt, not seen, can make a world of difference in a patient's life.

BY CHRISTOPHER LUFT, OD
WOODSTOCK, GA

Pain is one of the more common chief complaints when it comes to the eye. Though it is a subjective issue, the anatomy and physiology of pain have been the topics of more research investigations in recent years. We as clinicians treat signs more often than symptoms, so neuropathic pain usually falls outside of our typical order of operations. Time is of the essence in these cases, and when clinical findings do not match patient symptoms, a proper diagnosis can be difficult to make.

This article sheds light on what pain is, the neurobiology involved and what happens when the pain pathway is disrupted and dysfunctional. Keep the following phrase in mind as you work through the content: "Let me explain: pain, to the brain, with no stain."

Pain

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage."[1] From there, pain can be broken down into two broad categories: nociceptive and neuropathic.[1,2]

Nociceptive pain, which is usually transient, arises from the activation of nociceptors—the sensory receptors by which a nerve impulse is triggered—by actual or threatened damaging stimuli. Sites of nociceptive pain generation are located on, but not limited to, the dermis, muscles, cornea, periosteum, endosteum, synovial capsules and parietal pleural peritoneal membranes. These signals detect the conscious perception of mechanical, cutting, stretching, inflammatory, chemical, thermal and traumatic stimuli.

Neuropathic pain, on the other hand, is caused by an insult or disturbance to the nociceptive system, by either a chronic or acute etiology. This leads to overactive pain signaling, where symptoms far outweigh signs on clinical exam.[3] Ocular neuropathic pain, therefore, is "a diagnosis of exclusion which refers to the heightened perception of pain in response to normally non-painful stimuli."[2] To put it simply, it is pain with no benefit or purpose.

To the Brain

Pathways for ocular pain originate from a peripheral stimulus that then travels to the central nervous system along the afferent pathway.[4] Neural impulses respond to stimuli at the ocular surface—most notably at the cornea, the most innervated area of the body—and then project information from external stimuli to the central nervous system.[3,4] This triggers a mechanical and chemical response in the corneal nerve fibers to protect against danger, assist in maintaining a healthy cornea and modulate wound repair.[3]

The cornea is richly innervated by the ophthalmic division of the trigeminal nerve.[3-5] Corneal epithelium-derived innervation from the subbasal nerve plexus has illustrated that the plexus forms a delicate three-dimensional network in the epithelium, originating from the branches of the peripheral stromal nerves.[4,5] The tips of the stromal nerves penetrate Bowman's layer, predominantly in the peripheral cornea, and give rise to long bundles that run from the periphery to the center close to the subbasal epithelia and resemble wavy lines.[3-5] One millimeter into the corneal limbus, corneal nerve

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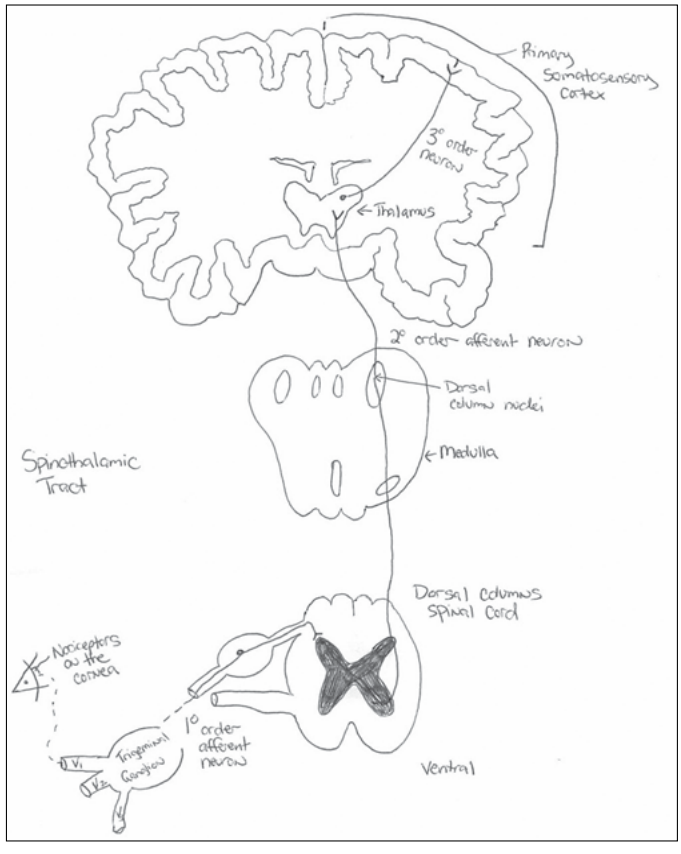
fibers lose their perineurium and myelin sheaths and are surrounded solely by Schwann cells.[3,5] Corneal nerve density increases and nerve diameter thins moving anteriorly through the stroma.[3] The overall density of epithelial nerves is greater centrally than peripherally, as the neural network has fully branched out.[3,5] Along their course, these long nerve bundles divide into numerous smaller branches that connect, constituting a delicate nerve network within the epithelium.[4,5]

The generation of a spinal nerve impulse from an external stimulus is called transduction.[1,6] This is a signal for "proper pain," as the stimulation is consistent with the response. The afferent signal travels across the sensory nerve to the relay synapses in the spinal cord, a process called conduction.[6] These sensory fibers decussate on the dorsal side of the spine, consistent with the notion that pain on one side of the body is processed on the contralateral side of the brain.[6] Once the signal is transmitted in the spine, it then travels up the spinothalamic tract to the thalamus, where the perception of pain originates.[1,6]

Localization of pain occurs in the sensory cortex of the brain, which tells us where the insult or injury is occurring to elicit a response.[6] This relaying of sensory information through the spinal cord, brainstem, thalamus and sensory cortex in the parietal lobe is known as the somatosensory system.[1-4,6]

Neuropathic pain disrupts the somatosensory pathway, causing "improper pain," in which a peripheral stimulus has an increased amplitude, duration, frequency or sensitivity to external stimuli.[1-4,6] Stimuli are received by receptors and generate an action potential, exciting the afferent sensory cortex of the brain.[6,7] Repeated stimulation can cause disproportionate glutamate release from presynaptic afferent nerves, triggering sodium channels in second-order neurons to commence.[7] Sensitization to higher-order pain pathways both centrally and peripherally can cause allodynia, or pain due to innocuous stimuli, and hyperalgesia, or enhanced pain perception.[7]

This discordance can occur at any level of the neural pathway and has many etiologies, including infection, allergy, herpes, trauma, compression, alcohol, vitamin B deficiency and certain neuropathies, all of which can cause a disconnect between signs and symptoms.[1-3] Women present with neuropathic findings more often than men, as they are more susceptible to autoimmune conditions that put them at higher risk.[2] Diabetes, which has seen an increase in the number of cases over the past decade, is also linked to neuropathic pain.[8]



The somatosensory pathway consists of fibers that carry information for pain, temperature, touch, position and vibration. Sensory receptors housed in the dorsal root ganglia project to the dorsal spinal cord, which decussate and extend to the thalamus.

The physiology of neuropathic corneal pain helps improve the quality of life for our patients while helping us understand corneal pain at a chemical level. Initiation of the arachidonic acid pain pathway bathes neural cells with cytokines that act on nociceptors, causing the neuron to fire more easily with increased amplitude and duration.[1,9] NMDA, another pain receptor, is also increased during bouts of cytokine release, allowing for more impulses to be transmitted.[1,9] Sodium channel activation along the neuron triggers neural impulses to fire more easily.[9] The most powerful prostaglandin, PGE 2, is released from the inflammatory pain pathway, causing an increase in neural impulses and worsening symptoms.[9,10]

Chronic inflammation may lead to aberrant connectivity of the nervous system, which may cause irreversible damage.[9,10] Pain blockades allow for an increased threshold for stimuli along the pain pathway and reduce neural activation.[11]

With No Stain

The debilitating nature of ocular pain compels urgency in management, balancing short-term symptomatic relief with long-term mitigation efforts.

Diagnosis. To properly diagnose true neuropathic pain, we have to confirm neurological impairment. This isn't as easy as it may sound; the pain is felt, not seen. There is no true clinical diagnostic test for neuropathic eye pain, as these abnormal firings take place at the neurological level and are too small to detect at the slit lamp.[12] Sodium fluorescein staining and typical dry eye workups typically come back unremarkable for pathology, with little to no ocular surface disease.[1,12]

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-2017 DEWS II Report

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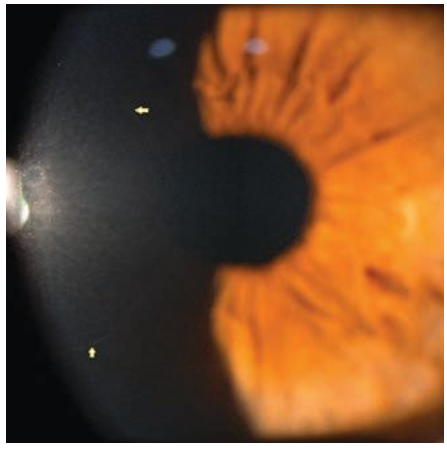
in the somatosensory pathway.[11,13] This test evaluates tactile stimulation of the ophthalmic branch of the trigeminal nerve using a cotton-tip applicator without topical anesthetics.[11] Touching the center of the cornea, we can subjectively judge a patient's reaction and determine nerve function.[11,13] Limitations with this method occur because of the all-or-none response to mechanical stimulation that patients are reporting.[11] This method fails to quantify corneal nerve sensitivity and may be better suited for neurotrophic corneal disease.

Functional somatosensory testing is also possible with the proparacaine test, which helps localize the initial pain stimulus to either a peripheral or central trigger.[1,6,11] Upon installation of anesthetic, if the patient reports full relief from pain we can localize the root cause to a peripheral stimulus. However, if there is no relief or the condition gets worse upon drop installation, we are dealing with a centralized stimulus, a marker for neuropathic pain.[1,11]

Luckily, there are diagnostic tests and technologies available to visualize corneal nerves, helping us confirm neural disruption. This doesn't negate the importance of diagnosing comorbidities on the ocular surface, such as dry eye disease, epithelial basement membrane dystrophy and keratitis, to give us a better clinical picture of inflammatory triggers for pain.[1-4,6] Managing comorbidities helps with neuropathic pain as we eliminate the underlying causes of cytokine and macrophage release arising from concurrent conditions.[1-3,6]

Assessment of corneal nerve integrity and morphology is possible with confocal microscopy.[1,6,11,13] While there is no objective criterion for the diagnosis of neuropathic pain, with this device we can visualize corneal structures at the cellular level.[13] Confocal microscopy acts as a noninvasive biopsy for corneal nerves, allowing for a high-resolution opportunity to pinpoint and confirm nerve damage that may be causing neuropathic eye pain.[11,13] Signs of corneal nerve damage apparent with microscopy include nerve beading, nerve loss, tortuosity and increased reflectivity.[13,14]



Yellow arrows mark normal corneal nerves *in vivo* under the slit lamp using specular reflection.

Confocal microscopy can also detect microneuromas in corneal nerve anatomy present in neuropathic eye pain but not in dry eye disease.[15] Microneuromas are defined as irregularly shaped, terminal enlargements of subbasal nerve endings with variable hyperreflectivity.[15] Findings such as these act as an objective, sensitive and specific biomarker for clinical diagnosis.[15] Keep in mind, visualization is more difficult when there is concurrent inflammation throughout the cornea from other comorbidities.[6,13-15]

Management. Therapies for neuropathic pain are designed to help alleviate any dysfunction along the somatosensory pathway.[2,7] The best treatment approach for neuropathic eye pain is one that involves multiple modalities to reduce external stimulation to corneal nociceptors and harmful cytokines and chemoattractants that disrupt the normal pain pathway. Neuropathic eye pain has many complex mechanisms that involve the central and peripheral nervous system, so treatment must target all of these impulses to alleviate the signs and symptoms of nerve damage.[2,7]

The first step in managing neuropathic ocular pain after establishing the proper diagnosis is treatment with preservative-free tears.[2,7] Benzalkonium chloride and other preservatives have been linked to the exacerbation of neuropathic pain due to their abrasive impact on the ocular surface. A regimen of non-preserved drops four times per day is recommended as the minimum starting point.[2,7,11] Topical corticosteroids such as the ester-based Lotemax (loteprednol, Bausch + Lomb) are particularly useful when initiating therapy.[2,7] Gel and ointment forms contain far fewer preservatives (Lotemax ointment is preservative-free) and offer a constant concentration of the drug upon application with fewer side effects.[2,7] Lotemax gel can be applied four times per day initially, with a slow taper over six weeks, diminishing the dosage by half every two weeks.[7,11]

Autologous serum tears are also part of the first-line therapy for neuropathic eye pain due to their powerful anti-inflammatory and restorative properties for neuronal regeneration.[2,7,11] Serum tears are formulated from a patient's own blood after removing red blood cells and clotting proteins.[2,7,16] This preservative-free solution serves as another option to relieve signs and symptoms of ocular pain and should be dosed about six times per day to start.[2,7]

Finally, diclofenac can be used QID to treat ocular surface pain, as it acts as a neuronal potassium channel opener.[16,17] The drug suppresses primary afferent neuronal excitatory and firing signals and attenuates excitatory neurotransmitter release and synaptic transmission, creating antiallodynic and antihyperalgesic effects.[16,17] Confocal microscopy has shown increased nerve density, reduced beading and reduced tortuosity *in vivo* in as little as eight weeks.[7]

The next step in therapy if symptoms have not quelled by this point is supplementation with the use of oral medications. Neurontin (gabapentin, Pfizer) and Lyrica (pregabalin, Pfizer) are the frontrunners, though gabapentin is not considered a controlled substance and therefore is more attractive to prescribe.[7] Gabapentin has been proven to relieve neuropathic pain by reducing the amount of inflow of calcium into the neurons, acting to stabilize their response in the central nervous system.[2,7] Dosage is 600mg by mouth the first day and then can

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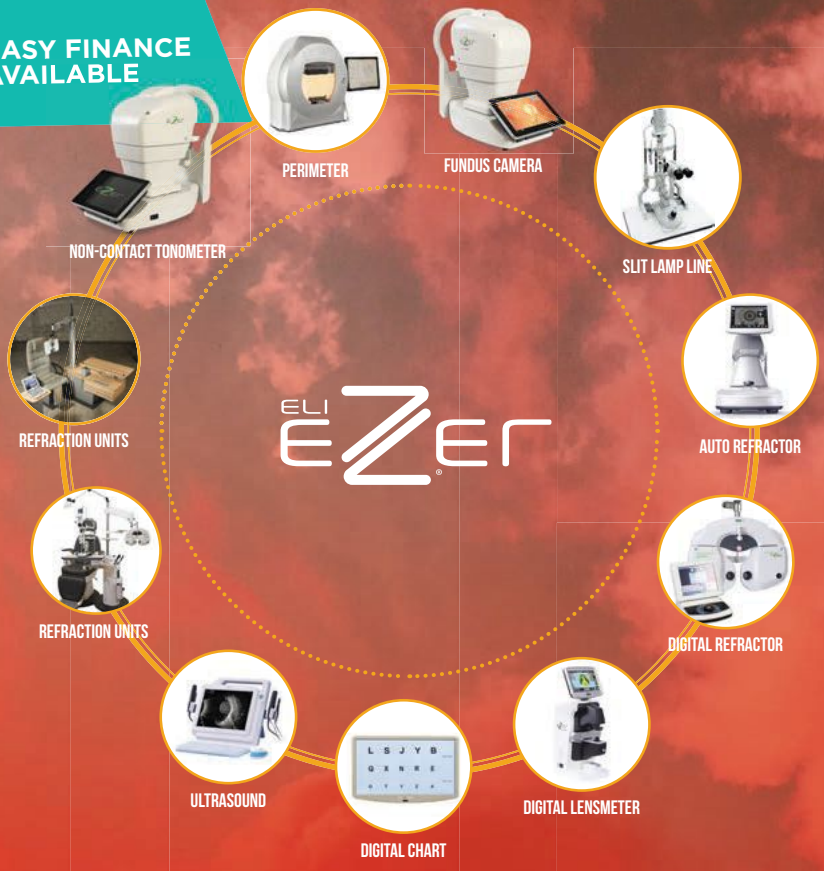

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be increased by 600mg increments to 3600mg (4x900mg daily) maximum.[2,7] Common side effects include fatigue, dizziness and confusion, though titration of dosage can be implemented to reduce adverse events.[2,7]

Doxycycline can also be used to inhibit matrix metalloproteinase, which degrades connective tissue, and increase tear film stability while helping to control ocular surface inflammation and nerve impulses.[2,7] Administer this drug at 100mg twice per day for three months and then 100mg once daily for three months before cessation.[2,7]

Upon implementation of oral medication, it is important to work in conjunction with a pain specialist to help provide relief with potentially stronger medications or more invasive methods.[2,7,11] We as optometrists may underestimate the degree of ocular pain these patients experience; however, it remains our duty to improve their quality of life while restoring proper corneal function. Luckily, the aforementioned therapies have been proven to provide structural and symptomatic relief for affected patients.

Takeaways

Corneal neuropathic pain is underrecognized, underdiagnosed and undertreated. Chronic dry eye and neuropathic eye pain may seem congruous but can vastly differ in presentation and treatment.[18] More research is needed to fully understand and manage neuropathic eye pain, but at the very least, grasping the complexity of the neuroanatomy and physiology of pain is crucial. ODs are the first line of defense against this debilitating condition and can greatly improve our patients' quality of life if we take the necessary steps to quell their symptoms. ■

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DON'T LET OSD COMPROMISE CONTACT LENS SUCCESS

Be proactive and manage the ocular surface upfront in order to ensure patient satisfaction.

BY IRENE FRANTZIS, OD
NEW YORK CITY

Managing ocular surface disease (OSD) is crucial for contact lens success. Contact lens dropout rates remain as high as 64% when symptoms such as discomfort and dry eye disease (DED) are present.[1] Ensuring a healthy ocular surface prior to your contact lens fitting can minimize the chance of contact lens issues down the road and increase patient satisfaction.

Baseline Evaluation

DED is a complex, multifactorial condition where symptoms and clinical signs do not always correlate well. Patients may be asymptomatic or could complain of pain, tearing or blurry vision. Many have found symptoms to be a more reliable indicator of dry eye than clinical signs.[2] As such, incorporate a validated dry eye questionnaire such as SPEED (Standard Patient Evaluation of Eye Dryness) or OSDI (Ocular Surface Disease Index) in your patient workup. The SPEED questionnaire has the advantages of fewer questions and easier interpretation. Contact lens dropouts have been found to have significantly higher scores on SPEED than successful lens wearers.[1,3]

Always consider the patient's medical history and medications while caring for their ocular health. Medical conditions that may contribute to DED include Sjögren's syndrome, rheumatoid arthritis, lupus and thyroid disorders amongst many others. The Tear Film and Ocular Surface Society's Dry Eye Workshop (DEWS) II report includes an extensive list of medications that can contribute to DED. Common classes of such medications include antihistamines, antidepressants, antispychotics, estrogen replacements and decongestants.[4] Chronic use of topical preservatives may also contribute to DED. Be aware of this in glaucoma and ocular hypertensive patients, as many of them are on such topical medications for many years.

Perform a careful slit lamp examination prior to initiating any contact lens fit. Eyelid position, closure and blink rate should be observed. Evaluate eyelids and lashes for signs of blepharitis or meibomian gland dysfunction (MGD).

