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ANNUAL CORNEA REPORT

Foreign Body Removal Start to Finish

These patients need your help—quickly. Here's how to prepare your office.

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A CXL Guide for the Surgically Savvy

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Understanding Corneal Nerve Function —and Dysfunction

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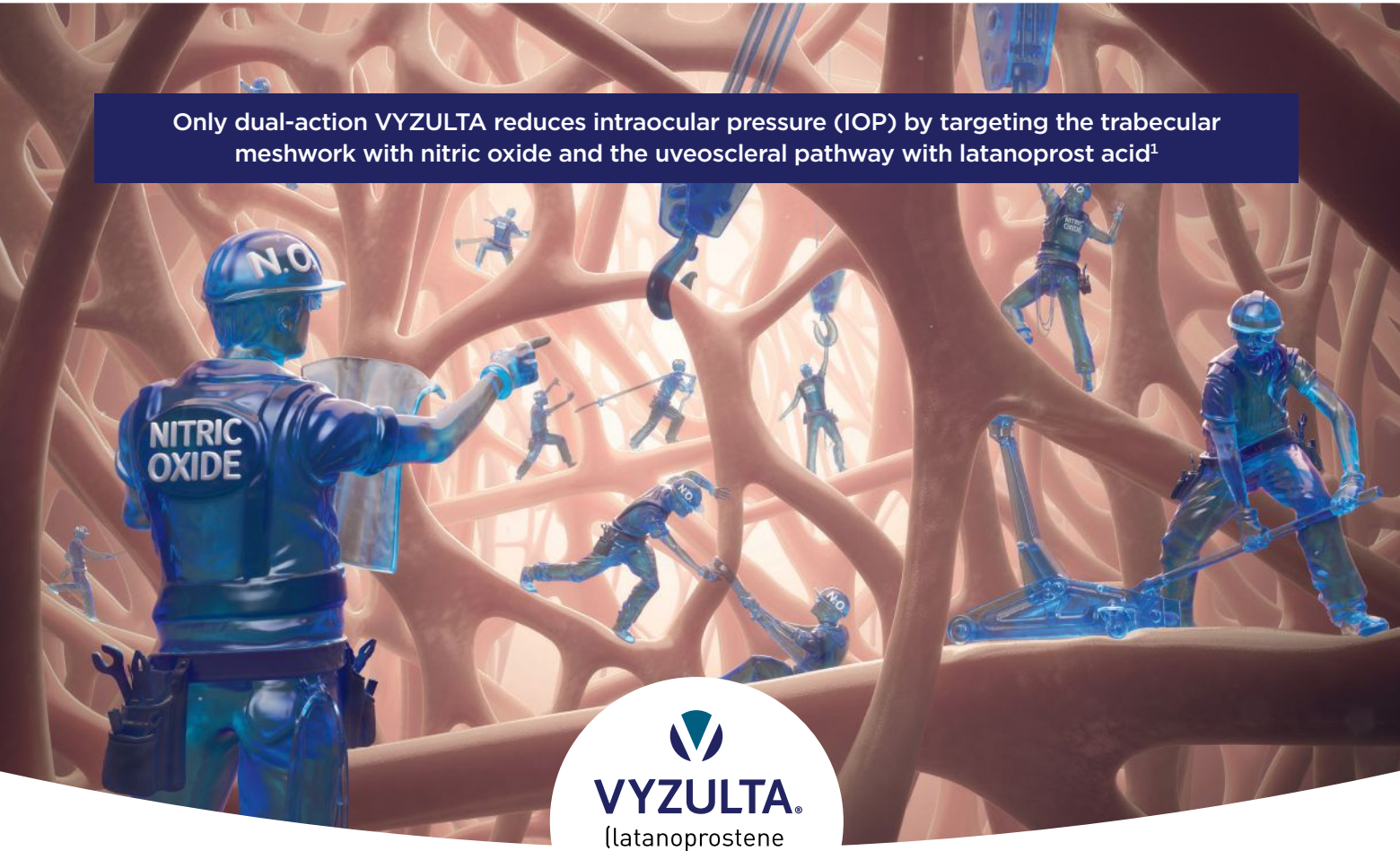

EXPAND THE TRABECULAR MESHWORK WITH THE POWER OF NITRIC OXIDE[2-6]

VYZULTA achieved significant and sustained long-term IOP reductions vs Timolol 0.5% in pivotal trials[7]

P<0.001 vs baseline at all pre-specified visits over 12 months in a pooled analysis of APOLLO and LUNAR clinical trials (N=831)

VYZULTA demonstrated safety profile in clinical trials

Only 6 out of 811 patients discontinued due to ocular adverse events in APOLLO and LUNAR clinical trials[1,8,9]

Visit VYZULTANOW.com to see our efficacy results

INDICATION

VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% is indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION

- Increased pigmentation of the iris and periorbital tissue (eyelid) can occur. Iris pigmentation is likely to be permanent
- Gradual changes to eyelashes, including increased length, increased thickness, and number of eyelashes, may occur. These changes are usually reversible upon treatment discontinuation
- Use with caution in patients with a history of intraocular inflammation (iritis/uveitis). VYZULTA should generally not be used in patients with active intraocular inflammation
- Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin analogs. Use with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema

IMPORTANT SAFETY INFORMATION cont'd

- There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products that were inadvertently contaminated by patients
- Contact lenses should be removed prior to the administration of VYZULTA and may be reinserted 15 minutes after administration
- Most common ocular adverse reactions with incidence ≥2% are conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%)

For more information, please see Brief Summary of Prescribing Information on next page.

References: 1. VYZULTA Prescribing Information. Bausch & Lomb Incorporated. **2.** Cavet ME. *J Ocul Pharmacol Ther*. 2018;34(1):52-60. DOI:10.1089/jop.2016.0188. **3.** Wareham LK. *Nitric Oxide*. 2018;77:75-87. DOI:10.1016/j.niox.2018.04.010. **4.** Stamer DW. *Curr Opin Ophthalmol*. 2012;23:135-143. DOI:10.1097/ICU.0b013e32834ff23e. **5.** Cavet ME. *Invest Ophthalmol Vis Sci*. 2015;56(6):4108-4116. **6.** Kaufman PL. *Exp Eye Research*. 2008;861:3-17. DOI:10.1016/j.exer.2007.10.007. **7.** Weinreb RN. *J Glaucoma*. 2018;27:7-15. **8.** Weinreb RN. *Ophthalmology*. 2016;123(5):965-973. **9.** Medeiros FA. *Am J Ophthalmol*. 2016;168:250-259.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use VYZULTA safely and effectively. See full Prescribing Information for VYZULTA.

VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024%, for topical ophthalmic use.

Initial U.S. Approval: 2017

1 INDICATIONS AND USAGE

VYZULTA® (latanoprostene bunod ophthalmic solution) 0.024% is indicated for the reduction of intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Pigmentation

VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% may cause changes to pigmented tissues. The most frequently reported changes with prostaglandin analogs have been increased pigmentation of the iris and periorbital tissue (eyelid).

Pigmentation is expected to increase as long as latanoprostene bunod ophthalmic solution is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of VYZULTA, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes are likely to be reversible in most patients. Patients who receive prostaglandin analogs, including VYZULTA, should be informed of the possibility of increased pigmentation, including permanent changes. The long-term effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly *[see Patient Counseling Information (17) in full Prescribing Information]*.

5.2 Eyelash Changes

VYZULTA may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and the number of lashes or hairs. Eyelash changes are usually reversible upon discontinuation of treatment.

5.3 Intraocular Inflammation

VYZULTA should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation as it may exacerbate this condition.

5.4 Macular Edema

Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin analogs. VYZULTA should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

5.5 Bacterial Keratitis

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

5.6 Use with Contact Lens

Contact lenses should be removed prior to the administration of VYZULTA because this product contains benzalkonium chloride. Lenses may be reinserted 15 minutes after administration.

6 ADVERSE REACTIONS

The following adverse reactions are described in the Warnings and Precautions section: pigmentation (5.1), eyelash changes (5.2), intraocular inflammation (5.3), macular edema (5.4), bacterial keratitis (5.5), use with contact lens (5.6).

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.

VYZULTA was evaluated in 811 patients in 2 controlled clinical trials of up to 12 months duration. The most common ocular adverse reactions observed in patients treated with latanoprostene bunod were: conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%). Approximately 0.6% of patients discontinued therapy due to ocular adverse reactions including ocular hyperemia, conjunctival irritation, eye irritation, eye pain, conjunctival edema, vision blurred, punctate keratitis and foreign body sensation.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available human data for the use of VYZULTA during pregnancy to inform any drug associated risks.

Latanoprostene bunod has caused miscarriages, abortion, and fetal harm in rabbits. Latanoprostene bunod was shown to be abortifacient and teratogenic when administered intravenously (IV) to pregnant rabbits at exposures ≥ 0.28 times the clinical dose. Doses ≥ 20 µg/kg/day (23 times the clinical dose) produced 100% embryofetal lethality. Structural abnormalities observed in rabbit fetuses included anomalies of the great vessels and aortic arch vessels, domed head, sternebral and vertebral skeletal anomalies, limb hyperextension and malrotation, abdominal distension and edema. Latanoprostene bunod was not teratogenic in the rat when administered IV at 150 mcg/kg/day (87 times the clinical dose) *[see Data]*.

The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2 to 4%, and of miscarriage is 15 to 20%, of clinically recognized pregnancies.

Data

Animal Data

Embryofetal studies were conducted in pregnant rabbits administered latanoprostene bunod daily by intravenous injection on gestation days 7 through 19, to target the period of organogenesis. The doses administered ranged from 0.24 to 80 mcg/kg/day. Abortion occurred at doses ≥ 0.24 mcg/kg/day latanoprostene bunod (0.28 times the clinical dose, on a body surface area basis, assuming 100% absorption). Embryofetal lethality (resorption) was increased in latanoprostene bunod treatment groups, as evidenced by increases in early resorptions at doses ≥ 0.24 mcg/kg/day and late resorptions at doses ≥ 6 mcg/kg/day (approximately 7 times the clinical dose). No fetuses survived in any rabbit pregnancy at doses of 20 mcg/kg/day (23 times the clinical dose) or greater. Latanoprostene bunod produced structural abnormalities at doses ≥ 0.24 mcg/kg/day (0.28 times the clinical dose). Malformations included anomalies of sternum, coarctation of the aorta with pulmonary trunk dilation, retroesophageal subclavian artery with absent brachiocephalic artery, domed head, forepaw hyperextension and hindlimb malrotation, abdominal distention/edema, and missing/fused caudal vertebrae.

An embryofetal study was conducted in pregnant rats administered latanoprostene bunod daily by intravenous injection on gestation days 7 through 17, to target the period of organogenesis. The doses administered ranged from 150 to 1500 mcg/kg/day. Maternal toxicity was produced at 1500 mcg/kg/day (870 times the clinical dose, on a body surface area basis, assuming 100% absorption), as evidenced by reduced maternal weight gain. Embryofetal lethality (resorption and fetal death) and structural anomalies were produced at doses ≥ 300 mcg/kg/day (174 times the clinical dose). Malformations included anomalies of the sternum, domed head, forepaw hyperextension and hindlimb malrotation, vertebral anomalies and delayed ossification of distal limb bones. A no observed adverse effect level (NOAEL) was established at 150 mcg/kg/day (87 times the clinical dose) in this study.

8.2 Lactation

Risk Summary

There are no data on the presence of VYZULTA in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for VYZULTA, and any potential adverse effects on the breastfed infant from VYZULTA.

8.4 Pediatric Use

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

8.5 Geriatric Use

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

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Latanoprostene bunod was not mutagenic in bacteria and did not induce micronuclei formation in the *in vivo* rat bone marrow micronucleus assay. Chromosomal aberrations were observed *in vitro* with human lymphocytes in the absence of metabolic activation.

Latanoprostene bunod has not been tested for carcinogenic activity in long-term animal studies. Latanoprost acid is a main metabolite of latanoprostene bunod. Exposure of rats and mice to latanoprost acid, resulting from oral dosing with latanoprost in lifetime rodent bioassays, was not carcinogenic.

Fertility studies have not been conducted with latanoprostene bunod. The potential to impact fertility can be partially characterized by exposure to latanoprost acid, a common metabolite of both latanoprostene bunod and latanoprost. Latanoprost acid has not been found to have any effect on male or female fertility in animal studies.

13.2 Animal Toxicology and/or Pharmacology

A 9-month toxicology study administered topical ocular doses of latanoprostene bunod to one eye of cynomolgus monkeys: control (vehicle only), one drop of 0.024% bid, one drop of 0.04% bid and two drops of 0.04% per dose, bid. The systemic exposures are equivalent to 4.2-fold, 7.9-fold, and 13.5-fold the clinical dose, respectively, on a body surface area basis (assuming 100% absorption). Microscopic evaluation of the lungs after 9 months observed pleural/subpleural chronic fibrosis/inflammation in the 0.04% dose male groups, with increasing incidence and severity compared to controls. Lung toxicity was not observed at the 0.024% dose.

U.S. Patent Numbers: 7,273,946; 7,629,345; 7,910,767; 8,058,467.

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VYZ.0058.USA.19 Issued: 3/2019

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IN THE NEWS

With retinal multimodal imaging, researchers are finding a higher incidence of reticular pseudodrusen than in previous studies that used fundus color images. After French researchers looked at data from 472 eyes, they identified an annual reticular pseudodrusen incidence per participant of 2.9% and an estimated 13.5% five-year incidence. Age, choroidal thinning and genetic background were all associated with incidence.

Dutheil C, Le Goff M, Cougnard-Grégoire A, et al. Incidence and risk factors of reticular pseudodrusen using multimodal imaging. JAMA Ophthalmol. March 12, 2020. [Epub ahead of print].

A study conducted in Japan with 169 adult patients has found that **cataract surgery** with intraocular lens (IOL) implantation **may increase patients' nonvisual light perception and improve their circadian alignment**, which also increased the concentrations of melatonin secretion. The researchers presume the effects of cataract surgery on melatonin secretion when blue light-blocking IOLs are used might be weaker because of reduced nonvisual light perception.

Nishi T, Saeki K, Miyata K, et al. Effects of cataract surgery on melatonin secretion in adults 60 years and older. JAMA Ophthalmol. March 5, 2020. [Epub ahead of print].

A study from the University of Alabama suggests that prescribing **overnight orthokeratology** (ortho-K) lenses for corneal reshaping **can help patients avoid contact lens discomfort during the day.** The investigators examined 29 subjects and found that, after only one month, questionnaire scores, conjunctival staining and flatter keratometry values showed significant improvement. At three months, the improvement was even more pronounced.

Duong K, McGwin G, Franklin Q, et al. Treating uncomfortable contact lens wear with orthokeratology. Eye Contact Lens. February 24, 2020. [Epub ahead of print].

Could Plaquenil Treat COVID-19 Illness?

The drug is being evaluated for use in pneumonia related to the pandemic.

By Bill Kekevian, Senior Editor

Researchers across the globe are scrambling to come up with treatments for the deadly COVID-19 virus affecting people on nearly every continent. While no vaccine or antiviral treatments are yet available, part of the virus's impact is that infected people can develop pneumonia. Now, researchers in Shanghai are aiming to evaluate the efficacy and safety of Plaquenil (hydroxychloroquine, Sanofi-Aventis) to treat that pneumonia.[1]

They're investigating a dose of 400mg per day—the standard for its use for rheumatoid arthritis, lupus and other inflammatory conditions.[1,2] Plaquenil toxicity can cause problems such as retinopathy and retinal atrophy that can lead to central vision loss.[3] Of course, these complications only seem to develop in patients on a long course of the medication.[3] The COVID-19 study is looking into the efficacy of a five-day course, so it shouldn't be alarming to optometrists, says Sara Wedimayer, OD, an optometrist with the Ann Arbor Healthcare System's Veterans Administration and a clinical instructor at the University of Michigan. Adverse ocular affects are rare, but patients taking Plaquenil require more stringent optometric oversight.[2-4]

"Plaquenil toxicity is not common, and it tends to occur in patients who have received a cumulative dose of >1,000g," Dr. Weidmayer explains. These patients are "chronically on a dose >5mg/kg/d of their actual weight, or have other risk factors. Even if 400mg of Plaquenil a day for five days ends up being regularly used for those with pneumonia from COVID-19, it's very unlikely that those patients would have any significant eye-related side effects from taking that short a course of the medication."

Plaquenil is commonly used in rheumatoid arthritis, but was originally developed as an antimalarial medication. A number of immunodeficient conditions may be treated with Plaquenil, including Sjögren's syndrome, a number of autoimmune diseases and *Coxiella burnetii*–related heart infections.[4-6]

1. Hongzhou Lu, Shanghai Public Health Clinical Center. US National Library of Medicine. Clinical Trials. clinicaltrials.gov/ct2/show/study/NCT04261517. March 4, 2020. Accessed March 13, 2020.
2. Demeritt M, Reynolds S, Shechtman D, Davidson J. How to succeed in Plaquenil screenings. Rev Optom. 2019;156(2):56-63.
3. Pandya H, Robinson M, Mandal N, Shah V. Hydroxychloroquine retinopathy: A review of imaging. Indian J Ophthalmol. 2015;63(7):570–4.
4. Marmor MF, Kellner U, Lai TY, et al. Recommendations on Screening for Chloroquine and Hydroxychloroquine Retinopathy (2016 Revision). Ophthalmology. 2016;123(6):1386-94.
5. Yeo K, Chen H, Chen Y, et al. Hydroxychloroquine may reduce risk of pneumocystis pneumonia in lupus patients: a nationwide, population-based case-control study. BMC Infectious Diseases. February 10, 2020 [Epub ahead of print].
6. Kersh G. Antimicrobial therapies for Q fever. Expert Rev Anti Infect Ther. 2013;11(11):1207-14.

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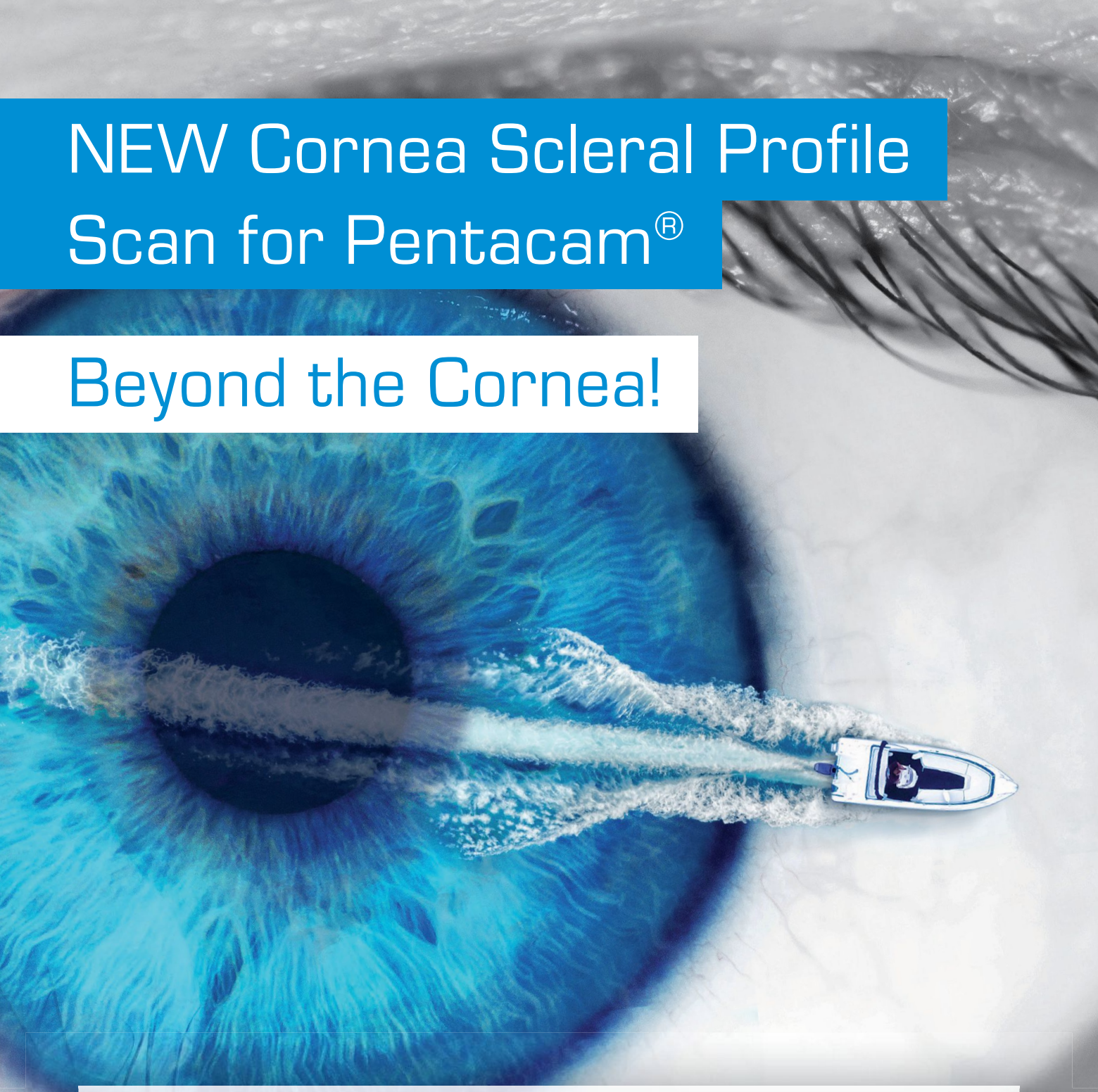

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Omega-3s and Autologous Serum Tested

Studies suggest neither are ideal for all types of dry eye.

Two studies looked at the limits of each treatment option of dry eye disease: one at omega-3 supplements and the other at autologous serum drops. The first study concluded that lower systemic levels of omega-3s aren't linked to worse symptoms and most signs of the condition, and the second stated that the serum drops may not work as well in cases of dry eye associated with systemic disease.[1,2]

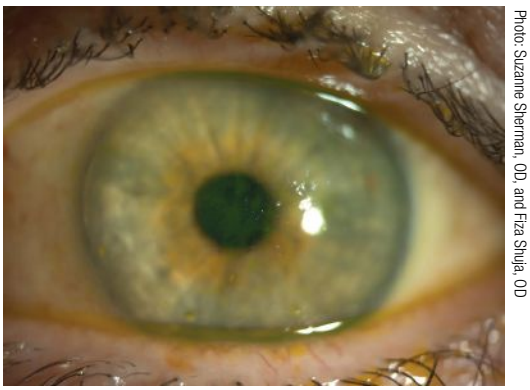


Photo: Suzanne Sherman, OD, and Fiza Shuja, OD

Autologous serum may not prove as effective for this patient with with Sjögren's syndrome and lupus as it would for someone with localized DED.

Doubting Omega-3s

In the latest offshoot of the Dry Eye Assessment and Management (DREAM) study, researchers upped their stance that omega-3 fatty acids don't help improve symptoms of dry eye disease. In the current investigation, researchers analyzed patients' blood samples for omega-3 and omega-6 to evaluate the relationship between systemic omega-3 levels and signs and symptoms at baseline in the DREAM investigation. The samples were measured as relative percentages by weight among all fatty acids in erythrocytes. The team evaluated symptoms using the Ocular Surface Disease Index, conjunctival staining, corneal staining, tear break-up time (TBUT) and Schirmer's test with anesthesia.[1]

The researchers found no correlation between the systemic omega-3 levels and dry eye symptoms. When assessing the signs of dry eye, the investigators observed a link between lower DHA levels and higher conjunctival staining with mean scores of 3.31, 2.96 and 2.82 for low, medium and high levels of DHA, respectively. None of the other signs were associated with DHA or the other omega-3 measures.[1]

The eligibility criteria of the DREAM study allowed people who were taking low doses of omega-3 supplements (1,200mg) to still enroll in the study. Erythrocyte analysis showed the 134 subjects who were taking omega-3 supplements before entering the study had significantly higher systemic levels compared with the 386 subjects who were not taking any supplements prior to the study.

However, despite the marked differences in systemic levels of omega-3 between the two groups, no statistically significant differences in severity of dry eye signs and symptoms were observed, the researchers noted.[1]

These findings help support the conclusion that systemic levels of omega-3 are not associated with the severity of dry eye disease and bring into question the assertion that omega-3 fatty acids are beneficial for treatment and the mechanism by which they affect dry eye, the investigators said.[1]

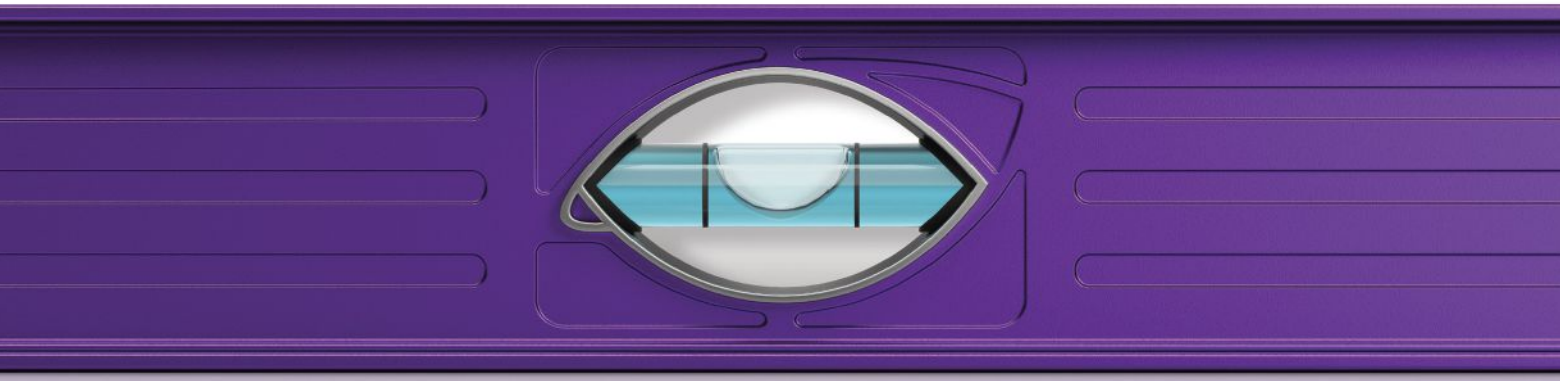
Serum Not Appropriate For Systemic DED

The other study suggested that eye drops engineered to contain growth factors and vitamins similar to those in human tears are a promising therapy for ocular surface disease and associated symptoms.[2]

This team of researchers evaluated 53 patients with either systemic diseases (group 1) or localized ocular surface diseases (group 2) who were prescribed autologous serum tears. They found that the average concentration of epidermal growth factor in group 1 (29.39±52.85pg/ml) was significantly lower than it was in group 2 (88.04±113.75pg/ml). They noted that levels of fibronectin, interleukin-8 and vitamin A were similar in both groups. The team also discovered a 24% reduction in Ocular Surface Disease Index scores six weeks after initiation in group 1 compared with a 36% reduction in group 2, both of which were significant.[2]

"The differences between levels of epidermal growth factor in patients with localized ocular surface disease and systemic inflammatory disease may account for differences in therapeutic outcome," the study concluded.[2]

1. Kuklinski EJ, Homm MM, Ying GS, et al. Associations between systemic omega-3 fatty acid levels with moderate-to-severe dry eye disease signs and symptoms at baseline in the dry eye assessment and management study. Eye Contact Lens. February 24, 2020. [Epub ahead of print].
2. Ripa M, Jabbehdari S, Yazdanpanah G, et al. The role of multisystem disease in composition of autologous serum tears and ocular surface symptom improvement. Ocul Surf. February 29, 2020. [Epub ahead of print].



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FLAREX® provides the precise level of potency when treating ocular surface inflammation[1,2]

By balancing efficacy and safety, you can tailor treatment to meet the exact needs of your patients[1]

- **Superior efficacy** vs FML® (fluorometholone ophthalmic suspension, USP) 0.1%*[2,a]
- **Similar efficacy** to prednisolone acetate 1.0%[2,a]
- **No differences** in adverse reactions vs FML* and prednisolone acetate 1.0%[2,a]
- The **lowest-cost branded** corticosteroid[3,b]
- **No generic equivalent**—prescribe **FLAREX** by name[4]

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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

CONTRAINDICATIONS
Contraindicated in acute superficial herpes simplex keratitis, vaccinia, varicella, and most other viral diseases of the 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.

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

[a]**STUDY DESIGN:** The efficacy and safety of FLAREX (n=41) vs FML* (n=37) were evaluated in a randomized, double-blind clinical trial in 78 patients with ocular surface inflammation (eg, conjunctivitis, episcleritis, scleritis) in one or both eyes. In a separate randomized, double-blind clinical trial in 82 patients with ocular surface inflammation in one or both eyes, the efficacy and safety of FLAREX (n=37) vs prednisolone acetate 1.0% (n=45) were evaluated. In these studies, patients administered either FLAREX or FML*/prednisolone acetate 1.0% 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. At each visit, investigators determined if symptoms in the involved eye were resolved (cured), improved, unchanged, or worsened. If a patient was rated as cured before the end of the study, steroid drops were discontinued and the patient was considered to have completed the trial.[2]

[b]Cost information based on Wholesale Acquisition Cost (WAC), 2019 data.

eyevance pharmaceuticals

FLA-09-19-AD-42

Flarex®
(fluorometholone acetate ophthalmic suspension) 0.1%

FLAREX® (fluorometholone acetate ophthalmic suspension) 0.1%
Brief Summary

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.

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.

CONTRAINDICATIONS
Contraindicated in acute superficial herpes simplex keratitis, vaccinia, varicella, and most other viral diseases of the 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 AND PRECAUTIONS
Topical Ophthalmic Use Only
For topical ophthalmic use only. Not for injection.

Intraocular Pressure Increase
Prolonged use may result in glaucoma, damage to the optic nerve, and defects in visual acuity and visual field. It is advisable that the intraocular pressure be checked frequently.

Cataracts
Use of corticosteroids may result in cataract formation.

Delayed Healing
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.

Viral Infections
Use in the treatment of herpes simplex infection requires great caution.

Bacterial Infections
Use of corticosteroids may suppress the host response and thus aid in the establishment of secondary ocular infections. Acute purulent infections of the eye may be masked or exacerbated by the presence of steroid medication.

Fungal Infections
Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use.

Contamination
Do not touch dropper tip to any surface, as this may contaminate the suspension.

Contact Lens Wear
Contact lenses should be removed during instillation of FLAREX but may be reinserted after 15 minutes.

Temporarily Blurred Vision
Vision may be temporarily blurred following dosing with FLAREX. Care should be exercised in operating machinery or driving a motor vehicle.

ADVERSE REACTIONS
Clinical Trials Experience
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 postmarketing use of FLAREX 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.

USE IN SPECIFIC POPULATIONS
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.

Lactation
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 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.

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

PATIENT COUNSELING INFORMATION
Risk of Contamination
Do not touch dropper tip to any surface, as this may contaminate the suspension.

Use with Contact Lenses
The preservative in FLAREX, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of FLAREX but may be reinserted 15 minutes after instillation.

Temporarily Blurred Vision
Patients should be advised that their vision may be temporarily blurred following dosing with FLAREX. Care should be exercised in operating machinery or driving a motor vehicle.

Rx Only
Distributed by: Eyevance Pharmaceuticals LLC. Fort Worth, TX 76102

References: 1. FLAREX [package insert]. Fort Worth, TX: Alcon Laboratories, Inc; 2017. **2.** 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. **3.** Data on file. Fort Worth, TX: Eyevance Pharmaceuticals LLC. **4.** US Department of Health and Human Services, Food and Drug Administration. *Approved drug products with therapeutic equivalence evaluations.* (Orange Book). 38th ed. Washington, DC: US Department of Health and Human Services, Food and Drug Administration; 2018.

FLA-09-19-AD-42

Fibrous Scarring Key to CNV Treatment

Lesion type's association with visual prognosis may help guide therapy decisions.

Choroidal neovascularization (CNV) patients with predominantly classic lesions may go on to develop fibrous scarring and subsequent rapid vision loss, a new study suggests. The investigation, published in *Ophthalmology Retina*, also found vision gains were achieved regardless of fibrosis status after 24 months of anti-VEGF treatment. Additionally, patients with extrafoveal fibrosis had the most significant visual gains by the study's end.

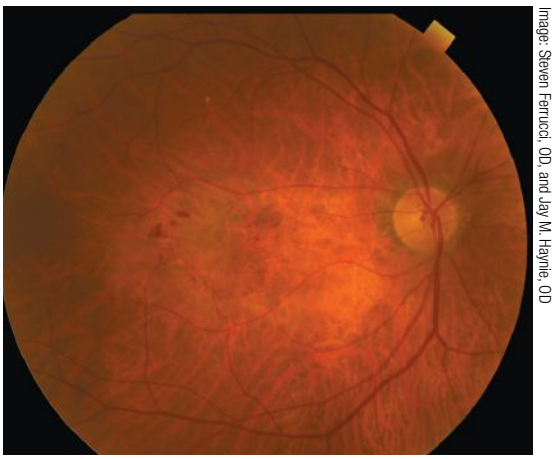

Image: Steven Ferrucci, OD, and Jay M. Haynie, OD

Patients with predominantly classic CNV at baseline were classified as having any subfoveal fibrosis.

Researchers examined the relationship between baseline CNV subtype and fibrosis development using HARBOR data that included 1,097 patients with wet AMD who were randomized to ranibizumab 0.5mg and 2mg injections for 24 months. The study also looked at associations among CNV subtype—predominantly classic, minimally classic or occult—fibrosis and best-corrected visual acuity (BCVA).