Signs of blepharitis include inflamed lid margins and debris along the lashes. Anterior blepharitis is found on the outer edge of the lid margin and is often a result of a bacterial infection. Posterior blepharitis is found on the inner edge and involves the meibomian glands. This is a critical step in your baseline evaluation because MGD is the major cause of evaporative dry eye and the odds of contact lens dropout increase with worsening levels of MGD.[1] Additionally, numerous studies demonstrate that contact lens wear negatively affects the meibomian glands, causing increased levels of gland dropout and lower-quality meibum.[5]

Evaluate the conjunctiva and eyelid margin with lissamine green staining. This vital dye stains epithelial cells with damaged cell membranes and is useful in diagnosing early to

About the author

Dr. Frantzis is an assistant clinical professor at SUNY College of Optometry, where she supervises interns in the Contact Lens and Myopia Control clinics. She also engages in clinical research with an emphasis on contact lens and myopia control studies. She has no financial interests to disclose.

TABLE 1. NORMAL VS. ABNORMAL TEST LEVELS FOR OSD

	Normal Value	Abnormal Value
Osmolarity	≤300mOsm/L	> 300mOsm/L
MMP-9 levels	<40ng/ml	≥40ng/ml
Phenol red	>20mm	≤20mm
Schirmer's without anesthetic	>10mm	≤10mm

moderate DED. Nine or more spots of lissamine staining are considered clinically significant.[4] Lissamine can also be used to examine the upper and lower lid margins to look for signs of lid wiper epitheliopathy. This staining represents increased friction that occurs when the lid margins contact an ocular surface with a thin or unstable tear film.[4] Examine the cornea with both white light and a cobalt blue filter with fluorescein, looking for subtle changes like punctate epithelial defects. Fluorescein will stain compromised cells, and five or more spots of staining are considered significant.[4] Remember to wait at least one minute after instilling these dyes for a more accurate assessment.

Fluorescein can also be used to assess tear break-up time (TBUT), but the sensitivity and specificity of the TBUT is less certain for patients with milder cases of DED.[4] Consider performing several TBUT measurements and averaging your results for greater accuracy.

If you have access to a TearLab device, consider obtaining tear film osmolarity. Hyperosmolarity is associated with proinflammatory stress that contributes to DED severity. A positive result is greater than 300mOsm/L or an interocular difference greater than 8mOsm/L. A study looking at variability of indicators, including corneal staining, conjunctival staining, meibomian grading, TBUT, Schirmer tests and OSDI, found that the osmolarity measurement was least variable in patients with dry eye.[6]

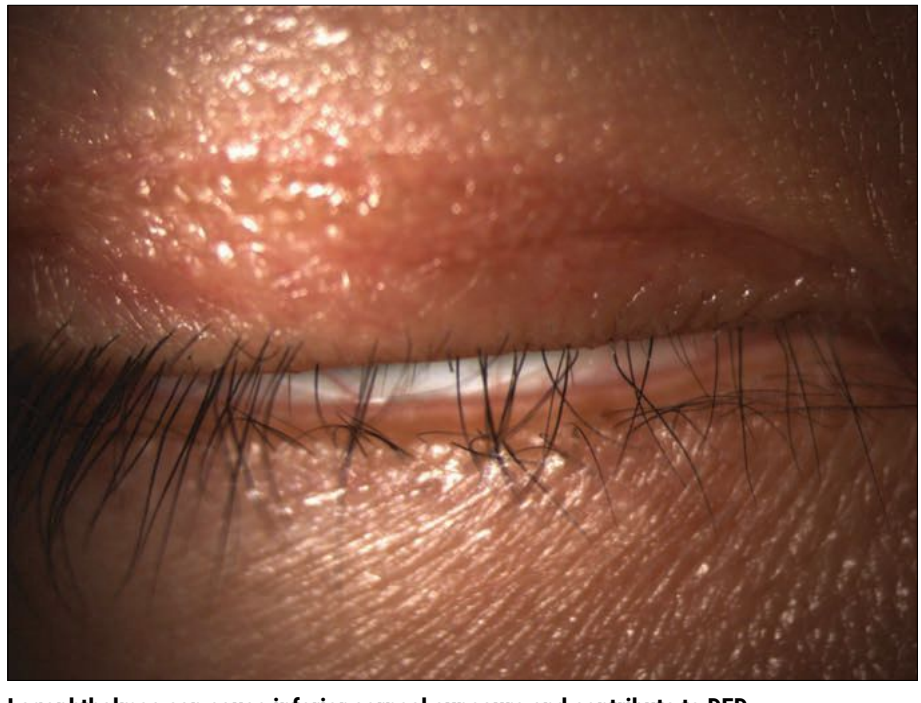
Tear hyperosmolarity initiates an inflammatory cascade that eventually causes damage to the ocular surface. Matrix metalloproteinase-9 (MMP-9) is one of many inflammatory markers that increases with increased levels of dryness. The InflammaDry (Quidel) device can measure MMP-9 levels, and levels 40ng/ml or greater are significant and produce a positive result.[4]

Also consider using the Schirmer or phenol red tests. The phenol red test involves inserting a thin yellow string into the eye for 15 seconds that turns red when moistened by tears. A normal result is greater than 20mm. Eyes are considered dry with a result less than 10mm and marginally dry with a result between 10mm and 20mm. Phenol red testing is less likely to cause reflex tearing than the Schirmer's test, which consists of a paper strip that is placed on the eye for five minutes. For Schirmer's testing without anesthetic, results less than 5mm are considered dry and between 5mm to 10mm are marginally dry. There is conflicting data on the sensitivity and specificity of these tests as well as the correlation between their results.[4] All

Differential Diagnoses

Other conditions such as allergic conjunctivitis, viral conjunctivitis and *Demodex* can present with symptoms of redness and tearing that mimic dry eye. Clinical findings that point to an allergic etiology include conjunctival papillae or chemosis and eyelid edema. Itching is a hallmark symptom of allergic conjunctivitis. Key signs of viral conjunctivitis include watery discharge, edematous lids and preauricular lymphadenopathy.

In viral infections, redness often begins unilaterally and then affects the other eye within a few days. Key signs of viral conjunctivitis include watery discharge, edematous lids and preauricular lymphadenopathy. Also consider *Demodex* in your differentials, as these mites can spread to the eyelids. During a slit lamp exam, cylindrical dandruff at the root of the eyelash is a key finding that suggests *Demodex*. The mites may also be viewed under high magnification after epilating a lash.



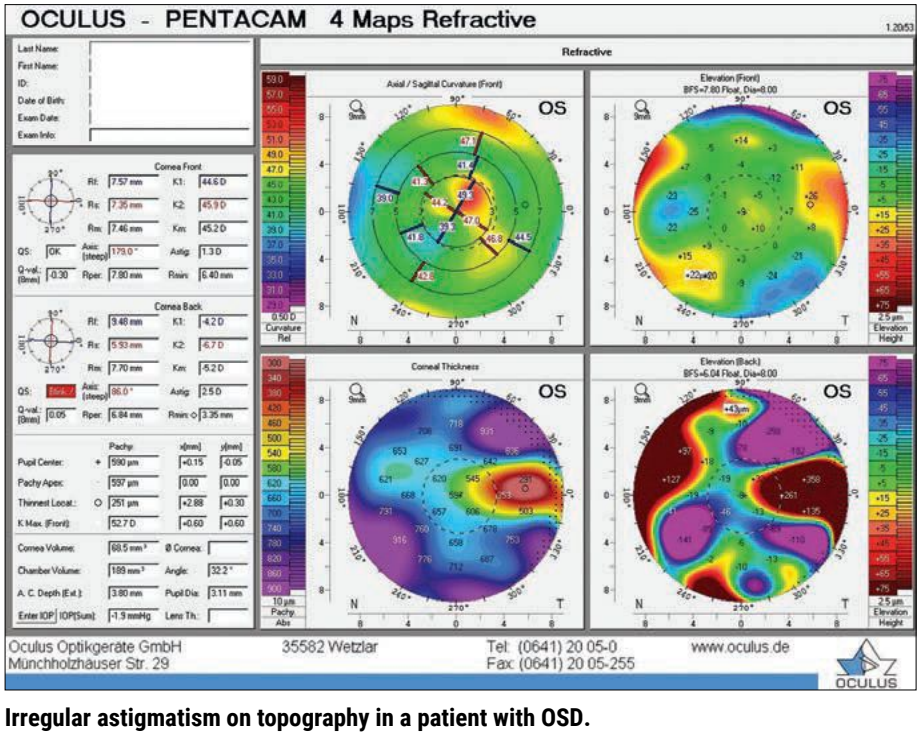
Lagophthalmos can cause inferior corneal exposure and contribute to DED.

of these testing values are provided (*Table 1*).

Baseline imaging will allow you to better monitor your patients with OSD over time and ensure that contact lens wear is not exacerbating any anterior segment findings. Anterior segment photos allow you to document existing corneal or conjunctival staining, corneal neovascularization or scarring. In moderate-to-severe OSD, you may also use topography to rule out the presence of irregular astigmatism. A device such as the LipiView (TearScience) or Keratograph (Oculus) can quantify additional indicators of DED such as lipid layer thickness and tear meniscus height.

DED is complex, and there is no one test to diagnose it. Consider all the diagnostic tools available as well as the patient's symptoms to formulate the best diagnosis and management plan.

Severe OSD may present as diffuse, whorl-like staining with fluorescein.



Irregular astigmatism on topography in a patient with OSD.

DED Management

A healthy ocular surface is critical in supporting healthy, comfortable contact lens wear. Contact lenses divide the tear film into a pre- and post-lens tear film. This affects the biochemical properties of the tear film and results in a thinner lipid layer and increased tear evaporation.[4] As such, you must proactively treat any patient with dry eye signs or symptoms prior to initiating a contact lens fit. Simple interventions such as lid hygiene and warm compresses may improve contact lens comfort and prevent future contact lens dropout.

According to the DEWS II guidelines, a stepwise approach is appropriate for dry eye management. First-level interventions include patient education, lid hygiene and artificial tears. For patients who remain symptomatic, step two recommendations include supplementing with overnight ointments, moisture chamber goggles, punctal plugs or in-office procedures like thermal compressive therapy such as LipiFlow (Johnson & Johnson Vision). Prescription medications that calm inflammation, including immunomodulators (*e.g.*, cyclosporine, lifitegrast), steroids or oral tetracyclines, are also indicated in step two.

For patients who require additional intervention, step three considerations include autologous serum and therapeutic contact lenses. For severe cases who do not respond to more conservative treatments, consider amniotic membrane grafts, tarsorrhaphy or salivary gland transplantation.[4]

Contact Lens Fitting

After thoroughly assessing and determining the patient's OSD severity, determine which lens option will benefit them.

Soft lenses. For patients with mild DED who are being managed

When it comes to ocular surface inflammation, FLAREX® is A PROVEN WINNER

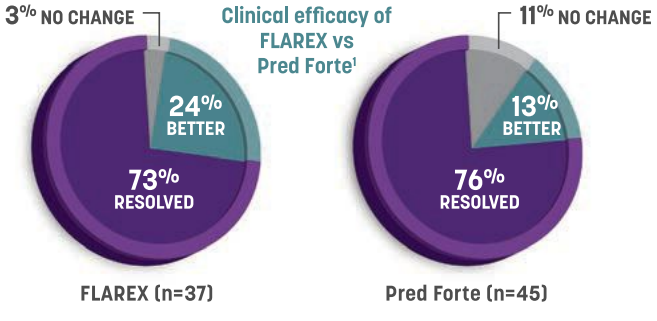
The power of Pred Forte* (prednisolone acetate ophthalmic suspension, USP) 1% with the safety of FML* (fluorometholone ophthalmic suspension, USP) 0.1%[1a]

Ocular surface inflammation is a key etiological factor in Dry Eye Disease[2]

FLAREX offers the efficacy of Pred Forte for ocular surface inflammation[1]

In the FDA pivotal trial evaluating patients with ocular surface inflammation,[a] there was no significant difference in clinical efficacy with FLAREX vs Pred Forte, *P*=0.49.[1]

97% of ocular surface inflammation was resolved or improved with FLAREX vs 89% with Pred Forte[1]



FLAREX is a steroid ester and the *only* acetate derivative of fluorometholone.[3-5] The acetate group improves lipophilicity, allowing greater penetration across the cell membrane.[6]

In clinical trials, there were no adverse reactions reported in the FLAREX and FML treatment groups and FLAREX and Pred Forte treatment groups.[1]

There is no generic equivalent of FLAREX—be sure to prescribe by name[4]

INDICATIONS AND USAGE
FLAREX® (fluorometholone acetate ophthalmic suspension) is indicated for use in the treatment of steroid-responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the eye.
IMPORTANT SAFETY INFORMATION
ADVERSE REACTIONS: Glaucoma with optic nerve damage, visual acuity and field defects, cataract formation, secondary ocular infection following suppression of host response, and perforation of the globe may occur.
Please see the Full Prescribing Information on the next page.

[a]**STUDY DESIGN:** The efficacy and safety of FLAREX were evaluated in two identical, randomized, double-blind clinical trials. In one trial of 78 patients with ocular surface inflammation (eg, conjunctivitis, episcleritis, scleritis) in one or both eyes, patients administered either FLAREX (n=41) or fluorometholone alcohol (n=37) every 2 hours for the first 2 days and then every 4 hours thereafter, with signs and symptoms of inflammation assessed at Days 1, 3, 8, and 13. In a separate but identical trial in 82 patients with ocular surface inflammation, patients administered either FLAREX (n=37) or prednisolone acetate 1.0% (n=45). At each visit, investigators determined if signs and symptoms in the involved eye were resolved, improved, unchanged, or worsened. If a patient was rated as signs and symptoms resolved before the end of the study, steroid drops were discontinued and the patient was considered to have completed the trial.[1]

Flarex®
(fluorometholone acetate ophthalmic suspension) 0.1%

FLAREX NDC NUMBER: 71776-100-05

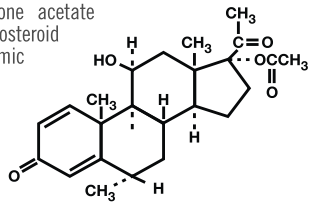
References: 1. Leibowitz HM, Hyndiuk RA, Lindsey C, et al. Fluorometholone acetate: clinical evaluation in the treatment of external ocular inflammation. *Ann Ophthalmol.* 1984;16(12):1110-1115. 2. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II Definition and Classification report. *Ocul Surf.* 2017 Jul;15(3):276-283. doi: 10.1016/j.jtos.2017.05.008. 3. FLAREX [package insert]. Fort Worth, TX: Alcon Laboratories, Inc; 2017. 4. US Department of Health and Human Services, Food and Drug Administration. *Approved drug products with therapeutic equivalence evaluations.* (Orange Book). 40th ed. Washington, DC: US Department of Health and Human Services, Food and Drug Administration; 2020. 5. National Center for Biotechnology Information, PubChem. Fluorometholone acetate. https://pubchem.ncbi.nlm.nih.gov/compound/ fluorometholone-acetate. Accessed September 10, 2020. 6. Sendrowski DP, Jaanus SD, Semes LP, et al. Anti-inflammatory drugs. In: Bartlett JD, Jaanus SD, eds. *Clinical Ocular Pharmacology.* 5th ed. St Louis, MO: Butterworth-Heinemann; 2008:221-244.

eyevance pharmaceuticals

When it comes to ocular surface inflammation, FLAREX® is

A PROVEN WINNER

DESCRIPTION: FLAREX® (fluorometholone acetate ophthalmic suspension) is a corticosteroid prepared as a sterile topical ophthalmic suspension. The active ingredient, fluorometholone acetate, is a white to creamy white powder with an empirical formula of C24H31FO5 and a molecular weight of 418.5. Its chemical name is 9-fluoro-11, 17-dihydroxy-6 -methylpregna-1, 4-diene-3, 20-dione 17-acetate. The chemical structure of Fluorometholone Acetate is presented above:



Each mL contains: Active: fluorometholone acetate 1 mg (0.1%). Preservative: benzalkonium chloride 0.01%.

Inactives: sodium chloride, monobasic sodium phosphate, edetate disodium, hydroxyethyl cellulose, tyloxapol, hydrochloric acid and/or sodium hydroxide (to adjust pH), and purified water. The pH of the suspension is approximately 7.3, with an osmolality of approximately 300 mOsm/kg.

CLINICAL PHARMACOLOGY: Corticosteroids suppress the inflammatory response to inciting agents of mechanical, chemical or immunological nature. No generally accepted explanation of this steroid property has been advanced. Corticosteroids cause a rise in intraocular pressure in susceptible individuals. In a small study, FLAREX (fluorometholone acetate ophthalmic suspension) demonstrated a significantly longer average time to produce a rise in intraocular pressure than did dexamethasone phosphate; however, the ultimate magnitude of the rise was equivalent for both drugs and in a small percentage of individuals a significant rise in intraocular pressure occurred within three days.

INDICATIONS AND USAGE: FLAREX (fluorometholone acetate ophthalmic suspension) is indicated for use in the treatment of steroid responsive inflammatory conditions of the palpebral and bulbar conjunctiva, cornea, and anterior segment of the eye.

CONTRAINDICATIONS: Contraindicated in acute superficial herpes simplex keratitis, vaccinia, varicella, and most other viral diseases of cornea and conjunctiva; mycobacterial infection of the eye; fungal diseases; acute purulent untreated infections, which like other diseases caused by microorganisms, may be masked or enhanced by the presence of the steroid; and in those persons who have known hypersensitivity to any component of this preparation.

WARNINGS: FOR TOPICAL OPHTHALMIC USE ONLY. NOT FOR INJECTION. Use in the treatment of herpes simplex infection requires great caution. Prolonged use may result in glaucoma, damage to the optic nerve, defect in visual acuity and visual field, cataract formation and/or may aid in the establishment of secondary ocular infections from pathogens due to suppression of host response. Acute purulent infections of the eye may be masked or exacerbated by presence of steroid medication. Topical ophthalmic corticosteroids may slow corneal wound healing. In those diseases causing thinning of the cornea or sclera, perforation has been known to occur with chronic use of topical steroids. It is advisable that the intraocular pressure be checked frequently.

PRECAUTIONS:

General: 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.

Information for Patients: Do not touch dropper tip to any surface, as this may contaminate the suspension. The preservative in FLAREX® (fluorometholone acetate ophthalmic suspension), benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of FLAREX (fluorometholone acetate ophthalmic suspension) but may be reinserted 15 minutes after instillation. Patients should be advised that their vision may be temporarily blurred following dosing with FLAREX (fluorometholone acetate ophthalmic suspension). Care should be exercised in operating machinery or driving a motor vehicle.

Carcinogenesis, Mutagenesis, Impairment of Fertility: No studies have been conducted in animals or in humans to evaluate the possibility of these effects with fluorometholone.

Pregnancy: Fluorometholone has been shown to be embryocidal and teratogenic in rabbits when administered at low multiples of the human ocular dose. Fluorometholone was applied ocularly to rabbits daily on days 6-18 of gestation, and dose-related fetal loss and fetal abnormalities including cleft palate, deformed rib cage, anomalous limbs and neural abnormalities such as encephalocele, craniorachischisis, and spina bifida were observed. There are no adequate and well controlled studies of fluorometholone in pregnant women, and it is not known whether fluorometholone can cause fetal harm when administered to a pregnant woman. Fluorometholone should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Systemically administered corticosteroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. It is not known whether topical administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Because many drugs are excreted in human milk, caution should be exercised when FLAREX (fluorometholone acetate ophthalmic suspension), 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 or effectiveness have been observed between elderly and younger patients.

ADVERSE REACTIONS: Glaucoma with optic nerve damage, visual acuity and field defects, cataract formation, secondary ocular infection following suppression of host response, and perforation of the globe may occur.

Postmarketing Experience: The following reaction has been identified during post-marketing use of FLAREX® (fluorometholone acetate ophthalmic suspension) in clinical practice. Because reactions are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reaction, which has been chosen for inclusion due to either its seriousness, frequency of reporting, possible causal connection to FLAREX, or a combination of these factors, includes: dysgeusia.

DOSAGE AND ADMINISTRATION: Shake Well Before Using. One to two drops instilled into the conjunctival sac(s) four times daily. During the initial 24 to 48 hours the dosage may be safely increased to two drops every two hours. If no improvement after two weeks, consult physician. Care should be taken not to discontinue therapy prematurely.