Using fluorescein angiography interpreted by three readers, the study clarified the presence of fibrosis if the median area of subretinal fibrous tissue or disciform scar was greater than zero and if there was any detectable fibrosis. The study also used red-free fundus photography to determine the fibrous locations, which were defined as not detected, any subfoveal, extrafoveal only or remote location only or not reported (other).

The investigation found the baseline distribution of CNV lesions was similar to findings in clinical practice, with 15.5% of patients having predominantly classic, 46.4% minimally classic and 38.1% occult CNV lesions. At month 24, a total of 513 patients had no detected fibrosis, 295 had any subfoveal fibrosis, 86 subjects had extrafoveal only fibrosis and 10 patients were found to have other fibrosis.

At two years, detectable fibrosis was found in 78.2%, 50.7% and 19.8% of patients with baseline predominantly classic, minimally classic and occult CNV lesions, respectively.

Patients achieved meaningful visual gains at months 12 and 24 regardless of the two-year status, the researchers noted. At month 12, patients who were later classified as having subfoveal fibrosis at month 24 gained 8.5 ETDRS letters compared with those with extrafoveal only fibrosis, who gained 16.7 letters. Patients with fibrosis not detected at two years gained 9.2 letters.

At month 24, patients with any subfoveal fibrosis gained 8.3 letters, those with extrafoveal only gained 14.5 letters and patients with fibrosis not detected at month 24 gained 8.2 letters. At both time points, visual gains in patients with any subfoveal fibrosis were no different from patients with undetected fibrosis.

Also of note: more patients with extrafoveal-only fibrosis achieved gains of 15 or more letters compared with patients with any subfoveal fibrosis or fibrosis that wasn't detected. This pattern was observed for all baseline lesion subtypes. Additionally, patients with fibrosis not detected at two years achieved similar visual gains from baseline over the course of the study compared with those who had any subfoveal fibrosis.

Also, more patients with predominantly classic CNV at baseline were classified as having any subfoveal (65.5%) vs. extrafoveal only (9.2%) fibrosis, which was consistent with real-world observations, the researchers noted. This trend also was observed in those with minimally classic and occult lesions (14.2% vs. 5.2%).

The findings may be beneficial in guiding treatment decisions in light of the possible development of new therapies that target subretinal fibrosis, the researchers noted in their paper.

Adrean SD, Morgenthien E, Ghanekar A, Ali FS. Subretinal fibrosis in HARBOR varies by choroidal neovascularization subtype. Ophthalmology Retina. February 27, 2020. [Epub ahead of print].

Widefield OCT-A Best for DR Detection

Researchers recently reported a higher detection rate of proliferative diabetic retinopathy (PDR) with widefield OCT angiography (OCT-A) when compared with clinical examination.[1] While this suggests that widefield OCT-A could be used noninvasively for the early detection and characterization of neovascularization, the question then becomes which scan protocol is the best.[1] Looking to answer this, one team found that angio 12x12mm images focusing on the fovea and the optic disc may achieve the best balance between speed and efficacy in detecting DR lesions.[2]

The first of two studies on the subject included 79 eyes of 46 patients—57 eyes had PDR and 22 had severe non-proliferative DR (NPDR). A pair of graders identified neovascularization on widefield OCT-A imaging using 12x12mm montage scans and compared their findings with clinical examination outcomes.[1]

The investigators detected neovascularization at the disc in the form of preretinal hyperreflective material on OCT-A B-scans in 39 eyes with evident flow signals in 79.5% compared with 51.3% when detected clinically. When they classified disc neovascularization on OCT-A into four subtypes, they found that subtypes one and two could not be seen on clinical examination alone.[1]

Beyond the disc, the team noted that OCT-A detected neovascularization in 81.0% of cases compared with 55.7% detected clinically. They added that widefield OCT-A resulted in a higher percentage of PDR grading (88.6%) than on clinical examination (72.2%). Ultra-widefield fluorescein angiography confirmed the OCT-A diagnoses in the majority of cases.[1]

Building on these results, another observational study imaged 176 eyes of 119 PDR, NPDR or non-DR patients with widefield swept-source OCT-A using the following scan protocols: angio 3x3mm centered on the fovea, angio 6x6mm centered on the fovea and the optic disc, montage 15x9mm and angio 12x12mm centered on the fovea and the optic disc. Two graders independently evaluated and compared the images for DR lesions.[2]

The team discovered that angio 6x6mm images centered on the fovea detected neovascularization at about half the rate of montage 15x9mm images. They noted that angio 6x6mm images centered on both the fovea and the optic disc increased this rate to about two thirds. They observed comparable detection rates between angio 12x12mm images and montage 15x9mm images for all DR lesions. In terms of microaneurysms, the investigators found that angio 6x6mm images performed better than montage 15x9mm images.[2]

1. Khalid H, Schwartz R, Nicholson L, et al. Widefield optical coherence tomography angiography for early detection and objective evaluation of proliferative diabetic retinopathy. Br J Ophthalmol. March 19, 2020. [Epub ahead of print].
2. Zhu Y, Cui Y, Wang JC, et al. Different scan protocols affect the detection rates of diabetic retinopathy lesions by wide-field swept-source optical coherence tomography angiography. Am J Ophthalmol. March 20, 2020. [Epub ahead of print].

Inflammatory Markers Found in Scleral Reservoirs

Researchers from the Ocular Surface Institute at the University of Houston College of Optometry recently discovered elevated levels of inflammatory markers—namely matrix metalloproteinase-9 and -10 (MMP-9, MMP-10)—in scleral lens fluid reservoirs compared with those found in basal tear samples, indicating potential clinical issues with these lenses.

Their study enrolled 15 normal, habitual soft contact lens wearers who were fitted with 14.8mm or 15.4mm scleral lenses. The investigators collected basal ocular surface tears and fluid reservoir samples after eight hours and again after four days of scleral lens wear.

After eight hours, the median concentration of MMP-9 in the fluid reservoir and basal tears were 62.7ng/mL and 15.2ng/mL, respectively. Likewise, MMP-10 was significantly greater in the fluid reservoir compared with the basal tears after eight hours and four days. Additionally, researchers reported interleukin-4 and -8 (IL-4, IL-8) were relatively high in the fluid reservoir, yet not significantly so, at eight hours and at four days.

While certain markers were elevated, MMP-7 remained unchanged at both time points.

No changes were found in visual acuity or corneal or conjunctival staining, but participants said their comfort was reduced while wearing the scleral lenses compared with their usual soft contacts.

This is the first study to compare the fluid reservoir with basal ocular surface tears, the researchers said. ■

Walker MK, Lema C, Redfern R. Scleral lens wear: Measuring inflammation in the fluid reservoir. Contact Lens & Anterior Eye. March 9, 2020. [Epub ahead of print].

BRIEF SUMMARY OF PRESCRIBING INFORMATION

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

LOTEMAX® SM (loteprednol etabonate ophthalmic gel) 0.38%

For topical ophthalmic use
Initial U.S. Approval: 1998

INDICATIONS AND USAGE

LOTEMAX® SM is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once to fill tip before instilling drops. Apply one drop of LOTEMAX® SM into the conjunctival sac of the affected eye three times daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period.

CONTRAINDICATIONS

LOTEMAX® SM, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, in mycobacterial infection of the eye and fungal diseases of ocular structures.

WARNINGS AND PRECAUTIONS

Intraocular Pressure (IOP) Increase: Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, intraocular pressure should be monitored.

Cataracts: Use of corticosteroids may result in posterior subcapsular cataract formation.

Delayed Healing: The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

Bacterial Infections: Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

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

Fungal Infections: Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.

Contact Lens Wear: Contact lenses should not be worn when the eyes are inflamed.

ADVERSE REACTIONS

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. Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with infrequent optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, delayed wound healing and secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera. There were no treatment-emergent adverse drug reactions that occurred in more than 1% of subjects in the three times daily group compared to vehicle.

USE IN SPECIAL POPULATIONS

Pregnancy: Risk Summary: There are no adequate and well controlled studies with loteprednol etabonate in pregnant women. Loteprednol etabonate produced teratogenicity at clinically relevant doses in the rabbit and rat when administered orally during pregnancy. Loteprednol etabonate produced malformations when administered orally to pregnant rabbits at doses 4.2 times the recommended human ophthalmic dose (RHOD) and to pregnant rats at doses 106 times the RHOD. In pregnant rats receiving oral doses of loteprednol etabonate during the period equivalent to the last trimester of pregnancy through lactation in humans, survival of offspring was reduced at doses 10.6 times the RHOD. Maternal toxicity was observed in rats at doses 1066 times the RHOD, and a maternal no observed adverse effect level (NOAEL) was established at 106 times the RHOD. The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2 to 4%, and of miscarriage is 15 to 20%, of clinically recognized pregnancies. Data: *Animal Data.* Embryofetal studies were conducted in pregnant rabbits administered loteprednol etabonate by oral gavage on gestation days 6 to 18, to target the period of organogenesis. Loteprednol etabonate produced fetal malformations at 0.1 mg/kg (4.2 times the recommended human ophthalmic dose (RHOD) based on body surface area, assuming 100% absorption). Spina bifida (including meningocele) was observed at 0.1 mg/kg, and exencephaly and craniofacial malformations were observed at 0.4 mg/kg (17 times the RHOD). At 3 mg/kg (128 times the RHOD), loteprednol etabonate was associated with increased incidences of abnormal left common carotid artery, limb flexures, umbilical hernia, scoliosis, and delayed ossification. Abortion and embryofetal lethality (resorption) occurred at 6 mg/kg (256 times the RHOD). A NOAEL for developmental toxicity was not established in this study. The NOAEL for maternal toxicity in rabbits was 3 mg/kg/day. Embryofetal studies were conducted in pregnant rats administered loteprednol etabonate by oral gavage on gestation days 6 to 15, to target the period of organogenesis. Loteprednol etabonate produced fetal malformations, including absent innominate artery at 5 mg/kg (106 times the RHOD); and cleft palate, agnathia, cardiovascular defects, umbilical hernia, decreased fetal body weight and decreased skeletal ossification at 50 mg/kg (1066 times the RHOD). Embryofetal lethality (resorption) was observed at 100 mg/kg (2133 times the RHOD). The NOAEL for developmental toxicity in rats was 0.5 mg/kg (10.6 times the RHOD). Loteprednol etabonate was maternally toxic (reduced body weight gain) at 50 mg/kg/day. The NOAEL for maternal toxicity was 5 mg/kg. A peri-/postnatal study was conducted in rats administered loteprednol etabonate by oral gavage from gestation day 15 (start of fetal period) to postnatal day 21 (the end of lactation period). At 0.5 mg/kg (10.6 times the clinical dose), reduced survival was observed in live-born offspring. Doses ≥ 5 mg/kg (106 times the RHOD) caused umbilical hernia/incomplete gastrointestinal tract. Doses ≥ 50 mg/kg (1066 times the RHOD) produced maternal toxicity (reduced body weight gain, death), decreased number of live-born offspring, decreased birth weight, and delays in postnatal development. A developmental NOAEL was not established in this study. The NOAEL for maternal toxicity was 5 mg/kg.

Lactation: There are no data on the presence of loteprednol etabonate in human milk, the effects on the breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for LOTEMAX® SM and any potential adverse effects on the breastfed infant from LOTEMAX® SM.

Pediatric Use: Safety and effectiveness of LOTEMAX® SM in pediatric patients have not been established.

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in the chromosomal aberration test in human lymphocytes, or *in vivo* in the mouse micronucleus assay. Treatment of male and female rats with 25 mg/kg/day of loteprednol etabonate (533 times the RHOD based on body surface area, assuming 100% absorption) prior to and during mating caused preimplantation loss and decreased the number of live fetuses/live births. The NOAEL for fertility in rats was 5 mg/kg/day (106 times the RHOD).

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

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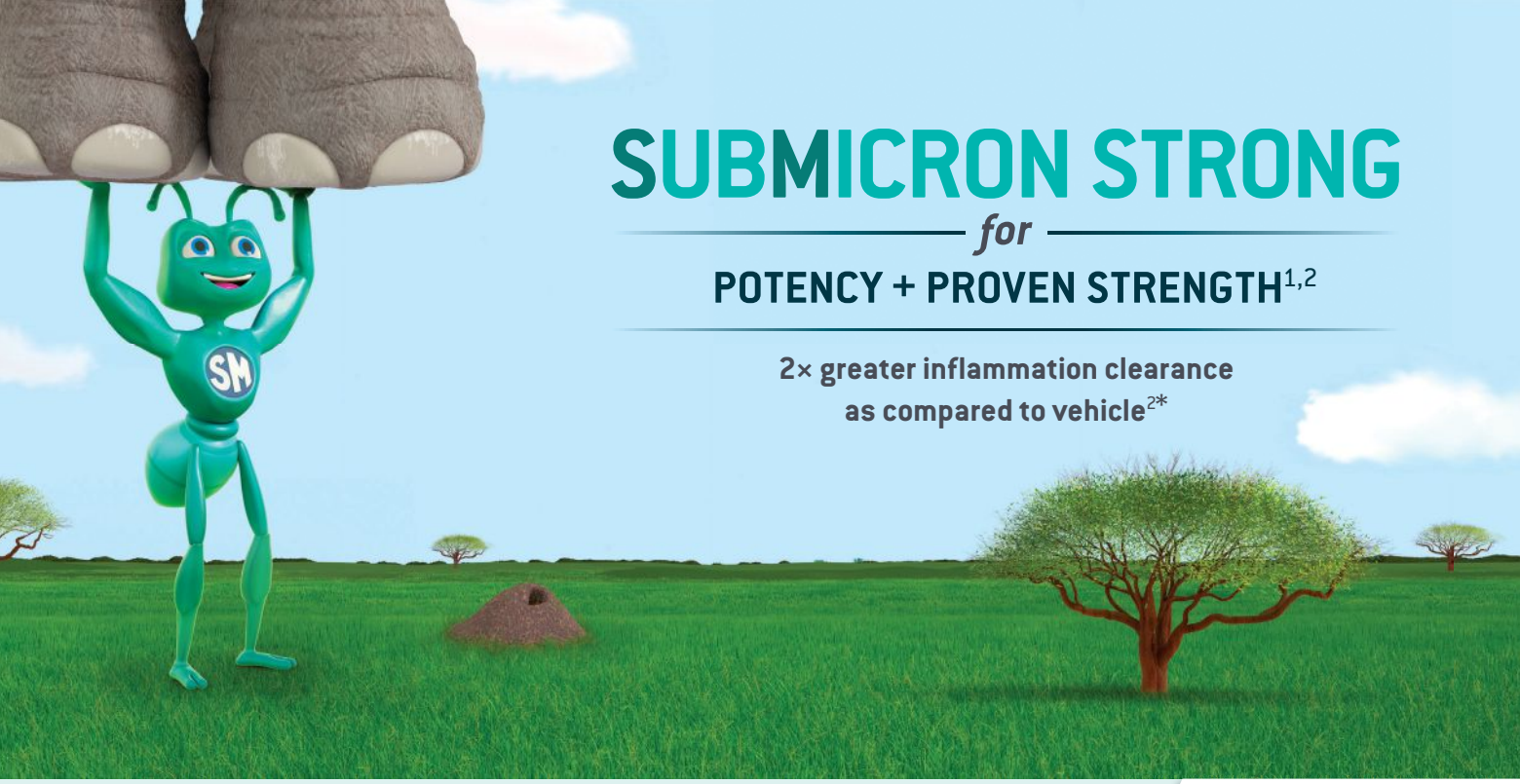
Based on 9669600-9669700 Revised: 02/2019



SUBMICRON STRONG

for

POTENCY + PROVEN STRENGTH[1,2]

2× greater inflammation clearance as compared to vehicle[2]*

SM TECHNOLOGY™

- **Engineered with SM Technology™ for efficient penetration at a low BAK level (0.003%)[1,3]**
- **~2× greater penetration** to the aqueous humor than LOTEMAX® GEL (loteprednol etabonate ophthalmic gel) 0.5%[3]

Clinical significance of these preclinical data has not been established.

LOTEMAX® SM
(loteprednol etabonate ophthalmic gel) 0.38%

SMALL & MIGHTY
SUBMICRON PARTICLES

*PROVEN STRENGTH

- **30% of LOTEMAX® SM patients had complete ACC resolution** vs vehicle (15%) at Day 8 (N=371, *P*<0.0001)[1,2†]
- **74% of LOTEMAX® SM patients were completely pain-free** vs vehicle (49%) at Day 8 (N=371, *P*<0.0001)[1,2‡]

†Pooled analysis of Phase 3 clinical studies. **Study 1:** 29% LOTEMAX® SM (N=171) vs 9% vehicle (N=172). **Study 2:** 31% LOTEMAX® SM (N=200) vs 20% vehicle (N=199); *P*<0.05 for all.

‡Pooled analysis of Phase 3 clinical studies. **Study 1:** 73% LOTEMAX® SM (N=171) vs 48% vehicle (N=172). **Study 2:** 76% LOTEMAX® SM (N=200) vs 50% vehicle (N=199); *P*<0.05 for all.

Indication

LOTEMAX® SM (loteprednol etabonate ophthalmic gel) 0.38% is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

Important Safety Information

- LOTEMAX® SM, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.
- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If LOTEMAX® SM is used for 10 days or longer, IOP should be monitored.
- Use of corticosteroids may result in posterior subcapsular cataract formation.

Important Safety Information (cont.)

- The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those with diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infections.
- Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).
- Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal cultures should be taken when appropriate.
- Contact lenses should not be worn when the eyes are inflamed.
- There were no treatment-emergent adverse drug reactions that occurred in more than 1% of subjects in the three times daily group compared to vehicle.

You are encouraged to report negative side effects of prescription drugs to the FDA. Visit **www.fda.gov/medwatch** or call **1-800-FDA-1088**.

Please see brief summary of Prescribing Information on adjacent page.

References: 1. LOTEMAX SM Prescribing Information. Bausch & Lomb Incorporated. **2.** Data on file. Bausch & Lomb Incorporated. **3.** Cavet ME, Glogowski S, Lowe ER, Phillips E. Rheological properties, dissolution kinetics, and ocular pharmacokinetics of loteprednol etabonate (submicron) ophthalmic gel 0.38%. *J Ocul Pharmacol Ther.* 2019. doi: 10.1089/jop.2019;35(5):291-300.

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April 15, 2020

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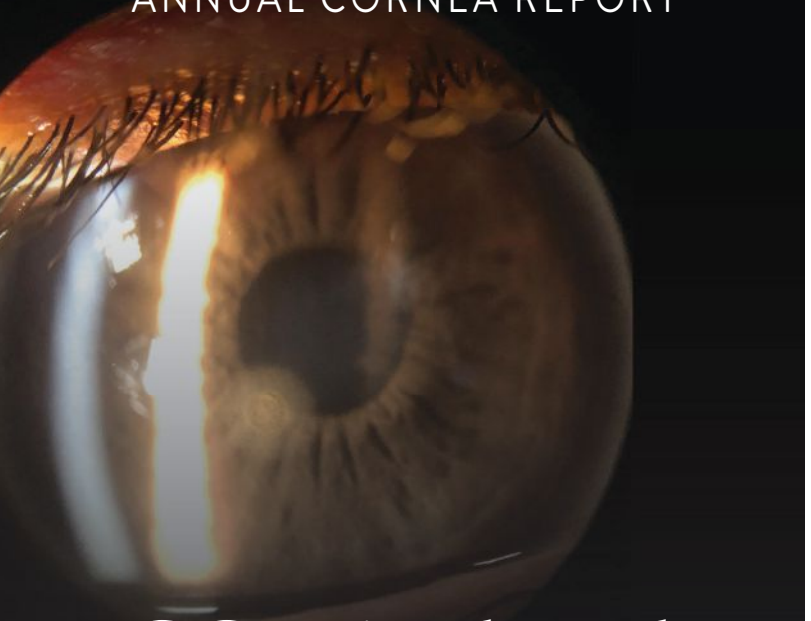

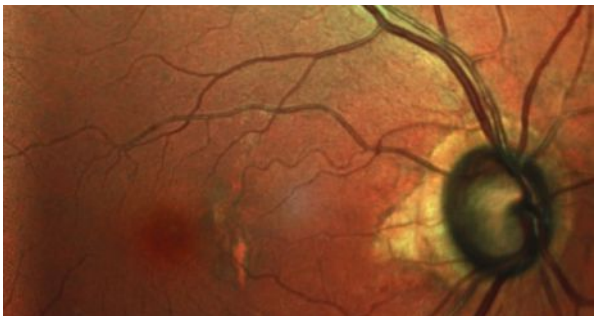

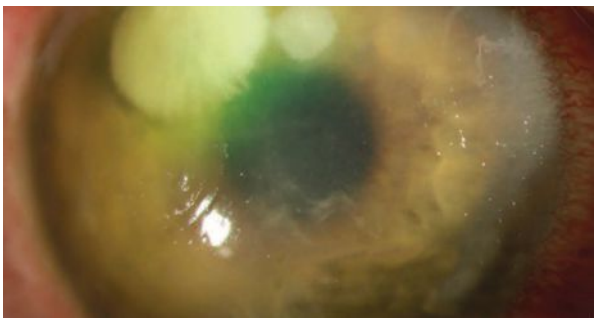

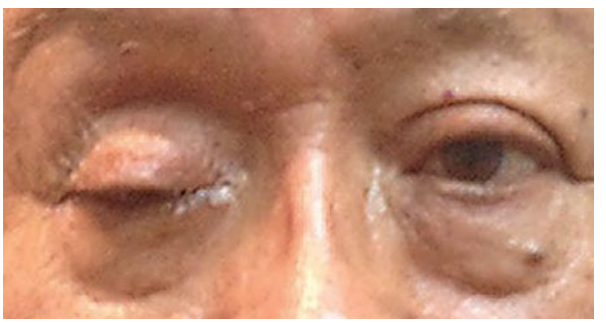

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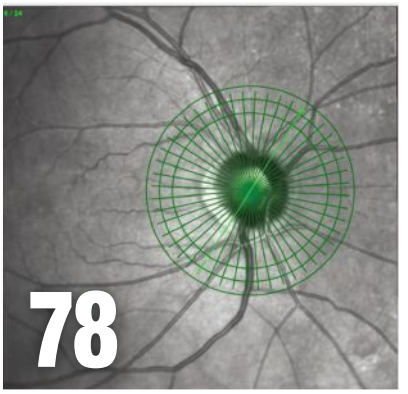

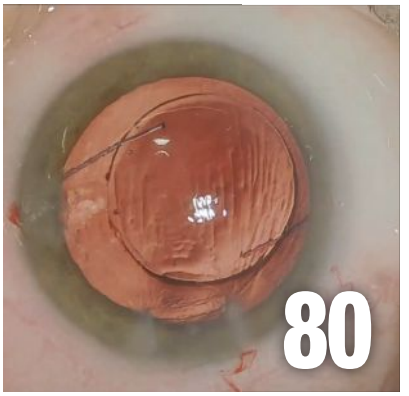

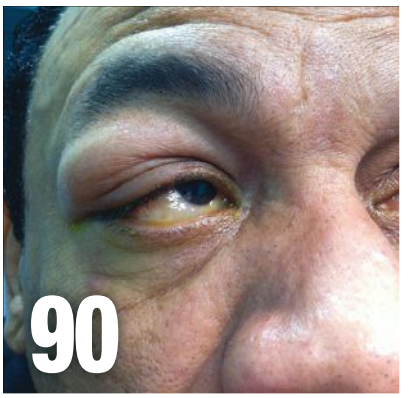

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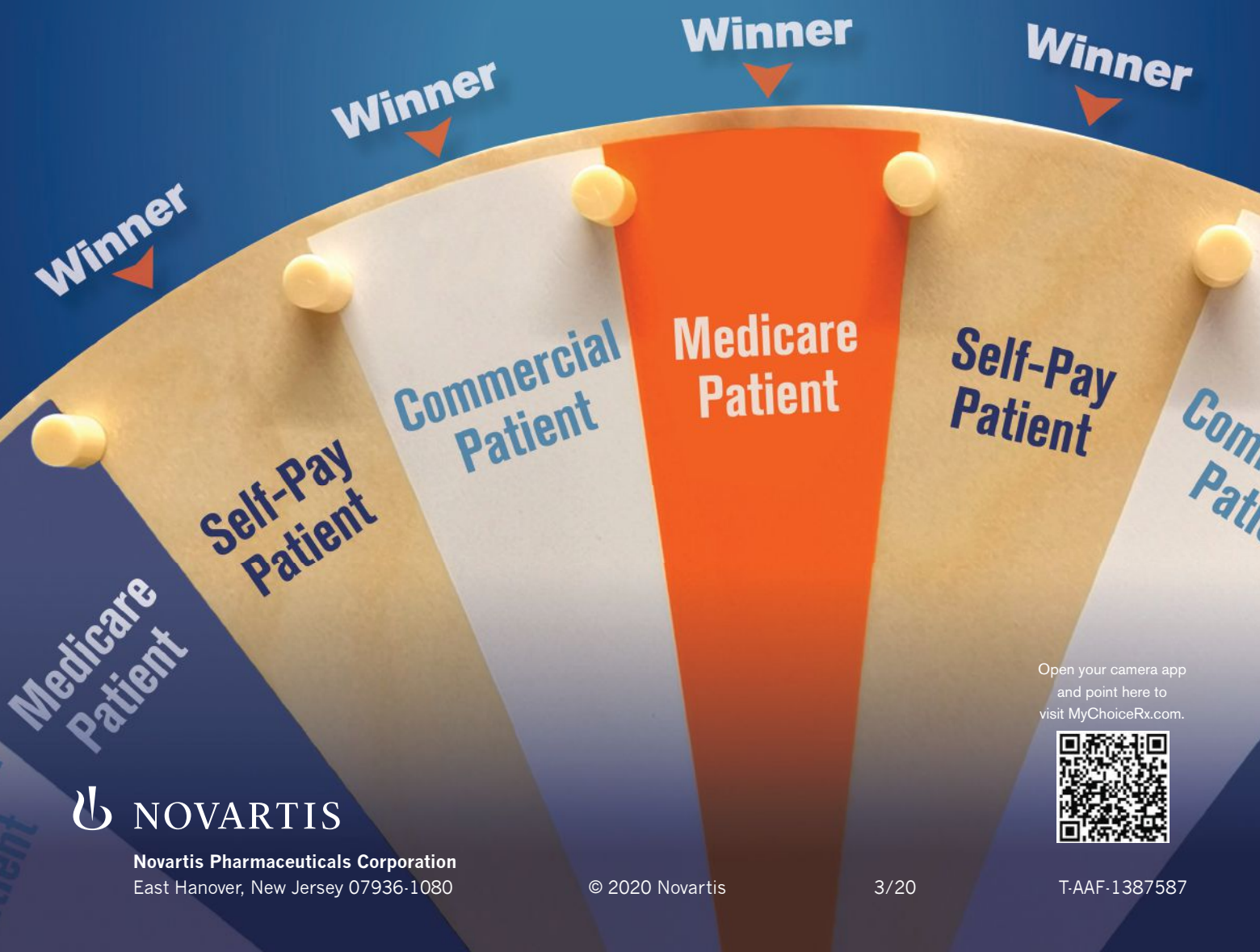

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Outlook

By Jack Persico, Editor-in-Chief

The Best Laid Plans

We're having a very different year than we expected, but discarding old routines might allow better ones to emerge.

On March 26, I was supposed to be in New York City, walking into the Jacob Javits Center for the first day of Vision Expo East. Instead, I was 'sheltering at home' and reading news stories about Javits being turned into a field hospital for COVID-19 patients. It was eerie to see the familiar environs of the cavernous hall filled not with extravagant eyewear displays but instead with hospital beds and stark white makeshift walls. The set-up has a 3,000-bed capacity. Sadly, it'll be no surprise if they all end up occupied.

The amount of suffering that's already occurred in just a matter of weeks, with more to come, is incalculable. But I believe it's been matched by an equal amount of courage, kindness and kinship. We've all read or watched stories about heroic hospital workers risking, and in some cases losing, their lives to save ours.

On a smaller scale, our personal and family connections may have been warped by a sudden reliance on glitchy conference calls and messaging apps, but these exchanges feel a little more empathetic right now.

I'm encouraged to find that same spirit strong within optometry, too. By now, the majority of eye care practices have closed to routine exams and are only seeing emergency cases, but ODs are looking out for each other. Online discussions show an eagerness to help colleagues work through their clinical and logistical problems. Doctors are even calling our offices offering to write articles because they have time on their hands and knowledge to share. And practice management guru Gary Gerber, OD, recently hosted a roundtable with over a dozen corporate executives, who put aside their competitive instincts and shared ideas on how to help ODs get through the crisis. A few interesting ideas from that:

(1) Use this downtime to retrain, retool and rethink. Lots of doctors are trying to implement telehealth out of necessity right now, but maybe it can become a part of your practice for the long-term. Now would also be an opportunity to delve into an area of care you've wanted to add but never had time to research.

(2) Stay in touch with staff during the furlough to keep them from moving on. If you want them to come back when you reopen, remind them they matter to you even when you don't need them. Offer them new training, too, so you all come out of this stronger and ready to rebound.

(3) Get comfortable with ambiguity. Which patients need to be seen now? When should you reopen? How can you prevent transmission of the virus in your office? What will happen to your practice's finances? Learning how to make decisions with incomplete and rapidly changing information is a great skill to have under any circumstances. There's nothing like an existential crisis for sharpening your wits.

I wish you, your families and your patients the best in these troubled times. Next March, when I walk into the Javits Center for Vision Expo East 2021, I'll stop and marvel at the surreal year that had just passed. Let's all hope the pain and anxiety will have dissipated by then, and left us with more growth and fewer scars. ■

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This month's issue covers several exciting anterior segment advances to help patients and your bottom line. **By Paul M. Karpecki, OD, Chief Clinical Editor**

Optometrists handling anterior segment concerns have a few new tools at their disposal lately. Here's an overview:

Corneal crosslinking. Still relatively new in the US but a mainstay internationally for more than two decades, this technology can halt progression of ectasia for conditions such as keratoconus. And while this is a wonderful tool, the real key to halting this disease is early diagnosis.

New imaging technologies such as Visionix and Pentacam can help you detect keratoconus early and find the right treatment path. With today's advances, these new tools may soon be accompanied by genetic testing. The AvaGen genetic test (Avellino Labs) measures more than 1,000 SNPs across 75 genes associated with keratoconus and numerous corneal dystrophies that may progress or exacerbate with certain surgeries such as LASIK.

Lid ptosis. It's imperative we start looking closely for this, even if it turns out to be longstanding blepharoptosis or a common acquired ptosis. Sometimes, it aids in the diagnosis of a life-threatening conditions such as an impending aneurysm or an acquired Horner's secondary to non–small cell lung cancer. In the next few months, the FDA will review clinical trial data for Vertical Pharmaceuticals' topical drop, RVL1201, for blepharoptosis. RVL1201 is a once-daily ophthalmic formulation of an alpha-1 agonist, which acts directly on Müller's muscle to elevate the upper eyelid.

Corneal nerves. Corneal innervation may be the key to numerous disease presentations. With the approval of Oxervate (cenegerminbkbj ophthalmic solution 0.002%, Dompé), we now have an effective treatment for neurotrophic keratitis, ranging from stage 1 with SPK to stage 3 with corneal ulceration. In clinical trials, Oxervate resulted in no corneal staining for 72% of cases after two months of therapy. One year later, 80% of the patients still had no signs of corneal pathology.

Another challenging condition to manage is neuropathic pain, or corneal neuralgia. These patients present with intense pain but no stain. The nerves are damaged and confocal microscopy shows 'burrs' on the nerve endings and numerous nerve branches—leaving patients prone to chronic pain from corneal nerve firing. Treatments involve topical loteprednol and autologous serum, oral nortriptyline, low-dose naltrexone and dry eye management.

The ophthalmic branch of the trigeminal nerve is another nerve we can't lose sight of. New research into trigeminal dysphoria caused by subtle eye misalignment results in frequent headaches, neck stiffness and a dry eye sensation. Research shows measurement and treatment with a spectacle lens called the NeuroLens (eyeBrain) can practically eliminate more than 50% of all frequent headaches and the accompanying dry eye sensation that occurs with most cases of trigeminal dysphoria.

New Solution for Profitability

With just one adjustment, we could add more than $3 billion per year to optometry: prevent contact lens dropout. The average contact lens wearer generates more than $300 annually to a practice (not including spectacle sales). However, statistics show the dropout rate is somewhere between 18% and 24% per year. Assuming the higher 24%, with 43 million people in the US wearing contact lenses, that means nearly 10 million drop out per year, or a loss of close to $3 billion.

The number one reason for dropout described by patients is dryness and irritation. So it's time to start treating dry eye and meibomian gland dysfunction early. A single Lipiflow (Johnson & Johnson Vision) treatment resulted in four hours of increased contact lens wearing time. A recent study found the new Eyeleve moist compress (Bruder) can increase contact lens wear time by three hours when used for 10 minutes per day.

If we focus on the underlying dry eye rather than simply changing lenses, we just may find a way to recoup that lost $3 billion in revenue per year.

It's time to look at opportunities to diagnose patients early and provide novel therapies to improve vision, stave off pain and keep patients happy in their lenses—true opportunities worth seizing. ■

Note: Dr. Karpecki consults for companies with products and services relevant to this topic.

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Can't Touch This

We are all finding out how much time is too much time with the kids—and how to doomsday shop. **By Montgomery Vickers, OD**

By the time this column goes to press, I hope the coronavirus has, at least mostly, run its course. All of us affiliated with *Review* have truly kept all of you in our daily thoughts and prayers.