HOW SUPPLIED: FLAREX (fluorometholone acetate ophthalmic suspension) is supplied in white low density polyethylene (LDPE) bottles, with natural LDPE dispensing plugs and pink polypropylene closures. The product is supplied as 5mL in an 8 mL bottle.
5 mL: NDC 71776-100-05

STORAGE: Store upright between 2°C -25°C (36°F -77°F). Protect from freezing.

Manufactured for:
Eyevance Pharmaceuticals, LLC
Fort Worth, TX 76102 USA

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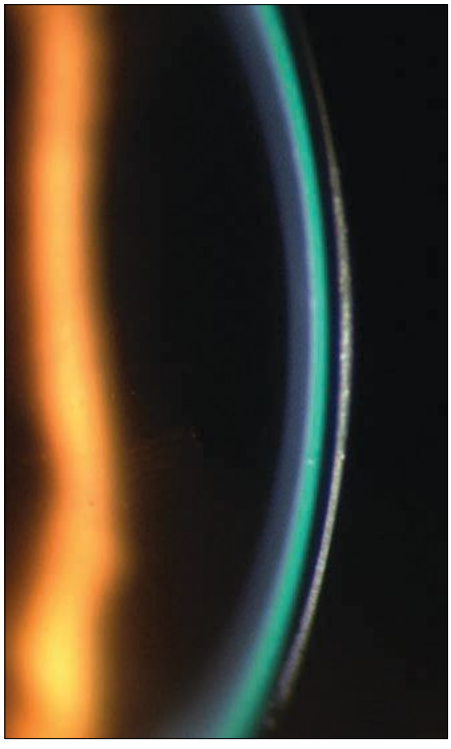


A scleral lens demonstrating a 1:1 ratio of lens thickness (dark band) to tear layer (green band).

appropriately, consider a soft contact lens fit. Ideally, select a daily disposable lens if available in the patient's prescription. The daily disposable modality minimizes the risk of lens deposits and lens care systems affecting the ocular surface.

Daily disposables have also been found to cause less damage to the ocular surface and lower levels of inflammation.[7] If the patient requires a reusable lens, recommend a hydrogen peroxide care system to minimize the risk of solution sensitivity.

As far as material selection, there have been several studies that refit hydrogel wearers into silicone hydrogel (SiHy) lenses and found less dryness, improved hyperemia and better comfort.[8] Conversely, higher levels of inflammatory markers were found in the tears of SiHy wearers. This is due to the higher modulus and lower wettability of SiHy lenses.[7] Many new SiHy materials have been created to combat this issue by promoting wettability and lowering the modulus while still maintaining high oxygen permeability.

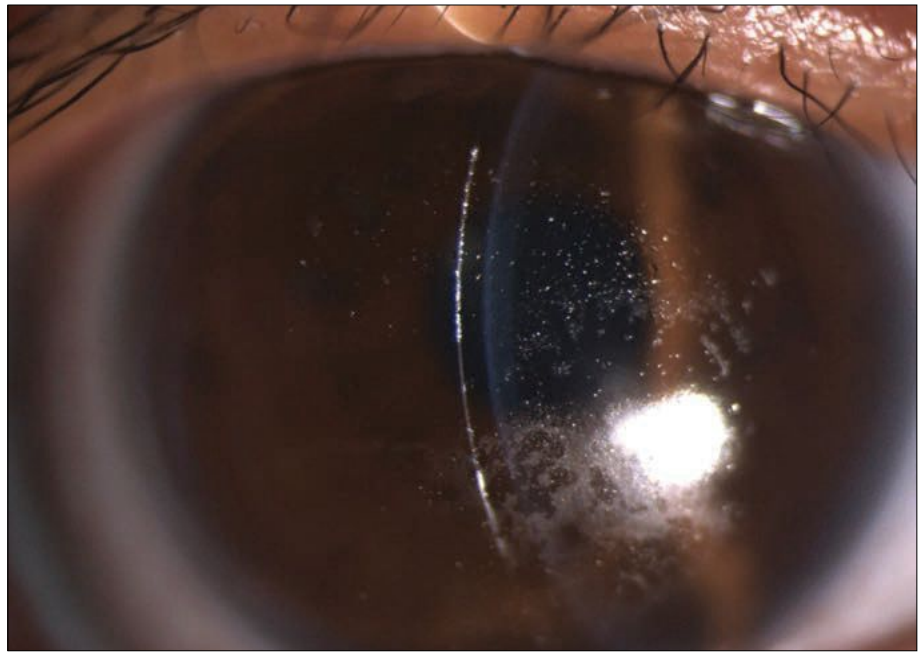
It is easy to get overwhelmed with all the contact lens options we have nowadays. A few notable SiHy advancements include Alcon's Dailies Total1 and Precision1 lenses, which feature a gradient design where water content increases towards the outside of the lens to promote lens wettability and patient comfort, and Bausch + Lomb's Infuse lens, which also promotes wettability and reduces discomfort. Coopervision's MyDay and Biofinity lenses also provide moisture and breathability. Johnson & Johnson's 1-Day Oasys with Hydraluxe features a wetting agent that mimics tears to improve comfort. All of these advancements allow for increased wear time and improved end-of-day comfort.

During every follow-up visit, verify your patient's lens care system and replacement schedule. Recently, one of my patients complained of severe dryness in his multifocal toric soft lenses. After further questioning, it turned out he had recently began using his partner's gas permeable (GP) lens solution to clean and store his soft lenses. After reinforcing proper hygiene with an approved soft lens multipurpose solution, his symptoms greatly improved.

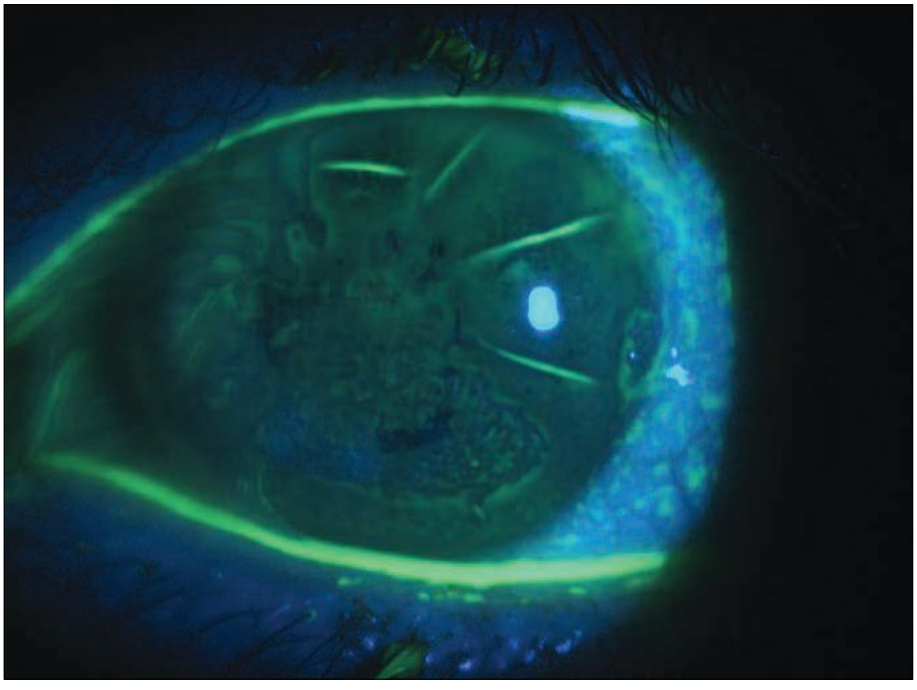
GP lenses. In moderate-to-severe cases of OSD, consider a specialty contact lens fit. GP lenses are an excellent choice for patients with high prescriptions or astigmatism with their sharp optics and high oxygen transmissibility. Orthokeratology, or corneal reshaping, is another GP option to consider for certain patients. Since these lenses are worn overnight, the patient does not need to be concerned with lens dryness during the day. The patient will also have easier access to the ocular surface for drop instillation.

Scleral lenses are an excellent treatment option for patients with moderate-to-severe cases of OSD who have failed with more conservative treatments. Studies have demonstrated the safety and efficacy of scleral lenses in improving ocular comfort, protecting the ocular surface and resolving epitheliopathy in patients with many types of OSD, including neurotrophic keratopathy, exposure keratopathy and limbal stem cell deficiency.[9] Scleral lenses are large-diameter GPs that vault the cornea and provide excellent vision with their GP optics and stability.

Sclerals protect the cornea from the environment and bathe it with fluid. Patients with OSD may benefit from



A Hydra-PEG coating would benefit this patient with heavy deposits on a scleral lens.



Diffuse corneal staining with fluorescein in a patient with severe dry eye and a history of radial keratotomy.

filling their sclerals with preservative-free artificial tears or a preservative-free saline mixed with several drops of preservative-free tears.

Fitting philosophies for scleral lenses vary, but remember that these are thicker lenses with a substantial tear layer. When fitting sclerals, use a highly oxygen permeable material. Lens vault is critical; excessive clearance will decrease oxygen to the cornea, but minimal clearance may cause the lens to settle and touch the cornea.

Similarly, lens thickness is crucial, as excessive amounts can decrease oxygen delivery, but minimal thickness may cause flexure and induce astigmatism.[10] See your scleral patients back for follow-up after they have worn their lenses for several hours to determine the amount of clearance that remains after lens settling.

Many patients with OSD have fogging and wetting issues with their contact lenses. For these patients, be sure to confirm their lens replacement schedule, cleaning regimen, current dry eye regimen and lens wear time. Consider additional intervention with an extra-strength treatment like Progent (Menicon) or a special lens coating like Tangible Hydra-PEG (Tangible Science). The Hydra-PEG coating can be added to certain GP materials to minimize lens deposits and fogging while improving wettability and lubricity. Take caution to not use any abrasive lens cleaner that will strip this coating.

When establishing a follow-up schedule for your patients, consider the severity of their OSD and the type of lens they are wearing. For new lens wearers and patients fit in specialty lenses, monitor them, at minimum, every six months to re-evaluate their corneas and symptomatology. Monitor patients with moderate-to-severe OSD every one-to-three months after finalizing their contact lens fit. For milder cases, follow-up every six months may be sufficient.

Case Study

A 42-year-old Hispanic male with a history of radial keratotomy (RK) and dry eye in both eyes was referred for a contact lens evaluation. His referral indicated a history of trialing soft and hybrid contact lenses with inadequate vision and comfort. His dry eye was managed with Xiidra (lifitegrast 5%, Shire) twice daily and preservative-free artificial tears four times daily in both eyes. Best-corrected spectacle vision was 20/40 in the right and left eyes. Externals were unremarkable. Slit lamp exam was remarkable for mild scurf, several capped meibomian glands, scattered RK scars and diffuse corneal staining with fluorescein in both eyes.

A scleral lens fit was initiated. In scleral lenses, the patient achieved 20/25 vision in each eye. The patient was urged to continue his current regimen of Xiidra and preservative-free tears as well as initiate warm compresses, lid hygiene and nightly ointment use. He has now been wearing scleral lenses successfully for two years. His corneal findings and symptoms have improved over this time.

Key Clinical Takeaways

Diagnosing and managing DED can be complicated, but managing the ocular surface upfront pays off in the long run and leads to more successful, satisfied contact lens patients. A careful assessment of the ocular surface could lead to increased success and reduced dropout rates. ■

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NaturalVue® Multifocal : The Benefits of High Relative Plus Power Across Your Patient Population

Douglas P. Benoit, OD, FAAO
Executive Director,
Professional Services for VTI

Pinhole Optics and EDOF

NaturalVue® (etafilcon A) Multifocal 1 Day Contact Lenses uniquely employs the principle of pinhole optics, creating an Extended Depth of Focus (EDOF).

To harness the power of pinhole optics in its design, the Neurofocus Optics® Technology of NaturalVue Multifocal relies on the rapid, continuous and uninterrupted progression in relative plus power outward from the center of the lens.

With this design, NaturalVue Multifocal can deliver spectacle-level visual acuity across all distances.[1]

A "Powerful" Effect: 3 or More Diopters of Plus Power

In the NaturalVue Multifocal, with no conventional "transition zones," the plus power increases rapidly from the center outward in a smooth, continuous and uninterrupted fashion—reaching 3 diopters or more. Because there's so much plus power near the treatment zone, the effect of the lens may be greater vs. traditional designs in terms of its ability to move defocused light rays inside the retina. Other published studies suggest that more plus power in the near periphery (closer to the fovea) may create a stronger effect.[2]

Additionally, the BLINK study supports the benefit of higher ADD power in a lens. That study concluded that treatment with the higher ADD power multifocal contact lenses tested was more effective with progressing myopes.[3]

Multiple Types of Patients Benefit from NaturalVue® Multifocal.

The versatility of this lens comes, in part, from a very unique extended depth of focus (EDOF) design. The high amount of relative plus can be tolerated well with all types of patients because the EDOF design creates pinhole optics that are unique to each person's own optical system. This enables clear vision at near, intermediate and importantly, distance.

NaturalVue® Multifocal

- ✓ **Power Range:** +4.00 to -12.25 D in 0.25 D steps
- ✓ **Add:** One effective add of +3.00 D for a simplified fit[1]
- ✓ **Relative Plus Power:** 3 diopters or more

For additional Information, please contact Dr. Doug Benoit at **dbenoit@vtivision.com** or VTI Technical Consultation **1-844-VTI-LENS (1-844-884-5367)**, ext. 102, or **TechnicalConsultation@vtivision.com**

References: 1. VTI data on file 2015. N=59. Data assessed after one week of wear. 2. Smith EL III. Optical treatment strategies to slow myopia progression: Effects on the visual extent of the optical treatment zone. Exp Eye Res. 2013 Sep;114:77-88 3. Walline JJ, Walker MK, Mutti DO, et al. Effect of High Add Power, Medium Add Power, or Single-Vision Contact Lenses on Myopia Progression in Children: The BLINK Randomized Clinical Trial. JAMA. 2020;324(6):571–580. doi:10.1001/jama.2020.10834

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HOW TO CONDUCT A GOOD DRY EYE ASSESSMENT

Perform a comprehensive evaluation and you'll be well on your way to the proper diagnosis.

BY JENNIFER GOULD, OD
NEW YORK CITY

While dry eye disease (DED) is common, proper diagnosis can be a challenge. Signs and symptoms don't always correlate, and patients can present with a wide range of symptoms, if they have any at all. Clinicians should be prepared to assess patients carefully for DED, which involves a combination of subjective and objective measures.

Proper diagnosis of DED requires an extensive understanding of the condition, detailed case history including symptom and risk factor assessment, and a systematic clinical evaluation. This detailed-oriented examination will aid in refining the subtype of DED and, therefore, in determining appropriate management of the condition.

During a dry eye evaluation, it is also important to rule out other ocular conditions that have similar signs and symptoms to ensure successful management. This article will provide a comprehensive discussion about the etiology of DED as well as aspects of evaluating and caring for symptomatic and asymptomatic patients.

Understanding DED

Classically, dry eye is characterized by inflammation of the eyelids, ocular surface and/or lacrimal gland.[1] DED is a source of ocular pain, irritation and tear film instability leading to visual fluctuations. These symptoms inevitably result in decreased quality of life for those coping with the disease.[1,2]

In 2017, the Tear Film and Ocular Surface Society (TFOS) published the Dry Eye Workshop (DEWS) II report with an updated definition of DED, which provides clues to the clinical picture of the condition. These clues—*e.g.*, symptoms, osmolarity, inflammation—are pivotal in guiding patient evaluation and determining the subtype of DED.[3]

We know from the TFOS DEWS II definition that DED results when the homeostasis of the tear film is not maintained. In a balanced environment, the tear film provides a clear, smooth refractive surface that protects the cornea.[4] Osmolarity is an indicator of the level of homeostasis of the tear film. Many factors can disrupt ocular surface homeostasis, including tear film instability, hyperosmolarity and ocular surface inflammation. A hyperosmolar state (*i.e.*, loss of homeostasis) triggers an inflammatory cascade resulting in corneal epithelial and goblet cell loss (the latter effect impairing mucin formation). Clinically, the loss of homeostasis can be seen through variable patient symptoms of DED, punctate epitheliopathy, conjunctival staining and tear film instability.

DEWS II recognized the neurosensory component of DED, a novel concept within dry eye and one not fully understood at this point in time. There are two types of ocular pain associated with DED: nociceptive and neuropathic. Nociceptive pain is an activation of sensory nerves secondary to ocular tissue damage that results in ocular pain. Neuropathic pain

About the author **Dr. Gould** is an assistant clinical professor at the SUNY College of Optometry University Eye Center and is responsible for clinical supervision of third- and fourth-year students in primary care. Dr. Gould receives consulting fees from Aerie Pharmaceuticals and Carl Zeiss Meditec.

results from neurological defects and has been described as "pain without stain."[5] These patients report symptoms consistent with dry eye but do not have correlating clinical signs. Patients with DED can also have some neuropathic symptoms, including spontaneous pain, sensitivity to light and wind, and an exaggerated sensation of pain response (hyperalgesia).[5,6] These neuropathic symptoms will remain even after a topical anesthetic is instilled during a clinical exam and can help to differentiate between nociceptive and neuropathic pain.[6]

It is also important to remember that chronic dry eye also causes corneal hypoesthesia.[7] This can explain the mismatch often noticed in patients with DED: minimal symptoms with severe signs of dryness on our clinical examination.[7] Corneal hypoesthesia can also be secondary to other conditions such as diabetes, previous herpetic keratitis, corneal surgery (such as LASIK) and long-term contact lens use.[5,8] These other conditions should be considered when evaluating our patients with DED.

Dry eye disease can be broken into two major etiological categories: evaporative (EDE) and aqueous-deficient (ADDE). Some patients also have mixed-mechanism dry eye, which combines both etiological categories of the disease.[3] The most common type of evaporative dry eye occurs secondary to meibomian gland dysfunction (MGD), a subtype of posterior blepharitis. It has been reported that 86% of patients with DED have MGD; this includes patients with either standalone EDE or mixed-mechanism DED.[9]

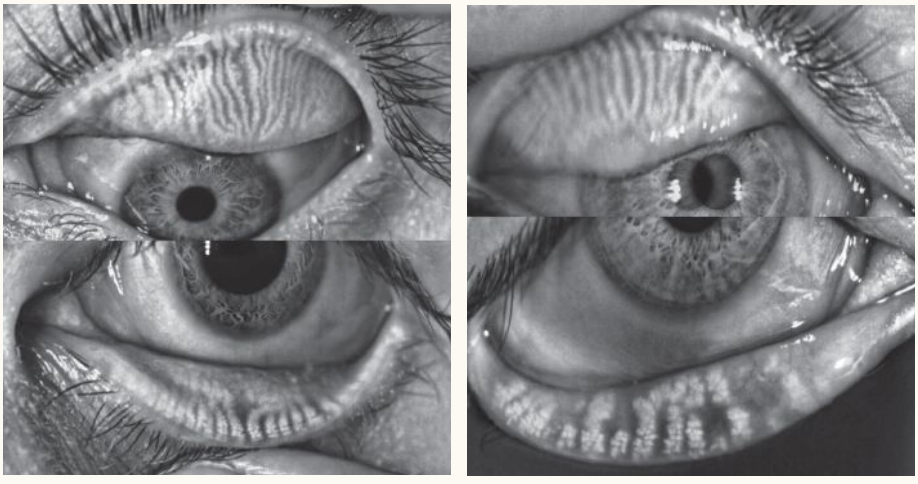

Fig. 1. These LipiView II meibography images show a normal meibomian gland anatomy of upper and lower eyelids (left) and normal upper lid meibomian gland anatomy with meibomian gland dilation and atrophy of the lower eyelid (right).

The most common cause of ADDE is inflammatory infiltration of the lacrimal gland. This ADDE can be associated with autoimmune disorders, such Sjögren's syndrome or non-Sjögren's autoimmune conditions. This inflammation of the lacrimal gland can result in a neurosensory block, further reducing aqueous release.

Assessment and Evaluation

It is important to take a systematic approach to dry eye patients with both objective and subjective testing during an evaluation. The DEWS II report and the American Society of Cataract and Refractive Surgery (ASCRS) algorithm for evaluating DED provide detailed test interpretation and methodical guides to aid eye care providers in identifying the disease.[10,11]

The ASCRS algorithm acknowledges the importance of effectively diagnosing and managing DED prior to cataract and refractive surgeries. It reports that properly treating ocular surface disorders

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Expiration Date: March 15, 2024

Estimated Time to Complete Activity: 2 hours

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Educational Objectives: After completing this activity, the participant should be better able to:

- Assess patients for dry eye disease.
- Review the clinical usefulness and real-world applications of DED questionnaires.
- Describe what the various dry eye diagnostic tools reveal about dry eye status.
- Distinguish between DED and conditions that present with similar symptoms.
- Educate patients on their disease.

Target Audience: This activity is intended for optometrists engaged in routine eye care and ocular surface disease management.

Accreditation Statement: In support of improving patient care, this activity has been planned and implemented by the Postgraduate Institute for Medicine and Review Education Group. Postgraduate Institute for Medicine is jointly accredited by the Accreditation Council for Continuing Medical Education, the Accreditation Council for Pharmacy Education, and the American Nurses Credentialing Center, to provide continuing education for the healthcare team. Postgraduate Institute for Medicine is accredited by COPE to provide continuing education to optometrists.

Faculty/Editorial Board: Jennifer Gould, OD, SUNY College of Optometry.

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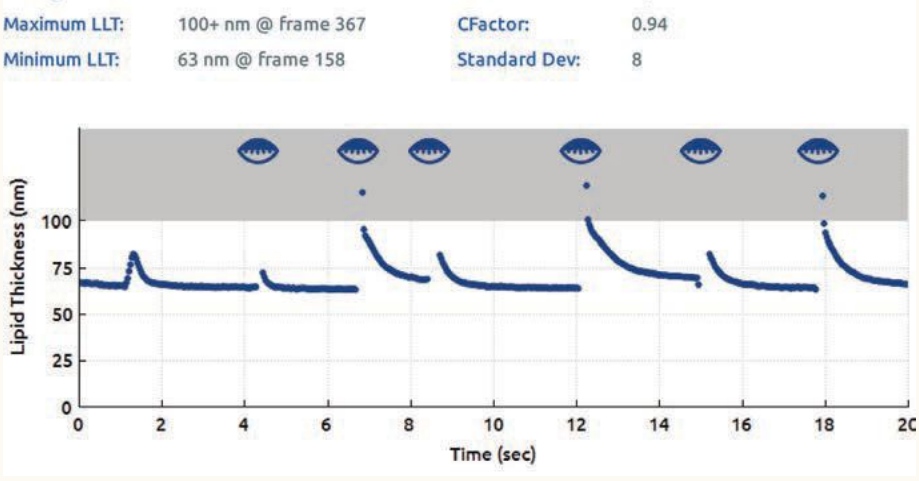

Fig. 2. LipiView II Surface Interferometer lipid layer thickness (LLT) and blink rate assessment. Results show reduced average LLT and high partial blink rate contributing to meibomian gland dysfunction.

improves visual outcomes and patient satisfaction postoperatively. This same concept can be applied to an optometric practice and can improve patient outcomes with enhanced refractions and reduced contact lens intolerance.

The ASCRS algorithm recommends a two-part DED evaluation: (1) screening of all patients for DED with symptom surveys and point-of-care testing and (2) clinical examination. Before this algorithm can be applied, a comprehensive ocular and medical history must be obtained.

Directed case history to identify DED. Case history is important during a dry eye evaluation to properly assess risk factors and rule out iatrogenic causes of dry eye. Risk factors can be modifiable or non-modifiable and can help to elicit the etiological subtype of a patient's condition (*Table 1*).[12] For example, patients with a history of LASIK have some level of corneal anesthesia, leading to ADDE. All risk factors should be discussed with patients to aid in comprehension of the multifactorial nature of this chronic condition.

Some of these risk factors can be easily added as supplemental questions to a symptom survey, while others can be incorporated into your case history (*e.g.*, medication reconciliation, computer use) or clinical exam (*e.g.*, MGD, *Demodex folliculorum* evaluation).

Iatrogenic conditions result from some form of medical or cosmetic treatment. Medication-related iatrogenic dry eye can result from both systemic and ocular drug use. *Table 2* shows a comprehensive list of systemic medications that have been shown or reported to be associated with DED in the DEWS II iatrogenic report.[13] Many of these medications are very commonly prescribed and taken by our patients, and include analgesics such as aspirin or antihypertensive medications such as hydrochlorothiazide. Different classifications of drugs have different effects on the tear film, a few of which are worth noting.

Anti-cholinergic medications (*e.g.*, antihistamines, antidepressants) affect muscarinic receptors in the lacrimal gland and conjunctival goblet cells and reduce overall aqueous and mucin production. Some drugs, including aspirin and chloroquine, are secreted into the tear film leading to ocular irritation and increased evaporation of the tear film. Retinoids like isotretinoin (used to treat severe acne) affect the epithelium of the meibomian glands and result in increased lipid secretion, tear osmolarity and tear film instability.

Topical ophthalmic drugs can have allergic, toxic and inflammatory effects on the ocular surface. This can result in tear film disruption, reduced aqueous secretion and/or neurotoxicity of the corneal nerves. Benzalkonium chloride (BAK), used to preserve many topical ophthalmic medications, has been shown to have a direct relationship on tear film osmolarity.[13] Glaucoma patients have a high prevalence of dry eye associated with their

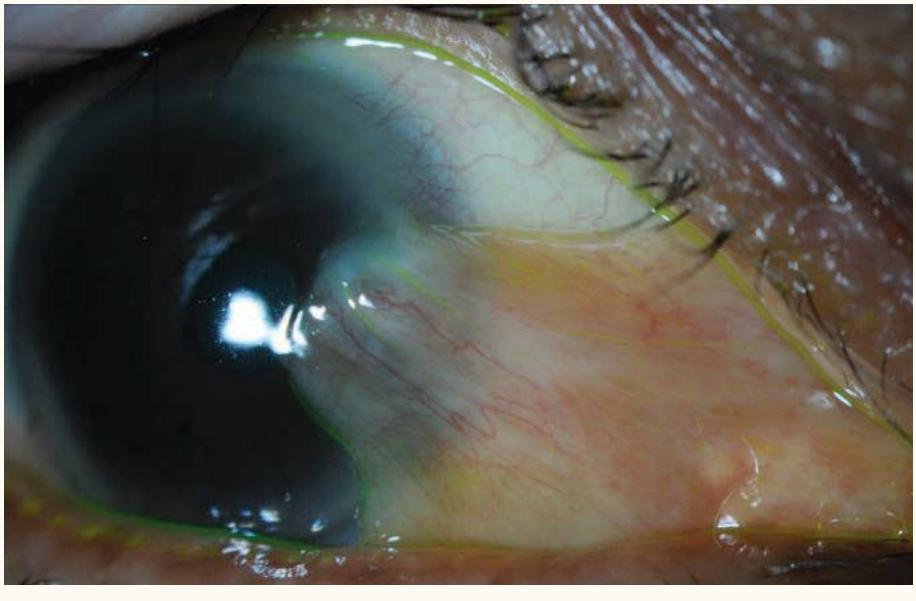

Fig. 3. Slit lamp photo demonstrating large, nasal, mildly inflamed pterygium and inferior lid scalloping secondary to MGD. In addition to managing the MGD-associated DED, we referred this patient for pterygium removal due to persistent ocular irritation.

glaucoma therapy; the more medications a patient is taking for glaucoma, the higher the prevalence of DED.[13] This is primarily due to the preservatives (often BAK) within the drops.

Some of the other causes of iatrogenic DED include contact lens wear, ocular/lid surgeries, eyelid tattooing and noninvasive ventilation. Contact lens–associated dry eye is a result of a reduced and disrupted lipid layer, lower basal tear turnover, increased tear osmolarity and decreased tear meniscus volume.[13] Common ocular surgeries that can contribute to DED include LASIK, PRK, cataract and blepharoplasty.[13]

Refractive surgeries (*e.g.*, LASIK, PRK) lead to sensory deficit of the corneal nerves, resulting in decreased lacrimal aqueous distribution.[13,14] Eyelid tattooing leads to meibomian gland atrophy, chronic conjunctival inflammation, decreased tear breakup time (TBUT) and increased fluorescein staining.[13] The use of continuous positive airway pressure machines for the treatment of obstructive sleep apnea has been shown to increase ocular irritation, based on the Ocular Surface Disease Index (OSDI), and decrease TBUT.[15]

Symptom surveys and point-of-care testing. We understand that signs and symptoms typical in dry eye care have variable correlation. For this reason, it is important to screen all patients for DED, as not all patients will be symptomatic. The ASCRS algorithm recommends using a symptom survey and point-of-care testing for this initial screening. The results of this screening can help guide other aspects of the clinical exam based on the findings.

As symptoms are very subjective and difficult to standardize and quantify, it is important to use a symptom survey when evaluating patients for DED.[10,16] The questionnaire can be used both in the initial workup of a patient and also repeated to evaluate the efficacy of treatment. Many questionnaires have been created. The DEWS II report recommends using a questionnaire that has been validated, such as the OSDI, Standard Patient Evaluation of Eye Dryness (SPEED), Dry Eye Questionnaire (DEQ) or Contact Lens Dry Eye Questionnaire (CLDEQ).

TABLE 1. RISK FACTORS FOR DED CATEGORIZED BY LIKELY ASSOCIATION[12]

	Consistent Association	Suggestive Association	Possible Association
Non-modifiable	aging	diabetes	Hispanic ethnicity
	female sex	rosacea	menopause
	Asian race	viral infection	acne
	meibomian gland dysfunction	thyroid disease	sarcoidosis
	connective tissue diseases	psychiatric conditions	
	Sjögren's syndrome	pterygium	
Modifiable	androgen deficiency	low fatty-acid intake	smoking
	computer use	refractive surgery	alcohol
	contact lens wear	allergic conjunctivitis	pregnancy
	hormone replacement therapy		*Demodex* infestation
	hematopoietic stem cell transplantation		
	environment: pollution, low humidity, sick building syndrome		
	antihistamines, antidepressants, anxiolytics, isotretinoin	anticholinergics, diuretics, beta-blockers	multivitamins, oral contraceptives

The OSDI survey combines questions related to symptoms, quality of vision and environmental triggers. This questionnaire has been the most widely accepted for research purposes, and many of the other surveys are validated against it. For this reason, the DEWS II report recommends the OSDI.[10] The ASCRS protocol uses a unique version of the SPEED survey that has an additional, non-validated question intended to ascertain the patient's personality type to aid in understanding their expectations and approaching patient education.[11]

We know from the definition of DED that both inflammation and hyperosmolarity play key roles in the condition. Point-of-care testing can be used to evaluate patients for the presence of these DED factors, especially in asymptomatic patients.[11] Two point-of-care tests are clinically available: InflammaDry (Quidel) and TearLab Osmolarity System (TearLab). Both have reimbursable CPT codes associated with them; they are 83516 and 83861, respectively.

InflammaDry provides an indication of whether or not inflammation is present within the tear film. Matrix metalloproteinase-9 (MMP-9) is an enzyme that is released into the tear film secondary to ocular inflammation. InflammaDry is a qualitative test that detects MMP-9 levels within the tear film. A positive result (presence of MMP-9) indicates that anti-inflammatory therapy may be useful in relieving patient symptoms and improving signs of DED. This should also be considered prior to the use of punctal plugs, as they will retain inflammatory mediators on the ocular surface, exacerbating signs and symptoms.

The TearLab Osmolarity System provides a qualitative measurement of the osmolarity of the tear film. The company reports that a measurement greater than 308mOsm/L or an inter-eye variability of greater than 8mOsm/L is considered abnormal. Since osmolarity can be increased in both aqueous-deficient and evaporative dry eye, the test result

does not narrow down the etiology. However, it can help to differentiate it from other conditions that result in similar symptoms, such as allergic conjunctivitis, anterior blepharitis, conjunctivochalasis, computer vision syndrome and epithelial basement membrane dystrophy (EBMD).[17] In these conditions, symptoms will be variably present, but osmolarity will be normal (less than 308mOsm/L).

According to the ASCRS algorithm, if one of the three components (questionnaire, InflammaDry, TearLab osmolarity measurement) is abnormal, DED is likely and further testing should be done to identify the etiology to aid in patient management. In addition to the screening, other noninvasive tests such as meibomian gland imaging, lipid layer thickness

TABLE 2. SYSTEMIC MEDICATIONS ASSOCIATED WITH DRY EYE[13]

Category	Subcategory	Drugs
ANALGESICS	antirheumatics	aspirin, ibuprofen
	cannabinoids	dronabinol, tetrahydrocannabinol
	opioids	buprenorphine, fentanyl, methadone, morphine, opium, oxymorphone, tapentadol
ANESTHETICS		ether, nitrous oxide
ANTICHOLINERGICS (ANTIMUSCARINICS)	antiarrythmics/bronchodilators	atropine, diphenhydramine, disopyramide, homatropine, ipratropium, methscopolamine, scopolamine, tiotropium, tolterodine
	antihistamines	azelastine, brompheniramine, carbinoxamine, cetirizine, chlorpheniramine, clemastine, cyproheptadine, desloratadine, dexchlorpheniramine, diphenhydramine, doxylamine, epinastine, fexofenadine, hydroxyzine, ketotifen, loratidine, olopatadine, promethazine, pseudoephedrine, tripelennamine, triprolidine
	antidepressants	agomelatine, amitriptyline, bupropion, clomipramine, citalopram, desipramine, doxepin, duloxetine, fluoxetine, fluvoxamine, imipramine, mianserine, mirtazapine, nortriptyline, paroxetinem, reboxetine, sertraline, tianeptine, trazodone, venlafaxine
	anti-Parkinson's drugs	benapryzine, benzhexol, bornaprine, levodopa, methixine, orphenadrine, pramipexole, procyclidine
	antipsychotics	aripiprazole, brompheniramine, carbinoxamine, chlorpheniramine, chlorpromazine, clemastine, clozapine, cyproheptadine, dexchlorpheniramine, fluphenazine, haloperidol, lithium carbonate, olanzapine, perphenazine, promethazine, quetiapine, risperidone, sulpiride, thiethylperazine, thioridazine, thiothixene, trifluoperazine, ziprasidone
	antispasmodics	fesoterodine, homatropine, oxybutynin, propantheline, propiverine, solifenacin, tolterodine, trospium
	decongestants	oxymetazoline, phenylephrine, phenylpropanolamine, pseudoephedrine, xylometazoline
ANTIHYPERTENSIVES	adrenergic blockers	acebutolol, atenolol, carvedilol, labetalol, metoprolol, nadolol, pindolol, clonidine, prazosin, oxprenolol, propranolol
	Na^+Cl^- co-transporters (diuretics)	bendroflumethiazide, chlorothiazide, chlorthalidone, hydrochlorothiazide, hydroflumethiazide, indapamide, methyclothiazide, metolazone, polythiazide, trichlormethiazide
ANTILEPROSY DRUGS		clofazimine
ANTIMALARIALS		chloroquine, hydrochloroquine
ANTINEOPLASTICS		busulfan, cetuximab, cyclophosphamide, docetaxel, erlotinib, gefitinib, interferon, methotrexate, mitomycin C, panitumumab, vinblastine, verteporfin
ANXIOLYTICS/HYPNOTICS		alprazolam, diazepam, eszopiclone, lorazepam, zolpidem, zopiclone
CHELATORS/CALCIUM REGULATORS		methoxsalen, alendronate, pamidronate, risedronate
DEPRESSANTS		ethanol
HERBAL AGENTS AND VITAMINS		isotretinoin, niacin, echinacea, kava
HORMONAL THERAPIES	antiandrogen/estrogen replacements	alfuzosin, doxazosin, finasteride, leuprorelin, tamsulosin, terazosin, estrogen/progesterone, medroxyprogesterone
NEUROTOXINS		Botulinum toxins A and B
SEDATIVES		primidone, phenobarbital

(LLT) evaluation and noninvasive tear breakup time (NI-TBUT) can also be performed to aid diagnosis.

Meibomian gland imaging can be performed using many different types of equipment, including the LipiScan Dynamic Meibomian Imager (Johnson & Johnson Vision Care), the LipiView II Ocular Surface Interferometer (Johnson & Johnson Vision Care) and the Keratograph 5M (Oculus). These devices allow for high-definition images of the meibomian glands to assess gland dropout, dilation and tortuosity, which, if present, aids diagnosis of MGD (*Figure 1*).

In addition to meibomian gland imaging, other measurements such as LLT, blink quality assessments and NI-TBUT can also be gathered using the LipiView II (*Figure 2*) and the Oculus Keratograph 5M. LLT allows the provider to understand the amount of meibum being excreted. A scant lipid layer can be due to MGD or abnormal blinking. For patients with reduced or low LLT (*i.e.*, less than 100nm), lipid-based tears may be recommended.[18] If the lipid layer alteration is associated with lagophthalmos (partial blinking), blinking exercises can also be used to supplement DED therapy.[19]

Clinical Evaluation

Once it has been determined that a patient likely has dry eye based on a screening, further clinical examination should be performed. The ASCRS algorithm lays out a simple, organized approach for ocular surface evaluation to confirm the subtype, severity and visual significance: *look*, *lift*, *pull and push*.[11] This four-step process is performed in addition to using vital dyes to better visualize the anterior segment and can be supplemented with other quantitative tests of tear film quality.

Look. During a slit lamp examination, many structures and conditions should be evaluated to rule in or out conditions associated with DED. The following is a non-exhaustive list of items that should be evaluated:

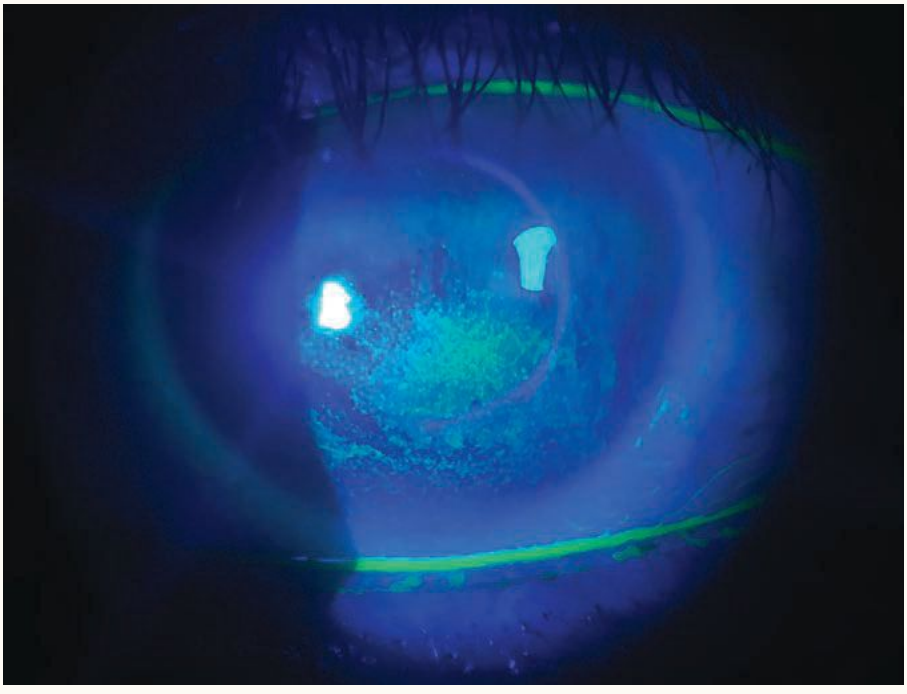

Photo: Alexander Kabiri, OD

Fig. 4. Slit lamp image showing diffuse punctate epithelial fluorescein staining secondary to lagophthalmos. Superior to the staining, the tear film has also "broken" as visualized during TBUT testing with fluorescein dye.