"Chairside" (you know, this column) is theoretically a humorous look at the world of optometry. It's kinda hard to find anything funny about this frightening pandemic, so I'll just make a few observations:

1. My wife and I were scheduled to visit Europe—Italy, to be exact—for the first time in mid April. That didn't happen. Don't tell my wife, but I wasn't over the moon about leaving the familiar confines of the US in the first place. I didn't invent the virus just to get out of the trip, but maybe it was not meant to be… the trip I mean.

2. Speaking of my home state, did anybody notice that West Virginia was the last state to have a coronavirus case? Oh, I know, you think it's because (a) nobody ever leaves the state and (b) if they did, they'd never come back. Me? I agree with the theory that Moonshine is an antiviral, and we always take our medicine in West Virginia.

3. I have always washed my hands before and after every patient. Mostly. Now I just do it in front of them. But it's a little intimidating. I am always paranoid the patient is counting to 20, ready to judge my scrub time. The result isn't cleaner hands but more splashed water on the front of my pants.

4. Now that we can only Facetime our grandkids, we have had more quality time together… more than ever… like hours and hours and hours. We ran out of interesting discussions by 4pm on day one, so now we are watching romantic comedies together. Why are all romantic comedies based on some guy cheating on his long-suffering wife (you know, the wife who didn't get to go to Italy, for example)?

5. The coronavirus has cut into my important budget-to-buy-stuff-I-really-don't-need. I now have to buy boring things like food. And don't get me started on toilet paper. Pay cuts suck.

6. OK, you got me started on toilet paper. I noticed early in the crisis that the sheets that you use to fill out your lottery numbers are roughly the size of two jumbo toilet paper sheets. Just remember to have them run the card through the machine first. Don't learn the hard way.

7. With so much time on my hands I found the perfect coronavirus shot. Any doctor will agree. Like all important medications, it has a funny name: Mezcal.

8. My 401K now has a new name: "401 dollars."

9. I wish we could choose who would get sick in our family. It's only right that I would choose myself, but I am also considering nominating my cousin, Carey, who got me grounded for a week in 1960 by convincing me to march down the middle of 6th Avenue in Montgomery screaming, "I'm a monkey," after sticking a curvy willow branch in the back of my pants.

10. I have great admiration for my three bosses for the huge efforts to keep our offices safe and afloat and their employees paid. I cannot imagine the angst doctor-owners are experiencing with COVID-19. There is always light at the end of the tunnel, but this is one long tunnel.

My friends, you are braver than you ever thought you could be. Eye care is a critically important part of the healthcare system. You've done all you can do!

Now, go wash your hands. ■

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In the Red Zone

Treating episcleritis involves a thorough review of systems for any underlying diseases. **Edited by Paul C. Ajamian, OD**

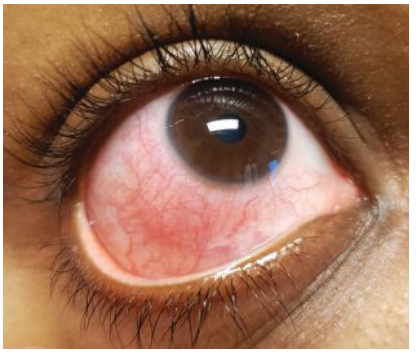
Q A 26-year-old female with sector injection presented with a history of a week on topical prednisolone QID with no improvement. What is my next step, and what are other differential diagnoses?

A "In my experience, it's unusual for simple episcleritis to be unresponsive to topical steroids after seven to 10 days," says Steven Ferrucci, OD, chief of optometry at the Sepulveda VA Ambulatory Care Center and Nursing Home in North Hills, CA. "Nodular episcleritis, which is less common and characterized by a raised nodule within the affected area, tends to last longer and may take up to two to four weeks to resolve."

If the episcleritis has not responded after a week or two, and the clinician is confident in their diagnosis, Dr. Ferrucci advises increasing the topical prednisone to a pulse dose, say every two hours for four days, or change steroids. "Durezol (difluprednate, Novartis) is a great choice and worth a try before switching to or adding orals," says Dr. Ferrucci. Adding an oral NSAID such as ibuprofen or indomethacin for a few weeks is often useful as well. "I typically prefer ibuprofen, 800mg three times a day, as it is relatively inexpensive, available over the counter and many patients already have it in their medicine cabinet," he says.

Workups

The vast majority of episcleritis is idiopathic and not associated with underlying systemic disease, but approximately 25% or so may be linked to systemic disease, with the most common condition being rheumatoid arthritis. This patient later admitted to this diagnosis, so Dr. Ferrucci recommends a thorough review of systems, as well as lab testing to look for an underlying cause.



Consider underlying systemic conditions first before diagnosing episcleritis.

Patients with nodular episcleritis, or those with severe and recurrent/persistent diffuse episcleritis may require a limited workup. Include complete blood count with differential, antinuclear antibody, rheumatoid factor, erythrocyte sedimentation rate, venereal disease research laboratory test and a fluorescent treponemal antibody absorption test.

A chest X-ray can help rule out some of the most common underlying diseases such as rheumatoid arthritis and lupus. If you suspect an underlying systemic disease, you might want to refer to their primary care physician or directly to a rheumatologist who can do a more extensive investigation.

"Of course, it is always a good idea to reconsider the initial diagnosis," Dr. Ferrucci says. One of the leading causes of sector injection that may throw clinicians off is a conjunctival abrasion. Before you jump to the diagnosis of episcleritis, be sure you stain with fluorescein to rule out a defect that would best be treated with an antibiotic, not a steroid. Bacterial conjunctivitis, phlyctenular conjunctivitis, subconjunctival hemorrhage and scleritis should also be on the differential list.

Perhaps the most important to rule out is scleritis, which typically does not respond to topical agents and requires systemic anti-inflammatory control, Dr. Ferrucci notes. One hallmark of scleritis is a deep, boring eye pain not present with episcleritis. Other signs may include an anterior chamber reaction and reduced visual acuity.

Blanching

According to Dr. Ferrucci, some practitioners advocate the use of 2.5% phenylephrine to aid in the diagnosis. The phenyl will blanch the superficial conjunctival and episcleral vessels but will not blanch the deeper scleral vessels. If the patient's eye clears up with installation, the diagnosis of episcleritis is strengthened. If the eye does not clear up, scleritis should be considered.

Once all the differentials are considered and everything but episcleritis is ruled out, don't be timid in your use of topical steroids, and don't forget to consider underlying systemic conditions. A consult to the appropriate specialist could make a big difference in the patient's health. ■

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Minor Procedures, Major Rules

Knowledge of the right coding process is power—and helps you sleep at night.

By John Rumpakis, OD, MBA, Clinical Coding Editor

The ability to perform surgical procedures is quickly becoming part of the OD's primary eye care role and, for some, is already second nature.

Mastering the clinical side of surgical procedures is only half of the successful integration into practice; mastering the coding is the other.

Count the Days

Surgical procedures follow their own set of rules, violation of which exposes ODs to the risk of an audit.

The first step to avoiding this is understanding the difference between major and minor surgery, which revolves around the concept of the "global period." The global period, or global surgical package, is a single payment for all care associated with a surgical procedure. Payment is based on the three phases of a procedure: pre-, intra- and post-operative. The difference between major and minor surgeries is the length (in days) of the global period. Any surgical procedure with a global period of less than 90 days is considered minor surgery. Any surgical procedure with a global period of 90 days is major. The rules differ significantly between the two. Let's focus on minor surgical procedures here.

Consolidate Your Codes

The vast majority of procedures performed on the cornea are minor, either with a zero- or 10-day global period. These include epilation (CPT 67820), corneal foreign body removal (65222), corneal debridement or curettage (65435), placement of amniotic membrane without sutures (65778) and occlusion of the puncta, by plug (68761).

In general, these are the rules surrounding minor surgical procedures:

1. There is no pre- or post-op period associated with the code, so the global period is only the date of the surgical procedure itself.

2. Unless special circumstances exist, a separate office visit on the same day as the surgery is not billable or payable.

Billing for that office visit is usually the stumbling block for ODs. The minor surgical codes already include an office visit, so the carrier appropriately denies payment for a second office visit on the same day. Many try to work around this by incorrectly using a modifier, thereby putting themselves at even greater risk of being audited for fraud.

The National Correct Coding Initiative (CCI) edits are explicit in addressing this issue and have remove much of the ambiguity with this. Only "a significant and separately identifiable E&M service unrelated to the decision to perform the minor surgical procedure is separately reportable with modifier 25. The E&M service and minor surgical procedure do not require different diagnoses. If a minor surgical procedure is performed on a new patient, the same rules for reporting E&M services apply. The fact that the patient is 'new' to the provider is not sufficient alone to justify reporting an E&M service on the same date of service as a minor surgical procedure."[1]

This policy addresses the use of CPT modifier -25, one of the most abused modifiers as reported by CMS, with a failure rate to meet necessity burden in more than 30% of claims.[2]

Other CCI edits impact your reporting process when performing multiple procedures on the same day. Consider a patient with a metallic corneal foreign body with a rust ring who requires removal of both and typically would have a bandage contact lens applied. You would think the coding would be: 65222, 65435 and 92071 (fitting of a contact lens for treatment of ocular surface disease).

However, based on the CCI edits, 65222 and 65435 are now bundled together, and you are no longer allowed to bill for the fitting of a bandage lens on the same day as any corneal procedure.[1]

So, for our clinical example, the coding and billing would be 65222-RT/LT (modifiers used to specify right or left eye and must correspond with laterality specific ICD-10), even if all three procedures are performed.

Incorporating surgical procedures into your practice broadens the depth of care you provide your patients and community. As you hone your clinical skills, make sure your coding skills keep pace to avoid preventable exposure and risk. ■

Send your coding questions to rocodingconnection@gmail.com.

1. NCCI Policy Manual 2020.
2. Department of Health & Human Services, Office Of Inspector General. Use of modifier 25. November 2005.

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Prescribing For Young Children

Follow these guidelines to ensure your prescriptions are well suited for this demographic. **By Marc B. Taub, OD, MS, and Paul Harris, OD**

For patients older than seven, we can usually start to incorporate subjective data they provide us into our examinations rather than relying exclusively on objective data. The same, unfortunately, isn't usually true for younger children. This column addresses how to approach refracting and prescribing in this population. Specifically, we will cover the protocols a focus group of optometrists—including us—who work with children helped develop for a handful of different ages. About 40 people came together in an effort to establish a shared evidence base that would act as a foundation for the emergence of clinical guidelines for the visual care of young children.

Don't Get Ahead of Yourself

The group consisted of optometrists who were mostly from the United States, but some came from the United Kingdom, Denmark and Norway. We shared a similar understanding of the process of emmetropization, how the optics of the eye develop in healthy children and how we prescribe today has an impact on the future. Emmetropization should be left to follow its natural progression, and our prescribing should help it along. We only need to prescribe to shift the visual system within an envelope of refractive tolerance, at which point emmetropization takes over from there.

We could not, however, come to the consensus that refractive status of the developing eye and visual system is plastic earlier on in life and the actions we take as optometrists can have large consequences over time. A retrospective study of a large patient population seen at SUNY over many years showed the following refractive trends in infants:[1]

- Less than +2.50D of hyperopia increases emmetropia
- Greater than +2.50D of hyperopia increases hyperopia until 3.5 years of age
- Greater than 3.00D of anisometropia increases the chances of still having anisometropia at age 10 to 90% and the chances of also developing amblyopia to 60%

Infants average almost 3.00D of cylinder at birth, which decreases to about 1.00D by 2.5 to five years of age. When we look at refraction as a whole, infants lose about one-third of their spherical equivalent and two-thirds of their astigmatism by two years of age. For most of this tuning to occur, though, we can't over-prescribe.

Just because you measure it doesn't mean you should prescribe it, especially in a younger child. Prescribing the full refraction earlier on often gets in the way of emmetropization and its active tuning process that helps the optics of the eye put clearer images on the retina.

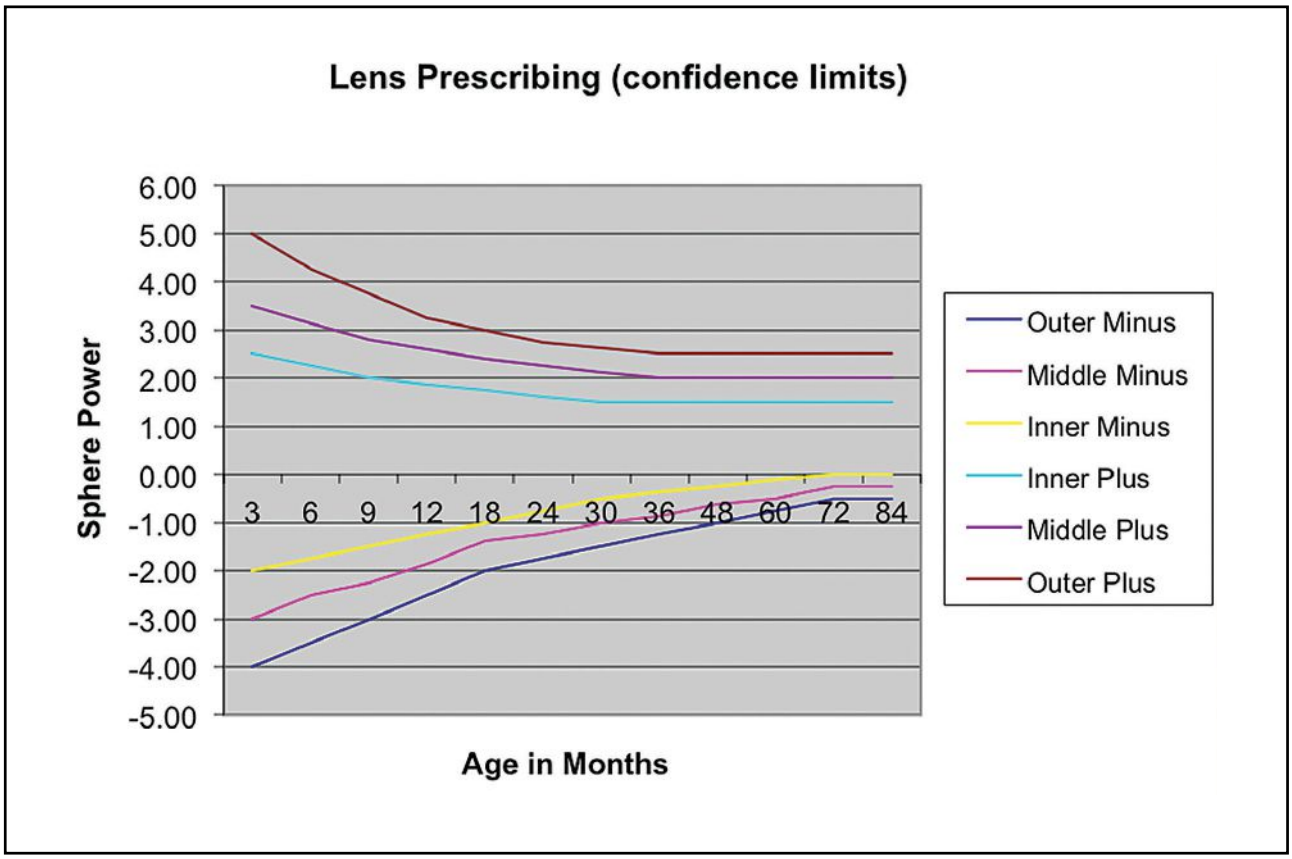
The Break Down

As the graph illustrates, the inner two lines show measurement tolerances. If a child's refraction at that age is inside the lines, we should not prescribe. For example, at three months of age it is advisable not to prescribe if the infant has a spherical power that falls within -1.75D to +2.50D. At 48 months of age, this range shrinks to between -0.25D and +1.50D.

The next most informative lines are the outer two. If a refraction falls outside of these lines, then action should be taken. For example, at three months of age, any hyperope in excess of +4.50D and any myope in excess of -3.50D should not be left alone. Some optometrists require the child to return for at least one additional visit at a different time of day, either with or without cycloplegia, before prescribing.

Between the inner and outer lines on either side of plano, we have a sort of sliding scale with "watch closely" toward the inner line to "take action" toward the outer. A child near the inner line might have to schedule a follow up appointment in four to five months, while a child near the outer line might have to be seen in two to four weeks. Generally, the younger the patient, the shorter the time between follow ups, and the older the patient, the longer the time between follow ups.

Once we decide to act, what



A focus group of optometrists who work with children came up with these guidelines to follow when prescribing for younger patients.

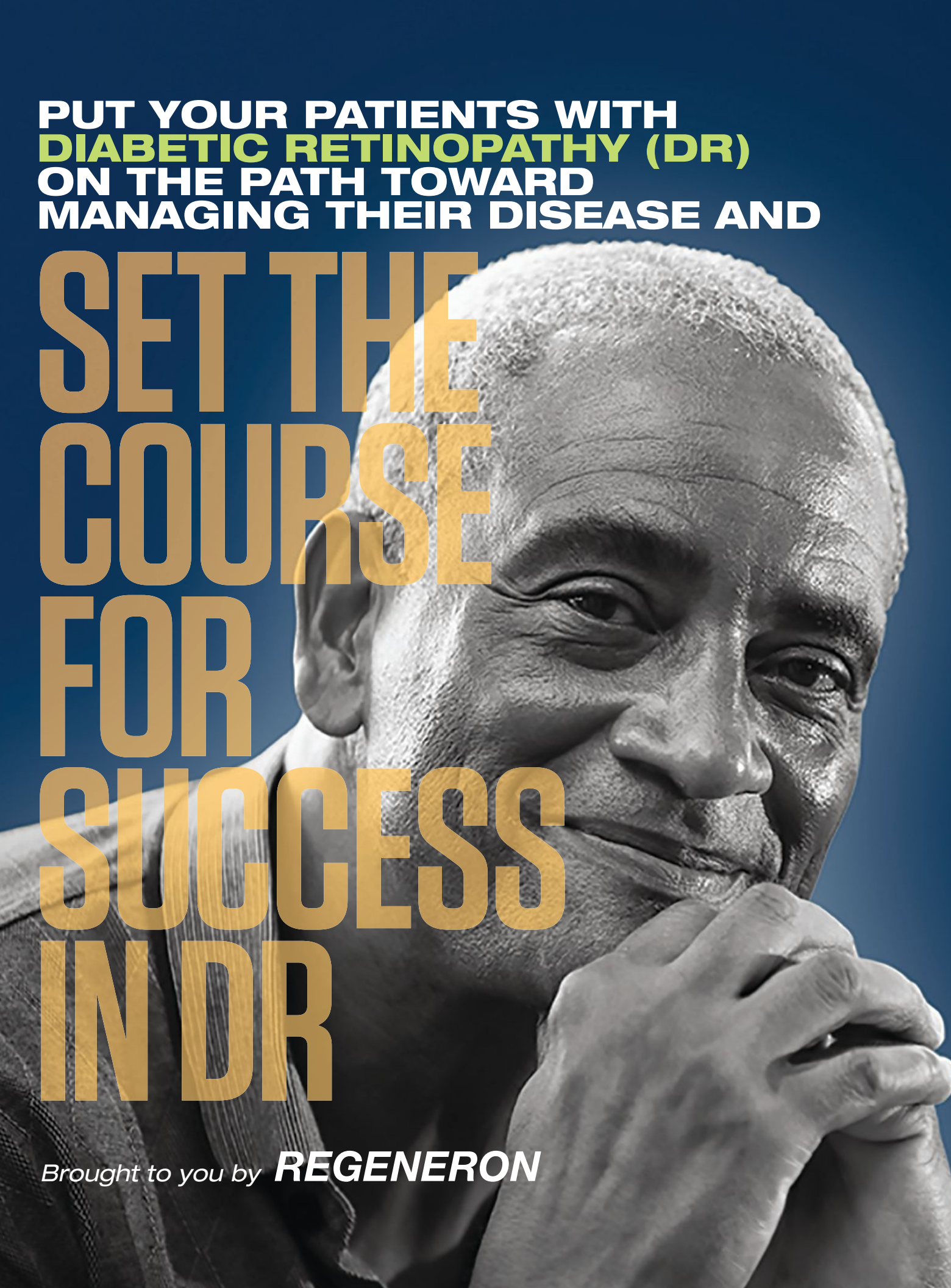
actions should we take and to what extent should we react? If we are prescribing a patient's first pair of glasses, it is advisable to shift the situation toward the inner line without fully correcting the refractive error.

For example, assuming both eyes are the same, let's say we measure +5.00D in an 18-month-old whose eyes are straight and demonstrate good binocularity. Looking at the top portion of the graph, the outer line is at about +3.00D and the inner line is at +1.75D for an 18-month-old. The minimum lens we might give would have a spherical power of +2.00D, which would require the patient to have to supply +3.00D of accommodation to see clearly at distance. This is when the emmetropization process kicks in and helps reduce the hyperopia over time. The maximum lens needed to stabilize the system, leaving +1.75D uncorrected, would be +3.25D. At this level of correction, with little chance of emmetropization, we should expect the total amount of hyperopia to remain the same.

Thus, our range is from +2.00D to +3.25D, with the +2.00D activating the refractive tuning mechanisms maximally and the +3.25D simply stabilizing the system in place. Each case is different, but the lenses prescribed for this particular patient should live between these two values. Schedule a follow up sooner the closer to +2.00D you prescribe (three to four months) and further away the closer to +3.25D you prescribe (five to six months). The hope is that by focusing less on the hyperopia at first, emmetropization will partially correct it over time.

Pay attention to these general guidelines and refer back to our graph findings when seeing and prescribing in younger patients. For concrete, real-world cases that show our evidence-based clinical protocols in action, stay tuned for our next installment. ■

1. Sethee SK, FitzGerald DE, Krumholtz I. Exotropia in a pediatric population less than six years of age. J Behav Optom. 2003;14(6):149-57.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Educate your patients about the severity of DR, especially when left untreated[3,4]

- Your early and frequent discussions about disease progression, treatment options, and referral will empower patients, which could help them avoid significant vision loss[3,4]

According to the AOA, you should refer patients with[3]:

- Severe nonproliferative DR (NPDR) within 2 to 4 weeks
- Proliferative DR (PDR) within 2 to 4 weeks
- High-risk PDR with or without macular edema within 24 to 48 hours

Ensure patients have followed up with a retina specialist who can treat DR

Monitor your patients with DR[3,4]

The AOA recommends frequent monitoring of patients[3]

- At least every 6 to 8 months in patients with moderate NPDR and more frequently for patients with greater disease severity[3]

Refer patients to a specialist who can treat DR[3,4]

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AOA = American Optometric Association.

References: 1. Diabetic Retinopathy. Centers for Disease Control and Prevention website. http://bit.ly/2BKTVCTS. Accessed August 7, 2019. **2.** 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. **3.** Care of the Patient With Diabetes Mellitus: Quick Reference Guide. American Optometric Association website. http://bit.ly/2M22OUJ. Accessed August 7, 2019. **4.** Ferrucci S, Yeh B. Diabetic retinopathy by the numbers. *Rev Optom*. June 15, 2016. http://bit.ly/2KNNJ4E. Accessed August 7, 2019.

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Corneal Disease Report

Foreign Body Removal Start to Finish

These patients are in need of help—quickly. Here's how to prepare your office.

By Cecelia Koetting, OD

Located in a city with a large shipyard, our office has its fair share of foreign body removal patients. Although incidence and severity are lower with the use of proper protective eye wear, accidents still happen. According to the National Institute for Occupational Safety and Health (NIOSH), each day approximately 2,000 American workers have a job-related eye injury requiring medical treatment.[1] NIOSH estimates that 90% of these injuries could be prevented or less severe if the correct eye protection was used.[1]

It is important for both you and your office staff to feel comfortable handling these emergency patients who require foreign body removal—from start to finish. This article discusses the step-by-step process of triaging, scheduling, examining, treating and following patients with a foreign body.

Office Prep

Most optometrists have all the tools they need to care for patients with corneal foreign bodies. The entrance tests are common practice for other conditions and include extraocular motilities, pupillary testing and confrontation visual fields. Abnormalities in these could be further indicators of orbital/globe penetration or full penetrating foreign bodies.

Other standard tests for suspected foreign body include documenting the entering visual acuities prior to any procedure and noting any pre-existing issues of amblyopia or decreased vision.

For all initial testing, train technicians to handle foreign body removal patients with "no touch" to avoid further irritating the eye

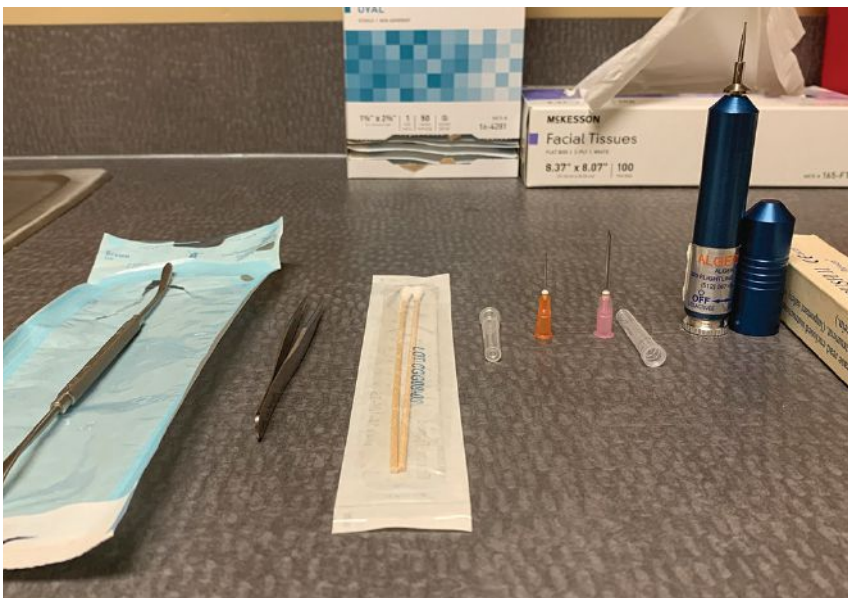


Fig. 1. The foreign body removal toolkit includes a spud, jeweler's forceps, cotton swabs, small-gauge needles and an Alger brush.

or the cornea. Ocular pressures can be checked after the slit lamp exam has been performed, ensuring it is safe. If the foreign body is embedded within the cornea centrally or there is concern for an open globe, it may be best to avoid checking the pressure.

During the slit lamp exam, a topical anesthetic will keep your patient more comfortable, while sodium fluorescein and a cobalt blue filter will help you examine the eye and detect any foreign bodies, wound leakage or a full penetrating injury. If the patient is struggling to keep their lids open, a lid retractor or lid speculum may be necessary.

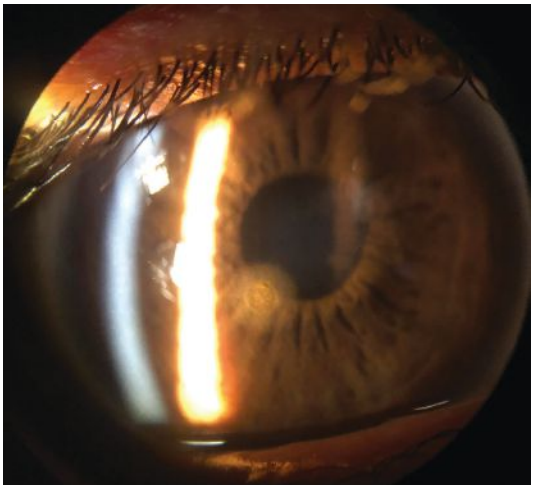


Fig. 2. This is a patient's cornea immediately after removal of a metallic foreign body but prior to rust ring removal. The object was superficial enough that it was removed with a sterile cotton swab after anesthetizing the patient's eye.

Clinicians should stock a few different handheld tools in the office to remove various foreign bodies (*Figure 1*):

• ***Superficial or loosely embedded cornea and conjunctival foreign bodies –*** The simplest method to remove loose pieces of material may be using only irrigation with sterile saline solution. If that isn't sufficient, a sterile cotton swab, spatula, spud or a small 25-gauge needle are all useful options. A magnetic spud is quite useful for metallic foreign bodies because you can often remove the object—and any residual metallic flakes—with little to no damage.

• ***Deeper within the corneal stroma –*** A spatula, spud or a 25-gauge needle are also good options here; while a spud or spatula reduces the risk of perforation, a needle often causes less damage to surrounding tissue.

• ***Protruding corneal and conjunctival foreign bodies –*** While any of the other methods mentioned may also be used, jeweler's forceps is an excellent option, as it may allow you to grasp the edge of the object and remove it.

• ***Corneal rust ring –*** This will require an Alger brush to remove.

In addition, stock a topical antibiotic to apply before and after any procedure to ward off infection.

Initial Encounter

When a patient calls or walks in complaining of a foreign body sensation, your front desk staff must understand what to ask the patient to triage and make sure they are seen or referred promptly. Front office and call center staff should begin the patient encounter, whether in person or on the phone, with the tried-and-true five Ws: who, what, where, when and why. These help to ensure patients who need urgent care get it, and those who don't can be scheduled accordingly.

For example, a patient who calls saying something got in their eye while doing yardwork yesterday requires different treatment than a patient who had the same thing happen to them a month ago. The latter situation is far less urgent and is less likely a true foreign body than the patient who sustained an injury the day before.

Patients who mention additional injuries related to the incident may require further testing or treatment. Head trauma requiring imaging or sutures should be sent to the emergency room to address those injuries first. However, keep in mind that MRI is contraindicated for patients with a suspected metallic foreign body. With their serious injuries cared for, the patient can be seen back regarding the ocular foreign body if it wasn't treated concurrently in the emergency room.

The five Ws can also help to correctly identify patients who may have had a work-related injury associated with a worker's compensation case. These situations often require extra paperwork to

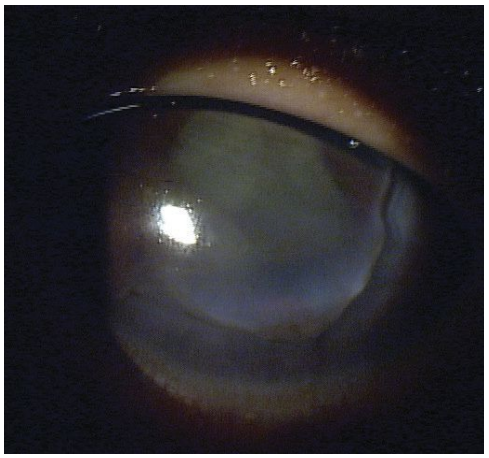


Fig. 3. This 13-year-old boy was hit in the eye with his pencil in school, leaving a laceration from 2 o'clock to 9 o'clock. It was pressure patched and seen by cornea specialist, who glued the cornea until the patient could get into the surgical suite, where the surgeon placed 20 sutures to close up the wound.

Fig. 4. Here is what you will typically need when removing a corneal rust ring with an Alger brush: start with topical proparacaine along with a broad-spectrum topical antibiotic. After the procedure is complete, instill a second drop of antibiotic into the patient's eye.

document the details. During documentation, also note if the patient was wearing appropriate personal protective eyewear.

In the Chair

Once you are sitting down with the patient, have a detailed discussion with them to understand what exactly is in their eye and how it got there. Depending on the type of foreign body and the timeline, there may be a concern for secondary infections. Patients with suspected vegetative matter warrant higher concern for the development of a fungal corneal ulcer, while a metallic object could cause a rust ring or, more rarely, introduce infectious material leading to bacterial keratitis.

We also know that the longer the foreign body is in the eye and there is an open abrasion, the higher the risk of developing bacterial keratitis that could lead to an ulcer or even an anterior chamber reaction.[2] A study of patients with corneal abrasions due to ocular foreign bodies found that no patients who were seen in clinic within 18 hours of the ocular injury and started on prophylactic antibiotic ointment developed an ulcer.[2] However, of those who presented 19 to 24 hours after injury, 3.7% developed an ulcer and 28.6% of those seen between 24 and 48 hours after developed an ulcer.[2]

A thorough slit lamp exam will help you determine if the foreign body is still there, its location, depth within the ocular tissue and if it has fully penetrated the cornea (*Figure* 2). If available, anterior segment OCT can be useful in identifying the depth of the foreign body.[3] Patients with a foreign body or abrasion are typically light sensitive and in pain. Instilling a drop of ocular topical anesthetic will help you perform the slit lamp exam.

Make sure to stain the patient's eye with sodium fluorescein and use a cobalt blue filter to check for multiple vertical lines on the cornea (tracking patterns) or conjunctival abrasions that may indicate trapped foreign material under or within the lid. Also evert the patient's lid to visualize all fornicies and ensure no trapped material is causing further corneal damage or later lodge itself within the cornea.

If the injury occurred from a high-velocity impact or while grinding, it is important to dilate to look for signs that the foreign body has fully penetrated the cornea or globe. Conjunctival penetration is easier to see because there will typically be an area of injection and chemosis surrounding the entrance point. When a conjunctival foreign body or full penetration of the cornea or globe is suspected, check the patient for a positive Seidel's sign with sodium fluorescein and cobalt blue light filter. Another indication of full penetration with a wound leak would be decreased intraocular pressure or a shallow anterior chamber.

When looking at the entrance wound on the cornea, check for tracks or disrupted tissue through the cornea stroma or endothelium. An object that has penetrated the ocular lens typically leaves a mark on the anterior portion of the lens, possibly damaging the iris—a wound that can be viewed with iris transillumination.