- Blink quality and tear meniscus height.
- Lid, lash and/or globe abnormalities (*e.g.*, entropion, ectropion, trichiasis, proptosis).
- Anterior blepharitis (*e.g.*, scurf, collarettes related to a *Demodex follicularum* infestation, frothy tears).
- Posterior blepharitis (*e.g.*, lid margin keratinization, capped meibomian glands, telangiectasias, scalloping of the lid margin as seen in *Figure 3*).
- Conjunctival abnormalities (*e.g.*, injection, follicles, papillae, conjunctivochalasis, pinguecula).
- Corneal abnormalities (*e.g.*, pterygia, EBMD, filamentary keratopathy, superficial punctate erosions, superior limbic keratopathy).

Lift and pull. The superior cornea should be evaluated while lifting the upper lids up. EBMD and superior limbic keratopathy can be easily missed by omitting this step during a slit lamp examination. In addition, the upper and lower eyelids should be slightly displaced from the globe to observe for potential rebound. This will aid in noting lid laxity associated with floppy eyelid syndrome.

Push. Light pressure should be applied to the lower lid margin to assess the meibum secreted from the meibomian glands. This can be done using your finger, a cotton tip applicator or the Meibomian Gland Evaluator (Johnson & Johnson Vision Care). This device mimics the pressure applied on the meibomian glands during a natural blink. Abnormal meibum secretion upon palpation is highly suggestive of MGD and, therefore, is an important part of each work-up.[20]

Vital dye staining. Fluorescein dye should be instilled as part of a dry eye workup. With this dye, the anterior segment can be assessed using a cobalt blue filter; the examination can be further enhanced by using a Wratten #12 yellow filter (optional). The clinical use of fluorescein dye has two purposes: to evaluate tear film stability through TBUT and highlight epithelial defects. A TBUT of less than 10 seconds is considered abnormal and indicates tear film instability. *Figure 4* demonstrates punctate staining as visualized with fluorescein dye.

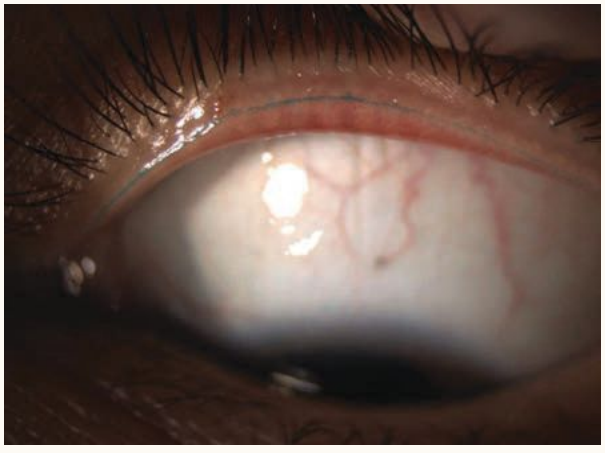

Fig. 5. Slit lamp photo with the line of Marx visualized with lissamine green stain. Lid wiper epitheliopathy, when present, is visible posterior to the line of Marx.

Fluorescein can also aid in visualizing the tear meniscus; however, ideally the height is evaluated prior to instillation of any eye drops/dyes as the tear volume is altered and measurement will be overestimated.

A secondary dye (rose bengal or lissamine green) that stains devitalized cells should be incorporated into a dry eye evaluation as well. Both of these dyes are best used with white light in the slit lamp. These stains aid in detecting conjunctival staining, which can be present prior to corneal staining and can help detect more subtle DED.[21]

Vital dyes can also aid in visualizing lid wiper epitheliopathy (LWE). The lid wiper is an area of the marginal eyelid conjunctiva that is responsible for spreading the tear film across the ocular surface. Both upper and lower lids have a lid wiper area. Clinically, it is easiest to evaluate this area on the upper lid after performing lid eversion with lissamine green or rose bengal stain.

LWE occurs when the conjunctival epithelium in the lid wiper area is disrupted due to mechanical friction.[22] LWE appears posterior to the line of Marx, which separates the epidermis of the eyelid and the conjunctival tissue. The line of Marx will variably stain with all dyes; it is important to use this as a reference point and exclude this staining from assessment for LWE (*Figure 5*).[22] LWE is commonly seen in all types of dry eye but is especially prevalent in contact lens–associated DED.[22]

Supplementary quantitative tear film testing. If ADDE is suspected and a reduced tear meniscus is also noted, additional analysis of tear film production can be measured using Schirmer's or phenol red threat tests. However, throughout the years, these tests are being used less and less due to variable diagnostic accuracy.[10,11]

Putting It All Together

By incorporating our knowledge of the etiological categories of DED with our clinical findings as related to both signs and symptoms, we are able to classify patients with ADDE, EDE or mixed-mechanism DED. Before making a management plan, it is important to rule out differential diagnosis, remembering that patients can have more than one condition and each condition requires proper management to reduce patient symptoms.

It is important to discuss with patients their risk factors and any iatrogenic causes of DED. Any modifiable risk factors should be reviewed in detail and addressed, if possible. As part of patient education, be sure to present any quantitative and qualitative data (*e.g.*, InflammaDry, questionnaire, osmolarity, TBUT). These test results will vary (and hopefully improve) over time and can be a very meaningful and encouraging for patients to maintain their treatment protocol.

By understanding the pathophysiology of DED and following systematic evaluation techniques, DED diagnosis and management can become patient-centric and identify unsuspecting patients. ■

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OPTOMETRIC STUDY CENTER QUIZ

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1. Which of the following items play a role in disrupting tear film homeostasis?
a. Tear film instability.
b. Hyperosmolarity.
c. Ocular surface inflammation.
d. All of the above.

2. Hyperosmolarity of the tear film results in which of the following clinical findings?
a. Pterygia.
b. Punctate epitheliopathy.
c. Neurotrophic keratitis.
d. Meibomian gland atrophy.

3. Which of the following is true regarding pain associated with DED?
a. Nociceptive pain results from ocular tissue damage.
b. Neuropathic pain results from neurological defects.
c. Neuropathic pain presents as "pain without stain."
d. All of the above.

4. What are symptoms of ocular neuropathic pain?
a. Spontaneous pain.
b. Sensitivity to wind.
c. Exaggerated pain response.
d. All of the above.

5. Which of the following conditions does not lead to corneal hypoesthesia?
a. Dry eye disease.
b. Diabetes.
c. Depression.
d. Herpetic keratitis.

6. What is the most common cause of evaporative dry eye?
a. Meibomian gland dysfunction.
b. Lagophthalmos.
c. Contact lens wear.
d. Ectropion.

7. Aqueous-deficient dry eye secondary to Sjögren's syndrome will likely result in which of the following clinical findings?
a. Decreased tear film osmolarity.
b. Decreased phenol red tear collection.
c. Increased tear break up time.
d. Negative InflammaDry.

8. Which of the following is considered a modifiable risk factor associated with DED?
a. Diabetes.
b. Meibomian gland dysfunction.
c. Contact lens use.
d. Pterygium.

9. Which of the following is considered a non-modifiable risk factor associated with DED?
a. Age.
b. Smoking.
c. *Demodex* infestation.
d. Refractive surgery.

10. Which types of medication have been shown to have a consistent association with dry eye disease?
a. Antihistamines.
b. Antidepressants.
c. Isotretinoin.
d. All of the above.

11. Which of the following is true about iatrogenic dry eye secondary to topical ophthalmic drug use?
a. Benzalkonium chloride lowers tear osmolarity.
b. Topical medications can lead to allergic, toxic and inflammatory effects on the ocular surface.
c. Dry eye prevalence is directly related to the number of topical medications used.
d. None of the above.

12. Which of the following is not a medication-related cause of iatrogenic dry eye?
a. Contact lens wear.
b. Cataract surgery.
c. Eyelid tattooing.
d. All of the above.

13. Which dry eye questionnaire is commonly used in research and for validation testing and is recommended by the DEWS II report for clinical use?
a. Contact Lens Dry Eye Questionnaire.
b. Dry Eye Questionnaire.
c. Standard Patient Evaluation of Eye Dryness.
d. Ocular Surface Disease Index.

14. The ASCRS protocol recommends the following as part of a screening for dry eye?
a. Symptom questionnaire, tear osmolarity testing, MMP-9 testing.
b. Case history, lissamine green staining, tear osmolarity testing.
c. Lid eversion, meibography, meibomian gland compression.
d. Symptom questionnaire, MMP-9 testing, Schirmer's testing.

15. You screen a new patient for DED. Their OSDI results in severe symptoms, MMP-9 testing is negative and osmolarity is found to be 299mOsm/L in each eye. Which of the following is true?
a. Further dry eye testing should be performed, neuropathic pain is likely.
b. Further dry eye testing should be performed, evaporative dry eye is likely.
c. Further dry eye testing should be performed, aqueous-deficient dry eye is likely.
d. DED is not present; no further testing is needed.

16. You perform a DED screening on a new patient who has Sjögren's syndrome. Their OSDI results in moderate symptoms and MMP-9 testing is positive. Meibography was performed as part of the screening and significant meibomian gland dropout was noted. Which of the following is true?
a. Further dry eye testing should be performed, neuropathic pain is likely.
b. Further dry eye testing should be performed, evaporative dry eye is likely.
c. Further dry eye testing should be performed, aqueous deficient dry eye is likely.
d. Further dry eye testing should be performed, mixed-mechanism dry eye is likely.

17. Refractive surgery can result in which of the following?
a. Corneal hypoesthesia.
b. Neuropathic pain.
c. Evaporative dry eye disease.
d. All of the above.

18. Which of the following correctly identifies the four-step clinical evaluation discussed in the ASCRS algorithm?
a. Look, ask, lift, stain.
b. Look, pull, flip, image.
c. Look, lift, pull, push.
d. Lift, pull, ask, stain.

19. Which stain(s) will enhance visualization of devitalized cells?
a. Fluorescein sodium.
b. Lissamine green.
c. Rose bengal.
d. Both B and C.

20. Which clinical test assesses tear film production?
a. Meibomian gland palpation.
b. Schirmer's strip.
c. Phenol red thread.
d. Both B and C.

Examination Answer Sheet

How to Conduct a Good Dry Eye Assessment
Valid for credit through March 15, 2024

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Directions: Select one answer for each question in the exam and completely darken the appropriate circle. A minimum score of 70% is required to earn credit.

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Credit: This course is COPE approved for 2 hours of CE credit. Course ID is 71556-AS.

Processing: There is a four-week processing time for this exam.

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Answers to CE exam:

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

Post-activity evaluation questions:

Rate how well the activity supported your achievement of these learning objectives. *1=Poor, 2=Fair, 3=Neutral, 4=Good, 5=Excellent*

21. Assess patients for dry eye disease. ① ② ③ ④ ⑤
22. Review the clinical usefulness and real-world applications of DED questionnaires. ① ② ③ ④ ⑤
23. Describe what the various dry eye diagnostic tools reveal about dry eye status. ① ② ③ ④ ⑤
24. Distinguish between DED and conditions that present with similar symptoms. ① ② ③ ④ ⑤
25. Educate patients on their disease. ① ② ③ ④ ⑤

26. Based upon your participation in this activity, do you intend to change your practice behavior? (Choose only one of the following options.)

Ⓐ I do plan to implement changes in my practice based on the information presented.
Ⓑ My current practice has been reinforced by the information presented.
Ⓒ I need more information before I will change my practice.

27. Thinking about how your participation in this activity will influence your patient care, how many of your patients are likely to benefit? (please use a number): ☐

28. If you plan to change your practice behavior, what type of changes do you plan to implement? (Check all that apply.)

Ⓐ Apply latest guidelines
Ⓑ Change in diagnostic methods
Ⓒ Choice of management approach
Ⓓ Change in current practice for referral
Ⓔ Change in vision correction offerings
Ⓕ Change in differential diagnosis
Ⓖ More active monitoring and counseling
Ⓗ Other, please specify: _____

29. How confident are you that you will be able to make your intended changes?

Ⓐ Very confident Ⓑ Somewhat confident Ⓒ Unsure Ⓓ Not confident

30. Which of the following do you anticipate will be the primary barrier to implementing these changes?

Ⓐ Formulary restrictions
Ⓑ Time constraints
Ⓒ System constraints
Ⓓ Insurance/financial issues
Ⓔ Lack of interprofessional team support
Ⓕ Treatment related adverse events
Ⓖ Patient adherence/compliance
Ⓗ Other, please specify: _____

31. Additional comments on this course: _____

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The following is your: ☐ Home Address ☐ Business Address
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Rate the quality of the material provided:

1=Strongly disagree, 2=Somewhat disagree, 3=Neutral, 4=Somewhat agree, 5=Strongly agree

32. The content was evidence-based. ① ② ③ ④ ⑤
33. The content was balanced and free of bias. ① ② ③ ④ ⑤
34. The presentation was clear and effective. ① ② ③ ④ ⑤

By submitting this answer sheet, I certify that I have read the lesson in its entirety and completed the self-assessment exam personally based on the material presented. I have not obtained the answers to this exam by any fraudulent or improper means.

Signature _____ Date _____ Lesson 120997 RO-OSC-0321

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VACCINES AND VULNERABLE EYES: WHAT TO LOOK FOR

Rare but on the rise, conditions that could be prevented by inoculation should be part of your differential.

BY PAULA McDOWELL, OD
BIG RAPIDS, MI
AND ALEXANDRA WILLIAMSON, OD
CLEVELAND

As we watch the ramp-up of COVID-19 vaccination, we can marvel at the ingenuity that brought these vital agents to market in under a year. But it also starkly underlines the importance of vaccines as a whole to society. Unfortunately, a decline in routine vaccination was among the unwelcome consequences of the pandemic lockdowns that began in March 2020, which significantly altered health care as we know it. Patient visits for routine and emergency care began to decrease.[1] This has resulted in a reduced rate of vaccinations for vaccine-preventable diseases (VPD) across the nation.

For individuals 18 years and younger, vaccine rates have been down by as much as 30% compared to previous years, although the rate for newborns remained generally stable (with some variability for individual states).[2] On a global scale, the disruption to vaccine distribution programs and access has also been altered.[3] The World Health Organization estimates that globally, 94 million children will not receive the measles vaccine because of COVID-related closures and decreased access to care. A recent report stated that measles cases in 2019 were the highest they have been since 1996, and are expected to rise.[3]

With the decrease in vaccine rates, both in the US and globally, there is increased potential for reemergence of VPD, particularly in children. VPDs have significant and wide-ranging systemic effects (including ocular manifestations) with the potential to be fatal, so the decrease in vaccine rates globally has significant ramifications for both at-risk individuals and health care providers.

This article provides an overview of the ocular manifestations of many VPDs so that we can be vigilant for them in appropriate patients.

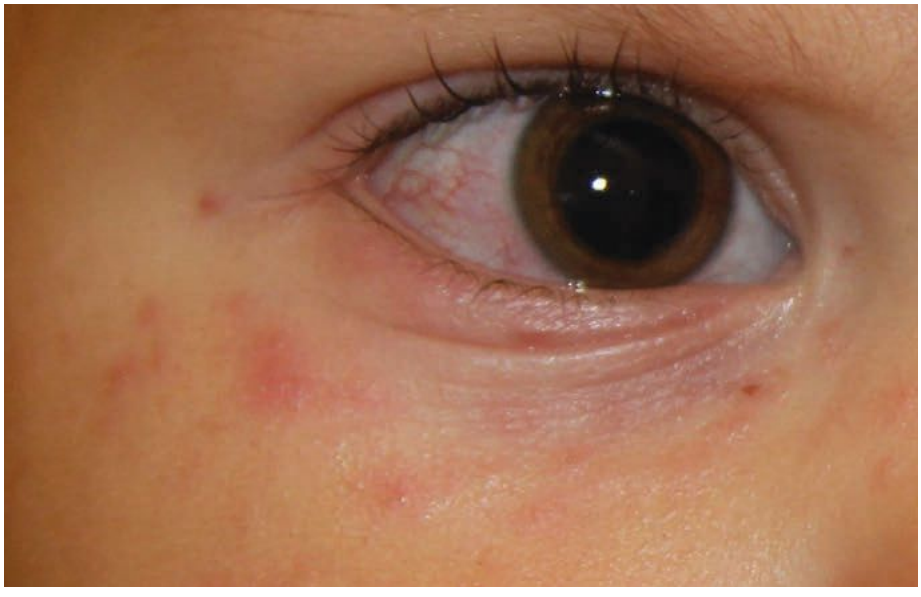
Ocular Signs of VPD

Pediatric vaccine-preventable diseases may present with ocular involvement, but more often will present with systemic signs or symptoms. Symptomatic patients usually present to the pediatrician, primary care practitioner or emergency medicine provider. Eye care providers (ECPs) in hospital or multidisciplinary settings may be more likely to encounter these cases as part of the patient care team, but sequelae of primary infections may present to ECPs in all settings, including community-based optometrists.

While the following conditions are rare in optometric practice, they might be considered in abnormal red eye presentations, or in cases where acute disease does not resolve with the typical treatment regimen. Providers may elect to add questions about vaccine history to intake questionnaires and consider VPDs when other systemic conditions present concurrently, especially rashes or persistent coughing.

About the authors

Dr. McDowell is an associate professor at the Michigan College of Optometry, where she serves as Chief of the Pediatric and Binocular Vision Service, and is the Pediatric Residency Supervisor. She is also involved in the Pediatric Eye Disease Investigator Group (PEDIG) and chairs the Michigan Optometric Association Children's Vision Care Committee. **Dr. Williamson** is a clinical assistant professor of ophthalmology at the Cleveland Clinic Lerner College of Medicine and associate staff member at the Cole Eye Institute. She is a PEDIG investigator and fellow of both the American Academy of Optometry and the Contact Lens Society of America.



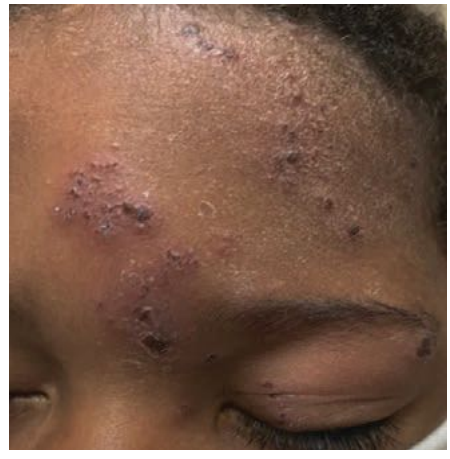


Fig. 1. At left, ocular involvement of herpes zoster with associated rash of the ocular adnexa and surrounding skin; above, classic presentation of herpes zoster.

Measles

This viral infection is highly transmissible due to its high R0 value and the trend for declining vaccine rates. There were several recorded outbreaks in the United States prior to the COVID-19 pandemic.[5] Measles infection has an incubation period of nine to 10 days followed by systemic signs, which include high fever, cough and Koplik spots (blue-gray lesions on an erythematous base) with an eventual onset of the classic skin rash.

Ocular manifestations include a non-purulent papillary conjunctivitis. Rarely, Koplik spots can be visualized on the conjunctiva. Keratitis leading to scarring and blindness can occur and is more likely in patients with poor vitamin A intake. Other reported ocular manifestations include subconjunctival hemorrhages, posterior uveitis and pigmentary retinopathy.[5-9] Measles-related posterior uveitis is characterized by disc swelling, arteriolar attenuation, diffuse retinal edema and scattered retinal hemorrhages with exudative stellate macular lesions.

Measles retinopathy is usually bilateral and occurs in immunocompetent patients. Upon resolution, signs such as disc pallor, peripapillary vascular sheathing and pigmentary changes result in a "salt and pepper" fundus appearance. In congenital cases, the electroretinogram (ERG) may be normal. In acquired cases, the ERG is reduced during active infection and can improve with time. Neuroimaging may show white matter abnormalities. Secondary outcomes of viral infection, such as acute disseminated encephalomyelitis (ADEM), have also been reported.[5-9]

A rare sequela of a mutant variant of measles relevant to all ECPs is subacute sclerosing panencephalitis (SSPE.) Patients are school-aged children whose primary infection occurred before age two. While the condition is rare, early SSPE mimics typical pediatric malingerers. Signs include painless vision loss and possibly chorioretinitis starting in the macula or posterior uveitis. Ocular findings are common and occur in up to 50% of cases.

SSPE results in cognitive decline and eventually death. Visual symptoms and retinal findings precede neurologic findings by weeks to years. Associated findings of focal necrotizing retinitis, ground-glass retinal whitening, RPE mottling, papilledema, optic atrophy, retinal folds, retinal hemorrhages, serous detachments and occlusive vasculitis with minimal vitreous inflammation have all be described.[5-9]

Mumps (Parotiditis)

Though primary infections of mumps are less common in the United States, sporadic outbreaks have been reported. The severity of

THE VALUE OF VACCINES

The goal of any vaccine is twofold: first, to keep the individual healthy and prevent future disease, and second, to halt spread within a population by increasing herd immunity. This is especially necessary for protecting vulnerable populations such as infants, pregnant women and immunocompromised individuals. The amount of herd immunity needed to stop the spread of infection varies by the contagiousness of the disease. This is defined by the basic reproduction number (R_0), which is the average number of individuals a single person is likely to infect in a completely susceptible population.[4] The higher the R_0 value, the more contagious the disease—and therefore the increased importance of vaccinations.

The Centers for Disease Control and Prevention (CDC) has a recommended vaccine schedule for people of all ages. The highest number and frequency of vaccinations are recommended during childhood. Most vaccines require several doses throughout the first six years of life (*e.g.*, DTap, MMR, polio, hepatitis A and B, pneumococcal, varicella, meningococcal), some require boosters and some—namely, influenza—require an annual administration.

the systemic illness is variable; prior to vaccine development 15% to 27% of infections were asymptomatic. After an incubation period of 12 to 25 days, patients develop parotiditis, fever, headache, muscle aches and malaise. Reported ocular signs include dacryoadenitis, follicular conjunctivitis, episcleritis, scleritis, keratitis, retinitis, optic neuritis, opsoclonus-myoclonus syndrome and facial nerve palsy.[5,10-20]

Rubella

This often presents to the eye care practitioner as a sequelae of a primary or congenital exposure. In primary cases, ocular signs are mild. Conjunctivitis is common, though

TABLE 1. OCULAR FINDINGS OF VACCINE-PREVENTABLE DISEASES

Disease	Anterior Segment Findings	Uvea/Retina/Choroid Findings	Optic Nerve/Neurologic Findings	Unique Ocular Clinical Features
Measles	Koplik spots, papillary conjunctivitis, subconjunctival hemorrhages, keratitis, ulceration, scarring	posterior uveitis, arteriolar attenuation, diffuse edema, hemorrhages, exudative stellate macular lesions, peripapillary vascular sheathing, pigmentary (salt and pepper) retinopathy, chorioretinitis, serous detachments	disc edema, disc pallor, papilledema, optic neuritis, optic atrophy	ADEM and SSPE possible, posterior uveitis and painless vision loss more likely in SSPE cases
Mumps	dacryoadenitis, follicular conjunctivitis, episcleritis, scleritis, keratitis	retinitis, bilateral outer retinal necrosis	optic neuritis, opsoclonus-myoclonus syndrome, facial nerve palsy	
Rubella	conjunctivitis and keratitis in primary infection	Fuchs' heterochromic iridocyclitis, pigmentary retinopathy, retinal hemorrhages	glaucoma (congenital cases), disc edema	congenital nuclear cataracts, posterior-to-cornea involvement more likely in congenital
Diphtheria	symblepharon, entropion, membranous conjunctivitis, corneal scarring, scarring if thrombosis of perilimbal vessels		toxic demyelination, nerve palsies	oculomotor, ciliary, abducens, and facial palsies possible
Tetanus			muscle rigidity	concern in penetrating ocular injuries
Pertussis	conjunctivitis, subconjunctival hemorrhages	retinal hemorrhages		rule out non-accidental trauma as cause of retinal hemorrhages
Human Papilloma Virus	papilloma, conjunctival lesions, pterygium			
Meningococcal	hyperacute conjunctivitis	retinal and peripapillary hemorrhages	meningitis, optic nerve edema	pediatric endophthalmitis without meningitis has been reported
Pneumococcal	conjunctivitis, keratitis			Eencapsulated strain reported in endophthalmitis cases
Varicella Zoster	skin/eyelid vesicles, conjunctivitis, episcleritis, keratitis, stromal and endothelial corneal involvement possible	anterior uveitis, congenital chorioretinal scars (likely in congenital)		retinal lesions less likely in children in primary cases; pseudodendrites likely in early disease
Influenza	orbital syndrome, acute conjunctivitis (commonly bilateral)	uveal effusion syndrome, iritis, vitritis, peripheral necrosis, choroiditis, submacular hemorrhages, macular edema, neuroretinitis, vaso-occlusive retinal vasculitis, exudative retinal detachment	optic neuritis, opsoclonus-myoclonus syndrome, facial nerve palsy	simultaneous retinal and LGN infarct has been reported in H1N1 infection
Human coronavirus	conjunctivitis, subconjunctival hemorrhages			

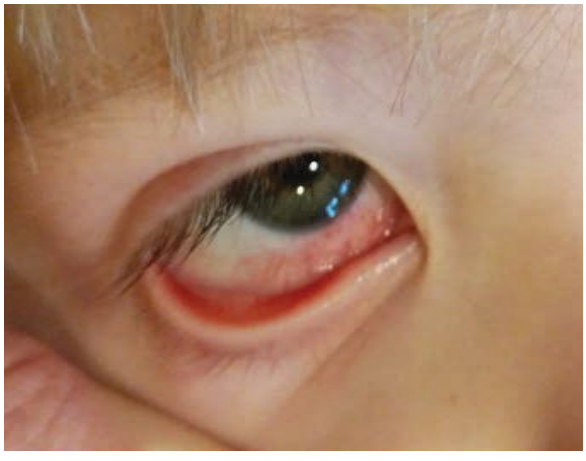


Fig. 2. Sectored red-eye presentation in a three-year-old. All pediatric red eyes, especially unusual presentations, should have a full vaccine history included in the work-up.

central epithelial keratitis has also been reported. Fuchs' heterochromic iridocyclitis—a unilateral uveitis with a triad of heterochromia, predisposition to cataract and glaucoma, and keratic precipitates—is associated with rubella infection. In congenital cases, severity is inversely related to gestational age at the time of maternal infection.

The triad of congenital rubella syndrome includes auditory, cardiac and ocular defects, which occur in 30% to 40% of cases. Nuclear cataracts, microphthalmos and congenital glaucoma are more likely in the first trimester. The most common outcome is pigmentary retinopathy, which can occur when maternal exposure occurs before gestational age of 20 weeks. Rubella retinopathy is usually benign, non-progressive and visually insignificant, though rare complications such as hemorrhages and disc edema can reduce vision.

Diphtheria

Once a leading cause of childhood death, widespread vaccine use has led to near eradication of diphtheria in the United States. As such, reports in the literature of ocular involvement are sparse but generally address two areas of concern: membranous conjunctivitis and nerve dysfunction secondary to toxic demyelination. Diphtheria conjunctivitis is described in the literature as both pseudomembranous and membranous, resulting from formation of a gray plaque of necrotic tissue. Though involvement of extra-respiratory sites is uncommon, this severe conjunctivitis can cause secondary problems such as symblepharon, conjunctival and corneal scarring, and other ocular surface irregularities.

Tetanus

This anaerobic infection is generally a concern in emergency cases of penetrating ocular injuries. *Clostridium tetani* spores can germinate, leading to production of toxins that act on the nervous system, resulting in the well-known associated muscle rigidity.[5,26,27]

Pertussis

Also known as whooping cough, this condition generally affects the eye in one of two ways. The most common ocular sign is a subconjunctival hemorrhage resulting from the characteristic cough. Less commonly, retinal hemorrhages have been reported, though it is essential in all pediatric cases involving retinal hemorrhages to fastidiously rule out non-accidental trauma. Although not currently employed as such, the conjunctiva has been proposed as a site for vaccine delivery.[5,26,27,30,31]

Human Papilloma Virus (HPV)

Vertical and contact transmissions of HPV are the most likely routes of ocular infections in children, though several routes exist, including sexual contact and autoinoculation. HPV is categorized into high risk and low risk subtypes; the former leads to anogenital and cervical cancers while the latter causes dysplasia that does not progress to cancer. HPV has been found in conjunctival and eyelid lesions such as inverted papillomas and pterygia. While both subtypes have been identified in ocular tissue, low-risk HPV is more commonly associated with ocular lesions.[5,6,33-39]

Meningococcus

Meningococcal disease earns its name due to its strong association with meningitis. While it is not the only organism which causes meningitis, *Neisseria meningitidis* is a leading cause of bacterial meningitis in babies, children and adults.

Pediatric cases of endophthalmitis without meningitis have also been reported. Other reported ocular signs include severe photophobia, hyperacute conjunctivitis, retinal and peripapillary hemorrhages, and optic nerve edema. Systemic signs can include fever, headache, neck stiffness, vomiting, lethargy and seizure. Meningococcal disease is potentially blinding and fatal and must be quickly treated both reactively and proactively. In these cases, immediate referral to emergency care is warranted.[5,40-46]

Pneumococcus

In children, pneumococci are generally involved in cases of bacterial meningitis and acute otitis media, but cases of pneumococcal conjunctivitis, keratitis and endophthalmitis have been reported. Pneumococcus is found in one third of bacterial keratitis cases.[5,47-56]

Varicella Zoster Virus (VZV)

Primary varicella infections have dropped dramatically since 1995, when the VZV vaccine was introduced, though reactivation of infections such as herpes zoster ophthalmicus (HZO) can occur. Postherpetic neuralgia is less likely in children than adults.

Primary VZV infections can cause eyelid lesions (*Figure 1*), conjunctivitis, episcleritis, keratitis and anterior uveitis. Retinitis, common in adults, is rare in children in primary infection, though congenital VZV infection can leave discrete white chorioretinal scars. After vaccination, mild

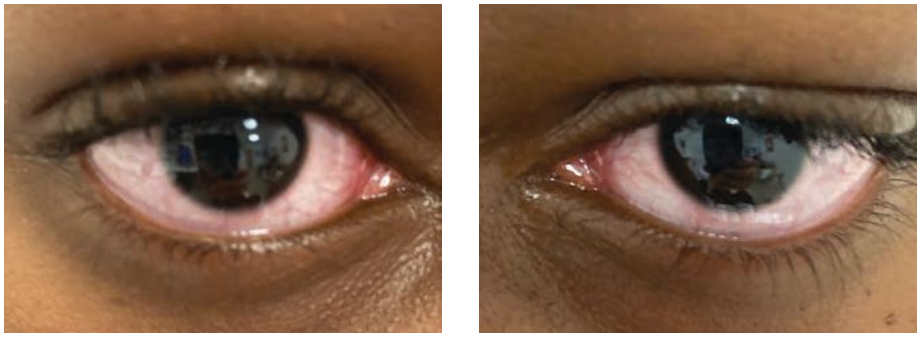


Fig. 3. Same patient, right and left eyes, respectively. Typical presentation of acute-onset red eyes in a school-aged child.

non-infectious keratitis has been reported.

Those who have had a primary VZV infection and those who received the vaccine are less likely to develop HZO. As is the case with adults, early anti-viral treatment, close follow-up and careful corneal management is important in pediatrics. Children who are immunocompromised or have systemic disease should be hospitalized and treated with IV antiviral therapy. Damage to ocular structures in the course of pediatric HZO can lead to deprivational amblyopia.[5,6,57-58]

Influenza

The seasonal flu can produce the following ocular signs: orbital inflammatory syndrome, acute conjunctivitis, conjunctival injection, anterior chamber inflammation, uveal effusion syndrome, vitritis, vasculitis, frosted branch angiitis, macular edema, submacular hemorrhaging, exudative retinal detachment, retinopathy, peripheral retinal necrosis, choroiditis, neuroretinitis and optic neuritis. Pain and decreased vision have been reported. Visual acuity loss has also been reported as the presenting sign of simultaneous retinal and lateral geniculate body infarct.

Influenza is unique in that a yearly vaccine is needed to reduce contraction, as the virus itself mutates frequently. However, both severity and duration of symptoms tend to be reduced in individuals who have received the vaccine.[5,59,60]

Human Coronavirus

Though they only became a household name in 2020, human coronaviruses are quite common, and often lead to fever, fatigue, rhinitis, headache, sore throat and other common cold-type symptoms. The hallmark signs of COVID-19 additionally include shortness of breath, and loss of taste or smell.

While literature on SARS-CoV-2 continues to develop, there are several reports of COVID-19 conjunctivitis developing in individuals who test positive for SARS-CoV-2. Red eyes generally present as a typical viral conjunctivitis, with a unilateral presentation that transitions to bilateral, watery discharge, and mild to moderate redness.[61,62] Children, especially those under 10 years of age, continue to have lower reported symptomology from COVID-19, although they may be asymptomatic carriers. Those who do show symptoms can rarely develop multi-system inflammatory syndrome in children (MIS-C).

Most reports of this condition show high levels of antibodies to SARS-CoV-2, indicating a previous infection. Associated signs and symptoms include fever in 100% of cases and bilateral conjunctival injection in 55% of cases, in addition to significant gastrointestinal, cardiovascular, hematologic and respiratory involvement; however, there is a high rate of recovery for these patients.[63]

There are several theories as to why children are less impacted by the coronavirus. One suggestion relates to the spike glycoprotein, which is present on the envelope of the coronavirus and helps the virus bind to ACE2 receptors. It has been theorized that children perhaps have less (or immature) ACE2 receptors, which reduces binding of the virus.[64] Another theory is that the proteins on the spike glycoprotein are similar to those found in measles and rubella. Since children are frequently exposed to both coronaviruses and the measles/rubella proteins through routine vaccinations, their immune systems may be able to ward off the Sars-CoV-2 virus more effectively than adults who have decreased antibody titers.[64]

Recognizing and Reducing Infectious Disease

As healthcare providers, optometrists should stay up to date on their own immunizations and encourage patients to do the same. Providers may consider keeping in place some or all of the general cleaning and sanitization protocols that have increased in the past year, to continue to prevent spread of any pathogen that may present to the office.

Clinicians should also be aware of local outbreaks of infectious disease to assist in differentiating ocular manifestations. In cases of red eyes or unusual presentations of ocular disease, it will become increasingly important to inquire about a patient's immunization history and consider vaccine-preventable disease as a differential once common causes have been ruled out, particularly in cases that do not improve with standard treatment or that present with associated systemic findings. ■

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One Bird, Two Stones

Here's what's likely to happen when you combine CXL and Intacs to treat keratoconus.

Q Is combining corneal crosslinking (CXL) and Intacs for keratoconus a viable option? What does it involve? What requirements do patients have to meet for candidacy? What other considerations need to be taken into account?

A Surgical treatment of keratoconus has substantially advanced over the past two decades, according to Brian Chou, OD, of San Diego. In July 2004, the FDA granted Humanitarian Device Exemption approval to Intacs (Addition Technology) for keratoconus. Then, in April 2016, the FDA granted approval for the KXL crosslinking system by Avedro (since acquired by Glaukos) for progressive keratoconus.

CXL decreases the progression of keratoconus and incrementally flattens the topographical shape of the cornea. Intracorneal ring segments (ICRS) for keratoconus, *i.e.*, Intacs or Ferrara rings (Mediphacos), can smooth out and flatten the corneal surface.

A Combined Effect

The safety and efficacy of CXL and Intacs, performed both concurrently and sequentially, was recently evaluated in 198 patients of the Cornea and Laser Eye Institute (CLEI) in Teaneck, NJ.[1] Enrolled keratoconus participants were 21 years or older. Excluded patients had a corneal thickness less than 350µm at the thinnest point or other conditions predisposing them to surgical complications.

John Gelles, OD, of CLEI, explains that, "in a concurrent treatment, the patient will first undergo an intrastromal ring dissection with a femtosecond laser, followed by CXL and finally the implantation of the ICRS." By contrast, in a sequential procedure CXL is performed first and ICRS happens weeks to months after. "In our randomized prospective clinical trial, we compared concurrent (same-day CXL and ICRS) with sequential (three months between CXL and ICRS) surgery."

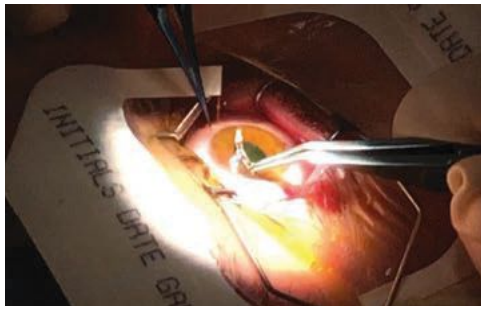

Photo: John Gelles, OD

An ICRS is placed into an intrastromal channel immediately after undergoing CXL. Note the riboflavin-induced yellow hue of the cornea.

The research team found that outcomes between the two were equivalent, the combined procedure was safe and there was no comparative increased risk associated with one or the other. Dr. Gelles notes that a well-placed, single segment ICRS implant provided the largest curvature reduction and visual improvement.

While adjunctive CXL and Intacs offers more flattening of the corneal distortion than either procedure alone, Dr. Chou says all patients undergoing combined surgery can expect to wear rigid-surface contact lenses afterwards for maximal vision. "No surgery at present can make the distorted cornea in keratoconus as smooth as the surface of a rigid-surface contact lens," he says. "However, combined CXL and Intacs may provide carefully selected keratoconus patients—including those with milder distortion and myopia—with sufficient vision with glasses or soft contact lenses."

Patient Selection

These patients must understand that undergoing CXL or Intacs may cause them to lose eligibility for necessary contact lenses under a vision plan, notes Dr. Chou. For example, one criterion of EyeMed Vision Care for "moderate/severe keratoconus" is a topographical steep keratometry value of 53.00D or greater.[2] "If CXL and/or Intacs causes the patient's keratometry value to fall below 53.00D but they end up as visually dependent on scleral lenses as beforehand, the EyeMed patient must bear the full cost of scleral contact lenses and prescribing services, which can exceed $3,000 each year," Dr. Chou says. To set realistic expectations, Dr. Chou recommends optometrists discuss this with patients preoperatively so they have the necessary information to decide which course of action makes the most sense for them moving forward.

Take-home Message

Combining CXL and Intacs is a suitable defensive play for select cases of keratoconus. CXL can prevent disease progression, while Intacs can provide functional vision with glasses or soft contact lenses. However, the offensive play to bring out maximal vision remains rigid contact lens optics, most commonly with scleral contact lenses. ■

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About Dr. Shovlin

Dr. Shovlin, a senior optometrist at Northeastern Eye Institute in Scranton, PA, is a fellow and past president of the American Academy of Optometry and a clinical editor of *Review of Optometry* and *Review of Cornea & Contact Lenses*. He consults for Kala, Aerie, AbbVie, Novartis, Hubble and Bausch + Lomb and is on the medical advisory panel for Lentechs.