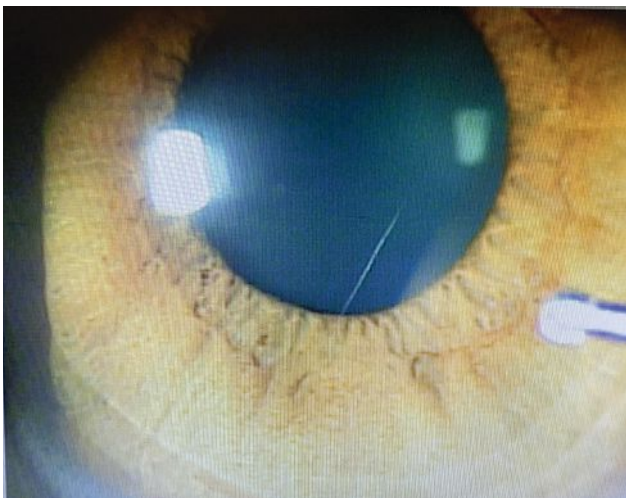


Fig. 5. When removing the rust ring from the cornea with the Alger brush, make sure to approach tangentially. This allows for better control of the instrument and pressure applied to the cornea.

Dilation aids in seeing these lenticular marks and helps us visualize the back of the eye to look for the retained object. If you suspect a penetrating intraocular foreign body but cannot directly visualize it, consider sending the patient for orbital radiographs,

B-scan or computed tomography to identify and pinpoint the object.[4] However, this is not mandatory and may not be a practical use of resources in all cases.

Removal Step-by-step

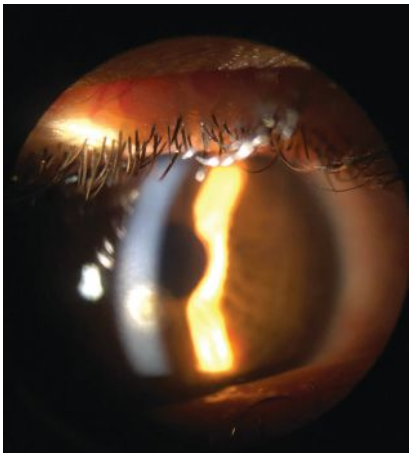
While most of us learned how to remove a foreign body during our education, its rarely an everyday occurrence. Many regional and national conferences provide workshops to help those who feel the need for new or additional training. Before performing any procedure, consult your state law and scope of practice to make sure that you are practicing within your guidelines.

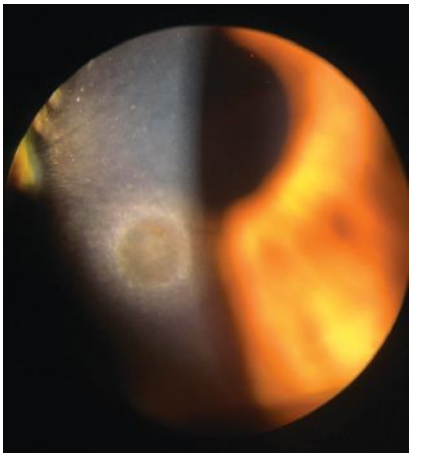
Before you begin, discuss the steps of the procedure with the patients to reduce their anxiety. In addition, obtain written consent or document in the chart that the patient verbally consented to the treatment plan. If a patient has poor cooperation or is struggling to keep their eyelids open, a lid speculum can help. Have the patient fixate on a target with the opposite eye to help the eye still. Instill a topical anesthetic and a broad-spectrum topical antibiotic.

The location and type of foreign body will often determine how you remove them. Most of us have a preferred method and instrument that we feel comfortable using to remove foreign bodies.

Superficial or loosely embedded corneal foreign bodies are often easily removed with a sterile cotton swab, spud or a small-gauge needle.

If the foreign body is deeper within the corneal stroma, use a spud or 25-gauge needle. Using the patients' forehead for stability, hold the needle head tangentially to the cornea with the beveled tip up, away from the cornea. Place the tip underneath the anterior projection of the foreign body and carefully tease it out. Once dislodged from the stroma, the object can be removed from the surface with a cotton swab or forceps.





Figs. 6 and 7. This patient is being seen at follow-up after a metallic foreign body was removed. While the epithelium has fully healed, there is a remaining rust ring.

Depending on the practitioner's comfort level, they should consider referring patients to a cornea specialist. In cases where there is full globe or corneal penetration or a concern for vision-threatening scarring, it is advantageous to consult with a cornea specialist regarding any further treatment or surgical procedures to reduce scarring (i.e., lamellar keratectomy).

Depending on the angle and size of the foreign body, jeweler's forceps are helpful in cases where the object is protruding from the cornea where an edge is easily accessible or when the foreign body is small such as a splinter or fiberglass.

If, during the slit lamp and dilation or with anterior segment OCT, you determine the foreign body is full penetrating, consult a surgeon for treatment and removal. If the patient has a positive Seidel's sign or suspected open laceration, give them a drop of topical antibiotic, pressure patch them to reduce the flow of the leaking aqueous and refer immediately (*Figure 3*).

Metallic foreign bodies containing iron may leave behind a rust ring in as little as three to four hours.[5] In the event that a rust ring forms, removal is performed using an Alger brush (*Figure 4*). Use a clean sterile tip and approach the area tangentially with the brush to better control the tool (*Figure 5*). Any remaining rust ring could cause inflammation and slow or even prevent healing of the corneal epithelial defect. When the rust is deep within the stroma, the patient may require a second treatment with the Alger brush during the follow-up visit to remove the entire rust ring (*Figures 6 and 7*). However, it is better to remove the entire ring on the initial visit, whenever possible, to reduce the necessity of retreatment.

When the foreign body seats itself within the conjunctiva, clinicians may be able to remove it in-office without surgery (F*igure 8*). The entering wound, if shallow and recent, sometimes functions as an access point for removal with jeweler's forceps. If it has been more than 48 hours or the material is seated too deeply, the removal may require incision and possible sutures and, in some cases, may warrant a referral.

Bacterial cultures are not routinely performed on patients with

corneal foreign bodies without a stromal infiltrate. One study found that only nine of 63 tested corneal foreign bodies were positive for bacteria.[6]

After any foreign body removal, scan the patient's eye to ensure no other possible foreign bodies are present and document the extent of the patient's treatment area.

Most importantly, educate the patient prior to leaving the office regarding proper protective eye wear to help decrease the likelihood of re-occurrence. Discuss not only what is considered proper protective eye wear but also when they should be wearing it (e.g., yard work, working on cars, grinding, cutting).

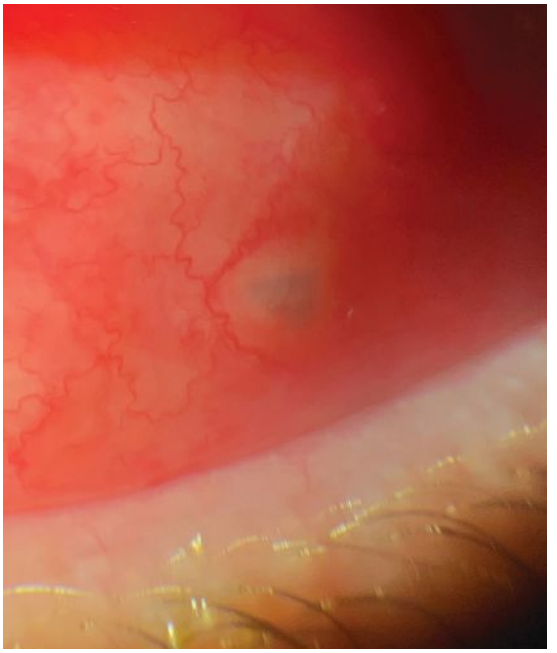


Fig. 8. This patient presented to the office within eight hours of being hit in the eye with a tree branch. A piece of bark had lodged itself under the conjunctiva. The foreign body was removed with forceps through the entry point with no sutures needed.

Homework

Patients should be started on a topical antibiotic immediately following the removal of the foreign body. Typically, a broad-spectrum topical antibiotic drop such as a flouroquinolone QID is appropriate, given the patient has no allergies. In the case of conjunctival involvement or large abrasions, the patient may be more comfortable using an ophthalmic antibiotic ointment such as tobramycin or Polytrim (polymyxin B/trimethoprim, Allergan) BID to QID. If vegetative matter involvement is suspected and a fungal ulcer is present, the patient should be started on topical and oral anti-fungal medication.

Pain management for these patients can vary depending on situation and the patient. The use of a therapeutic bandage contact lens, while not necessary, can provide sufficient relief but should be avoided if there is any formation of secondary ulcer at the time of exam. Some patients find comfort from pressure patching the eye, although this can be cumbersome with the requirement of frequent ocular drops. To avoid this, it is preferable to use ophthalmic antibiotic ointment, instilled prior to pressure patching. Topical nonsteroidal anti-inflammatory agents can aid in pain management, as can atropine.

Oral analgesics and anti-inflammatory medications such as Tylenol and ibuprofen may be added as needed. The use of narcotics can be considered on a case-by-case basis in appropriate patients but is often unnecessary.

Patients with larger lesions and those with a bandage contact lens or pressure patch should have a follow up in 24 hours. Smaller or peripheral lesions can have an extended follow up of up to a week for non-complicated cases if no ulcer or infection is present. When an ulcer has formed or infection is present, the patient should be seen the next day to monitor for improvement.

Amniotic membranes or amniotic drops can also be considered for patients with deep central foreign bodies.[7] If the patient's injury was due to vegetative matter, it is important to watch for possible infiltrate and ulcer development prior to starting any steroid, as this will worsen a fungal infection.

Knowing how to help established or new patients with an urgent foreign body situation is essential for your community and your practice. The need for foreign body removal is a common and frequent complaint. As optometrists, we should feel comfortable in treating, or in the very least, triaging these patients. Once you establish yourself as knowledgeable and competent, you will enjoy increased personal fulfillment—and referrals. ■

Dr. Koetting is the referral optometric care and externship program coordinator at Virginia Eye Consultants in Norfolk, VA. She is a fellow of the American Academy of Optometry and a trustee of the Virginia Optometric Association.

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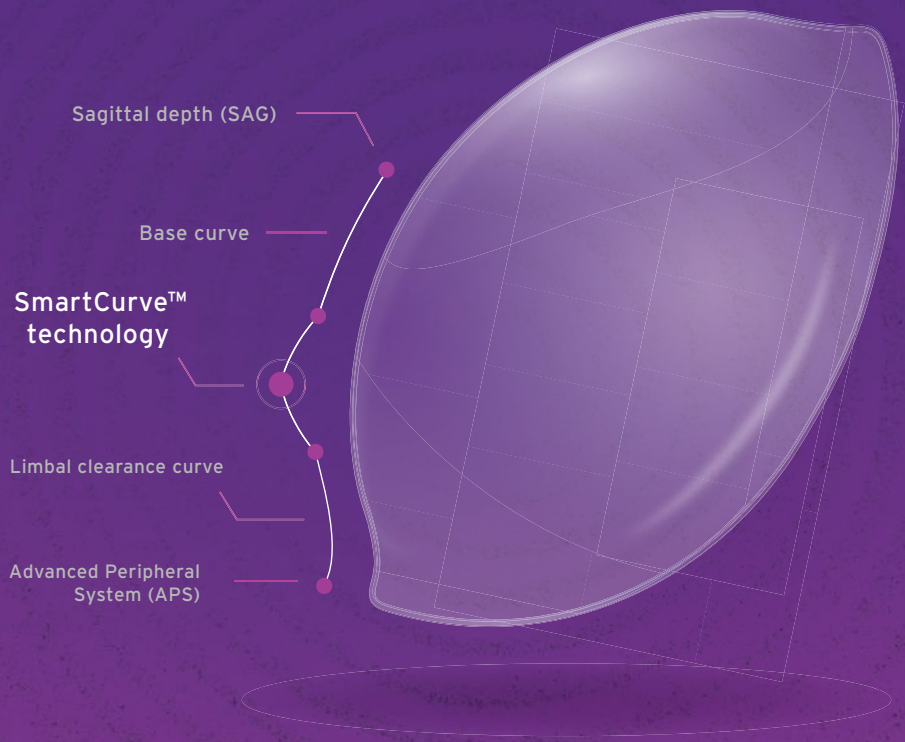

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Corneal Disease Report

A CXL Guide For the Surgically Savvy

Here's what you need to know about the procedure—what it can do, who can do it and what the future might hold. By Catherine Manthorp, Associate Editor

Patients with thin corneas susceptible to warpage and steepening had little more than corrective lenses and high-stake surgeries to turn to up until a few years ago. It's no surprise, then, that corneal collagen crosslinking (CXL), approved in the United States in 2016, has been widely hailed as a quantum leap forward in the management of progressive keratoconus and, to a lesser extent, post-LASIK corneal ectasia.[1] For the majority of patients, CXL slows disease progression and prevents further visual acuity loss, advanced disease and corneal transplantation, according to John Gelles, OD, who works at an OD/MD practice in Teaneck, NJ. Although CXL is not intended to cure keratoconus, reduce its severity or improve vision, the latter two have been documented, albeit inconsistently, in the literature.[1]

"This treatment holds great therapeutic value for corneal diseases associated with reduced biomechanical strength, such as keratoconus or corneal ectasia following refractive surgery," remarks Clark Chang, OD, of Wills Eye Hospital in Philadelphia. But doctors who practice in the United States are playing catch-up. "Due to the late adoption of CXL in the United States, clinical use of this important treatment is still slowly emerging," says Dr. Chang.

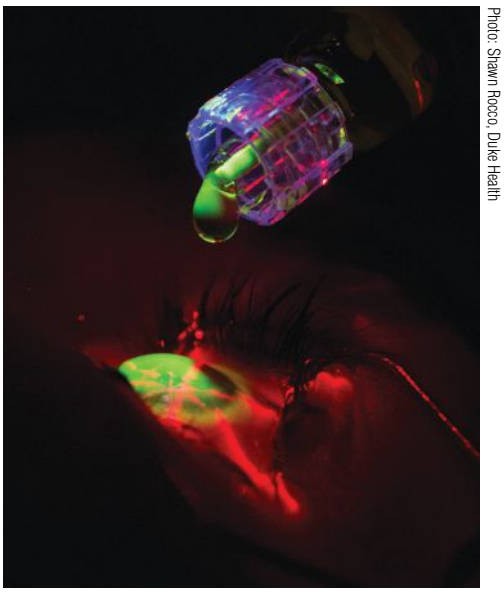

Photo: Shawn Rocco, Duke Health

UV light is applied to the eye of a CXL patient.

As the procedure gains traction in the United States, researchers and clinicians are pushing forward with experimental new treatment protocols, techniques and indications. If you're interested in comanaging these patients, here are insights from ODs and MDs well-versed in what CXL offers today and how it might evolve over time.

Laying Down Roots

The corneal stromal can become thin either from pathologic processes (e.g., keratoconus, pellucid marginal degeneration) or iatrogenic ones, most notably LASIK surgery. Ectasia occurs when the thinning is severe enough to cause distension of the cornea—especially the cone-like bowing that gives keratoconus its name—resulting in refractive shift and, in severe cases, risks to the structural integrity of the eye. Crosslinking seeks to strengthen the bonds between the remaining collagen fibrils to

mitigate this process. After bathing the cornea in riboflavin, a dose of UV light catalyzes a reaction that creates reactive oxygen species, which then form new covalent bonds among stromal fibrils. The cornea remains thin but, hopefully, emerges stronger than before.

First developed about 20 years ago in Europe, CXL has been a mainstay of treatment throughout Europe for the last 15 years and around the rest of the world for a decade, according to Christopher J. Rapuano, MD, chief of the Wills Eye cornea service. Drs. Rapuano and Chang have been involved with CXL research since 2008. At that time, the influx of data on success of the 'epi-off' technique, which requires debridement of the epithelium, in other countries led the United States to pursue this protocol for FDA approval. Epithelium removal improves penetration of riboflavin but, as can be expected, results in significant pain for patients during the healing phase.

In 2016, the KXL system from Avedro (now part of Glaukos) became the only FDA-approved collagen crosslinking device in the country thus far.[2] The data that led to the device's approval showed that, on average, the maximum keratometry values of patients with progressive keratoconus decreased by 1.60D one year after the procedure.[3]

Since then, the technique continues to find success in halting keratoconus progression in the majority of patients, with most studies suggesting control of progression in more than 90% of treated participants.[4] A small percentage continue to experience progression after CXL, which Dr. Rapuano suggests could be due to eye-rubbing—a significant risk factor for progression—or severe disease.

Making Links

The procedure, while relatively simple, requires upwards of two hours of chair time for the patient, according to Dr. Rapuano. Here, he outlines the procedure steps he and his team follow:

- Numb the eye with topical anesthetic, instill antibiotic drops and lay the patient down.
- Sterilize the area around the eye with povidone-iodine, and apply an eyelid speculum.
- Use a semi-sharp blade to remove the epithelium (~10mm diameter, a technique known as epi-off or the Dresden protocol), and then remove the lid speculum.
- Administer riboflavin drops every two minutes for 30 minutes.
- Sit the patient up and, behind the slit lamp, check that the riboflavin has been absorbed throughout the cornea and into the anterior chamber.
- Lay the patient back down, and check corneal thickness. If the measurement is not at least 400µm, the next step is to apply hypotonic riboflavin drops every five to 10 seconds for as long as it takes the cornea to reach this parameter, which could mean an additional 20 minutes for some.
- Once the eye is prepped, apply ultraviolet (UV) light to the cornea for 30 minutes while administering riboflavin and numbing drops periodically. The care team must make sure the UV light is centered on the eye and the limbus is protected from any extraneous UV, advises Dr. Rapuano.
- Upon completion of the procedure, rinse off the riboflavin, put in a bandage contact lens and clean off the povidone-iodine.

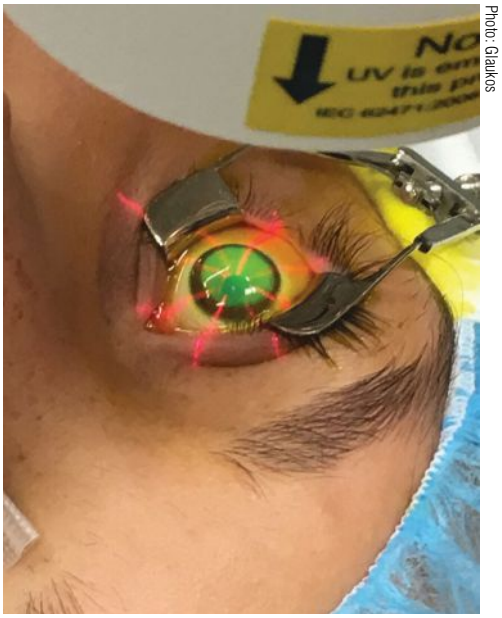

Photo: Glaukos

In this part of the procedure, UV light is focused on the eye for 30 minutes.

Dr. Rapuano performs the entire procedure personally but may ask a technician to administer some of the riboflavin drops. He emphasizes the importance of operating the UV light device himself "because I think that's kind of the critical part of the procedure."

Patients should expect discomfort for a few days post-op, with vision returning to baseline within one to three months. During the first few postoperative days, Dr. Rapuano says it's important that they use ice packs and over-the-counter pain medication, antibiotics and a bandage contact lens for the corneal epithelial defect and steroid drops for the inflammation.

Dr. Gelles suggests scheduling follow-ups at one day, four to five days and one, three, six and 12 months. He notes the first visit is aimed at ensuring there are no obvious complications, while the second is to remove the bandage lens and confirm epithelial healing. The later visits allow clinicians to evaluate changes to baseline measurements.

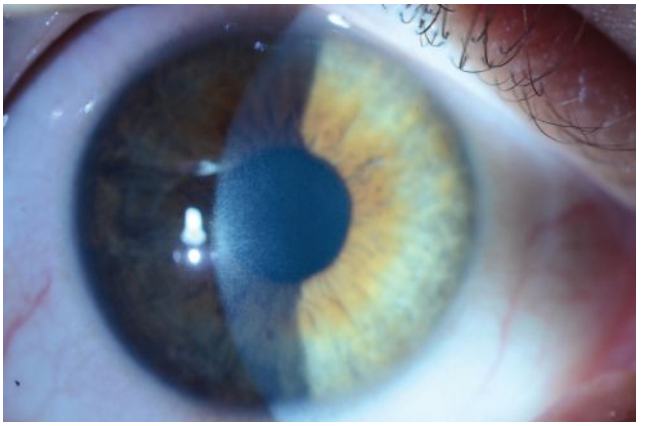

Photo: Christopher J. Rapuano, MD

Mild stromal haze can be seen one month after epi-off CXL.

"Though rare, we have seen patients who have been lost to follow-up after CXL treatment only to return with a more advanced disease state," says Dr. Gelles. "The need for appropriate follow-up on these patients cannot be overstressed. Continuous monitoring, despite treatment with CXL, is extremely important."

Shortcomings and Complications

The current technique has seen some updates to shorten procedure duration, reduce recovery time and create a more robust effect. Still, it's not perfect.

"Removal of the epithelial tight junction was thought to permit better riboflavin penetration into the corneal stroma, although it also increases the risks for potential complications," according to Dr. Chang. While the benefits of CXL are well documented, the technique is associated with certain drawbacks that, when not managed appropriately, may mean the difference between a satisfied patient and an unsuccessful outcome.

Procedural risks could include infectious or non-infectious keratitis, corneal haze or opacity and persistent epithelial defects, says S. Barry Eiden, OD, a keratoconus specialist from Chicago and president of the International Keratoconus Academy. He adds that some patients may struggle with the post-op healing process and experience challenges with discomfort or pain, slow visual recovery, corneal shape changes requiring a contact lens or spectacle refitting and the initial inability to wear contact lenses.

The riboflavin solution causes stromal dehydration, which elevates the risk of scarring, swelling and melting; Dr. Rapuano includes these possibilities in what he characterizes as a 1% chance of complications. "That 1% is why we don't do CXL on everyone with keratoconus who walks in," he says. "If they're not progressing or getting worse, then we don't want to take even a small 1% risk of creating a bigger problem."

CXL may halt disease progression, but it doesn't answer the patient's visual needs, Brian Chou, OD, of San Diego, notes. "CXL is a defensive play against progression, while specialty contact lens care is an offensive play to bring out maximal vision," he remarks. This is why it is important for the patient and practitioner to carefully weigh the benefits and risks of CXL.

According to Dr. Chou, improving practitioner understanding and setting patient expectations go hand-in-hand for success with CXL. Some advocates overlook the fact that the procedure may not help keratoconus patients who have already achieved disease stability in older age or those with advanced distortion, he says. Those in their teenage years to early 20s whose keratoconus is detected soon after onset stand to reap the greatest value of CXL, explains Dr. Chou.

Potential Improvements

The rest of the world remains a few steps ahead of the United States, with access to protocols that allow transepithelial (or 'epi-on') CXL, accelerated CXL (which delivers higher doses of UV over a shorter time period) and other already well-known procedure options. But these are most likely headed to our shores eventually. "Now that epi-off CXL study data is well-established, many clinical trials are investigating the comparative treatment efficacy of different delivery protocols with the purpose of improving the overall patient experience," Dr. Chang notes.

Here's a quick look at each:

Epi-on. One study found that an investigational crosslinking protocol avoiding epithelium removal can safely stop disease progression in corneas as thin as 302nm and may offer faster visual recovery than other methods. The researchers used a new riboflavin formulation and application technique and a pulsed dosing of UVA to allow better oxygen transmission into the cornea.

They observed improvements in uncorrected and corrected distance visual acuities (DVA), total higher-order aberrations and coma and maximum keratometry values. There was no progression or loss of effect, nor did the team note any complications. Participants were only uncomfortable for 24 hours post-op, with blurred vision lasting two to three days and contact lens wear resuming within a week.[5]

Also looking into oxygen flow—this time for the epi-off technique—a team found that increasing oxygen concentration around the cornea during UVA radiation can improve the efficacy of conventional CXL.[6]

Accelerated. Other studies are looking into protocols employing a stronger UV light for less overall treatment time. Conventional CXL uses 3mW/cm for 30 minutes, while research into the accelerated technique documents anywhere from 9mW/cm for 10 minutes to 30mW/cm for four minutes.[7] Investigators found that both accelerated protocols and conventional CXL had similar visual acuities, refractive outcomes and stabilization rates, although more parameters showed significant improvements 12 months after the standard protocol. While their results are promising, they also indicate the need for a better understanding of the effects of accelerated CXL.[7]

Around the same time, another team confirmed that accelerated CXL is a contender for keratoconus treatment, finding that the technique can safely halt progression within 24 months.[8] After two years of follow-up, they observed an increase in the number of eyes with a corrected DVA of 0.3logMAR and a significant reduction in maximum and mean keratometry values.[8] Other researchers demonstrated that the accelerated procedure is also associated with less corneal haze and a smaller risk of continuous flattening.[9]

A new method known as custom fast CXL does not disrupt the epithelium and features 15 minutes of corneal presoaking with a riboflavin-vitamin E solution and a 370nm UVA radiation beam centered on the most highly curved region of the cornea. The study noted "a significant, rapid and lasting cone progression stoppage, astigmatism reduction and visual acuity improvement."[10]

Accelerated CXL may also aid in keratitis therapy. Researchers have recommended a technique called photoactivated chromophore for keratitis (PACK) CXL to treat moderate-sized, therapy-resistant bacterial corneal ulcers.[11] The same reactive oxygen species that create new covalent bonds within the stroma have the added benefit of killing pathogens in the treated area; also, the stronger cornea is more resilient against pathogenic attack.

Another group of investigators provided further support for adjuvant PACK-CXL, finding that the procedure can expedite the resolution of infectious keratitis with bacterial or fungal etiologies by reducing healing time and infiltrate size.[12] PACK-CXL's usefulness may extend to fungal keratitis treatment as well, especially when combined with voriconazole therapy, a different study proposed.[13]

Combinations. Accelerated CXL may not provide any added benefits when combined with LASIK, though. A team looking into the efficacy of combining the two did not find any difference between the combination procedure and conventional LASIK in uncorrected DVA or refractive stability.[14]

Other simultaneous procedures involve CXL and corneal rings or photorefractive keratectomy (PRK). These may present effective options for keratoconus and other corneal ectasias, researchers suggest. They found that the changes in corrected and uncorrected DVA and maximum keratometry values were significant for both combinations. The team concluded that combined CXL and ring implantation may be more effective for eyes with irregular astigmatism and worse corrected DVA, while CXL and PRK may be more useful for eyes with irregular astigmatism but better corrected DVA.[15]

Another study looking into CXL combined with topography-guided PRK warned against the swift adoption of this procedure for keratoconus after observing various complications and continuous progression post-op. Adverse events included corneal haze, primary herpes simplex keratitis, persistent epithelial defects and central corneal stromal opacity. Related to removal of the epithelium were post-op pain, photophobia, lacrimation, foreign body sensation and healing difficulties.[16]

Combination procedures may be beneficial beyond keratoconus, with investigators reporting that

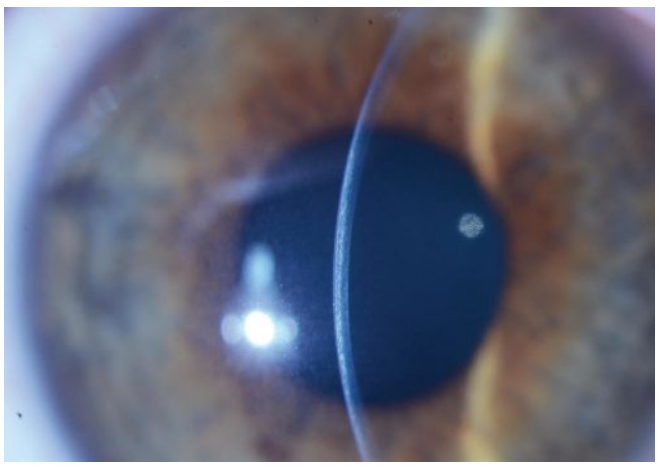

Photo: Christopher J. Rapuano, MD

The slit beam in this patient demonstrates a demarcation line at about 50% to 60% corneal depth.

Many Hands Make (UV) Light Work

So far, only ophthalmologists can perform CXL and, as would be expected, most practitioners are cornea and refractive surgery specialists.

Where the procedure stands within optometric scope of practice is a little hazier and depends on specific state licensure. Dr. Chou says there is speculation that if CXL expands to include an epi-on approach, it may fall within the scope of optometric care for some states. Eliminating the need to debride the cornea raises the potential for optometrists in all 50 states to qualify to perform CXL if further legistion is enacted.

Even if optometrists are not performing the procedure themselves, Dr. Eiden believes they are crucial members of the treatment team. Early disease and progression detection, timely treatment referral and proper follow-up scheduling, post-op care and visual rehabilitation with contact lenses all fall within the scope of optometry and play a critical role in optimizing visual outcomes.

performing transepithelial phototherapeutic keratectomy simultaneously with accelerated CXL may be an effective treatment option for pellucid marginal degeneration. Among the study's highlights were improvements in cylindrical value, spherical equivalent value, keratometry value, corneal thickness and the occurrence of myriad adverse events.[17]

A Bright Future Ahead

"I see the field of CXL moving in the direction of less invasive forms of treatment with better safety profiles, lower complication risks, faster visual recovery times and the ability to return to contact lens wear relatively quickly," Dr. Eiden says. He suggests CXL refinement will improve the treatment's predictability and make it a good option for combination procedures.

In addition to anticipating an epi-on technique for United States CXL procedures, which would significantly improve post-op comfort, Dr. Chou foresees other advances, such as use of iontophoresis to draw riboflavin into the corneal stroma and variable patterns of UV light with intraoperative oxygen supplementation to enhance crosslinking. Avedro currently markets this overseas as photorefractive intrastromal crosslinking (PiXL).

Dr. Chang adds that CXL could eventually incorporate topography-guided technology to deliver different treatment plans across different corneal areas, which may produce more corneal regularization and refractive benefits. Avedro calls this the customized remodeled vision (CuRV) in international markets.

As for the prospect of epi-on CXL with an accelerated and pulsed UV light device, Dr. Chang believes that by keeping most of the epithelium intact and shortening CXL treatment time with a higher-energy light, patients may be more comfortable during the early post-op period and have a quicker visual recovery. Dr. Rapuano, however, mentions significant issues with epi-on that must be overcome first, including how the epithelium prevents riboflavin absorption, UV light transference and oxygen transmission, which are all necessary for CXL success.

CXL has come a long way from its humble origins in 1997.[18] New protocols, techniques and indications are shifting the procedure out of the periphery and into the mainstream. They may, one day, also move the procedure within an expanded scope of optometric practice. Now's the time to start preparing for this possibility. ■

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Corneal Disease Report

PEER • REVIEWED • PRA • ARTICLE •

Understanding Corneal Nerve Function —and Dysfunction

These ocular structures are crucial to ocular health, and knowing the conditions that affect them will help optometrists better care for their patients. **By Lindsay Sicks, OD**

Corneal nerve structure and function have been extensively examined both *in vivo* and *ex vivo*.[1] A solid understanding of these factors will help clinicians recognize the signs and symptoms of corneal nerve damage and assist them in making the proper diagnosis. It will also help them initiate treatment, when appropriate, for ocular surface disease, ocular pain and corneal disease, infection or trauma.

Structure & Function

The corneal nerves begin to form at five months gestation in humans, as neural crest cells differentiate from the lateral border of the neural plate.[1] This process is induced and regulated by several proteins that control the differentiation of the neural crest cells. Some of the cells develop into cranial neural crest cells, and among those derivatives is the trigeminal ganglion, a sensory ganglion of the trigeminal nerve.[1] Also known as cranial nerve (CN) V, the trigeminal is the largest of the cranial nerves with three branches: the ophthalmic, maxillary and mandibular. Together they span the face up to the vertex of the scalp and cover the oral and nasal cavities. The ophthalmic and maxillary branches are purely sensory (e.g., touch, pain, temperature) while the mandibular branch also has a motor component. Recall that the branches of the ophthalmic nerve are the frontal, lacrimal and nasociliary branches.[2]

The cornea is the most densely innervated tissue in the human body, containing 70 to 80 large nerves and approximately 7,000 free epithelial nerve endings (nociceptors) per 1mm^2.[1,3] The tissue has been defined and characterized using light microscopy, electron microscopy and confocal microscopy.[1]

Most corneal nerve fibers arise from the ophthalmic branch of the trigeminal nerve, forming thick bundles that approach the cornea

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

- Describe the anatomy and function of the corneal nerves.
- Discuss the ways in which various pathologies disrupt corneal nerve function.
- Clinically assess corneal nerves.
- Review what treatment options are available.

Target Audience: This activity is intended for optometrists engaged in the care of patients with corneal nerve dysfunction.

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.

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radially to form the limbal plexus.[4,5] At 1mm to 3mm away from the limbus, the nerves lose their perineurium and myelin sheath, aiding in corneal transparency. These stromal nerves, encased in only Schwann cells, run at a mean depth of approximately 300µm from the corneal surface.[1,6] Within the stroma, they extend laterally and anteriorly, running parallel to the collagen lamellae.[3] Branches form the anterior stromal plexus and continue anteriorly to form the subepithelial nerve plexus (between Bowman's layer and the anterior stroma), penetrate Bowman's layer to form the subbasal nerve plexus and branch further to enter the corneal epithelium where they terminate.[5-8]

Corneal nerves play a role in the maintenance of a healthy cornea, including the blink reflex, wound healing and maintenance of the ocular surface. Nerves release neuromediators that provide nutritional support and elicit protective reflexes, such as tear production and blinking, in response to injury. When there is sensory nerve damage, corneal homeostasis mechanisms are affected and neurotrophic signaling is lost, negatively impacting corneal nerve function. The cornea could experience a reduction in epithelial cell turnover and blink rate as well as disruption of tear formation. As a result, the corneal epithelium releases neurotrophins—a family of growth factors related to nerve growth factor (NGF)—that help regulate the growth, proliferation, function and survival of the corneal epithelium, thereby maintaining a healthy ocular surface.[4]

Clinical Assessment

Corneal nerve structure and function are adversely affected by many ophthalmic and systemic conditions.[6,9,10] Therefore, it is critical to have tests for corneal nerve structure and function with good diagnostic capability.[10] Several important advancements have emerged recently for imaging and assessing corneal nerves.

Corneal confocal microscopy. *In vivo* confocal microscopy (IVCM), invented in the 1950s, became widely used in the early 1990s.[10-12] The imaging systems available today allow for high-resolution, real-time assessment of corneal nerve structure, including the epithelial nerves, subepithelial nerve plexus, subbasal nerve plexus and stromal nerves.[1,9] The introduction of IVCM enabled imaging of the live subbasal nerve plexus, leading to the theory that nerve bundles are preferentially oriented in the superior-inferior direction at the corneal apex and in a nasal-temporal direction in surrounding areas.[3]

Imaging with IVCM requires the proper instrumentation, patients who will cooperate while images are obtained, expertise in the interpretation of confocal imaging and software tools for automated analysis.[13] The tool is also limited in its ability to image the ultrastructure of various nerve bundles. If clinicians can obtain reliable images with IVCM, they can evaluate corneal nerve morphology and any abnormalities that occur due to various ocular and systemic diseases without altering the tissue microenvironment.[1]

Fig. 1. A Cochet-Bonnet esthesiometer is designed for rapid assessment of corneal sensitivity.

Cranial nerve and corneal sensitivity testing. Since CN V is implicated in corneal nerve sensitivity, it is important to review the appropriate testing of the cranial nerves. During evaluation of the ophthalmic branch, a blink reflex upon corneal touch is expected. Clinicians could also test the patient's forehead and/or scalp response to a light touch on each side, asking if both sides feel the same. To assess the maxillary branch, compare the touch response on the cheek or side of the nose. For the mandibular branch, compare touch on each side of the lower jaw.[14]

Current techniques for assessing corneal sensitivity have limited accuracy due to their subjective nature. The simplest involves touching the cornea gently with a wisp of cotton from a swab to initiate a blink response.[6,15] The Cochet-Bonnet esthesiometer can provide a more formal measurement with quantitative

The Corneal Layers

The cornea is an approximately 0.50mm thick avascular tissue with five distinct layers.[6] The outermost epithelial layer provides a smooth refracting surface as well as a barrier against infection.[62] Bowman's membrane, which lies under the epithelium and its associated basement membrane, has a function that is unclear in the literature. Some postulate that it may act as a physical barrier to protect the subepithelial nerve plexus, thereby facilitating rapid stromal wound healing, recovery of anterior corneal transparency and restoration of epithelial innervation after trauma.[63] The corneal stroma is the largest layer, accounting for 90% of the total corneal thickness. It is made up of intertwined fibrils of collagen lamellae that provide structure to the cornea. Descemet's membrane and the single-layer corneal endothelium form the innermost layers. The endothelial cells employ a sodium-potassium-ATPase pump to maintain tissue clarity by achieving an appropriate level of corneal dehydration.[17]

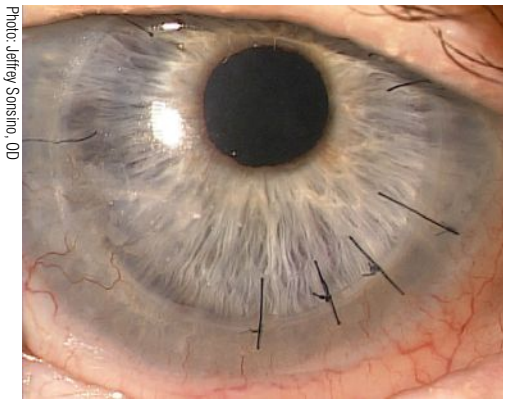
Photo: Jeffrey Sonsino, OD

Fig. 2. A full-thickness PKP with several interrupted sutures visible. All of the corneal nerves are transected when a PKP is performed.

results (*Figure 1*). It measures corneal sensitivity using a fine nylon filament that is introduced from the side and just touches the corneal surface. The longer the filament, the more flexible it is, indicating that more corneal sensation is present.[6]

Both of these approaches suffer from lack of diagnostic sensitivity and are generally disliked by patients.[10] Non-contact (or "air puff") instruments for corneal esthesiometry could be a potential improvement, but no such device to assess corneal nerves is currently commercially available. Further, such a device would likely require the patient to verbally confirm whether they felt the stimulus, introducing an element of subjectivity that may be undesirable.[13,16]

Researchers have proposed one novel approach to screening corneal sensitivity whereby hyperosmolar drops are instilled to cause a reflex eyelid squinting in rats.[13] The more hyperosmolar the solution, the stronger the blink response. Applying the various hyperosmotic solutions caused an osmolarity-dependent increase in squinting of the treated eye in control rats. In contrast, the squinting response of diabetic rats to the most hyperosmolar solution was significantly reduced compared with healthy rats.[13]

The motor innervation of CN V affects the muscles of mastication. Testing for the temporalis and masseter muscle motor function involves palpation for symmetry while the patient bites down and clenches their teeth. Testing the pterygoid muscles involves having the patient move their jaw from side to side. A lesion of the motor fibers of CN V will result in asymmetry of muscle action or deviation of the jaw toward the weak side upon closing of the mouth.[14]

Corneal Nerve Disruption

Disruption of the normal corneal architecture by ocular or systemic disease can affect the structure and function of the corneal nerves.[9,10]

Post-surgical complications. Corneal surgical procedures lead to varying degrees of corneal nerve damage, and subsequent regeneration of these nerves takes time. For example, in the creation of a classic LASIK flap with a microkeratome, the superficial afferent sensory nerves in the anterior one-third of the stroma are transected.[17,18] This disrupts ocular surface tear dynamics, resulting in symptoms of irritation and a reduction in corneal sensitivity.[18,19] As a result, dry eye disease (DED) is the most common complication following laser refractive surgery and is correlated to the amount of preoperative myopia and the depth of laser treatment.[20,21]

Several possible mechanisms have been proposed for DED after LASIK, including the above-mentioned afferent sensory nerve damage during flap creation, a reduction in the blink reflex, reduced tear production, increased tear evaporation and injury to the goblet cells at the limbus.[20]

One study found the incidence of post-LASIK DED was less with the newer femtosecond laser–created flaps (9%) than with a traditional microkeratome (46%).[22] Flap thickness does not correlate with dry eye symptoms, suggesting that other factors are important in the pathophysiology of LASIK-induced DED. One explanation for the decrease in dry eye with a femtosecond flap is that there is less damage incurred by the corneal nerves during flap creation and less damage to the limbal stem cells and goblet cells from the femtosecond fixation ring.[20,23]

The stromal nerves will usually reinnervate the cornea within five to eight months after LASIK surgery, improving dry eye symptoms.[17,20,23] During a penetrating keratoplasty, all of the corneal nerves are cut, so the recovery of innervation may be slower (months to many years) or even non-existent.[24]

Patients may also experience corneal nerve dysfunction after a neurosurgical procedure (brain, spinal surgery, etc.) during which the trigeminal nerve is damaged. Research shows that 2.8% of patients undergoing surgical intervention for trigeminal neuralgia develop neurotrophic keratitis (NK).[25,26]

Penetrating keratoplasty. A full-thickness penetrating keratoplasty has been the standard of care for replacing diseased and compromised corneas.[6] The procedure requires transection of all corneal nerves in both the host and donor cornea (*Figure 2*). Penetrating keratoplasty eyes can have marked central anesthesia or hypoesthesia for at least 18 months and up to 32 years following corneal transplantation.[17,24,27] Factors such as age, preoperative diagnosis, contact lens wear, diabetes and elapsed time since surgery had no correlation with the timeline for return of sensitivity to the graft.[24]

Diabetes. This disease can affect a wide variety of corneal nerve characteristics. In animal studies, diabetic rats had reduced corneal nerve den-

sity in the subepithelial layer and reduced cornea mechanical sensitivity by esthesiometry. Both motor and sensory nerve conduction velocity and total nerve fiber length in the subepithelial layer were also significantly decreased in diabetic rats.[13]

Diabetic NK is not well-described in the literature. However, the effects of diabetes on the corneal nerve structure are better understood. The degree of reduction in corneal sensitivity in diabetic patients often correlates to the severity of diabetic neuropathy.[28,29] A reduction of corneal nerves in diabetes patients may be the sole presenting feature of diabetes or may present concomitantly with proliferative diabetic retinopathy.[30] Conversely, through the use of confocal imaging, improvement in corneal nerve morphology can be seen when risk factors for diabetic neuropathy improve.[31]

Infection. Herpetic viral infection, either simplex or zoster, is a leading cause of neurotrophic keratitis (*Figure 3*).[32-34] After herpetic infection, the corneal nerves can undergo a loss of sensory fibers and a deficient or abnormal reinnervation process. Following herpes simplex keratitis, affected eyes have reduced nerve density, reduced total nerve count, reduced corneal sensation and the nerves themselves undergo regression.[35,36] The corneal nerves can also be altered after other forms of corneal infection, such as *Acanthamoeba* and fungal infections, where central subbasal corneal nerve density and nerve fiber length are significantly diminished and there is a marked decrease in nerve branching.[32,36]

Further studies are needed to investigate whether these nerve changes are caused directly by the virus or indirectly by the elicited immune response and resulting inflammation; however, some research does suggest a role for interleukin factors in the inflammatory response.[37] One study suggests corneal nerve alterations may be even more pronounced in *Acanthamoeba* and fungal infections than in herpetic infections.[32]

Dry eye disease. A study examining corneal nerves in patients with non-Sjögren's dry eye found reduced corneal sensitivity, changes in nerve morphology and reduction in nerve density with confocal imaging in the dry eye group compared with the control group.[38]

In select patients with DED, suspicion should remain high for early NK. To ensure prompt diagnosis, clinicians should conduct a thorough case history with emphasis on past herpetic infection, diabetes, surgery or trauma. Upon clinical exam, the presence of punctate epithelial erosions and/or epithelial irregularities should prompt clinicians to consider the addition of corneal sensitivity testing, confocal imaging or both, if available. In the absence of such technology, clinicians must carefully monitor patients who do not respond to standard therapy, as it raises the clinical suspicion for NK.

Neurotrophic keratitis. This rare degenerative corneal epithelial healing disorder arises after denervation of the corneal surface.[33] It is estimated that the prevalence of NK is fewer than five in 10,000 individuals and may be as low as 1.6 in 10,000.[25,39-41] There are fewer than 65,000 people affected in the United States.[42]

All of the conditions already described here can lead to neurotrophic keratitis, as can chemical burn, radiation, corneal injury and corneal trauma. Various types of intracranial space-occupying lesions or related surgical treatments affecting trigeminal innervation to the cornea can also be a cause of NK.[25]

The clinical presentation of NK includes an array of signs and symptoms such as painless blurry vision, punctate keratitis, tearing, light sensitivity, epithelial thinning, increased epithelial permeability, neovascularization, persistent epithelial defect, corneal edema, corneal scarring and corneal ulceration (*Figure 4*).[6,33,39]

NK is typically described as a persistent, non-healing, epithelial ulceration that can progress to corneal melt and perforation in severe cases.[39] Patients can be asymptomatic at advanced stages due to reduced corneal sensation. There is a risk of superinfection with bacteria or fungi and a risk of corneal melt precipitated by inappropriate use of topical steroid medications.[33,43] Comorbidities, such as exposure keratitis, DED or limbal stem cell deficiency can negatively influence the outcome of NK and require prompt treatment.[25]

NK is classified into three overlapping stages based on severity.[25,39] Staging is useful because some interventions are based on stage, and prompt treatment may halt progression to the next stage.[43]

Stage 1 (mild): Corneal epithelial

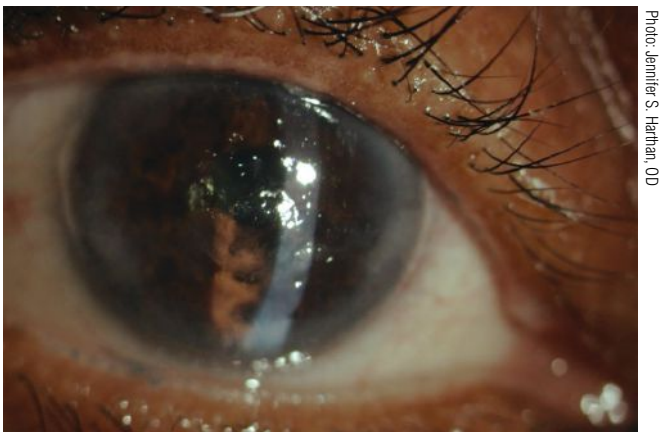

Photo: Jennifer S. Harthan, OD

Fig. 3. This African-American female patient developed HSV-associated neurotrophic keratopathy.

irregularity, superficial punctate staining, mild stromal scarring, corneal edema and neovascularization.

Stage 2 (moderate): Persistent epithelial defect, Descemet's folds, stromal swelling and possible anterior chamber reaction.

Stage 3 (severe): Corneal ulceration with stromal thinning that can progress to stromal melting, perforation or both.[39]

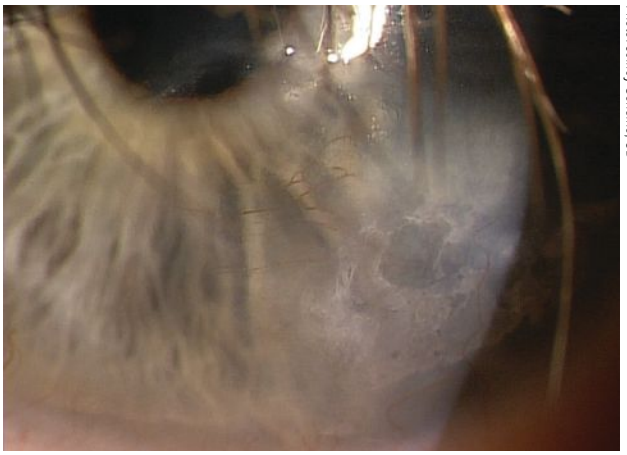

Photo: Jeffrey Sonsino, OD

Fig. 4. Here, neurotrophic keratitis presents with epithelial irregularity, corneal scarring and neovascularization.

Restoring Function

Following clinical assessment, there are a number of treatment approaches to consider when addressing disruptions to the structure and function of the corneal nerves.

Contact lenses. Bandage soft contact lenses (BCLs) have many functions in the treatment of corneal disease, including protecting the ocular surface from exposure. A bandage lens decreases necrosis and desquamation of the corneal epithelium by prevention of blink-associated mechanical stress, allowing for subsequent acceleration of wound healing.[44,45] In the treatment of NK, a BCL can prevent the need for tarsorrhaphy, with autologous serum dosed over the top, or in conjunction with cyanoacrylate glue to prevent corneal perforation.[25,45]

Scleral lenses have also been used in the treatment of refractory cases of DED and NK, as they can provide a tear reservoir for healing and contribute to corneal protection and hydration and present an alternative to tarsorrhaphy.[46,47]

Amniotic membranes. Applying one or more layers of amniotic membrane (AM), the innermost layer of the placenta, can be effective for the treatment of DED, herpetic infection and NK. In one study of NK, more than more than 75% of patients achieved re-epithelialization in 16 days while another study found an average time of 21 days.[48,49] AM procedures have traditionally been performed in the operating room, but sutureless amniotic membranes (SAMs) are now available for in-office application.[50]

Autologous serum. These are non-allergenic, non-preserved drops derived from blood serum—the component of blood that remains after clotting. Research speculates that the biochemical and biomechanical similarity of autologous serum to natural tears is inherent to its utility in the treatment of ocular surface disorders.[51] Several tear factors are important in the maintenance of the corneal and conjunctival epithelium, such as epidermal growth factor, vitamin A, transforming growth factor β, fibronectin and other cytokines.[45] In contrast, commercial artificial tear substitutes are typically optimized solely for their biomechanical properties.

Autologous serum can be useful in the treatment of DED, graft-vs.-host disease, limbal stem cell deficiency, recurrent corneal erosion, superior limbic keratoconjunctivitis, persistent epithelial defects and NK.[15,52-54]

Corneal nerve regeneration has been documented in NK patients with the use of autologous serum dosed six to eight times a day for the first month, tapering to four times a day.[55]

The concentration (ranging from 20% to 100%), dosing and preparation methods for autologous serum vary widely in both the literature and clinical practice.[53]

Managing NK Patients

Management of NK typically involves a stepwise approach depending on disease severity and staging. Stage 1 treatment consists of preservative-free tear supplementation, removal of any offending agents, prolonged patching and/or the addition of topical cyclosporine, lifitegrast or autologous serum tears.[42] Topical steroids are controversial—their use may increase the risk of corneal melt and perforation secondary to upregulation of collagenases.

At stage 2, BCLs, scleral lenses or amniotic membranes may be added.[46,47] Stage 3 may warrant the addition of debridement or punctal occlusion as well as consideration of more invasive procedures such as a tarsorrhaphy or Gundersen flap.[33] Surgical options are typically considered off-label and palliative in nature.[42]

An ideal treatment would go beyond palliative care and also stimulate epithelial healing, provide trophic support for the corneal tissue and restore sensation to the corneal nerves.[42] Autologous serum and medications containing NGFs, such as Oxervate, have the potential to provide some of these benefits.[55]

Two randomized controlled multicenter, double-masked trials of 151 patients demonstrated complete corneal healing in 70% of patients treated with this drug. The recommended dosing schedule for Oxervate is six times daily for eight weeks. Potential adverse reactions include eye pain (16%), conjunctival hyperemia, eye inflammation and eye irritation.[40,59] The eye pain and irritation could be associated with patients regaining corneal nerve function that was lost due to NK.[60]

Oxervate. This drug received FDA approval in August 2018 for the treatment of NK at any stage of the disease and is the first topical biologic agent approved for eyecare.[40,41] Oxervate (cenegermin-bkbj ophthalmic solution 0.002%, 20 mcg/m, Dompe) is a recombinant form of human NGF that aims to target the underlying pathology of NK, rather than solely addressing its symptoms. The medication is structurally identical to the endogenous NGF protein found in human ocular tissue and works through binding of specific NGF receptors in the anterior segment of the eye to ensure the proper growth and development of neurons that, in turn, support corneal integrity.[15,39] It is also the first such treatment to help prevent decreased vision or loss of vision caused by NK.[39]

Several studies supported the use of topical NGF in NK to restore corneal integrity and improve corneal sensitivity before Oxervate was approved.[43,56-58] Two pivotal trials, REPARO and NGF0214, established the efficacy of Oxervate for stage 2 and 3 NK in the United States.[39,59-61]

Treatment for corneal nerve dysfunction can be challenging, with many options available. A thorough case history, proper diagnostic testing and prompt identification of the disease process can help minimize serious corneal complications and reduce the need for invasive surgery. Employing the latest in imaging technology, medical devices and topical treatments can also prevent progression to the later stages of disease. Whether clinicians choose to manage some or all of these conditions, they are equipped to identify corneal nerve dysfunction and ensure patients get the care they need to recover. ■

Dr. Sicks is an assistant professor at the Illinois College of Optometry and serves as a clinical attending in the Cornea Center for Clinical Excellence at the Illinois Eye Institute. She lectures and participates in research on specialty contact lenses.

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OSC QUIZ

You can obtain continuing education credit through the Optometric Study Center. Complete the test form and return it with the $35 fee to: Jobson Healthcare Information, LLC, Attn.: CE Processing, 395 Hudson Street, 3rd Floor New York, New York 10014. To be eligible, please return the card within three years of publication. You can also access the test form and submit your answers and payment via credit card at *Review Education Group* online, revieweducationgroup.com.

You must achieve a score of 70 or higher to receive credit. Allow four weeks for processing. For each Optometric Study Center course you pass, you earn 2 hours of credit from Pennsylvania College of Optometry.

Please check with your state licensing board to see if this approval counts toward your CE requirement for relicensure.

1. What is the density of free epithelial nerve endings in the human cornea?
a. 2,000.
b. 5,000.
c. 7,000.
d. 10,000.

2. The corneal nerves form at how many months gestation?
a. Two.
b. Three.
c. Four.
d. Five.

3. What growth factors help regulate growth, proliferation, function and survival of the corneal nerves?
a. Neurotrophins.
b. Neuromodulators.
c. Neurotransmitters.
d. Neuropeptides.

4. Which neurotrophic keratitis treatment leads to re-epithelialization in more than 75% of patients within three weeks of treatment?
a. Autologous serum.
b. Amniotic membrane.
c. Oxervate.
d. Bandage contact lens.

5. Which of the following is not a main branch of the trigeminal nerve?
a. Nasociliary.
b. Ophthalmic.
c. Mandibular.
d. Maxillary.

6. What explanation is given for the side effect of eye pain experienced by some patients taking Oxervate?
a. The osmolarity of the drug's vehicle.
b. The eye regaining corneal nerve function.
c. The severity of the patient's comorbid DED.
d. The binding of the growth factor in the eye.

7. Which of the following corneal characteristics is affected by diabetes in rat studies?
a. Nerve cell density in the subepithelial layer.
b. Corneal sensitivity.
c. Motor nerve conduction velocity.
d. All of the above.

8. In a study looking at a novel approach for testing corneal sensitivity, what occurred when hyperosmolar solutions were applied to the rat cornea?
a. The more hyperosmolar the solution, the stronger the blink response.
b. The more hyperosmolar the solution, the weaker the blink response.
c. A change in hyperosmolarity had no effect on the rat cornea.
d. A change in hyperosmolarity increased the thickness of the rat cornea.

9. Each of the following is a sign of stage 1 neurotrophic keratitis, *except*:
a. Epithelial irregularities.
b. Anterior chamber reaction.
c. Corneal neovascularization.
d. Punctate staining.

10. Which of the following can be used to test corneal sensitivity?
a. Cochet Bonnet esthesiometer.
b. Wisp of cotton from a cotton-tipped swab.
c. Finger or fingernail.
d. Both a and b.

11. All of the following are functions of nerve growth factor (NGF) in the corneal epithelium, *except*:
a. Stimulate cell growth.
b. Regulate cell proliferation.
c. Maintain a healthy ocular surface.
d. Promote apoptosis.

12. Which corneal condition has *not* been implicated in the disruption of corneal nerve function?
a. *Acanthamoeba*.
b. Corneal abrasion.
c. Herpes simplex.
d. Fungal infection.

13. On average, how long after LASIK surgery does it take the corneal nerves to start to regenerate?
a. Six days.
b. Six weeks.
c. Six months.
d. Six years.

14. Which of the following treatment options is *not* preferred in stage 1 neurotrophic keratitis?
a. Topical steroids.
b. Patching.
c. Lifitegrast ophthalmic solution.
d. Autologous serum

15. Which problem-related test should be added to the exam if neurotrophic keratitis is suspected based on case history and slit lamp findings?
a. Corneal topography.
b. Endothelial cell count.
c. Corneal sensitivity.
d. Schirmer testing.

16. Which of the following is not a function of a bandage contact lens in the treatment of neurotrophic keratitis?
a. Prevent mechanical stress.
b. Provide pain relief.
c. Accelerate wound healing.
d. Prevent the need for tarsorrhaphy.

17. Which treatment is derived from the blood of the patient?
a. Oxervate.
b. Compounded cyclosporine ophthalmic emulsion.
c. Autologous serum.
d. Amniotic membrane.

18. All of the following surgical procedures have been suggested for the treatment of recalcitrant neurotrophic keratitis, except:
a. Gundersen flap.
b. Tarsorrhaphy.
c. Amniotic membrane graft.
d. Dacryocystorhinostomy.

19. Neurotrophic keratitis occurs in 2.8% of patients undergoing surgery for which of these conditions?
a. Brain tumor.
b. Trigeminal neuralgia.
c. Spinal tumor.
d. Eyelid ptosis.

20. All of the following areas of the cornea contain a nerve network branching from cranial nerve V, except:
a. Midstromal region.
b. Subepithelial region.
c. Endothelial region.

Examination Answer Sheet

Understanding Corneal Nerve Function—and Dysfunction

Valid for credit through April 15, 2023

Online: This exam can be taken online at revieweducationgroup.com. Upon passing the exam, you can view your results immediately and download a real-time CE certificate. You can also view your test history at any time from the website.

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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Payment: Remit $35 with this exam. Make check payable to Jobson Healthcare Information, LLC.

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

Answers to CE exam:

1. Ⓐ Ⓑ Ⓒ Ⓓ
2. Ⓐ Ⓑ Ⓒ Ⓓ
3. Ⓐ Ⓑ Ⓒ Ⓓ
4. Ⓐ Ⓑ Ⓒ Ⓓ
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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. Describe the anatomy and function of the corneal nerves. ① ② ③ ④ ⑤
22. Discuss the ways in which various pathologies disrupt corneal nerve function. ① ② ③ ④ ⑤
23. Clinically assess corneal nerves. ① ② ③ ④ ⑤
24. Review what treatment options are available. ① ② ③ ④ ⑤

25. 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.

26. 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): ☐

27. 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 pharmaceutical therapy ⓒ Choice of treatment/management approach ⓓ Change in current practice for referral ⓔ Change in non-pharmaceutical therapy ⓕ Change in differential diagnosis ⓖ Change in diagnostic testing ⓗ Other, please specify: _____

_____

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

ⓐ Very confident ⓑ Somewhat confident ⓒ Unsure ⓓ Not confident

29. 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:

30. Additional comments on this course:

_____
_____
_____
_____
_____

Please retain a copy for your records. Please print clearly.

First Name _____
Last Name _____
E-Mail _____

The following is your: ☐ Home Address ☐ Business Address

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Address _____
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ZIP _____
Telephone # _____ - _____ - _____
Fax # _____ - _____ - _____

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

Signature _____ Date _____

Lesson 119432 RO-OSC-0420

Rate the quality of the material provided:

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

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

Moving Optometry Forward in Glaucoma

Insurance and equipment limitations hold ODs back more than a lack of talent or motivation. Here's how to get the momentum going. **By Bill Kekevian, Senior Editor**

Just outside of downtown Los Angeles, a big box retailer employs two optometrists. About twice a week, a patient will enter for a refractive exam and leave with a glaucoma diagnosis. That's when "things get dicey," explains one of the clinicians, who didn't want to share his name. To save himself the trouble, he sends them to a nearby hospital.

This doctor's situation isn't uncommon. And the constraints he faces don't stem from his retail setting alone. If anything, it's emblematic of a blind spot that affects a sizable chunk of optometry—private practitioners and corporate ODs alike. When encountering glaucoma patients, only about one-third of optometrists practice to the full extent of their scope of practice. The rest pull the trigger on referral earlier than they might otherwise need to.

And that's a shame, because America is on the verge of a glaucoma influx. In 30 years, the rate of glaucoma is projected to more than double, from today's three million to more than seven million.[1,2] Prevalence isn't even clear because more than half of glaucoma cases in the US remain undiagnosed.[3] And with the number of ophthalmologists in the United States continuing to erode, patients are going to look to optometrists to fill that gap.[4]

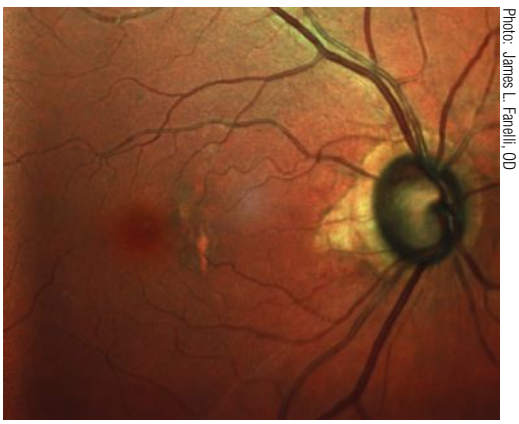


Photo: James L. Fanelli, OD

This 77-year-old patient's fundus image shows advanced glaucomatous damage and macular changes consistent with her age.

When they don't, some may chalk it up to a dearth of clinical expertise in glaucoma care or else blame economic pressures dictating that optometrists focus on selling glasses and contacts.

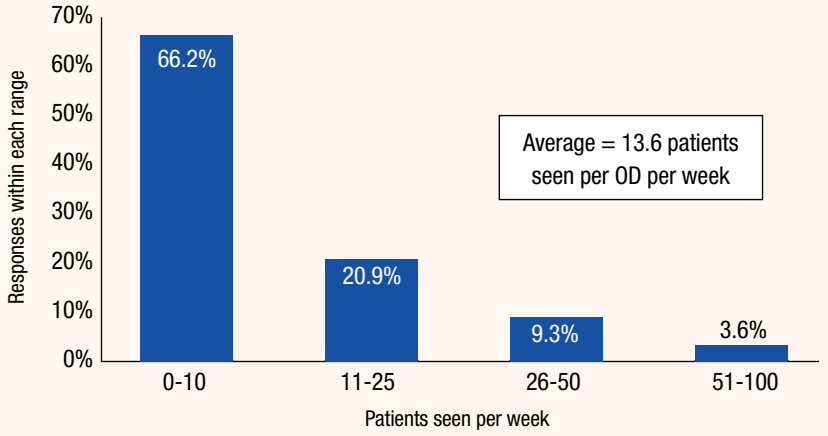
But for many optometrists, neither are true. The fact is that our big-box doctor is quite skilled at medical treatment, has an optical coherence tomography (OCT) device in his office, and communicates fluently with his multilingual community. The retailer doesn't prevent him from treating glaucoma—circumstances do. The obstacles have a lot more to do with the laborious time commitment and insurance-related red tape associated with glaucoma.

These are the key findings of a survey conducted by *Review of Optometry*, in which 364 optometrists shared their frustrations and aspirations in glaucoma care. Here's what they told us.

Overcoming Reluctance

For optometry to realize its potential in glaucoma care, two basic things need to happen: patients have to come into the clinic, and doctors have to be ready to provide

Fig. 1. Weekly Glaucoma Patient Volume



the care they need. Each component faces setbacks, our survey found.

First, take patient access. Respondents to this survey reported that, on average, 13.6 glaucoma patients or suspects present to their practices each week. That number was skewed slightly higher by a few respondents who report seeing 100 such patients per week. The most commonly reported number (the mode, in statistics parlance) was 10 patients per week. Another way of thinking about it: 66.2% of optometrists in our survey see 10 or fewer glaucoma patients or suspects per week (*Figure 1*). That just won't cut it when there's a population of about three million glaucoma patients needing anywhere from one to four eye exams per year.

And what happens when those patients do arrive? About one in five leave that day with a referral, most often to an ophthalmologist, according to our survey respondents (*Figures 2 and 3*). Another 12.1% of ODs treat only until they note progression, after which they too refer out. Only 34.9% of respondents told us they care for the patient to the full extent of their state's scope of practice law, including the provision of pre- and post-op care. Another 34.3% do actively manage the patients up to the point when surgery is required, however.

On balance, that combined 69.2% of ODs who are treating glaucoma does indicate broad acceptance of this as a fundamental optometric task; the challenge ahead is to break down barriers to entry for the other 30.8% and to help everyone push the envelope on the care provided in their practices.

Optometrists fought for decades to obtain the privilege to treat glaucoma medically. It's now a standard aspect of training and education. Michael Chaglasian, OD, president of the Optometric Glaucoma Society, fears that, if optometrists don't embrace a larger role in the care of glaucoma patients, one that partners with ophthalmic surgeons, "ophthalmologists will find some other profession—physician assistants, medical assistants, ophthalmic assistants," to partner with instead.

With some states still less than 20 years into topical glaucoma treatment indications—and Massachusetts still locked out altogether—patients aren't always aware of how broad optometry's scope of practice is. To many patients, optometrists might still be just the glasses-and-contacts people. Convincing them otherwise is going to require a little patient education. The American Optometric Association's "Think About Your Eyes" campaign educates the public on vision health and promotes the importance of annual comprehensive eye exams. But a number of respondents asked to see something specific to glaucoma. "A public awareness campaign that ODs treat glaucoma and a legislative push to allow privileges as-taught would be game changing," wrote one doctor from Blue Island, IL.

Fig. 2. How Do You Handle Glaucoma Patients/Suspects in Your Office?

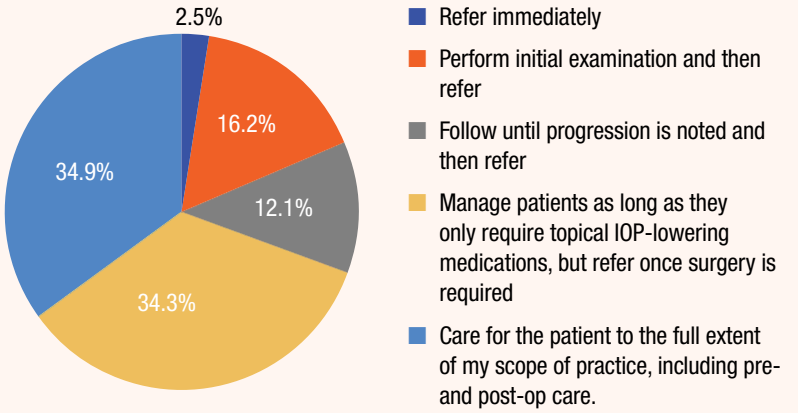
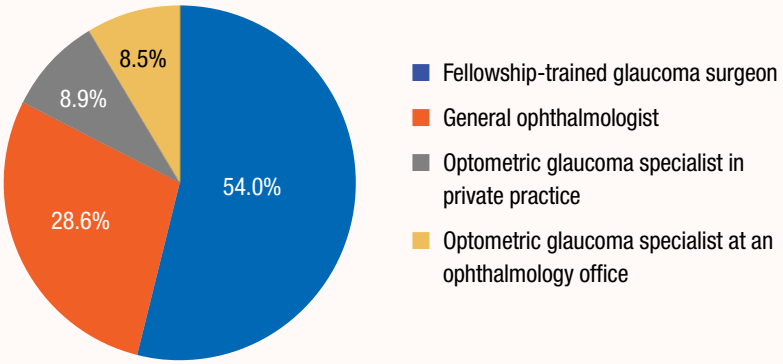


Fig. 3. If You Don't Manage Glaucoma, Where Do You Refer Cases?