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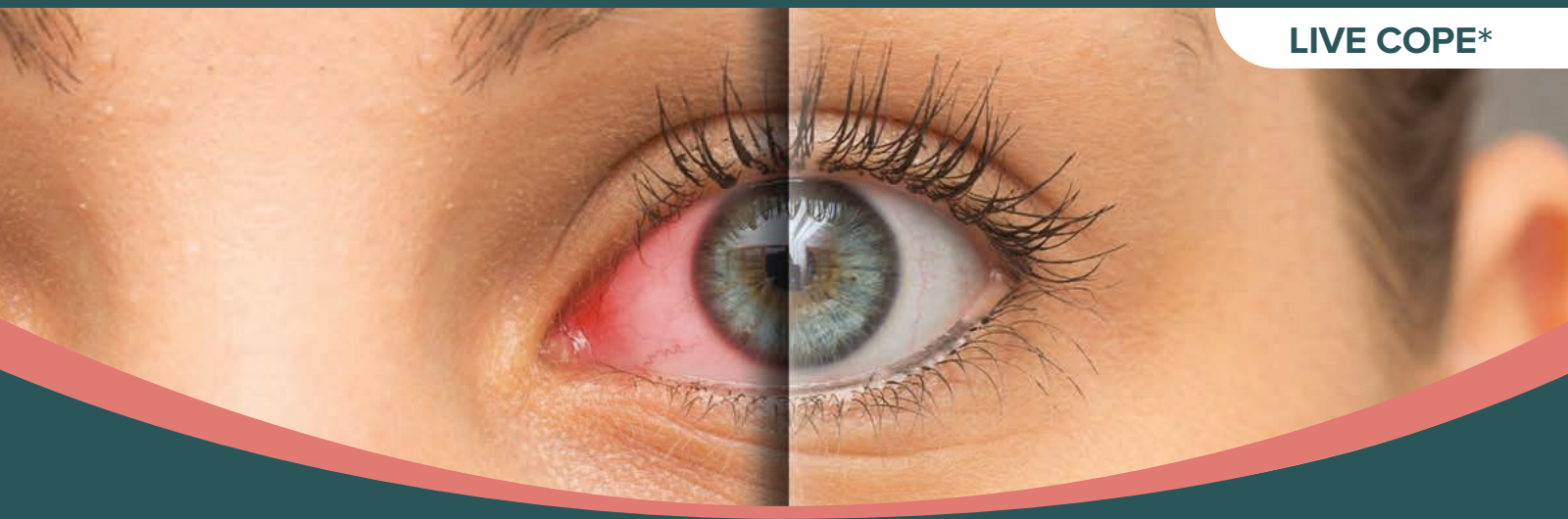

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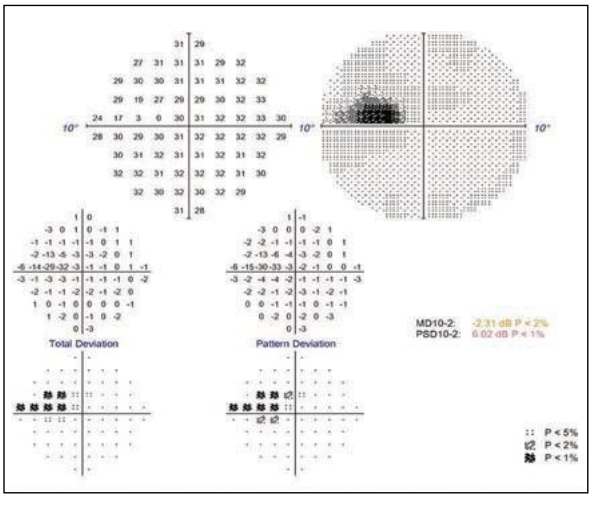
Fish Out of Water

A patient presenting with a unique-looking floater needed our help to figure out how to proceed.

BY PAUL HAMMOND, OD
MINNEAPOLIS

An 81-year-old man presented with a new "fish-shaped" gray floater in his left eye that had been a constant for the last three days. He reported that reading had become difficult. However, his visual acuity was 20/20 OS, and he had no other visual symptoms, eye pain, photopsia or headache. Notably, the patient specified that the floater was stationary relative to fixation and did not move with eye movement as his other floaters did.



This 10-2 visual field displays our patient's paracentral scotoma.

The patient's medical history was positive for thyroid disease, hypertension, prostate cancer, anemia and rheumatoid arthritis. His ocular history consisted of intermediate-stage dry age-related macular degeneration, pigment dispersion syndrome, posterior vitreous detachment and pseudophakia.

The anterior segment was within normal limits, and intraocular pressures and pupillary responses were normal. On dilated examination, there were no retinal breaks, hemorrhages or optic nerve abnormalities. The macula had a small demarcated area of retinal whitening just off the optic nerve, which corresponded with inner retinal thickening on OCT. A 10-2 Humphrey visual field showed the fish-shaped floater that had brought this patient in to seek help.

Case Discussion

The OCT findings were consistent with nerve fiber layer ischemia and the classic pattern of inner retinal edema with mild outer retinal shadowing seen in acute retinal artery occlusions. Given the shape and location of ischemia, the patient was diagnosed with a cilioretinal artery occlusion (CLRAO).

The cilioretinal artery is only present in approximately one in three people and provides a secondary blood supply to the inner layers of the macula.[1] CLRAO comprises only 5.3% to 7.1% of all retinal artery occlusions.[1] It has been associated with embolism, lupus, antiphospholipid syndrome, sildenafil, pregnancy and systemic hypertension.[2]

CLRAO can present in three ways: with ischemic optic neuropathy in giant cell arteritis (GCA), with concomitant central retinal vein occlusion (CRVO) or in isolation. It is important to distinguish which of these scenarios is at play, as the etiology will guide the treatment process and visual prognosis.

Fundus photography of the retinal whitening corresponds with the cilioretinal artery.

If there is reason to believe GCA is at the heart of the problem, either from associated symptomatology or clinical optic nerve appearance, it is critical to arrange for same-day erythrocyte sedimentation rate and C-reactive protein testing and intravenous steroid treatment. The inflammatory vasculitis of GCA has a predilection for medium-sized arteries like the ophthalmic artery, of which the cilioretinal artery is a branch. This disrupts the blood supply to both the ciliary circulation and the central retinal artery, which is why CLRAO usually occurs in conjunction with a central retinal artery occlusion and/or anterior ischemic optic neuropathy. The lack of redundant circulation is why GCA-associated CLRAO has the worst prognosis and, if not treated in a timely manner, could result in severe bilateral vision loss.

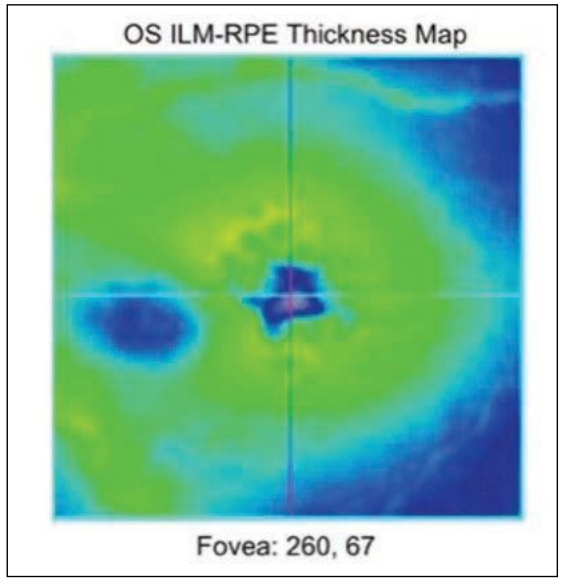
About Dr. Mangan

Dr. Mangan is a board-certified consultative optometrist from Boulder, CO, and a fellow of the American Academy of Optometry. He is an assistant professor in the department of ophthalmology at the University of Colorado School of Medicine. His focus is on ocular disease and surgical comanagement. He has no financial interests to disclose.

When CLRAO is associated with a CRVO, there is a better prognosis, as the vein occlusion tends to be non-ischemic. The exact etiology as to why these conditions sometimes occur simultaneously is unclear, and the incidence may be underreported.[3] The most widely accepted theory is that the initial CRVO raises the pressure in the capillary bed, causing hemodynamic block and a subsequent CLRAO.[4] Supporting this hemodynamic theory are reports that emboli are rarely, if ever, identified in eyes with concomitant CRVO and CLRAO.[5] Treatment focuses on the presence of macular edema and neovascularization in cases of isolated CRVO.

The third subtype has the best visual prognosis and can be seen in this patient. Isolated CLRAOs tend to be embolic in nature; therefore, treatment aims to dislodge the embolus and restore blood flow to the retina as soon as possible. Treatments include ocular massage, paracentesis and intra-arterial thrombolysis.[6] Perhaps most promising is hyperbaric oxygen treatment, the goal of which is to increase oxygen levels in the choroidal circulation to allow for diffusion into the inner layers until sporadic recanalization occurs, usually within the first 72 hours.[7]

This approach has shown significant improvement in subjective vision compared with observation and has a more favorable safety profile compared with thrombolysis.[8] Irreversible retinal damage is known to occur after four hours of CLRAO in animal models, though this may not directly translate to clinical practice given the multiple variables of acuteness of onset, degree of occlusion and patient-specific factors regarding perfusion pressure required to avoid permanent injury.[7,9] A widely accepted rule of thumb is that hyperbaric oxygen treatment should be performed within 24 hours of symptom onset.[10]



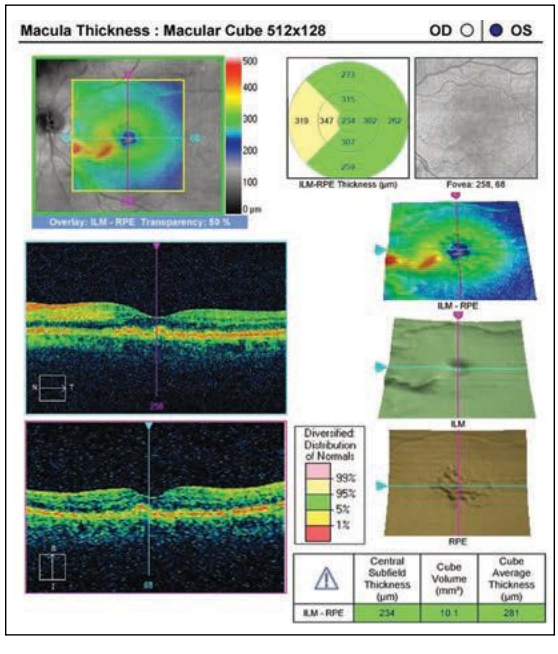
Repeat OCT was taken two months after the patient first presented, and you can see the area of thickening has now thinned due to atrophy.

Case Wrap-up

Fortunately, this patient had excellent presenting acuity, even though it was too late for hyperbaric oxygen treatment. After confirming there was no GCA or concomitant vein occlusion, the patient's case was deemed likely to be embolic and isolated in nature.

The patient was already being treated for systemic hypertension and on a daily aspirin regimen. It was recommended he follow-up that same day at the hospital for a full stroke evaluation, as up to 31% of patients with acute retinal artery occlusion may have concurrent cerebral infarction.[11]

Upon following up for an additional workup, imaging did not detect cerebral ischemia, but the MRI did incidentally reveal a pituitary tumor. The patient was kept overnight for observation, started on atorvastatin and scheduled for a follow-up with neurosurgery. The visual field defect persisted, but his vision remained 20/20 and the scotoma was not as bothersome. ■



Note the warmer colors on this macular OCT, indicating edema in the corresponding area. On the B-scan, you can see the hyperreflectivity of the edematous inner retinal layers.

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ABOUT THE AUTHOR

Dr. Hammond is a consultative medical optometrist at North Suburban Eye Specialists in Minneapolis. He has no financial interests to disclose.

Dead Spot

Determine what underlying condition is associated with these lesions.

BY ERIC DILLINGER, OD,
OWATONNA, MN

A 23-year-old white female presented for an evaluation of blurred vision in both eyes. She reported the right eye had been worse for over six months, and she felt like there was a "dead spot" in her central vision. The left eye had been getting worse over the past one month. She reported having been very near-sighted all her life and started wearing glasses at a very young age.

Her past medical history was significant for Crohn's disease, which was diagnosed at age 14, that she treats with Entyvio (vedolizumab, Millennium Pharmaceuticals) IV once a month. She reported having a recent flare-up.

On exam, her best-corrected visual acuity measured 20/400 OD with eccentric viewing and 20/70 OS. Her prescription measured -8.00D with 2.00D of astigmatism in each eye. Extraocular motility testing was normal. Confrontation visual fields were full-to-careful finger counting OU.

Amsler grid showed a central scotoma in both eyes but was very dense in the right eye. Her pupils were equally round and reactive to light; there was no afferent pupillary defect. The anterior segment examination was unremarkable. Tensions by applanation were 12mm Hg OD and 11mm Hg OS.

The dilated fundus examination revealed a clear vitreous in both eyes. The optic nerve was slightly tilted but had good rim coloration and perfusion. There was situs inversus of both optic nerves. She had a myopic-appearing fundus, and other significant changes were noted (*Figure 1*). An OCT was performed and is available for review (*Figure 2*).

Take the Retina Quiz

1. What is the patient's underlying condition?

a. Degenerative myopia
b. Ocular histoplasmosis
c. Pseudoxanthoma elasticum (PXE)
d. Punctate inner choroidopathy (PIC)

2. How would you characterize the macula in her right eye?

a. Fibrotic disciform scar
b. Active choroidal neovascularization (CNV)
c. Fuchs' spot
d. Angioid streak

3. How would you characterize the macula in the left eye?

a. Fibrotic disciform scar
b. Active CNV
c. Fuchs' spot
d. Angioid streak

4. How should our patient be treated or managed?

a. Observation in both eyes
b. Intravitreal steroid in one or both eyes
c. Treatment with anti-VEGF injection in both eyes
d. Treatment with anti-VEGF in left eye

5. What is the patient's likely visual outcome at this point?

a. Good vision in the left eye is likely
b. Poor in both eyes—worse than 20/200
c. Too early to determine
d. Could go either way

For answers, see page 106.

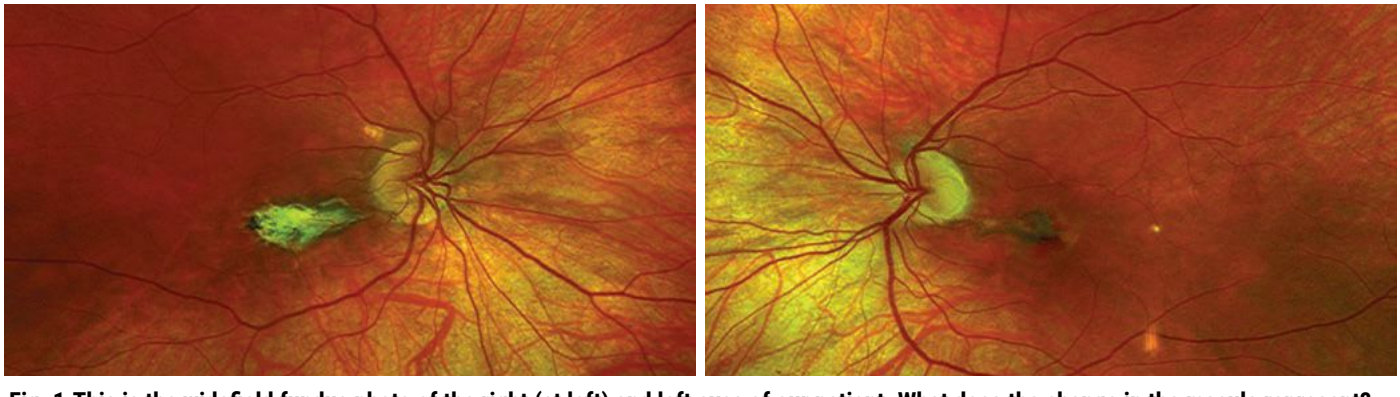

Fig. 1.This is the widefield fundus photo of the right (at left) and left eyes of our patient. What does the change in the macula represent?

About Dr. Dunbar **Dr. Dunbar** is the director of optometric services and optometry residency supervisor at the Bascom Palmer Eye Institute at the University of Miami. He is a founding member of the Optometric Glaucoma Society and the Optometric Retina Society. Dr. Dunbar is a consultant for Carl Zeiss Meditec, Allergan, Regeneron and Genentech.

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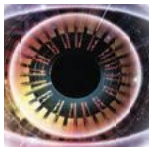

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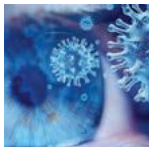

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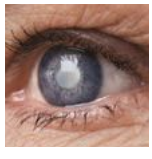

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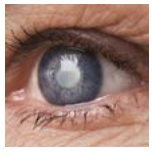

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Discussion

In the right eye, there is a fibrotic disciform scar forming that involves the patient's fovea and thus explains why she is 20/400 eccentrically viewing. In the left eye, there is a gray-green pattern that is visible between the optic nerve and macula. In addition, there is also a subretinal hemorrhage present on the temporal side near the fovea.

Unfortunately, our patient has bilateral CNV. The right eye is inactive and in the process of forming a fibrotic, disciform scar, but the CNV in the left is more recent. Subretinal fluid can be seen on the OCT in addition to a broad, dense reflective area anterior to the retinal pigmented epithelium (RPE), which likely represents the CNV. The CNV is likely above, or anterior to, the RPE because we were able to visualize the gray-green pattern on our clinical exam. Categorically, this represents a type 2 CNV, instead of a type 1, which is located below the RPE.

So, what is the underlying etiology for the CNV? It's not a straightforward, easy answer. She has significant myopia and clearly has myopic degenerative changes, so myopia could be a possibility. CNV associated with degenerative myopia is common and represents one of the top CNV causes, behind macular degeneration and ocular histoplasmosis.

Could this be from histoplasmosis? She does have some focal depigment spots in the posterior pole of both eyes that resemble "histo" spots. But there aren't that many spots, and there are none in the periphery. What's more, there isn't any pigment hypertrophy surrounding the spots, which is characteristic of histo spots, nor is there any peripapillary atrophy around the optic nerve. These are all classic features of ocular histoplasmosis. However, our patient is from Minnesota and, though maybe not typically considered to be part of the "Histo-belt" (Ohio and Mississippi River Valley), histoplasmosis is common in areas of Minnesota.[1]

Coupled with Myopia

More likely, our patient has PIC, an inflammatory disease of the choroid and RPE that affects young myopic women. Over 90% affected are female, and 85% have myopia with a median age of 30 (range 15 to 55).[2-4] It is characterized by multifocal, well-circumscribed, yellow-white choroidal lesions in the posterior pole in the absence of anterior segment inflammation and vitreous cells.

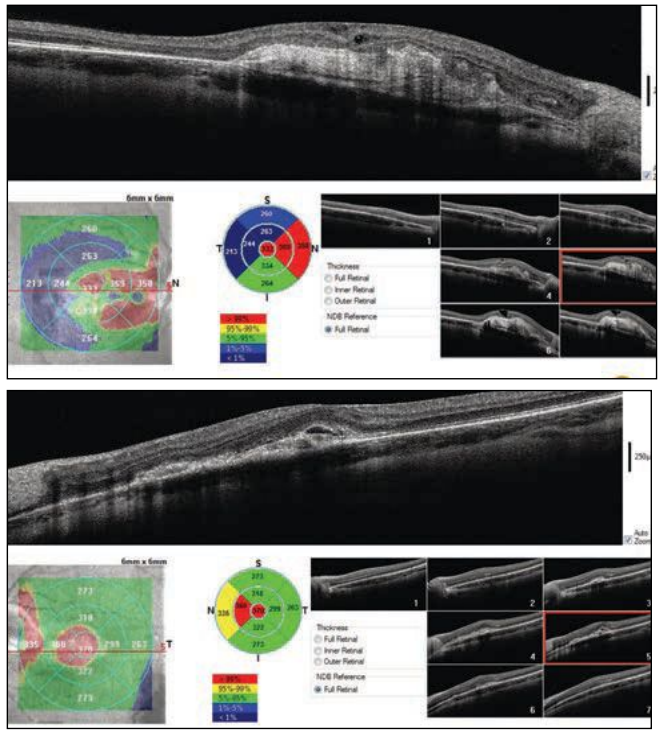

Fig. 2. This is the OCT through the macula of the right (on top) and left eyes.