On a smaller scale, optometrists can take it upon themselves to advocate for the profession and explain to patients that optometry is a primary care discipline that has the ability to treat almost any eye disease that doesn't require surgery.

Still, the loud voice of the medical lobby keeps optometry back, too. "The requirement in Texas to have to comanage glaucoma with an ophthalmologist is a pain and might be a deterrent for many," a reader from Fredricksburg, TX, notes.

Headwinds

Review's survey finds some optometrists have the expertise to treat, but not the tools (literal or administrative) while others say they do feel their clinical skills need polishing.

Some of the strongest motifs in our survey responses include:

Insurance hassles. The most heavily weighted response to the survey, with more than a third of respondents ranking it as either the biggest or second biggest barrier to embracing glaucoma care, involves issues with billing and coding (*Figure 4*). Many of those who answered *Review's* survey say they can't bill medical insurance. "There are too many panels that are OMD-only, or just closed to ODs," a reader from Laguna Niguel, CA, commented. "This forces me to refer a lot of patients out for something I can manage and treat in-office."

Others encounter pushback from patients who can't understand why their optometrist is suddenly asking about medical insurance when they've only ever asked about a managed vision plan.

The big-box optometrist in our first example owns his own OCT, but still doesn't bother billing insurance. "I haven't even tried it," he says. "We just charge a $35 flat fee for OCT—that's for the scan and the report. Typically, for a glaucoma work up, we'll do the OCT and we'll do the threshold visual field for another $20. That's really affordable, in my opinion."

He's also more apt to simply refer them out. "It's easier for me to do it that way, because I don't have the knowledge or the resources to do proper coding," he explains. If they're uninsured, he'll do what he can by starting them on drops, but eventually refers them to an MD.

It wasn't always this way. "When I first started, I did try to treat [glaucoma] and kept my fees very low, but it didn't work out. I found myself spending more time explaining the things I need to do to provide good care and when I tell patients the cost of the drops, it usually stops them dead in their tracks." That's not ideal when your two-doctor practice sees 40 patients a day, seven days a week.

Diagnostic tools. A close second to insurance headaches, our

Optometrists Sound Off!

Candid comments on the challenges of glaucoma integration.

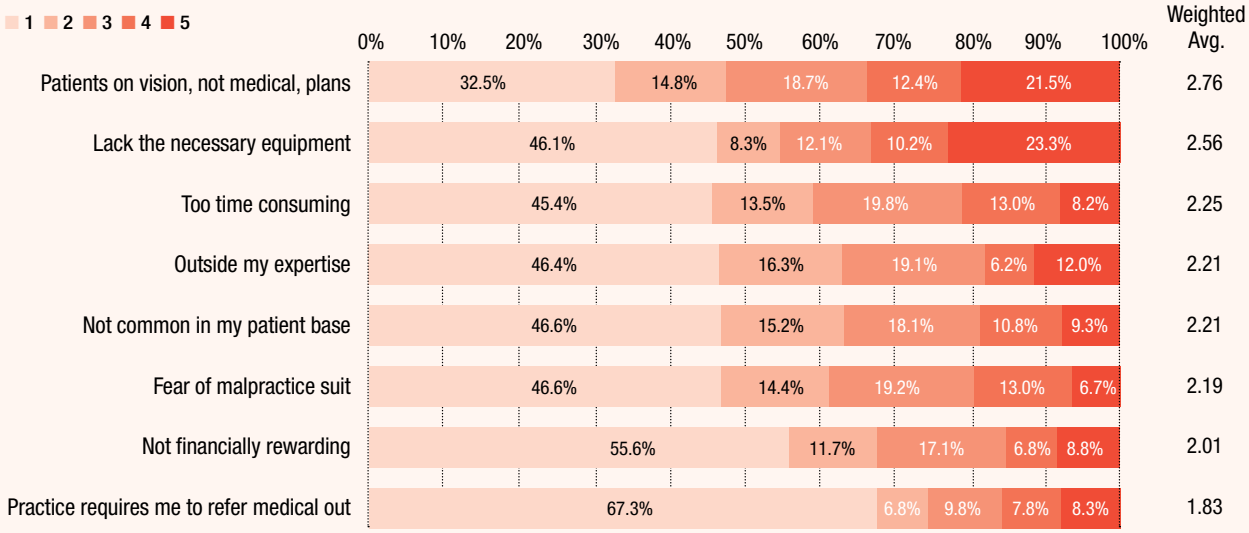
We need more support from PCPs. They often don't understand that optometry can diagnose and treat conditions such as glaucoma.

I think it's easy to know when someone has a glaucoma defect and OCT correlation. We need more information on making the decision to treat.

The challenges are all inter-related. Glaucoma is time consuming. As our knowledge increases, more variables need to be evaluated. This requires more delegation and appropriate reimbursement to practice at the high level that patients deserve.

Fig. 4. Barriers to Greater Optometric Care of Glaucoma Patients

Rated on 1-5 scale (1 = least impact, 5 = most impact)



respondents say, is a simple lack of necessary equipment, with 23.3% ranking this a "5 out of 5" in negative impact on their ability to practice. OCT instrumentation "is now at the low end of $40,000—no longer $60,000 to $80,000, but still huge for many small offices," explains Dr. Chaglasian.

There's a bit of a Catch-22 problem that keeps many practices from getting more involved in glaucoma: you can't pay for the equipment without the patients, and you can't build the patient base without the equipment.

"If a practice mostly sees younger families for refractive care, they might not have the volume to justify the equipment purchases," a reader from Mansfield, OH, explains. "That, in turn makes it difficult for the doctor to build a glaucoma practice and gain confidence and experience. I think there are still a substantial number of practices that work this way and that is the most common reason I hear in practices that choose not to treat glaucoma."

When asked what would enable them to take a more active role in glaucoma, respondents to our survey put 'better equipment' at the top of their wish lists (*Figure 5*). Nearly 40% chose it as something that would help. Tellingly, when forced to name the single most important factor that could turn the tide for them, 26.7% still picked better equipment. The second most commonly cited reply was, not surprisingly, easier ways to bill medical codes; still, the need for equipment outpaced it significantly.

Expertise. But simply having equipment isn't enough. "If they buy an OCT, they still need to learn how to use it," notes Dr. Chaglasian.

"Classroom teaching helps a little

I feel patients are calmed by a specialist and would prefer to be watched by them. Glaucoma is a big responsibility and losing vision is scary. I would feel comfortable comanaging with an OD-friendly OMD until I felt more comfortable managing them alone.

Step up to the plate and start treating glaucoma patients. It's extremely fulfilling and well within the scope of optometry.

Not all patients are willing to come back after their initial exam for further testing. Even with education, people don't understand glaucoma, so lots feel you are trying to swindle them.

There are no real classes or info educating general ODs on how to bill insurance and get reimbursed.

Space is an issue for having more equipment and establishing proper patient flow.

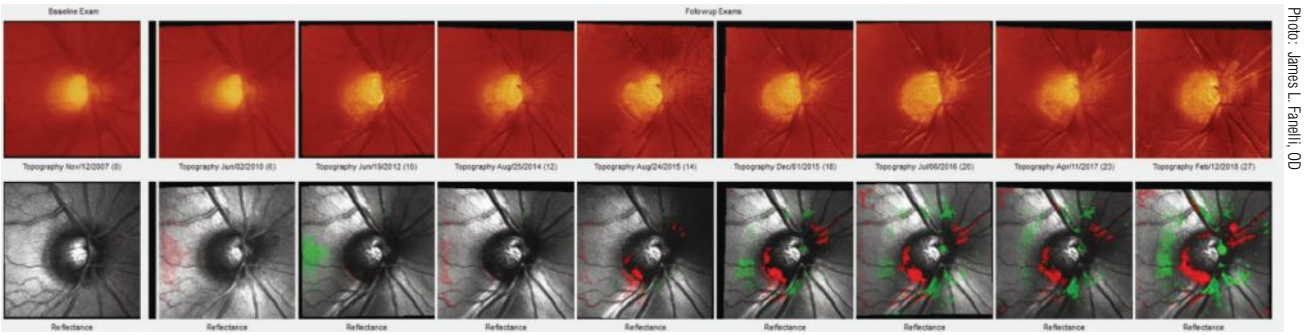


Photo: James L. Fanelli, OD

Heidelberg Retina Tomograph-3 imaging shows a distinct change in the inferotemporal neuroretinal rim of a 57-year-old patient. This series shows this change progress over the course of 11 years. Monitoring this kind of change over time is elemental to caring for glaucoma patients and suspects.

bit," Dr. Chaglasian explains, "but when the optometrist can come to a small group discussion and compare it with the IOP, the threshold visual field and the fundus photographs, and re-teach how to take care of a glaucoma patient, that can get them over their discomfort."

In *Review's* survey, 12% ranked "outside my expertise" as the number one reason they don't treat glaucoma patients to the full extent allowed by their state. When asked what would help them take a more active role in glaucoma treatment, respondents again indicated that increasing their clinical acumen would get the ball rolling. Specifically, 24.6% selected "better training in clinical work-up," 20.8% said "better understanding of the available medical treatments" and 19.8% answered "better understanding of the disease."

Prescribing topical drops for glaucoma is a hard-won privilege optometrists spent much of the 1990s fighting to obtain.[5] Texas only approved it in 1999, Vermont in 2004.[5] Massachusetts remains the only state in the nation without glaucoma indications for optometrists.[5] And yet, many ODs allow ophthalmology to dominate the field, as demonstrated by a recent study that shows MDs prescribe both a wider variety of glaucoma medications than optometrists (8.1 vs. 3.6) and to more patients (222.7 vs. 60.4).[6]

Part of this phenomenon can be attributed to the optometrist's career path, several experts speculated. Many optometrists fresh out of school opt to work for "corporate optometry"—that is, a retail chain primarily focused on frames and contact lens sales—before even considering opening up their own practice. This can help them catch up on student loan bills and establish some stability before taking on the financial commitment, risk and long hours of practice ownership. However, with so much of their day centered around refraction (and potential rules put in place by their employer), they may fall behind in the latest in medical knowledge.

A doctor with a Pearle Vision franchise simply answered that she "can't bill medically" so she refers all suspects to a general ophthalmologist. In *Review's* survey, 8.3% said the number one reason they don't treat glaucoma is because their practice requires them to refer out. But even privately run optometric offices can fall into a "refractions-and-eye-exam-only" routine.

Whichever the case, "for many of these practitioners, there's been a long gap between the time they were in school and in training programs and when they got to a location where they can practice to the fullest extent of their education," says Dr. Chaglasian.

Taking Action

Those optometrists who feel they've plateaued—at whatever level—in how they address glaucoma in their practices do have plenty of ways to push through.

Ask for help. Encouragingly, optometrists are sharing expertise, and patients, with their colleagues. "I have an OD contact in a large surgical practice I bounce diagnostic info off all the time—wish there were more than one available," wrote an OD from Hilliard, OH. "I have recently resorted to sending scans to other classmates for their input and that has been fruitful." OD-to-OD referrals comprised 17.4% of the patient hand-offs cited by our survey respondents.

Not every optometrist will be able to invest in all equipment needed, but that doesn't mean it's off-limits to you. If you don't have an OCT, one of your optometric colleagues in town likely does, explains James Fanelli, OD, a North Carolina clinician with a special interest in glaucoma. Then, you can have that doctor send you

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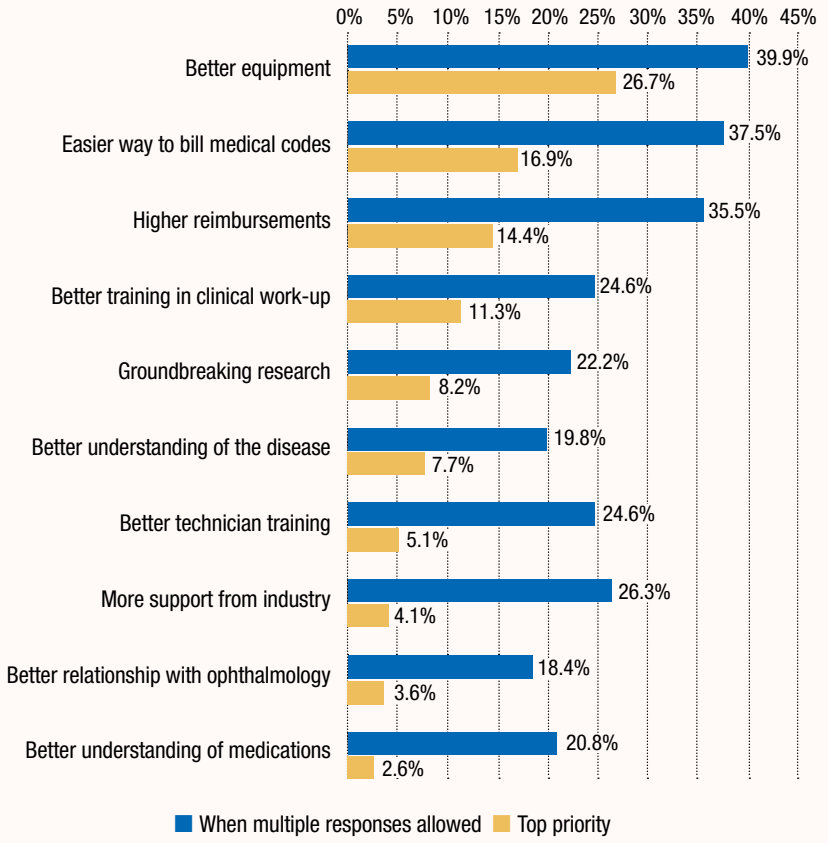
Fig. 5. What Would Enable You to Take a More Active Role in Glaucoma?

Readers were first asked to choose all options that apply, then were asked to select their single-biggest need.



the results, they can collect their portion for the technical component using code 91233-TC and you can collect for the interpretation, code 92133-26.

The same principle can be applied to fundus photography, pachymetry or threshold visual fields.

Get paid the right way. It's a bit of an understatement to point out that there are no easy ways to simplify the state of medical insurance in the United States. But experts have a few thoughts to share. If you're not already taking private medical insurance, you could consider attending courses on proper billing and coding at an optometric conference. The downside there is that these courses rarely qualify for relicensure, as coding is often considered "practice management," explains John Rumpakis, OD, a consultant on coding and practice strategy. But, he says, go anyway and fill in that gap in your knowledge. One-time commitments like these can get you started down the road to providing better care to that coming influx of glaucoma patients.

Those afraid of billing improperly need to keep a few pointers in mind. For starters, when a patient appears for a vision health checkup, that visit is billed to a patient's managed vision care plan, not medical insurance—even if you find a medical problem such as glaucoma. "It's always the purpose of the visit, never the findings" that you code for, Dr. Rumpakis says.

However, once the basic comprehensive exam portion of the visit is completed and the doctor makes a diagnosis of the patient as a glaucoma suspect, the medical insurance company is billed for any tests that the doctor orders on the basis of that finding. Both can be billed during one visit—but a strict line is drawn between the visit, the refraction and the comprehensive exam, which is billed to the managed vision plan and the rest of the appointment. This is where the doctor has to explain to the patient that they're showing potential glaucomatous changes and it will require additional testing to learn more. Those additional tests are billed to the medical carrier. Clinicians should explain that, if patients haven't yet met their deductible, they'll be responsible for the full cost.

Of the five medically necessary diagnostic tests in glaucoma—gonioscopy, pachymetry, threshold visual fields, fundus photography and OCT—the first three are allowed on the same day as the general exam but, Dr. Rumpakis explains, fundus photography and OCT are generally not allowed on the same day, except in the case of a vision-threatening necessity. Misusing a CPT modifier to get around this—even if your intentions are good and you're just trying to save your patient a second trip—is a violation of carrier rules.

Not all glaucoma suspects need to be tested with every piece of equipment you can get your hands on. "You can't apply the same protocol across the board for all glaucoma suspects," explains Dr. Rumpakis. "Clinicians have to look at the individual, their personal history, their physical exam and their family history, and then determine which tool

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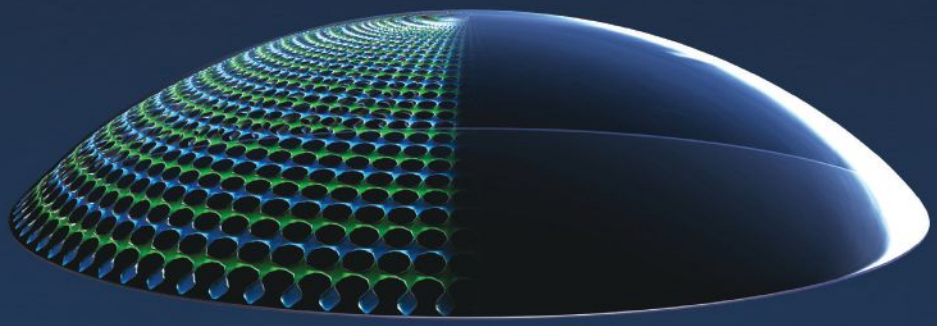

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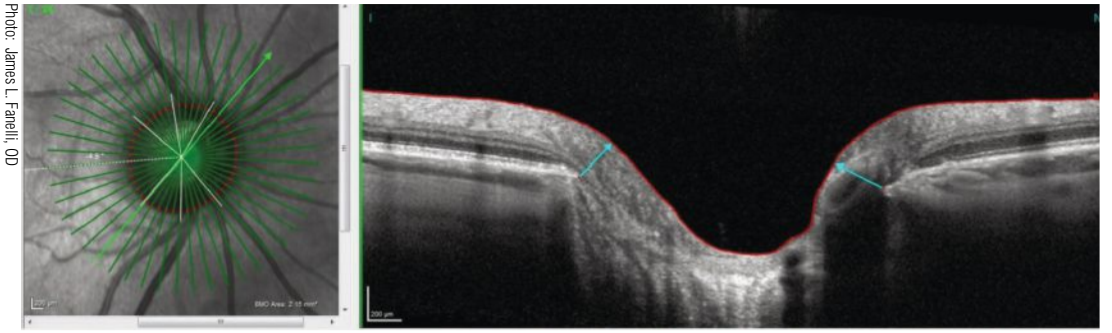

Photo: James L. Fanelli, OD

OCT images, such as this radial OCT of a steep nasal margin and sloping inferotemporal margin, offer deep insight into glaucoma patients.

is going to be most appropriate and effective." When coding, your office is responsible for properly establishing the path of medical necessity from what you observe in the general exam to ordering a specific series of tests appropriate for that patient.

Build your knowledge. A recent report into dry eye defines the condition as the "loss of homeostasis on the ocular surface."[7] Minus the ocular surface part, that's a fitting description for what you're looking for when monitoring glaucoma suspects and confirmed cases, according to Dr. Fanelli. Their visits, he says, "are geared toward stability. If things change, you know something needs to be done differently."

"Right now, there's no place to go that's widely available for clinical guidance on helping ODs overcome their anxiety and fear about not knowing what to do with a patient," Dr. Chaglasian explains. But he has an idea. The OGS ran a pilot project last year that brought together 45 to 50 optometrists across the country in a weekly web-based case discussion group on glaucoma care. Think of it as an interactive classroom, unencumbered by COPE oversight. There, "doctors could present their own cases and ask questions like, 'When do I add the next medication?', 'What should I look for on an OCT?' or 'When do I perform this type of visual field?'" The format, should it take off, would exist purely for learning. That outlet isn't currently available, but the OGS hasn't given up on it. A looser form of candid, collaborative discussion can be found online at ODs on Facebook and similar groups.

Dr. Fanelli shared a more DIY idea. "Try going to a fellow OD's office who does treat glaucoma and asking if you can spend a couple days with them." It couldn't hurt to ask.

Being the Change

A conservative mindset erroneously prevails throughout optometry about glaucoma care. "Optometrists worry about the liability," Dr. Rumpakis says. "They get scared and think 'Oh, my god, the patient's going to go blind.' What they don't understand is that the liability with failing to diagnose significantly outweighs the liability with losing somebody's sight." The vast majority of glaucoma is a slowly progressing disease, he explains, and you have plenty of time to assess and formulate a plan if you're monitoring a patient appropriately—two to three times a year.

One survey respondent explained why they don't treat glaucoma patients to the full extent allowed by their state. "I practice in California. Only recently have we been able to treat glaucoma. The glaucoma specialist in my area confuses me. He tends to disagree and not treat patients, only to treat them a year or two later. I also feel patients are calmed by a specialist and would prefer to be watched by them. Glaucoma is a big responsibility and losing vision is scary. I would feel comfortable comanaging with an OD-friendly ophthalmologist until I felt more comfortable managing them alone."

This doctor is exactly who Dr. Fanelli has in mind when he says advocates for optometrists to take on a bigger role in glaucoma, because ophthalmology will always try to take it from you, and relying on them at the first warning sign permits it. "If you're punting patients out the door, you're never going to develop that confidence. If you're referring most patients, you're never going to get any better," Dr. Fanelli says.

"Get up to the edge of your comfort zone and step just a little beyond it. Work there for a couple of months. Then, when you check in on the barrier of your comfort zone again, you'll find it's moved," he says. "That's when you step over it again." ■

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Put the Brakes on Contact Lens Dropout

Here's how to keep your lens wearers from heading down the wrong path.

By Amanda Tompkins, OD

I've been known to get caught up singing to a good song in the car and miss a turn or two. Just one of these wrong turns can make an easy drive a lot more frustrating. Some of our contact lens patients may know the feeling, as they find themselves heading down the road toward contact lens dropout.

While ranges vary, research shows up to half of new contact lens wearers drop out within the first three years.[1] Myriad complications can lead to drop out, but a lack of patient education, a compromised ocular surface and the wrong lens design are the big three I've noticed. Here's how you can identify a potential problem before it leads your patients down the road to dropout—and how to steer them toward the path of success.

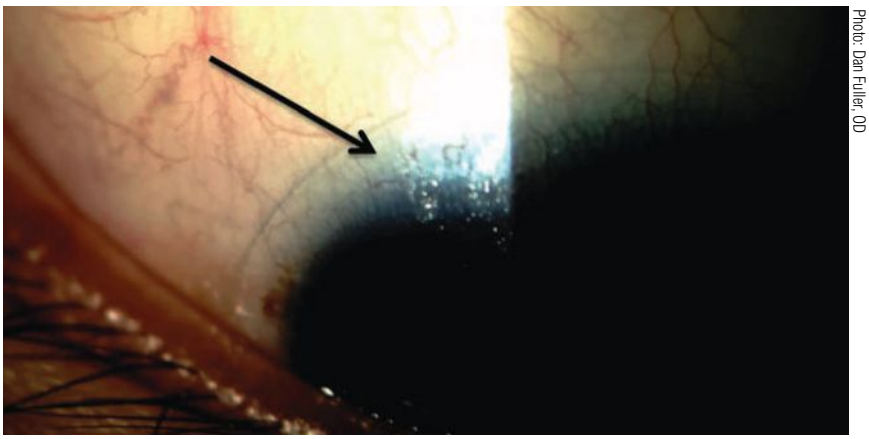

Photo: Dan Fuller, OD

Uncovering poor tear film stability caused by meibomian gland dysfunction, which results in the lipid layer thinning (arrow), can help you treat patients before they struggle with contact lens wear.

Invest the Time

Many patients drop out of contact lens wear because of a miscommunication or lack of communication somewhere along the way, especially at the outset. In practice, contact lens fittings add time to the exam, even when everything runs smoothly. It's tempting to save a few minutes by skipping or delegating patient education about different aspects of the lens design, materials and expectations. However, this costs much more than just a few minutes of your time in the long run, and it dismisses an opportunity to connect with the patients and understand their visual needs. Instead, clinicians can focus on three main categories during the fitting and education process: motivation, goals and expectations.

Motivation. This reflects strongly on the patient's chance for success. It's obvious when a patient is highly motivated. They are typically the patients that cram the lens between their lids during insertion and removal training. They have a good idea about contact lens use from self-driven research and show a willingness to heed professional direction. Highly motivated patients are often more attentive during the training process, more interested in new fit instructions and are generally

in a better position for long-term success. Motivation is especially important with potentially tricky toric and multifocal fits.

Goals. Patients ready for contact lens wear understand and have thought about what they want from their lenses. They've talked to contact lens wearing friends and have their own goals. They will be prepared to answer questions such as:

- Are you going to wear these full time or will these be reserved for certain activities?
- Do you value distance vision over near vision?
- Are you prepared for the hygiene requirements?
- What is the working distance of your computer?

It's crucial that you ask these questions to better understand the patient's visual goals, which will guide the fitting process. The majority of the contact lens fit is not about the actual fit—it's about understanding the patient and why you are fitting the lenses in the first place.

Expectations. The motivated patient with specific goals likely has equally specific expectations. The road to dropout is paved with mismatches between patient expectations and the reality of what current soft lenses can offer. It's your responsibility to bridge the gap, and nothing does this better than honesty.

For example, consider a new wearer with -0.75D cylinder or an oblique axis. I always let them know first that they will see better out of their glasses than their contact lenses and why. I never hide the fact that they will have visual fluctuations. These situations can be delicate, and you can put the patient on the road to success if they are first prepared for these discrepancies.

The same goes for established wearers when their prescription changes, whether they now need toric, multifocal or monovision. Optics are complex but highly effective within a multifocal lens and the more the patient knows, the more likely they are to accept the lenses' benefits and limitations.[2]

Use visual aids such as clinical images and the fitting guide to demonstrate the potential limitations in their vision to prepare them for any differences while wearing these designs. The use of loose lenses in the office for a monovision fit helps determine dominance and acceptance of the setup and shows the patient what to expect.

Never let the time required to show and tell patients about that which you are an expert deter you from offering them what you know can best suit their visual needs. If you invest the time, they will perceive the value, appreciate your attention and will be less likely to drop out of contact lens wear.

Set the patient up for success by telling them up front what to expect with any change and focus on the visual enhancements. Avoid words such as "sacrifices" or "compromises" and instead remind them what there is to gain.

Look First

Introducing a foreign object to the ocular surface is "intrinsically" inflammatory.[3] The natural protective process of inflammation (as when something is foreign in the body) can go awry by adding a contact lens to the ocular surface. The presence of soft contact lenses can increase the presence of inflammatory cells, causing the classic signs of redness, pain and swelling, as well as alter tear film osmolarity causing ocular surface discomfort and dryness.[4,5] When pre-existing ocular surface issues are ignored prior to lens introduction, the chance of dropout increases considerably.

One of the leading culprits of contact lens discomfort and dropout is dry eye disease.[6] In combating this, we must be proficient at identifying the presence of dry eye and treating it appropriately.

When I have a new wearer, one of the first things I do is reach for my slit lamp. This enforces the priority I put on their ocular health as a precursor and requirement of successful lens wear. I want to make sure that the ocular surface is ready to accept a contact lens—something I am sure to communicate with the patient.

I start with a tear film assessment with and without fluorescein, not in combination with a numbing agent, as a thick drop that can mask tear film characteristics.[7] I also perform a lid and lash assessment and document any signs and symptoms. The efficacy of the blink, the natural blink rate and the tear break-up time are all important factors, as

Dry But Determined

A patient presented who had discontinued contact lens wear secondary to dry eye. She was 21 and had previously been prescribed Restasis (Allergan) but was using is as needed, mistaking it for an artificial tear. A chart review revealed that she had tried almost every lens available that was appropriate for her —in total, about eight different lenses. She was wearing none of them when I talked with her. At this visit, she said she was frustrated but not quite ready to give up.

I reviewed the importance of Restasis as a medication, its dosing and its role in her contact lens life. With new understanding, she agreed to be adherent to the prescription and return in three months for her contact lens fit. She left happy, hopeful she would likely be able to wear any of the previously fit lenses once the ocular surface was healed and she was not "out of options."

is a gross assessment of meibomian gland status and any signs of anterior blepharitis. Ask the patient to describe how their eyes feel, being careful not to prompt them.

When preparing the eye for the introduction of a contact lens, clinicians should focus on quantification rather than qualification to accurately measure improvement with treatment and determine an appropriate timeline for lens introduction. Metrics such as tear break-up time and Schirmer testing are valuable.[8] A patient with a normal ocular surface and, in my opinion, ready for contact lenses would have a tear break-up time of approximately 10 seconds and a Schirmer score of at least 10mm after five minutes.[9,10]

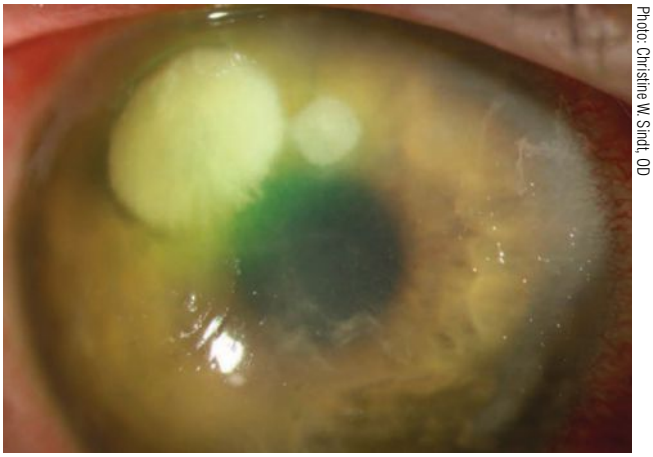

Photo: Christine W. Sindt, OD

Patients who have a history of a corneal ulcer, such as this one with a *Pseudomonas* ulcer, may do better with a daily disposable lens option—and plenty of patient education on proper lens wear and care.

For patients diagnosed with dry eye and not ready for contact lens wear, I usually prescribe an aggressive dose (consistent and frequent) of over-the-counter artificial tears, preferably using a preservative-free version, in combination with warming masks twice a day. In cases where the dry eye is significant and mostly aqueous deficient, I prescribe a cyclosporin in addition to the lubricant.[11] I bring them back to assess the ocular surface as frequently as needed until it is healed.

In a world of instant gratification, it can be hard to get the patient on board with forgoing contact lens wear until any underlying ocular surface issues are addressed. However, most patients seem to appreciate when you go the extra mile to make sure they are successful, especially highly motivated patients or those who have had negative experiences in the past.

Unless you are routinely performing a dry eye workup, you are likely allowing these patients to zoom right past you. You can rectify this by asking established wearers what you can do to make their contact lens experience better or if they wished something could be improved with their contact lenses rather than the typical "how are your lenses working?" which will often elicit a vague, "fine, thanks."

When asked differently, they almost always mention something about end-of-day comfort. In most cases, this is, in part, related to a dry ocular surface. You can reassure them that a motivated dry eye patient is not excluded from contact lens wear and relief can be as simple as changing materials or modalities. One study suggests the use of low-water content lenses such as silicone hydrogels reduce tear film deposition on the lens surface, optimizing lens wettability and tear film stability, ultimately improving comfort.[6] Although not as easily quantifiable, patient comfort truly is the bottom line in preventing dropout.

Furthermore, the modest use of rewetting drops should not be shrouded in a negative cloud; it's not a sign of contact lens wear failure. When you consider the environment in which we live and work, rewetting drops should be an expected part of contact lens wear. A change to a more dry eye-friendly material and establishing rewetting drop use as a norm for your patients could ultimately decrease drop out.

Taking action on their behalf will allow your patients to feel heard and understood, which will build their trust in you. When they are comfortable, they are more likely to open up when you ask them how you can improve their contact lens life year after year, perpetuating continued wear.

Find the Best Route

Knowing the various lens designs and modalities is important when patients are about to undergo a change in their lenses. Patients may prompt a change on their own or, more often, a change will be practitioner led for various reasons. Some of these include convenience, reduced over-wear potential, comfort, improved vision, freedom from glasses and improved overall ocular health. Established wearers usually change in one of two ways:

1. Change in modality (e.g., extended wear modalities to a daily disposable option)
2. Lens design change (e.g., toric or multifocal/monovision)

Change can be challenging, plain and simple. In all cases, the situation needs to be handled with care. Recognizing the switch as a potential change in their daily life and finances and showing that you understand

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this will strengthen trust, ultimately decreasing the chance the patient will drop out of contact lens wear after the switch. Be careful to reiterate and demonstrate the benefits that prompted the change instead of potential compromises.

Making a good first impression with the new lens is important and requires a good working knowledge of the options on the market:

Parameters: It's tough to backpedal from a ten-minute conversation focused on a daily lens when you later find out that it does not come in the patient's oblique axis.

Materials. Several "workhorse" daily lenses you likely have in your trial set are actually high water content, non-silicone hydrogel materials, which may not be ideal for dry eye patients who may currently be in an extended wear lens.

Designs. Be creative with multifocal and monovision fits. Understand designs such as aspheric and distance/near center and be willing to use a modified version to meet your patient's goals. For distance centric patients, you may need to have a designated distance center (in one eye or both) and knowledge of which lenses provide this will help ensure a good first impression.

Furthermore, do not limit your knowledge to the trials you have in your office. While these will always be your go-to options (consider stocking a variety of designs and materials), another lens might be the best option for a patient, and you should be prepared to know what it is and offer it to them.

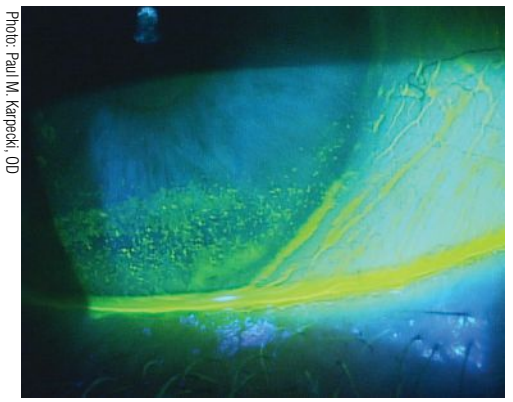

Photo: Paul M. Karpecki, OD

Patients with inferior corneal staining secondary to lagophthalmos, as seen here, may struggle with contact lens wear if it's not addressed first.

Get Back on Track

Patients who are considering dropping out or who have already done so aren't lost. Getting them back on track will be challenging, but possible. In my experience, after an initial episode of contact lens dropout, patients often develop a negative attitude toward lens wear. Two recurring statements I often hear my patients make are:

"I can't wear contact lenses." Many patients seem to think "contacts don't come in bifocals" or they "have the 'stigma'." This vague, defeated tone is an excellent opportunity for intervention, and I greet their disbelief with a "challenge accepted" mindset. With the wide range of parameters, materials and modalities we have at our disposal, almost anyone can be a successful contact lens wearer. With proper communication and a good fit, those previously fallen from contact lens wear can be reclaimed.

"I've had an ulcer in the past, so I cannot wear them again." I don't push a patient to try lenses again if they have any sense of dread or fear. In addition, I will refit this patient only if they are motivated and agree to adhere to prescribed lens wear habits and hygiene. If I sense they want a second chance, I offer daily disposables and explain that this would likely be their only option going forward. Most patients value the health of their eyes and my recommendation rather than pushing back on this stipulation.

With proper patient education, we can help restore confidence in these patients and get them back into their lenses. Some of my happiest patients are the ones who return to contact lens wear after thinking they were the exception.

Our role as optometrists is to make sure we are providing the best vision correction options to help our patients meet their goals. For many, contact lenses provide the freedom they want and the practice boost you need. Contact lenses have the power to solve many of our patient's problems and help them meet their visual goals in a way that could significantly impact their lives. ■

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The OD's Guide to Ptosis Workup

Droopy eyelids can stem from a number of conditions. Differential diagnosis is key for these patients. This guide will help navigate those cases.

By Eric Reinhard, OD, and Heather Spampinato, OD

Ptosis, formally known as blepharoptosis, is a common finding characterized by upper eyelid drooping in primary gaze. Commonly, ptosis is merely a reality of aging, but some occurrences are related to systemic diseases or genetic disorders. While cosmesis may be the primary concern for some individuals with ptosis, more advanced cases are associated with visual field disruption, eyelid strain, altered head position in an effort to compensate and headaches due to forehead and scalp muscle strain.[1] All this can decrease a patient's quality of life.

Here, we describe some of the causes of ptosis, with an emphasis on acquired forms, and will offer guidelines on monitoring and working up patients.

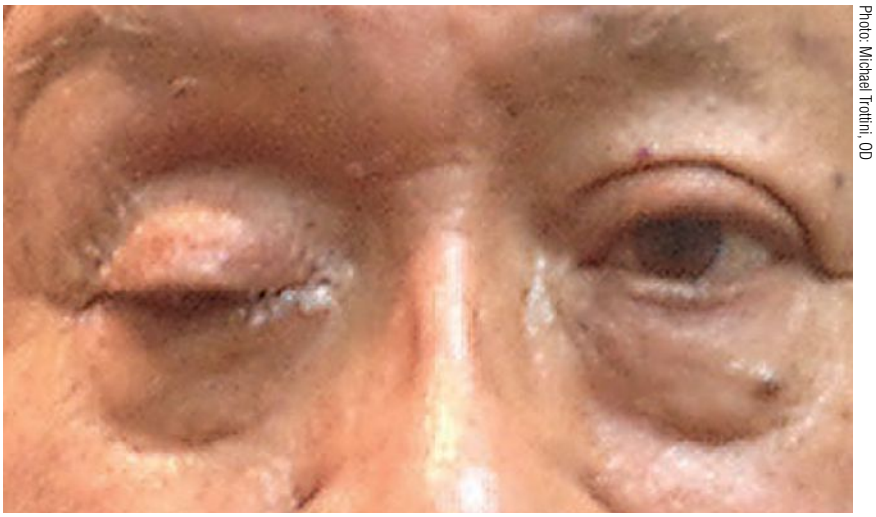


Photo: Michael Trottini, OD

Complete ptosis could indicate the presence of an emergent neurological condition.

Anatomical Explanation

Mechanically, ptosis is linked to dysfunction of the muscles responsible for eyelid elevation. These are the superior palpebral levator and the superior tarsal muscle, also called Müller's muscle. Loss of tonus in either of them results in ptosis.[2]

However, the superior palpebral levator is the main retractor of the upper eyelid and therefore deficiency in its function produces a more significant ptosis.[2] The levator originates from the lesser wing of the sphenoid bone and becomes a fan-shaped tendinous expansion, the levator aponeurosis, as it enters the eyelid.[2] The fibers of the aponeurosis penetrate the orbital septum and extend into the upper lid, fanning out across its entire length and insert on the anterior aspect of the tarsal plate. The levator receives its innervation from the superior division of the cranial nerve III (CN III).[3]

Müller's muscle originates from the inferior aspect of the levator, just posterior to the fornix, and inserts on the superior edge of the tarsal plate.[4]

This muscle is innervated by sympathetic fibers; denervation of Müller's muscle will cause only a mild ptosis of 1mm to 2mm.[3-5]

Patient Evaluation

When an individual presents with complaints of ptosis, the first step is to obtain a thorough clinical history. This should include a careful review of past systemic and ocular medical history, any changes in health and medication use.

Ptosis can be either congenital or acquired, monocular or binocular and progressive or non-progressive. These characteristics should be noted in the case history along with an inquiry of any associated neurologic and ophthalmic symptoms, including blurred vision, diplopia, pain, peripheral field loss, headaches or generalized muscle weakness. Inquire about any trauma or past ocular surgeries, along with a history of past botulinum toxin injections or ophthalmic steroid use.[6,7]

Understanding the course with regard to duration of the ptosis and whether it is progressing, resolving or unchanged from onset is important along with any indication of diurnal variability. An acute onset of hours or days prior to examination raises concern for serious pathologic etiology.

Reviewing old photographs can always help confirm any change if the patient is a poor historian.[8]

Clinical Examination

Evaluating patients with ptosis incorporates many of the standard components of a comprehensive eye exam. Visual acuity and binocular vision assessment can aid in indicating a possible causative systemic disease as well as in assessing for amblyopia or misalignment. If patients were to undergo surgical correction of the ptosis, amblyopia or phorias could indicate potential fusion issues. Pupil and extraocular motility testing along with external observation for globe asymmetry are critical to evaluate for other related pathology discussed later. Observing the patient's head position and visual field testing can help determine the impact and severity of the ptosis.

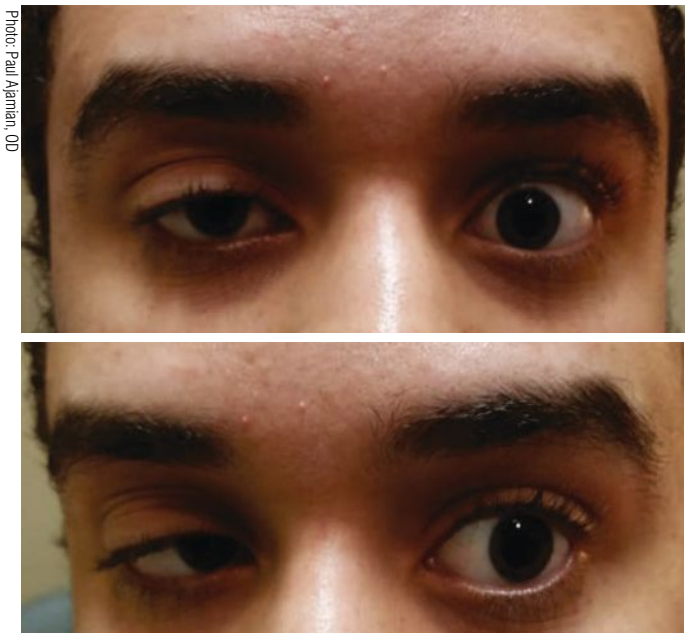


Photo: Paul Ajamian, OD

Acquired ptosis in one eye and a motility restriction in the other should be considered myasthenia gravis until proven otherwise.

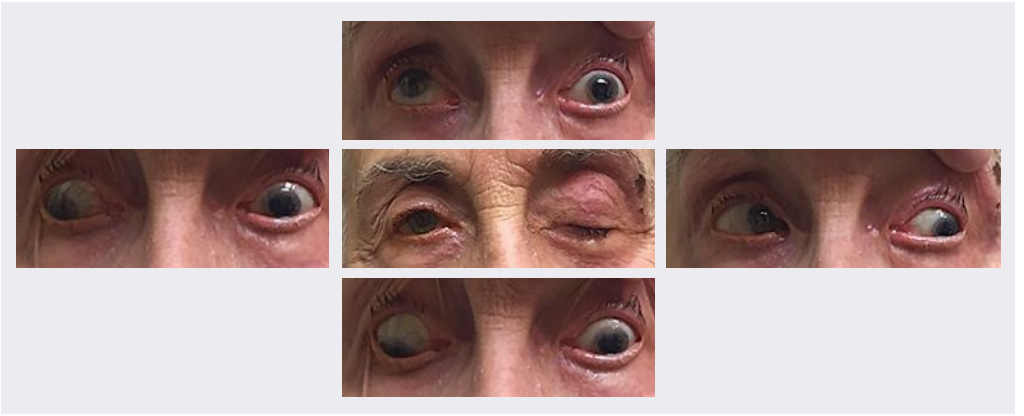
Quantitative measurements of eyelid position aid in assessing retractor muscle function, identifying anatomical abnormalities and can also be helpful to monitor for progression or improvement of ptosis over time.

Primarily, these measurements, called margin reflex distance (MRD) 1, 2 and 3, are performed using a penlight directed at the patient's eyes while in primary gaze. For MRD1, the distance in millimeters between the central portion of the upper eyelid margin and the pupillary reflex is recorded for both eyes.[9-11] A normal MRD1 is 4mm to 5mm.[5] The difference in MRD1 between the normal and the ptotic eye is the amount of ptosis. If the ptosis is significant enough that the pupillary reflex cannot be visualized, then the distance in millimeters that the eyelid must be raised until the pupillary reflex can be seen is recorded as the MRD1 in negative numbers.[9]

MRD2 differs in that it measures in the primary gaze, from the corneal light reflex to the central portion of the lower lid.[12] MRD3 determines how much levator to resect in patients with congenital ptosis, who have a vertical strabismus associated with ptosis and in whom strabismus surgery is not indicated.[12]

Levator function can be measured by determining the total movement in millimeters of the upper eyelid from downgaze to upgaze. This measurement is important for the surgeon when determining the most appropriate corrective procedure. Normal levator function is typically greater than 15mm, while 12mm to 14mm is considered good, 5mm to 11mm is considered fair and anything less that 4mm is poor.[5]

The upper eyelid crease represents the junction of the levator aponeurosis to overlying orbicularis muscle. The area from the upper eyelid margin in downgaze to the lid crease normally measures approximately 8mm in men and 9mm to 10mm in women, although it can vary by race.[10] In patients with congenital



Photos: Michael Trottini, OD

At this patient's initial visit, she had ptosis with restricted upgaze, downgaze and adduction. She was eventually diagnosed with a complete, pupil-sparing left 3rd nerve palsy secondary to herpes zoster. She resolved in approximately two weeks using an antiviral (*see page 72*).

and myogenic ptosis, the upper eyelid crease is often absent or subtle. While in patients with aponeurotic ptosis, the upper eyelid crease is positioned much higher.[11]

The palpebral fissure is simply the widest distance between the upper and lower eyelid margins in primary gaze and provides an overall comparison of relative ptosis. Average values are between 8mm and 11mm.[10]

Acquired Ptosis Classification

After performing an exam, the next step is to classify your patient's presentation. Based on etiology, ptosis can be classified as aponeurotic, myogenic, neurogenic, mechanical or traumatic. However, they may also have something called pseudoptosis, which describes an eyelid that appears ptotic due to structural changes that indirectly affect lid position.

Aponeurotic ptosis is the most common acquired ptosis. Typically seen in older individuals, it can present at any age as a result of trauma, frequent eye rubbing or prolonged use of contact lenses with hard lens wearers at higher risk.[6] Levator function is generally good in these patients, but the levator aponeurosis is stretched or thinned due to repetitive stress and effects of gravity and aging.[6] Younger patients exhibiting this form of acquired ptosis may display a higher eyelid crease due to levator disinsertion.[13] These patients generally respond well to surgical correction.

Mechanical ptosis can be caused by any abnormality that weighs down or alters the structure of the lid, including blepharochalasis, cellulitis, hordeolum, orbital fat prolapse and lid or orbital tumors. Scarring from inflammation, surgery, Stevens-Johnson syndrome or ocular pemphigoid can also lead to mechanical ptosis.[6] Always perform orbital imaging in patients with an underlying mass or infiltrative lesion. Addressing the causative factors is the initial management strategy in these patients.

Traumatic ptosis can develop as the result of any trauma to the orbit. The causes can include disinsertion of the levator muscle or damage to the levator tendon with scar formation. Alternatively, CN III damage can also sustain damage leading to the ptosis.[6,14] In severe cases that result in significant damage to the levator, patients may require multiple surgeries with a poor probability of restoring natural eyelid symmetry.[6,14] Patients who are at increased risk for CN III involvement include those with head injuries, post-traumatic cavernous sinus thrombosis, orbital apex fractures and nerve compression by foreign bodies.[14] Patients with CN III damage will typically resolve on their own with time and should be observed for spontaneous recovery over a period of three to six months before considering surgical intervention.[6,14]

Pseudoptosis can result from numerous conditions, including blepharospasm, dermatochalasis with hooding, brow ptosis, microphthalmos, enophthalmos and phthisis bulbi.[8] Lid retraction in the contralateral eye, as in thyroid eye disease, can also cause a relative ptotic appearance to the unaffected eye.[8]

Neurogenic Ptosis

This decreased innervation to the muscles of the upper eyelid can stem from a number of potential etiologies, some of which can be life threatening. Prompt identification and management of these conditions are critical.

Third nerve palsy is the most common cause of neurogenic ptosis.[1] This nerve innervates the superior, inferior and medial rectus muscles, the inferior oblique, the levator, and the pupillary sphincter muscle.[15] When ptosis is accompanied by symptoms of diplopia or pupillary mydriasis, a third nerve palsy must be considered.

Third nerve palsies cause the eye to assume a "down-and-out" position with significant weakness of

elevation, depression and adduction on motility testing.[16] The degree of severity of a third nerve palsy can vary greatly depending on the cause and anatomical location of the lesion.[15]

Ptosis associated with a third nerve palsy may be partial or complete. Patients presenting with an incomplete third nerve palsy in which there is only partial paresis of the extraocular muscles or only partial ptosis should be evaluated very closely for progression to complete palsy with pupillary mydriasis. Pupillary involvement associated with a third nerve palsy is concerning for a compressive lesion such as an aneurysm or neoplasm.

In patients older than 50, the most common etiology of third nerve palsy is microvascular ischemia in the presence of cardiovascular risk factors, followed by aneurysm, neoplasm, trauma, and various inflammatory and infectious etiologies.[16] Patients with third nerve palsy and pupillary involvement need to be sent for urgent neuroimaging of the head to rule out life threatening aneurysm, particularly aneurysm of the posterior communicating artery.[15,16]

Horner syndrome is characterized by unilateral ptosis, pupillary miosis and facial anhidrosis secondary to interruption of sympathetic innervation to the eye. The ptosis associated with Horner syndrome is mild, typically only 1mm to 2 mm, and is due to lack of innervation to Müeller's muscle in the upper eyelid. Ptosis in Horner syndrome can be variable and may even be absent in up to 12% of cases. Miosis occurs due to loss of sympathetic tone of the pupillary dilator muscle. The resulting anisocoria is more pronounced in the dark and a dilation lag is often evident within the first five seconds of dark exposure.[17]

Horner syndrome can result from a lesion anywhere along the three-neuron oculosympathetic pathway. Confirmation can be made through pharmacological testing with 0.5% apraclonidine or, less commonly, cocaine.[17,18] A positive apraclonidine test will result in dilation of the miotic pupil due to hypersensitivity of the iris dilator muscle as well as normalization of lid position.[1,17]

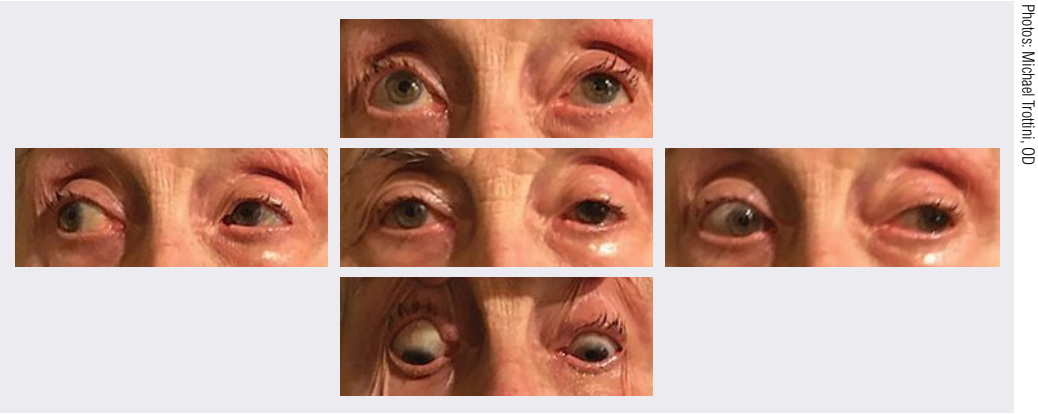
Hydroxyamphetamine can be used to determine if a lesion is pre- or postganglionic; however, this is rarely used in modern practice since neuroimaging will typically be ordered regardless.[17,18]

Emergent imaging for adults is not necessary unless Horner syndrome presents acutely with pain. Recent studies argue that in patients with new-onset isolated Horner syndrome and no localizing signs or symptoms, imaging should focus on the entire oculosympathetic pathway using MRI and angiography since potential etiologies are so numerous. A causative lesion is typically identified in 20% of cases, the most common being carotid artery dissection, which can occur spontaneously or secondary to trauma.

Other serious etiologies that must be ruled out are malignancy, vascular lesions of the brainstem, and cavernous sinus thrombosis.[1,17,18] In cases of longstanding Horner syndrome, typically considered two years or longer, imaging may not be warranted unless new symptoms develop.[17]

Myasthenia gravis is a rare disorder characterized by an antibody mediated immune attack on the nicotinic acetylcholine receptor (AChR).[19] In up to 65% of patients, the initial signs and symptoms of myasthenia gravis include ptosis, extraocular muscle weakness, weakness of the orbicularis oculi or ocular misalignment.[20] All symptoms

can present unilaterally or bilaterally and tend to be recurrent and variable with progressive worsening with fatigue. Typically, more than 90% of patients will experience some or all of these symptoms to some degree during the course of the disease.[21,22] Purely ocular myasthenia gravis occurs in approximately 50%.[21] Approximately half will progress to generalized disease within two years.[23-25]



Photos: Michael Trottini, OD

At follow-up, the same patient's (from page 70) ptosis and motilities significantly improved in two weeks.

Any patients with confirmed or even suspected myasthenia should also undergo CT imaging in order to evaluate for thymic hyperplasia or thymoma.[21] Thymoma occurs in approximately 10% to 15% of patients with myasthenia and requires surgical resection.[26]

Myogenic Ptosis

This most common congenital ptosis can be either acquired or congenital and is due to dysgenesis of the levator muscle with fibroadipose tissue found in place of skeletal muscle fibers.[6] Acquired myogenic ptosis describes a rare form of typically bilateral progressive ptosis, caused by systemic muscular dysfunctions.[6,27,28] This can include muscular dystrophy, myasthenia gravis (discussed previously), oculopharyngeal dystrophy and chronic progressive external ophthalmoplegia (CPEO).[6] Less commonly, steroid-induced and HAART-associated myogenic ptosis have been reported.[27,28]

Myotonic dystrophy is the most common form of adult-onset muscular dystrophy. Ocular findings include symmetrical ptosis, blepharospasm, ophthalmoplegia, and Christmas tree cataracts. Myotonia (delayed relaxation of skeletal muscle after contraction) is often the initial symptom; thus, affected individuals may be diagnosed prior to onset of ocular symptoms. Affected patients may also present with early-onset frontal alopecia, wasting of temporal and masseter muscles and distal limb weakness exacerbated by cold, excitement or fatigue.[29,30] Respiratory disease and cardiac myopathy are the most common causes of death.[30]

Myogenic ptosis may be corrected with an eyelid crutch or surgery; however, use caution when recommending either of these, as these patients have a higher risk of postoperative dry eye disease and exposure keratopathy due to poor Bell's phenomenon and incomplete blink.[31,32]

Myasthenia Gravis Testing

Two tests that can easily be performed in the exam room to evaluate for myasthenia gravis are the rest and ice tests. For the rest test, patients with ptosis are told to keep their eyes gently closed for two minutes. Approximately 50% of patients with myasthenia gravis will show an improvement in ptosis of 2mm or more with the rest test.[1] Researchers believe this happens because the amount of ACh within the synapse accumulates, improving muscle response.

The ice test is performed by placing ice on the ptotic eyelid for two minutes and then re-evaluating the ptosis. Like the rest test, an improvement of 2mm or more is a positive test result.[1,2] Ptosis secondary to other causes will not improve with either the rest or ice tests.[1]

Lab testing for AChR antibodies should also be performed in suspected cases of myasthenia. Keep in mind that anywhere from 30% to 65% of patients with purely ocular myasthenia gravis will be seronegative.[3,4] Studies show the level of AChR antibodies does not correlate with severity of disease or aid in prediction of who will develop generalized disease.[3,5]

The Tensilon test has long been regarded as the primary diagnostic test for myasthenia gravis, though today it is used less frequently than in the past due to risk of cardiac complications, syncope and cholinergic crisis. It also has a high incidence of false negatives and false positives.[1]

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When a patient presents with ptosis, a thorough case history and clinical exam are critical in determining when further work-up or referral is necessary as ptosis may be the initial presenting symptom of a number of potentially fatal medical conditions.

As a general clinical pearl, any time ptosis, pupillary anomaly, extraocular motility dysfunction, globe asymmetry or dystopia is detected on clinical exam, a thorough evaluation of each is warranted as they may give clues to concurrent disease.[8,33] Depending on the etiology, some cases of ptosis will resolve spontaneously, others will require management of systemic disease, and some will require surgery. As with any procedure, postsurgical complications can occur, including, but not limited to undercorrection, overcorrection resulting in lagophthalmos and dry eye, eyelid crease abnormalities and distortion of the lid margin.

Optometrists must have an awareness of potential etiologies and the ability to discern when ptosis presentation is an emergent situation requiring prompt diagnostic testing, treatment, and referral. ■

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Blood For Tears

Autologous serum drops give dry eye patients an effective treatment option.

Edited by Joseph P. Shovlin, OD

Q I have a few patients with significant anterior segment staining (corneal and conjunctival) who seem to be good candidates for autologous serum. Can you talk about how to acquire these drops and what concentration works best?

A "Dry eye disease is one of the most common concerns that brings patients to eye care professional offices," says Eric Donnenfeld, MD, a Long Island ophthalmologist who specializes in refractive, corneal and cataract surgery. He notes that the severity of the disease varies from mild to severe and influences treatment, the response to which depends on the patient. In general, artificial tears and lid hygiene are effective in cases of mild dry eye. When this approach is not sufficient, Dr. Donnenfeld suggests moving to immunosuppressive agents, such as cyclosporine, lifitegrast and corticosteroids. For moderate to severe dry eye patients, autologous serum tears may be their best option.

An Ideal Replacement

Physiological tears are complex in nature and contain more than 100 different proteins that help support the ocular surface. Many of these same proteins, including growth factors, fibronectin and laminin, are also found in our blood. This makes autologous serum tears created from the patient's own blood an ideal replacement, according to Dr. Donnenfeld.

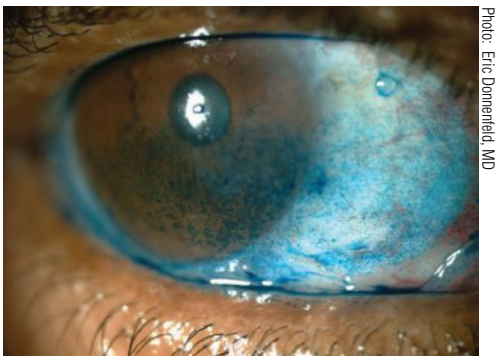

Photo: Eric Donnenfeld, MD

Severe dry eye patients with advanced corneal staining are ideal candidates for autologous serum tears.

Serum tears stand out even more when compared with artificial tears, which often only contain a few components, such as sodium, potassium and chloride. Further widening the gap, Dr. Donnenfeld adds that serum tears help promote epithelial growth and stability as well as corneal nerve regeneration and are comfortable for the patient, as tears and blood have almost identical salinity and pH.

The Production Process

Dr. Donnenfeld's clinic has a registered nurse who draws several vials of blood from the patient and sets it aside to clot for an hour. The blood is then spun down with a centrifuge to separate the red blood cells from the clear serum. The red blood cells are discarded, and the clear serum is filtered through a 25mm polyethersulfone disc filter. The remaining serum is then mixed with sterile, non-preserved saline to produce serum tears in varying strengths, ranging from 20% to 50%.

For practices that don't do their own blood draws, local hospitals, blood labs and compounding pharmacies can work with clinicians to create autologous serum tears that they can use as an alternative option. Pharmacies typically charge $15 per 5mL bottle of drops, and the fee for the blood draw is usually around $10. Draws should produce anywhere from six to eight bottles, which can last four to six months, so the patient should expect to pay about $115 out-of-pocket for the entire process, as this often isn't covered by insurance.

Serum tears are typically used between four and eight times per day, much like artificial lubricating drops. They are non-preserved, so patients don't have to worry about preservative toxicity, but they must be refrigerated when not in use. Dr. Donnenfeld says those with more significant dry eye will often carry serum tears in a cold container for use during the day. He notes that bottles of serum tears may be frozen for a short period of time and recommends defrosting them in the refrigerator or by twirling the frozen bottle vigorously between the palms of the hands.

Dr. Donnenfeld has found serum tears to be one of the most effective treatments for dry eye disease and an excellent addition to the management of moderate to severe dry eye patients. ■

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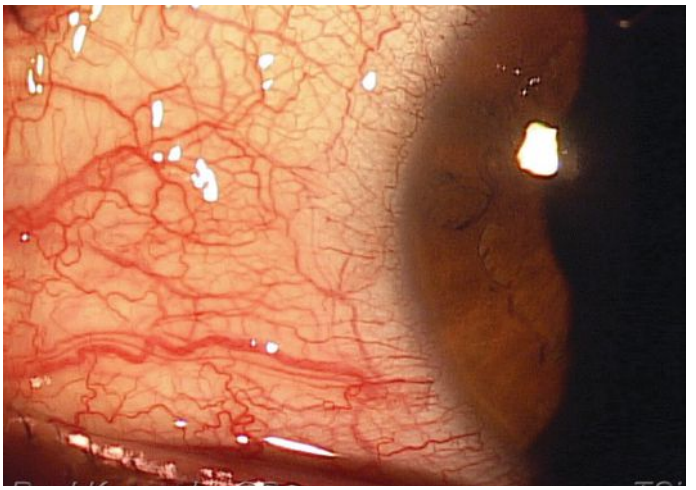
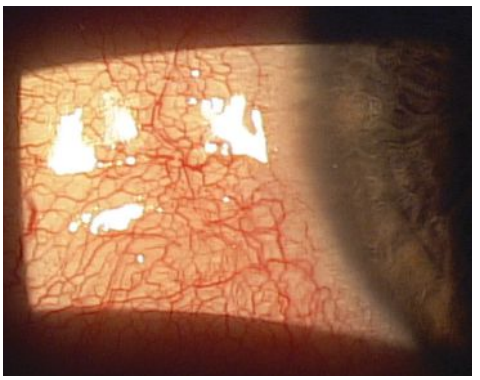
Coronavirus: Proceed Cautiously

The opposite of panic isn't calm—it's preparedness. Here's how to navigate clinical exams in uncertain times. **By Paul M. Karpecki, OD**

Writing about a disease we know so little about is challenging, especially considering how rapidly this public health crisis is evolving. At the risk of being outdated before the ink on this page dries, I'd like to attempt to share with you what we currently know about coronavirus, highlighting what it means for optometrists in particular.





These images show different patients with a common disease—viral conjunctivitis. The novel coronavirus currently threatening the planet can present quite similarly to these patients.

Coronavirus and Influenza Are Not Comparable

Over the past few weeks, our understanding of coronavirus has evolved. Initially, many healthcare providers worried about alarming patients and compared the disease to the flu when discussing prevention. This seemed to quell fears about the unknown virus that patients only heard about on international news broadcasts.

In the long run, making Americans feel too safe may isn't always ideal either. We see evidence of this every day in patients who assume that common-sense hand washing will stop this virus in its tracks and it will vanish from existence in no time. This approach is one of several reasons why, on March 11, the World Health Organization (WHO) officially declared coronavirus a pandemic, with the agency's Director General citing "deep concern" about "alarming levels of inaction."

Unlike influenza, coronavirus has no vaccine, is exceedingly virulent and has a high transmissibility rate. To put it into perspective, every year about 0.1% of people who get the flu die. This is why we advocate so strongly for influenza vaccination. But with no vaccine for coronavirus, the mortality rate of coronavirus is exponentially higher. Consider the mortality data out of Italy, which as of March 10 was above 5% and rising. In other words, for every person who dies of the flu, 50 could die as a result of this coronavirus.

Admittedly, Italy has an unusually high elderly population, but even in communities where mortality is closer to 1%, we're looking at a disease that's at least 10 times more deadly and spreads much more quickly. Consider: on February 20, Italy had identified only a single case of coronavirus. Less than 20 days later, more than 9,000 people in Italy had contracted it.

Promote Preparedness

The WHO didn't declare a pandemic so the world would fall into a state of hysteria or despair. They did it to prevent the situation from getting worse, assuring a world audience that "all countries can still change the course of this pandemic."

What does this mean for optometrists? In short, although we should continue to reassure patients, we

must balance our rhetoric so that we impress upon them how important it is to prevent the spread of disease to at-risk patients. As citizens, it is our social responsibility to protect the welfare of elderly patients, newborns and anyone else in harm's way. Primary care providers must make this a key takeaway when counseling patients.

Social media is buzzing with debate on this hot topic, and patients' views are highly politicized and polarizing, but the one piece of advice that I personally took to heart came from a doctor who reminds us that "the opposite of panic isn't calm—it's preparedness."

ODs to the Front

Eye care practitioners have a unique role to play in preparedness. Coronavirus is predominantly transmitted through direct or indirect contact with mucous membranes in the eyes, mouth or nose.[1] In fact, according to an American Academy of Ophthalmology alert, several reports suggest the virus can cause conjunctivitis and possibly be transmitted by aerosol contact with the conjunctiva.

The conjunctivitis presents similarly to other viral conjunctivitis cases with conjunctiva injection and hyperemia and discharge that is typically clear or mucin-like. A study of 30 patients hospitalized for COVID-19 in China suggests that it can infect the conjunctiva and cause conjunctivitis, and virus particles are present in ocular secretions.[2] As such, a report in *Lancet* says doctors examining suspected cases should wear protective eyewear and gloves.[3]

Until we know more about virus, we need to focus on prevention. This begins with a healthy diet, plenty of rest and vigilance about good hygiene. I've taken active steps to remind every patient to wash their hands often, stay hydrated and eat healthy foods. I also recommend they consider taking vitamin C and purchasing hypochlorous acid spray. Hypochlorous acid demonstrates broad-spectrum activity and may help prevent or treat ocular symptoms, while vitamin C is currently in Phase II trials for the clinical management of severe acute respiratory infection due to coronavirus.[4]

We must question patients with conjunctivitis about recent or current flu-like symptoms, including fever, cough or respiratory difficulties. We may need a thermometer such as a tympanic or forehead type device on hand.

The optometrist's role here is to educate patients who present to us regularly on the importance of good hygiene habits, nutrition and health. Additionally, ODs must be especially cognizant of any conjunctivitis that presents to our clinics at this time. ■

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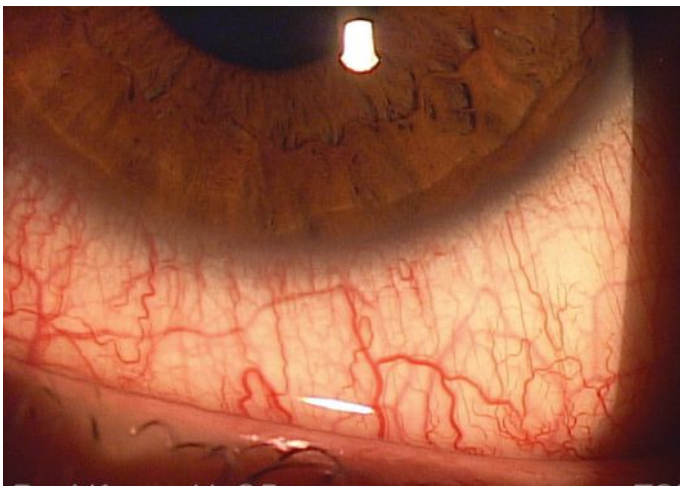
Frames and Contacts are Both a Risk

As is often the case in times of national crises, misinformation can run rampant. Here's some ways optometrists can use their authoritative positions to keep patients informed.