These yellow-white lesions are present in our patient. In the right eye, a lesion can be seen adjacent to the optic nerve, and in the left eye, two are clearly present: one temporal to the macula and the other one along the inferior arcade and even a possible third one just above the macula.

Patients with PIC may be completely asymptomatic unless the lesions affect the fovea. If this occurs, patients can have blurred vision, scotoma, metamorphopsia and even photopsia. CNV can develop in up to 70% of patients with PIC, in which case severe visual loss may occur unless it is treated.[2,4]

The exact cause of PIC is poorly understood. One thought is that it results from an autoimmune response to previous viral infections coupled with a genetic predisposition or family history. Environmental triggers, such as stress, may also play a role.[3]

For many patients with PIC, visual function is unaffected, and there is no need for treatment. For patients who develop active lesions in the macula, corticosteroids may be effective, as this is considered to be an inflammatory disease, and steroids have shown a beneficial effect. For patients who develop CNV, anti-VEGF is the treatment of choice, either alone or in combination with oral corticosteroids.

To Sum Up

In our patient, the CNV in the right eye was inactive, and because she is already forming a fibrotic scar, there would be no benefit of treating it. But the CNV in the left eye is active and, for that reason, she was referred to a retina specialist where anti-VEGF therapy was initiated. She continues to be followed on a monthly basis by the retina specialist. ■

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ABOUT THE AUTHOR

Dr. Dillinger practices at Horizon EyeCare in Owatonna, MN. He has no financial interests to disclose.

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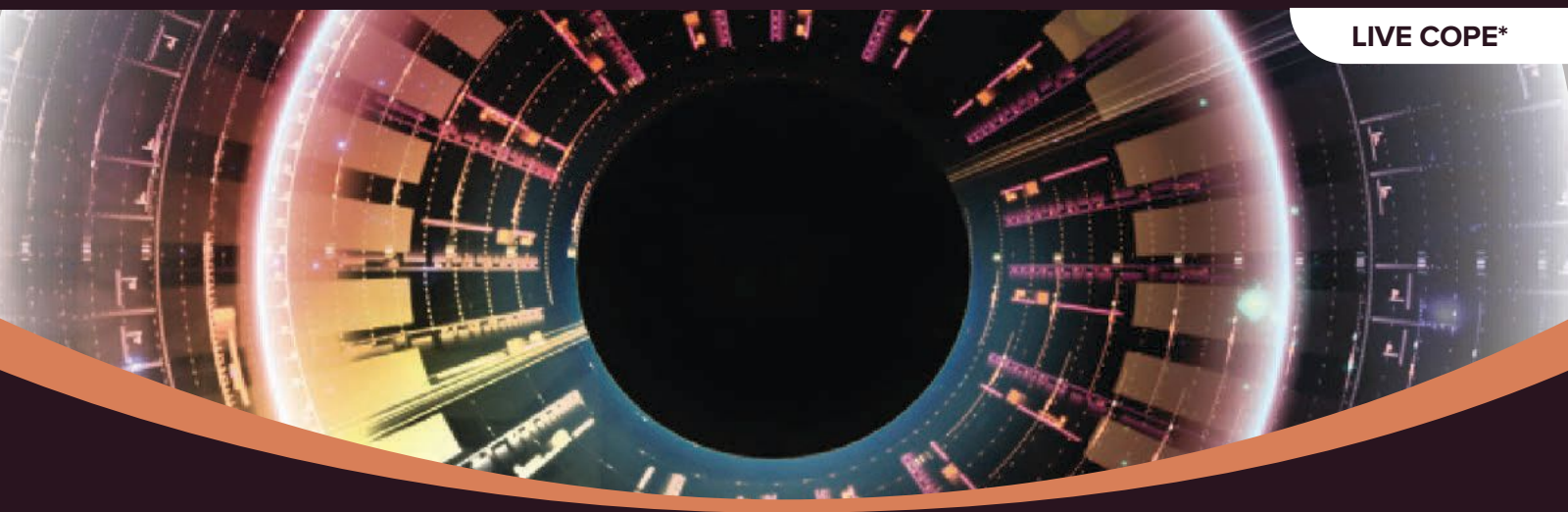

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BY BISANT A. LABIB, OD

Wild and Woolly

Take a closer look at how cotton wool spots manifest.

A careful retinal examination is critical in order to evaluate each patient for various pathologies, some of which yield an underlying systemic cause. One of these potential retinal findings is the cotton wool spot (CWS). A CWS appears as a white and fluffy superficial lesion 0.1mm to 1.0mm in diameter that obscures the underlying retinal detail.[1,2] This small but important finding can be a marker for potentially life-threatening conditions, making it of great clinical utility. To understand the health implications that cotton wool spots may carry, it is necessary to explore the process behind their formation.

Deep Dive

A CWS is thought to originate in cases where there is reduced perfusion, leading to focal or diffuse retinal ischemia. The retina is comprised of several kinds of neurons, including the retinal ganglion cells (RGCs), which are located within the superficial retinal nerve fiber layer (RNFL). In the ischemic retina, both orthograde and retrograde axonal transport of RGCs is disrupted. The CWS is a manifestation of this interruption of flow and is an accumulation of axoplasmic debris within the unmyelinated axons.[1,3]

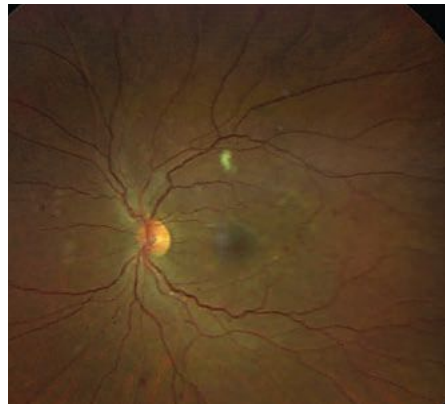
The "cytoid body," or end bulb of Cajal, is the histological landmark of the CWS and represents the terminal swelling of an RGC axon from the disruption of flow and hypoperfusion of the underlying retina.[4] Because the RNFL thickens as we move toward the periphery of the retina, a cotton wool spot is most evident within the post-equatorial region.[1] Although patients are typically asymptomatic, some reports indicate either local or arcuate scotomas at the site of the CWS.[3]

Besides the typical funduscopic appearance, a CWS can also be identified and monitored using optical coherence tomography (OCT). Since these lesions accumulate within the RNFL, the abnormality on OCT is typically found within this inner retinal layer. A scan over the area of the CWS will reveal marked thickening and hyper-reflectivity of the RNFL and inner neurosensory retina. Following clinical resolution of the CWS, retinal thinning may be evident in the corresponding area.[1]

In contrast to OCT, fluorescein angiography (FA) of a CWS manifests as a focal area of hypofluorescence that corresponds with the lesion. The reason for the darkened area is twofold. First, the presence of the CWS, to some extent, masks the underlying fluorescence. Second, the disruption of flow is presumed to be from an obstructed arteriole, in some cases, thus impairing normal vessel filling.[4]

Clinical Correlates

A CWS may present as a solitary retinal finding or be accompanied by additional pathology that can contribute to the overall clinical picture. In most cases, the finding is related to systemic disease.[1-7] At first, it was believed to be solely of hypertensive origin; however, this was later refuted when diabetic patients without hypertension also presented with a CWS.



Diabetic retinopathy and a CWS along the superior temporal RNFL arcade.

Furthermore, a CWS may be a retinal characteristic in patients with AIDS, anemia, collagen disease, bacterial endocarditis, radiation retinopathy, vascular occlusive disease, leukemia and systemic lupus erythematosus.[1,2] While the systemic causes are many, the mechanism is the same, in that it is found predominantly in diseases where there are circulatory abnormalities.[2]

The two most common causes of a CWS, by far, are hypertension and diabetes. In hypertension, a CWS is often found in conjunction with a narrowed arteriovenous ratio, nicking, flame-shaped retinal hemorrhages and exudates. This stage of hypertensive retinopathy, stage three, signifies poor blood pressure control.[5,6] In diabetic retinopathy, however, a cotton wool spot may be present even in milder forms and accompanied by dot and blot hemorrhages, microaneurysms, lipid exudates, edema and neovascularization.[2,7]

Though many of the retinal findings in these two etiologies overlap, the clinical course of a cotton wool spot differs in each. In hypertensive retinopathy, CWSs appear initially as a gray discoloration, days before

About Dr. Labib

Dr. Labib graduated from Pennsylvania College of Optometry, where she now works as an associate professor. She completed her residency in primary care/ocular disease and is a fellow of the American Academy of Optometry and a diplomate in the Comprehensive Eye Care section. She has no financial interests to disclose.

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developing their classic white and fluffy appearance. Studies that used FA demonstrated that nearby arterioles are leaky right before the CWS is evident, triggering a surrounding ring of capillary aneurysm formation during the course of the CWS. The arteriolar occlusion is the source of this ischemic cascade. However, following tight hypertensive control, resolution occurs within eight to 12 weeks. At this stage, the capillary bed returns to normal and few microaneurysms persist.[2]

In contrast, a CWS arising from diabetic retinopathy exhibits a similar clinical appearance but follows a different course. Capillary disease, especially microaneurysms, is the primary source of dysfunction triggering the ischemic events that lead to CWS formation. Since the capillary bed takes longer to recover, a CWS secondary to diabetes may last up to 17 months. This persistence may be attributed to the source of CWS clearance: macrophages. Macrophages are responsible for the clearing of cellular debris and arrive via the capillary circulation. As such, direct impairment to this transport system inhibits timely clearance, even with tight glucose control.[2]

Take-home Message

A CWS is a common retinal manifestation of many systemic diseases that affect circulation. Some, or many, of these conditions are life-threatening, necessitating prompt diagnosis and workup, or referral when applicable. The ability to identify this finding and its cause is an imperative skill, facilitated by the understanding of many of these aforementioned characteristic features. ■

DISTINGUISHING FEATURES OF THE TWO MOST COMMON CAUSES OF COTTON WOOL SPOTS

	Hypertension	Diabetes
Source of CWS Formation	arteriolar obstruction	capillary non-perfusion
Systemic Control	poor	mild to severe
Accompanying Retinal Findings	arteriolar narrowing, arteriovenous nicking, flame hemorrhages, microaneurysms, disc edema	microaneurysms, dot and blot hemorrhages, intraretinal microvascular abnormalities, neovascularization of the disc or retina, venous beading
Duration of CWS	eight to 12 weeks	up to 17 months

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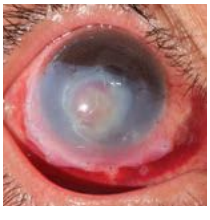

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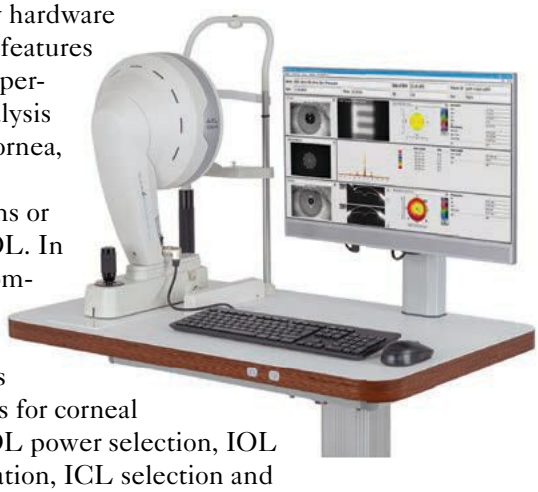
▶ DIAGNOSTIC EQUIPMENT

Anterior Seg Analysis, Inside and Out

The Oculus Pentacam, already a Swiss Army knife of sorts for anterior segment measurement, has added a few new tools. The latest model, called the Pentacam AXL Wave, retains the established functions of anterior segment tomography and optical biometry, but adds retroillumination and a Hartman-Shack sensor for total eye wavefront and objective refraction, a company press release explains.



These new hardware and software features allow optical performance analysis of the total cornea, total eye and crystalline lens or implanted IOL. In addition, a comprehensive overview display shows all parameters for corneal screening, IOL power selection, IOL power calculation, ICL selection and calculation, and pupil diameter under dim and dark conditions.

A new exam routine guides the user through the imaging process and allows both eyes to be examined in under five minutes, Oculus says.

The standard software package with the IOL calculator and its built-in IOL database provides verification of findings in numerous clinical applications such as corneal and lens refractive surgery, presbyopia solutions and standard cataract surgery, according to the manufacturer.

▶ OCULAR SURFACE CARE

Lubricant Targets Digital Eyestrain

Prolonged screen use is inevitable but the eye strain that accompanies it need not be, according to Allergan, which recently launched a topical lubricant called Refresh Digital to combat it. A company press release notes that Americans spend about 13 hours per day on some type of digital device, and this tends to reduce blink rates by as much as half. The result: some combination of dryness, burning, irritation and discomfort.

Many people have simply learned to live with this experience, thinking it's an inevitable consequence of digital technology. Allergan believes they could get relief from Refresh Digital, which it says is formulated to specifically relieve dryness and irritation that may occur from excessive screen time. It contains a glycerin-based solution intended to enable hydration and maintain the volume of cells on the ocular surface. Allergan calls this HydroCell, and says it supports all three layers of the tear film to keep eyes hydrated.

Refresh Digital is available in both preserved, multi-dose bottles and preservative-free, single-use vials.

Allergy Relief in an OTC, Nonpreserved Drop

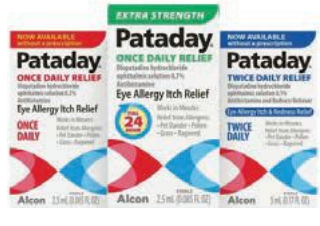
As allergy season approaches, patients will be looking for ways to ease discomfort quickly. Bausch + Lomb says its new topical antihistamine, Alaway Preservative Free (ketotifen fumarate ophthalmic solution 0.035%), provides relief within minutes and lasts up to 12 hours with one dose. The company also notes that it's the only over-the-counter preservative-free antihistamine eye itch relief drop available in the United States. The absence of preservatives should also reduce risk of irritation in eyes already inflamed by allergy flare-ups, B+L says.

Alaway Preservative-Free will be available at most national retailers, with a suggested retail price of $14.99.

Pataday Now OTC, Provides 24-hour Relief

If you used to write prescriptions for Pazeo and want to offer your allergy patients that same level of relief, now you can recommend an over-the-counter version known as Pataday Once Daily Relief Extra Strength, Alcon recently announced. The company has transitioned its popular antihistamine olopatadine 0.7% from professional to retail distribution, and says it's now available in select US stores and online retailers.

A company press release explains that the agent provides a full 24 hours of eye allergy itch relief from pollen, ragweed, grass, animal hair and dander for people ages two and older with just one drop once a day.



This launch will be supported by a full-scale media plan to reach eye allergy sufferers and get the word out, Alcon says.

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BY ANDREW S. GURWOOD, OD

DIAGNOSTIC QUIZ

Double Trouble

Examination of a hypertensive patient reveals worrisome retinal vascular findings. What might be the cause?

A 68-year-old African American female presented for an initial comprehensive ocular examination with a chief complaint of intermittent burning of both eyes over the past two years. The patient denied any additional ocular history and reported a medical history of hypertension for which she was properly medicated with lisinopril/hydrochlorothiazide, an angiotensin-converting enzyme (ACE) inhibitor. She denied having allergies of any kind.

Diagnostic Data

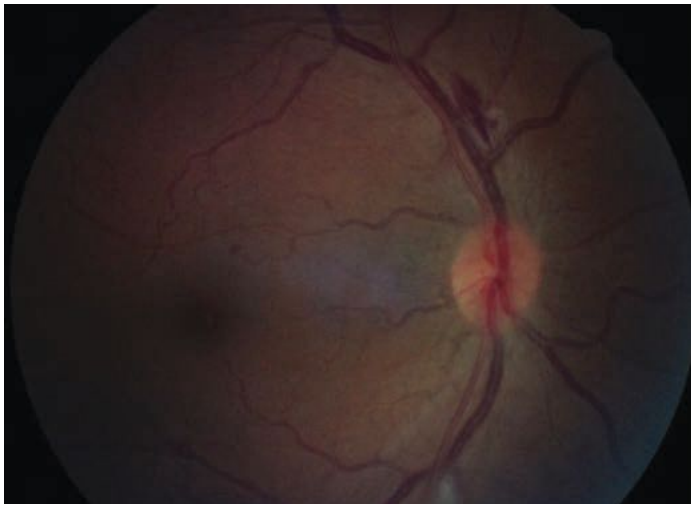
Her best-corrected entering visual acuity was 20/20 OU. Her external examination was unremarkable with no evidence of afferent pupillary defect. Biomicroscopic evaluation of the anterior segment was normal. Goldmann applanation tonometry measured 17mm Hg OU. The pertinent bilateral retinal findings are demonstrated in the photographs.

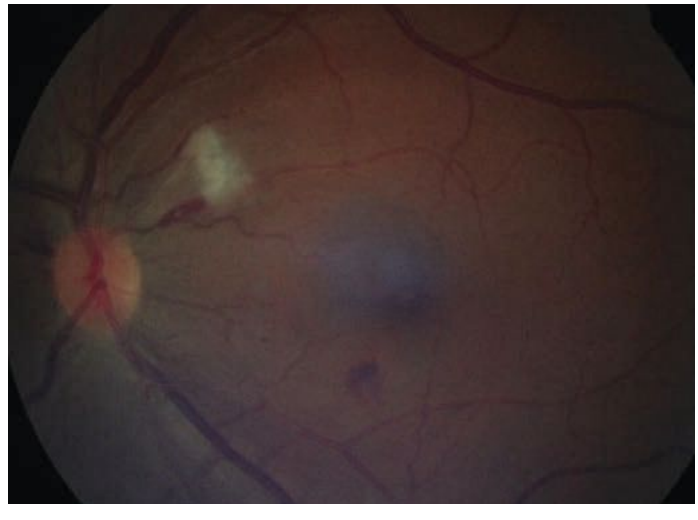
Additional testing included a lab workup for diseases capable of producing cotton wool spots, intraretinal flame-shaped hemorrhages and Roth spots, including coagulopathy, hyperviscosity, diabetes, hypertension, dyslipidemia, cardiopathy and carotid artery disease. The tests included a complete blood count with differential and platelets (CBC), an erythrocyte sedimentation rate (ESR), liver function studies (LFT), C-reactive protein (CRP), fibrinogen, fasting blood glucose, lipid panel, electrocardiogram (ECG) and carotid duplex.

Your Diagnosis

What would be your diagnosis in this case? What is the patient's likely prognosis? To find out, please read the online version of this article at www.reviewofoptometry.com. ■

Dr. Gurwood thanks Chris Brennan, OD, for his contributions to this case.





Dilated exam revealed the presentations shown here. How might they relate to the case history she described?

About Dr. Gurwood Dr. Gurwood is a professor of clinical sciences at The Eye Institute of the Pennsylvania College of Optometry at Salus University. He is a co-chief of Primary Care Suite 3. He is attending medical staff in the department of ophthalmology at Albert Einstein Medical Center, Philadelphia. He has no financial interests to disclose.

Retina Quiz Answers (from page 94)—Q1: d, Q2: a, Q3: b, Q4: d, Q5: a

NEXT MONTH IN THE MAG

In April, we present our annual cornea report. Articles will include:

- What's the Consensus on Keratoconus?
- Savvy Uses of Steroids and Antibiotics to Treat Keratitis
- Corneolimbal Concerns: Trouble at the Border
- ROCK Inhibitors for Endothelial Disease
- Comanagement Series: Elevate Your Cornea Care

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- Five Questions on Dry AMD Monitoring and Management
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