Contacts are safe, but keep hands clean—By now, vigilant hand washing should be a no-brainer, but be sure to emphasize "careful and thorough hand washing with soap and water followed by hand drying with unused paper towels" for contact lens wearers "before every insertion and removal."

Spectacles aren't immune—Sure, spectacle wearers don't touch their eyes with the frequency that contact lens wearers do, but that doesn't mean they're risk-free. The virus can remain on hard surfaces for hours to days and can be transferred to spectacles from fingers, faces or just from sitting around on other unclean surfaces, as reading glasses especially often do.

CORE. COVID-19 and contact lens wear: what do eye care practitioners and patients need to know? Contact Lens Update. March 16, 2020. Accessed March 17, 2020.



The conjunctiva is among the tissues that are likely to be penetrated by the conronavirus. No treatment exists yet, but identifying infection early can assist in management.

When Red Disease Gets Real

It takes a keen eye and an appreciation for change over time to distinguish a false positive from developing disease. **By James L. Fanelli, OD**

Red disease can confound therapeutic care and, if you're not careful, result in unnecessary treatment. 'Red disease' is the term used when one of the indices of a particular test, most often OCT imaging, falls outside statistical normal limits and is flagged on most printouts (in red). The term implies a finding that falls outside the statistical norm, but that finding is normal for the patient and not indicative of actual disease. Use caution when you see flagged indices of OCT scans as red because their presence does not indicate frank disease; they *may*, but they also may *not*. They need to be carefully evaluated.

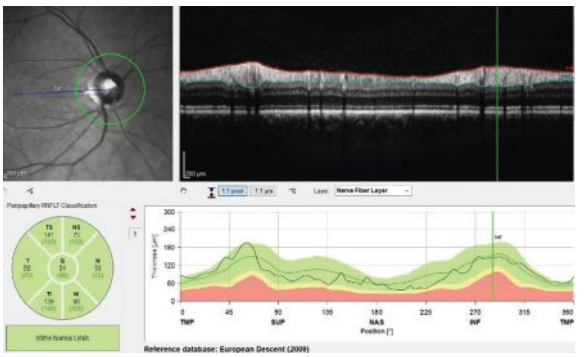


Fig. 1. This image shows an entirely normal RNFL circle scan on initial presentation of the right eye.

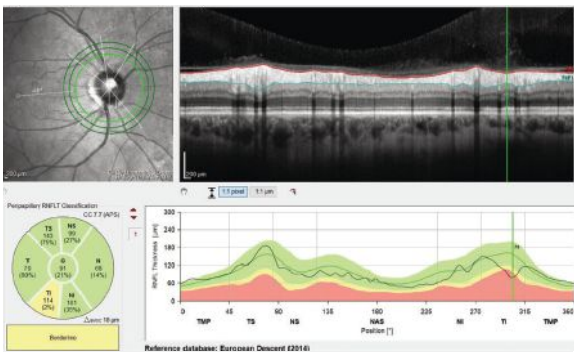


Fig. 2. This scan demonstrates a small area of potentially deceased RNFL thickness in the inferotemporal sector of the patient's right eye.

In Practice

Take, for instance, the case of this mild ocular hypertensive patient. In 2008, she was a 52-year-old with a family history of glaucoma. She presented for a comprehensive evaluation related to refractive changes, but initial scans were normal. But when newer scanning techniques demonstrated what we considered red disease, things got a little clouded.

Her intraocular pressure (IOP) by applanation at that initial visit was 22mm Hg OD and OS, and pachymetry readings were 525µm OD and 522µm OS. Anterior segment evaluations were entirely normal, with well-formed and deep anterior chambers, open angles and normal iris anatomy. Her best-corrected visual acuities were 20/20 OD, OS, OU. Her crystalline lenses were clear OU. Through dilated pupils her cup-to-disc ratio was approximately 0.50 x 0.55 OD and 0.50 x 0.50 OS. The neuroretinal rims were plush and well perfused. Her retinal vascular evaluation was entirely normal, as was her macular and peripheral retinal evaluations. Ultimately, a baseline threshold visual field was obtained, which was reliable and indicated no field defects associated with glaucoma. Baseline OCT measurements were performed and demonstrated no abnormalities in the RNFL scans (*Figure 1*).

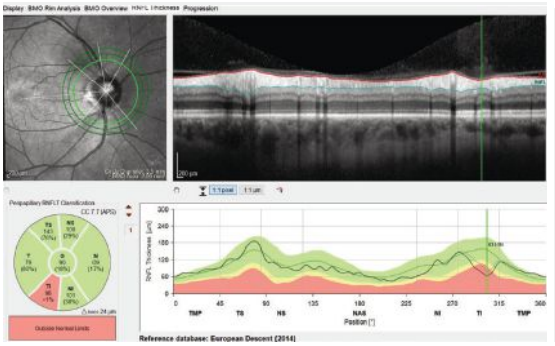
The patient was seen regularly, with periodic OCT scans, visual fields, optic nerve photos and stereoscopic disc evaluations. In all that time, no changes were observed.

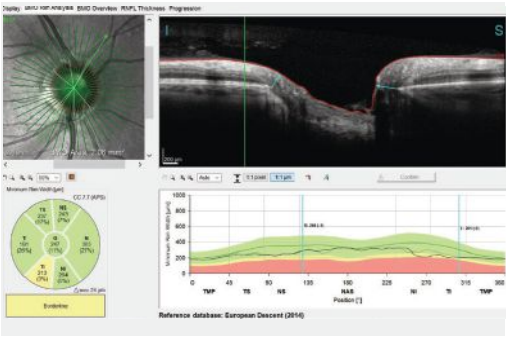
Changing Over Time

But, as time when on and technologies improved, a new glaucoma protocol evolved. Her first set of scans using three different diameter retinal nerve fiber layer (RNFL) circle scans, as well as Bruch's membrane opening (BMO), showed a small sector of the inner RNFL in the right eye that slightly falls outside the normative reference database (*Figure 2*). In other words, the first indication of red disease. However, this being a new scanning technique, absolute comparison with the earlier scan was not possible.

As time passed, the patient returned for follow-up visits as scheduled. In 2017, a subsequent

set of OCT scans was obtained, and, interestingly, revealed a demonstrable change in this inferotemporal segment of the RNFL (*Figure 3*). Also, a small change could be seen in the BMO scan (*Figure 4*). These findings indicate that the area of change is more noticeable in the RNFL than in the neuroretinal rim.





Figs. 3 and 4. Left, this scan demonstrates a loss of 15µm of the patient's RNFL thickness in the inferotemporally segment. Right, this scan demonstrates a change the inferotemporal neuroretinal rim consistent with the RNFL scans, indicating thinning of the BMO-MRW measurement.

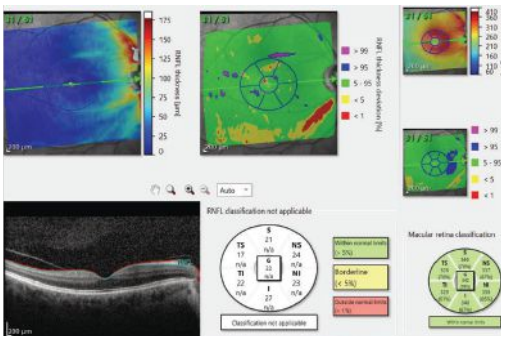


Fig. 5. This scan shows our patient's RNFL defect in red in the center top image.

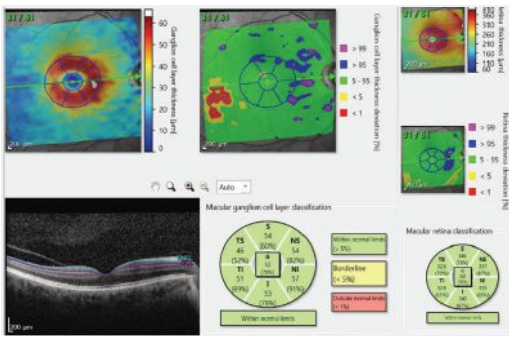


Fig. 6. The top center image, in red, shows the patient's GCL deviation map. Note that the location of these ganglion cell bodies is consistent with the location of their axons as seen in Figure 5.

Interpretation

The ultimate question is whether the difference seen on subsequent scans is real change that represents actual damage or progression. To answer this question, dig deeper into the information available. The deviation maps show aberrations in these same RNFL areas and corresponding ganglion cell layer (GCL), thereby giving a reasonable degree of certainty that the change demonstrated is actual progression of the disease process (*Figures 5 and 6*). Furthermore, a demonstrable change in the BMO-MRW scans can be seen compared with the characteristics of the neuroretinal rim in Figure 4.

Given the reliable change seen in the last set of OCT scans, it is clear that the patient has progressive disease, and therapy was initiated. This case exemplifies several lessons for any ODs who manage glaucoma:

1. By far, the hallmark of glaucoma is change over time. If you're seeing change, you're most likely looking at progressing disease.

2. Just because a finding is outside of normal limits does not mean that it is actual disease. It may be red disease.

3. As this case shows, red disease can become real disease—if it changes over time.

4. Change may occur first in the RNFL and progress toward the neuroretinal rim, or it may occur first in the neuroretinal rim and then progress outward into the RNFL. Be aware of both possibilities.

5. Change may be detected in the macula if your instrument is sensitive enough to discern 3µm to 4µm changes in the GCL thickness.

6. Technology changes. The OCT that you have now will be improved upon. Generally that translates into better image information, but not always. Updating your instrumentation is certainly something to consider.

7. If you do upgrade your technology, even with the same platform, be careful when comparing new data to old data. Be specifically aware of the nuances of the technologies and software.

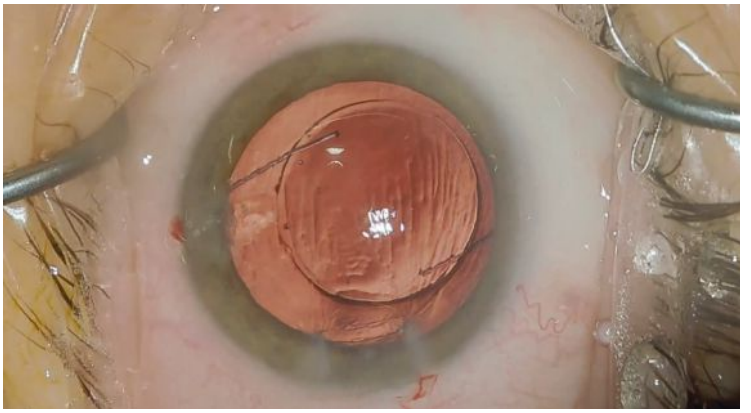
8. Your old instrument may not show damage, whereas your new instrument may. That requires you to delve deeper in to the nuances of the case and make a determination based on conflicting data. Sometimes that is tough to do, but it may become clearer as time elapses. ■

When Surgery Isn't Sufficient

A new IOL can be adjusted post-implantation to provide more optimal outcomes.

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

A new intraocular lens (IOL) technology allowing for postoperative vision refinement like we have never seen before is now available in the United States. The Light Adjustable Lens (RxSight) is made of an ultraviolet (UV) light-activated macromer that an be reshaped after cataract surgery to fune-tune the refraction. This technology is unique in that the shape and focusing characteristics of the lens can be changed after implantation (weeks to months).



The Light Adjustable Lens after insertion in the eye.

How it Works

An office-based light source called the Light Delivery Device (LDD, RxSight) focuses UV light on different areas of the lens, causing theilluminated macromers to connect with other particles and form polymers. This changes the curvature of the lens to adjust for residual refractive error after cataract surgery. The light-adjustment treatment requires a fully dilated pupil and takes between eight and 120 seconds each session.

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

Once the optimum focal power is achieved, the LDD then "cures" the lens to lock in the optical power. The curing process activates all remaining marcomers in the lens without changing the lens shape, effectively stabilizing the lens.

Post-op Do's and Don'ts

Although surgical implantation of this lens is no different than any other three-piece IOL, the post-op journey looks quite different. The patient must wear special UV-blocking glasses at all times—both indoors and outdoors—until several days after the lens is "cured," which might take a few months. This additional step requires explicit patient education, as exposure to incidental UV light could cause the lens to change in an unpredictable fashion or even use up all the potential macromers. Sunglasses, clear glasses and glasses with bifocal adds are given to the patient.

The post-op process may present a significant commitment for the patient, as multiple treatments (two to five) are necessary to fully adjust the lens. At each visit, the patient undergoes a careful refraction and gives feedback about their visual performance. For instance, if they elected for monovision and the eye was targeted at a refractive error of -1.50D, the patient could then ask for the focal point to be moved in (or out) several inches at one of the follow ups.

The treatment does have its limitations. You can only reliably change up to 2.00D of sphere and up to 2.00D of cylinder in the lens. The treatment is based on what the phoropter refraction can achieve, meaning it may not correct irregular corneas and irregular astigmatism as well as you'd hope.

Commercially, there is an aspheric monofocal lens option offered in the United States, meaning patients can be precisely corrected to any focal point in each eye. This technology is currently not available in other forms, but, as the lens can be molded into any shape, the future may hold multifocal and extended depth-of-focus options. An FDA study is now looking into an extended depth-of-focus variation of this lens. ■

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Meetings + Conferences

NOTE: Information was compiled prior to the pandemic. Please contact meeting organizers to confirm events and dates.

May

■ **2.** *Coastal California Optometric Conference.* Kimptom Goodland Hotel, Santa Barbara, CA. Hosted by: Tri-County Optometric Society. Key faculty: Bryant Lum, Robert Avery, Scott Schachter, Adam Harcourt. CE hours: 8. For more information, email Steve Langsford at doctorlangsford@gmail.com.

■ **14-17.** *VT3/Strabismus & Amblyopia.* Vision Sense Optometry, Halifax, Canada. Hosted by: the Optometric Extension Program (OEP) Foundation. Key faculty: John Abbondanza. CE hours: 35. For more information, email Karen Ruder at karen.ruder@oepf.org, call 410-561-3791 or go to www.oepf.org.

■ **17.** *Glaucoma Symposium.* Salus University, Elkins Park, PA. Hosted by: Salus University. Key faculty: G. Richard Bennett, Alissa Coyne, Andrew Meagher, Carlo Pelino. CE hours: 6. For more information, email Natalie Standig at nstandig@salus.edu, call 215-780-1381 or go to www.salus.edu/events.

■ **28-30.** *Virtual Great Lakes Eyecare Conference.* Hosted by: the Michigan Optometric Association. Key faculty: Bradley Habermehl, Nathan Lighthizer, Jason Duncan, Pinakin Davey, Alan Glazier. For more information, email the Michigan Optometric Association at info@themoa.org, call 517-482-0616 or visit www.themoa.org.

June

■ **1-4.** *Indian Health Service Biennial Eye Care Meeting.* Marshall B. Ketchum University, Fullertown, CA. Hosted by: the Southern California College of Optometry & Indian Health Service. CE hours: 26. For more information, email Bonnie Dellatorre at ce@ketchum.edu, call 714-449-7495 or go to www.ketchum.edu/ce.

■ **3-7.** *VT1/Visual Dysfunctions.* Vision Care Specialists, Southborough, MA. Hosted by: the OEP Foundation. Key faculty: John Abbondanza. CE hours: 35. For more information, email Karen Ruder at karen.ruder@oepf.org, call 410-561-3791 or go to www.oepf.org.

■ **3-7.** *VT2/Learning-related Visual Problems.* Nova Southeastern University, Fort Lauderdale, FL. Hosted by: the OEP Foundation. Key faculty: Robin Lewis. CE hours: 35. For more information, email Karen Ruder at karen.ruder@oepf.org, call 410-561-3791 or go to www.oepf.org.

■ **6-7.** *IU Summer CE.* Indiana University School of Optometry, Bloomington, IN. Hosted by: IU School of Optometry. CE hours: 16. For more information, email Cheryl Oldfield at coldfiel@indiana.edu, call 812-856-3502 or go to expand.iu.edu/browse/iuso-ce.

■ **6-8.** *Ocular Disease Update.* Big Cedar Lodge, Ridgedale, MO. Hosted by: the Oklahoma College of Optometry. Key faculty: Doug Devries, Justin Schweitzer, Spencer Johnson. CE hours: 16. For more information, email Callie McAtee at mcateec@nsuok.edu, call 918-316-3602 or go to optometry.nsuok.edu/continuing-education/schedule-of-events.

■ **7-19.** *TPA Certification/Board Review Course & Workshop.* NSU Fort Lauderdale/Davie Campus, Fort Lauderdale, FL. Hosted by: the NSU College of Optometry. CE hours: 100. For more information, email Michelle Morgado at oceaa@nova.edu, call 954-262-4224 or go to optometry.nova.edu/ce.

■ **11-14.** *GOA Annual Meeting.* Wild Dunes Resort, Isle of Palms, SC. Hosted by: the Georgia Optometric Association. Key faculty: Mohammad Rafieetary, Andrew Rixon. CE hours: 15. For more information, email Vanessa Grosso at vanessa@goaeyes.com, call 770-961-9866, ext. 1 or go to www.goaeyes.com.

■ **11-14.** *UOA Annual Congress.* The Zermatt Resort, Midway, UT. Hosted by: the Utah Optometric Association. CE hours: 22. For information, email Alyssa White at alyssa@utaheyedoc.org, call 801-364-9103 or go to www.utaheyedoc.org.

■ **12-13.** *MOA 2020 Summer Convention.* Sandestin Golf & Beach Resort, Miramar Beach, FL. Hosted by: the Mississippi Optometric Association. Key faculty: Randall Thomas, Ron Melton, Andrew G. Lee. CE hours: 10. For more information, email Sarah Link at selink@mseyes.com or go to www.mseyes.com.

■ **12-14.** *NCOS 2020 Spring Congress.* Embassy Suites Kingston Plantation, Myrtle Beach, SC. Hosted by: the North Carolina Optometric Society. CE hours: 18. For more information, email Christy Santacana at christy@nceyes.org, call 919-977-6964 or go to nceyes.org/spring-congress.

■ **14.** *Wine Country CE: A Flight of Ocular Courses.* Vintners Inn, Santa Rosa, CA. Hosted by Redwood Empire Optometric Society. Key faculty: Paul Karpecki. CE hours: 6. For more information call Margot Shipley at 707-681-1535 or go to www.reosvision.com.

■ **17-21.** *VT2/Learning-related Visual Problems.* InDepth Vision, Milton, Ontario, Canada. Hosted by: the OEP Foundation. Key faculty: John Abbondanza. CE hours: 35. For more information, email Karen Ruder at karen.ruder@oepf.org, call 410-561-3791 or go to www.oepf.org.

■ **18**. *PECAA Optical Merchandise Workshop.* Indianapolis. Hosted by: Professional Eye Care Associates of America. Key faculty: Doug Martin, Samantha Toth. CE hours: 3 COPE, 3 ABO, 3 NCLE, 3 CPC. For more information, email Cathi Zerba at cathi@pecaa.com or call 503-670-9200.

■ **24-28.** *AOA Optometry's Meeting.* Gaylord National Resort & Convention Center, Washington, DC. Hosted by: the American Optometric Association and the American Optometric Student Association. CE hours: total: 234, maximum per OD: 39
For more information, email Sarah Sutherland at ssutherland@aoa.org, call 314-983-4124 or go to optometrysmeeting.org.

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Critical Mass

An unusual finding was seen in a patient with blurred vision. Can you tell how the signs and symptoms are connected? **By Mark T. Dunbar, OD, and Jimmy Nguyen, OD**

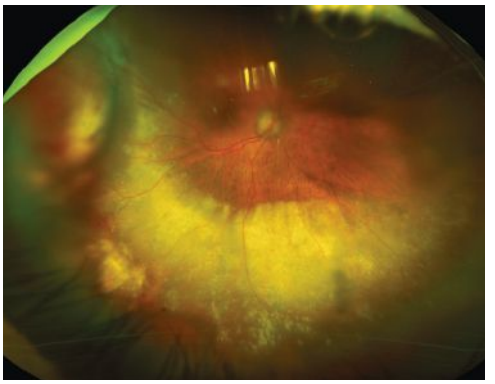
An 86-year-old Hispanic female presented to our office with complaints of blurred vision of the right eye for the past two months. She denied flashes, floaters, double vision or eye pain. Her medical history was remarkable for tachycardia, for which she was being treated with propranolol. She reported no personal or familial history of cancer, including ocular and cutaneous melanoma.

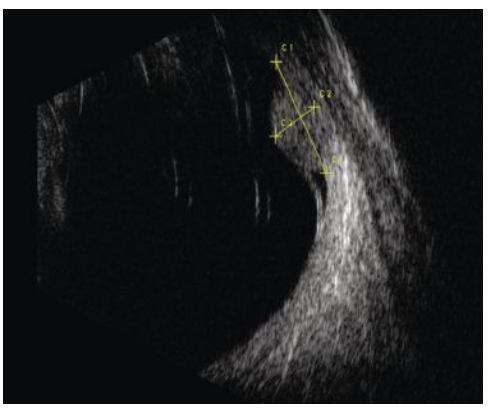
Evaluation

On examination, her best-corrected visual acuity was 20/200 OD and 20/20 OS. Her right eye's confrontation visual fields were constricted nasally and were full-to-careful finger counting in the left. Ocular motility testing results were normal and the pupils were equally round and reactive to light without an afferent pupillary defect.

The anterior segment was significant for meibomian gland dysfunction and confluent corneal guttae of both eyes without corneal edema. The anterior chambers were deep with no evidence of cell or flare. She had posterior chamber intraocular lens implants with 2+ posterior capsular opacification of the right lens and open posterior capsule of the left lens. Her intraocular pressures were 17mm Hg OD and 20mm Hg OS.

On dilated fundus exam, the vitreous was clear with no cells. The optic nerves appeared pink and healthy with good rim coloration and perfusion in both eyes. A reddish subretinal mass was visible in the far temporal periphery in the right eye at 9 o'clock associated with overlying subretinal hemorrhage and a shallow inferior exudative retinal detachment with subretinal lipid exudation (*Figure 1*). The peripheral retinal exam of the left eye was normal.





Figs 1 and 2. At top, our patient's right eye, seen in widefield image, has an elevated lesion. Below, the B-scan through the lesion below also shows its thickness and the overlying retinal detachment.

Additional Testing

Echography was performed of the right eye and showed a broad, non-vascularized, medium-high reflective lesion in the temporal quadrants straddling the equator anteriorly and posteriorly. The maximum thickness of the lesion was on the anterior side of the equator at 9 o'clock measuring 3.1mm. A shallow retinal detachment is noted over and adjacent the lesion (*Figure 2*).

Fluorescein angiography (FA) of the right eye showed early phase perifoveal petaloid leakage, temporal far peripheral aneurysmal dilatations with telangiectatic vessels and evidence of late leakage (*Figure 3*). The left eye was normal.

SD-OCT of the right eye showed cystoid macular edema, vitreomacular traction and blunting of the foveal contour (*Figure 4*). The left was normal.

Take the Retina Quiz

1. What is the likely diagnosis?
a. Amelanotic choroidal melanoma.
b. Vasoproliferative tumor.
c. Retinal capillary hemangioblastoma.
d. Choroidal osteoma.

2. What genetic conditions are associated with this lesion?
a. Tuberous sclerosis.
b. Neurofibromatosis.
c. Von-Hippel Lindau.
d. None of the above.

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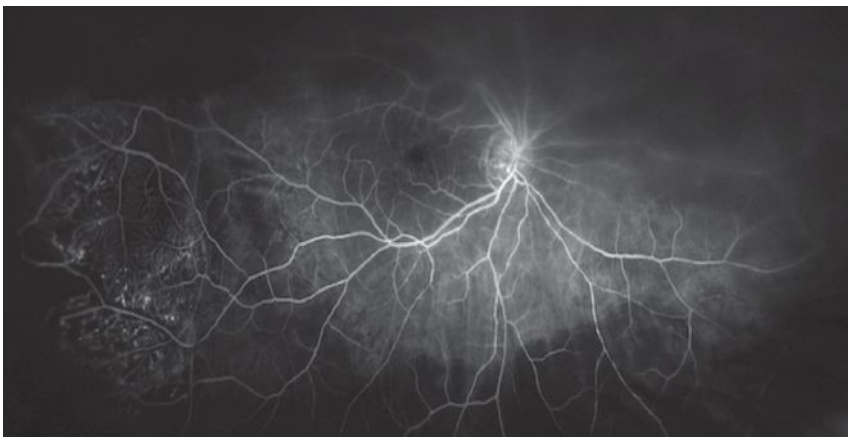
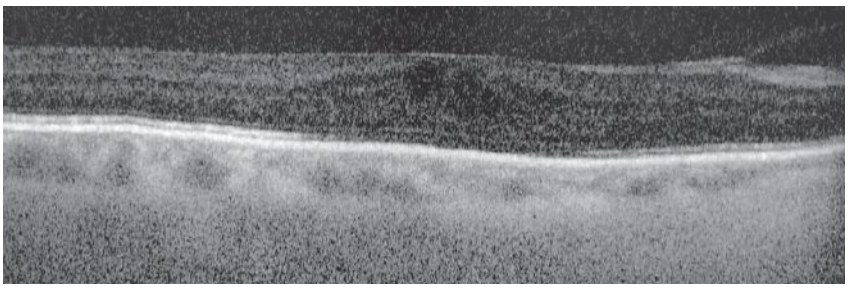
3. Which statement best describes the histology of this lesion?
a. Reactive astrocytic glial proliferation.
b. Composed of capillary-like vascular channels between large foamy cells.
c. Benign ossifying choroidal tumor.
d. Mixture of spindle cells and epithelioid cells.

4. Which if the following pre-existing ocular conditions are associated with development of this lesion?
a. Retinitis pigmentosa.
b. Coats' disease.
c. Previous retinal detachment repair.
d. All of the above.

For answers, see page 90.





Figs. 3 and 4. In the above fluorescein angiogram, the patient's aneurysmal dilations and leakage are visible. Below is an OCT.

Diagnosis

We can clearly see temporally in the right eye an elevated mass with a significant amount of exudation extending inferiorly circumferentially. One of the biggest concerns was the possibility of a choroidal melanoma, but aside from the elevation, the clinical picture didn't really fit a melanoma diagnosis. In addition, the ultrasound showed the lesion to have medium-to-high reflectivity, which is not typical for a choroidal melanoma, which usually exhibits low-to-medium reflectivity.

So, we must consider other causes, and the massive amount of exudation should be an important clue. The exudation combined with the FA, which shows significant aneurysmal vascular changes in the periphery, points to Coats' disease.

Coats' disease is an idiopathic vascular anomaly characterized by aneurismal dilations and telangiectasia of the retinal vessels.[1-2] It's often unilateral and most (more than 90%) cases occur in males between the first and second decade of life.[1-2]

Our patient is female (and much older), so this would be extremely unusual. The retinal capillaries tend to be most affected, but changes can also be seen in the major retinal vessels. These vessels become incompetent and leak fluid in the form of exudate. The hallmark of this condition is an exudative retinopathy. The extent of involvement and degree of severity can be variable.

That doesn't completely explain why there is a large elevated mass. Putting this all together, our patient likely has a vasoproliferative tumor as a secondary complication of Coats' disease. Less likely possibilities include peripheral exudative hemorrhagic chorioretinopathy (PEHCR), amelanotic choroidal melanoma, retinal hemangioblastoma, choroidal hemangioma and choroidal metastatic tumors.

Discussion

Vasoproliferative tumors appear as ill-defined reddish-yellowish globular masses, most frequently involving the inferotemporal periphery. These tumors are difficult to visualize ophthalmoscopically and are easily confused with other choroidal tumors or eccentric disciform lesions.

Vasoproliferative tumors are classified into two categories: idiopathic or secondary to pre-existing ocular diseases. Histology demonstrates that these tumors are comprised of a preponderance of reactive astrocytic cells, as opposed to vascular proliferation, despite the nomenclature.[3] The terms *reactionary retinal glioangiosis* and *retinal reactive astrocytic tumor* reflect the histopathology.

These tumors are generally thought to be reactive lesions that arise in response to chronic chorioretinal injury. The most common conditions leading to secondary vasoproliferative tumors include retinitis pigmentosa, intermediate uveitis, Coats' disease and previous retinal detachment repair.[4]

Vasoproliferative tumors themselves are benign; however, they can produce significant intraretinal and subretinal exudation, exudative retinal detachment, cystoid macular edema (CME), epiretinal membrane and hemorrhage leading to visual symptoms, including floaters, distortion, photopsia and poor vision. Anterior segment complications related to vasoproliferative tumors are rarely reported.[4]

Management of these lesions depends on the tumor size, location, amount of exudative retinopathy and patients' symptoms. Close observation to watch for growth is recommended for small peripheral lesions with minimal exudation.[5] These lesions are typically seen in the setting of an epiretinal membrane and vitreoretinal traction, and therefore a pars plana vitrectomy and membrane peel may be indicated.

Intravitreal anti-VEGF injection and intravitreal steroid injections may be used to manage the exudative retinopathy and macular edema.

Cryotherapy, brachytherapy and argon laser photocoagulation are the mainstay treatments used for tumor regression.[6]

Our patient had developed CME because of the massive amount of exudation. We recommended a pars plana vitrectomy with a membrane peel. She also had an intravitreal injection of an anti-VEGF medication on the initial visit and an intravitreal injection of Triesence (triamcinolone acetonide, Novartis) at the time of surgery. We are also considering performing low-energy, long-duration argon laser to the subretinal lesion and abnormal overlying vasculature. ■

Dr. Nguyen is currently an OD Resident at Bascom Palmer Eye Institute in Miami.

1. Do D, Haller J. Coats' Disease. In: Ryan SJ. Retina, vol. II: Medical retina. 4th edition St. Louis: Mosby; 2006:1417-23.
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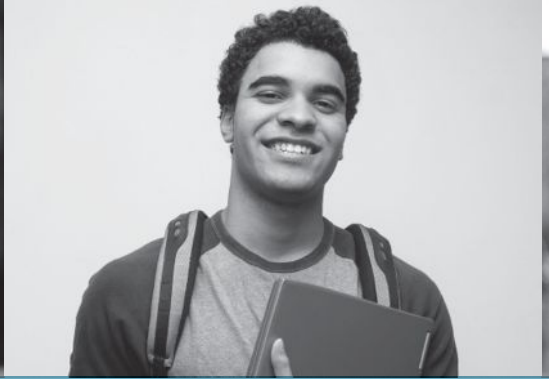


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Diagnostic **Quiz**

Overnight Sensation

Can you identify what happened to this patient's lid while he slept?

By Andrew S. Gurwood, OD

History

A 57-year-old Black male reported to the office with a chief complaint of a swollen eyelid that had been bothering him for a day. He explained that he had gone to sleep feeling normal, but when he woke up, he had a swollen lid. His systemic and ocular histories were unremarkable and he denied exposure to chemicals or knowing of any allergies.

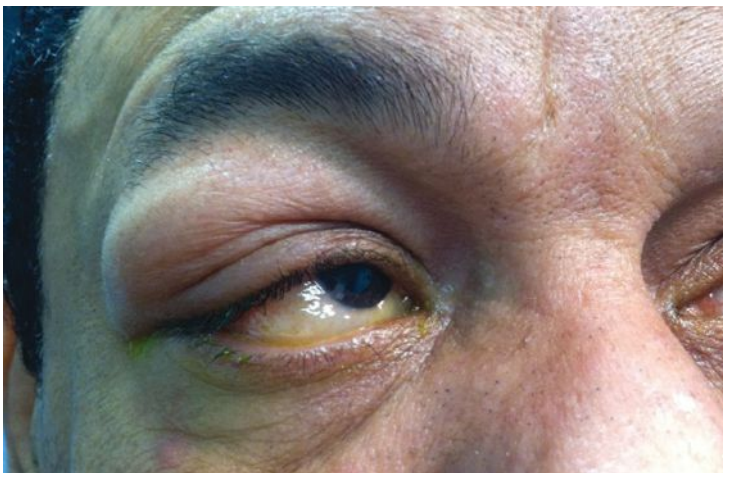

Fig. 1. This patient went to sleep feeling fine, but something went bump in the night—his eyelid. Can you identify what caused this and how he should be treated?

Diagnostic Data

His best-corrected entering visual acuities were 20/20 OU at distance and near. Extraocular muscles and confrontation fields were normal and he showed no evidence of afferent pupillary defect. The biomicroscopic examination of the anterior segment was normal and the external examination is demonstrated in the photograph (*Figure 1*). Goldmann applanation tonometry measured 15mm Hg OU.

The dilated fundus findings were normal peripherally and centrally with normal nerves and maculae.

Your Diagnosis

Does the case presented require any additional tests, history or information? Based on the information provided, what would be your diagnosis? What is the patient's most likely prognosis? To find the answers, please visit us at www.reviewofoptometry.com. ■

Retina Quiz Answers *(from page 84):* 1) b; 2) d; 3) a; 4) d.

Next Month in the Mag

Coming in May, Review of Optometry will present its Annual Dry Eye Report. Topics include:

- Treat Before the Cut: Managing Dry Eye in Cataract Patients
- Diet and Dry Eye: What You Need to Know
- Don't Overlook Aqueous-deficient Dry Eye

Also in this issue:

- Statins and the Eye: What You May Not Know
- Practical Tips on OCT Interpretation in Glaucoma (Earn 2 CE Credits)
- Top Five Cases You Shouldn't Refer Out

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