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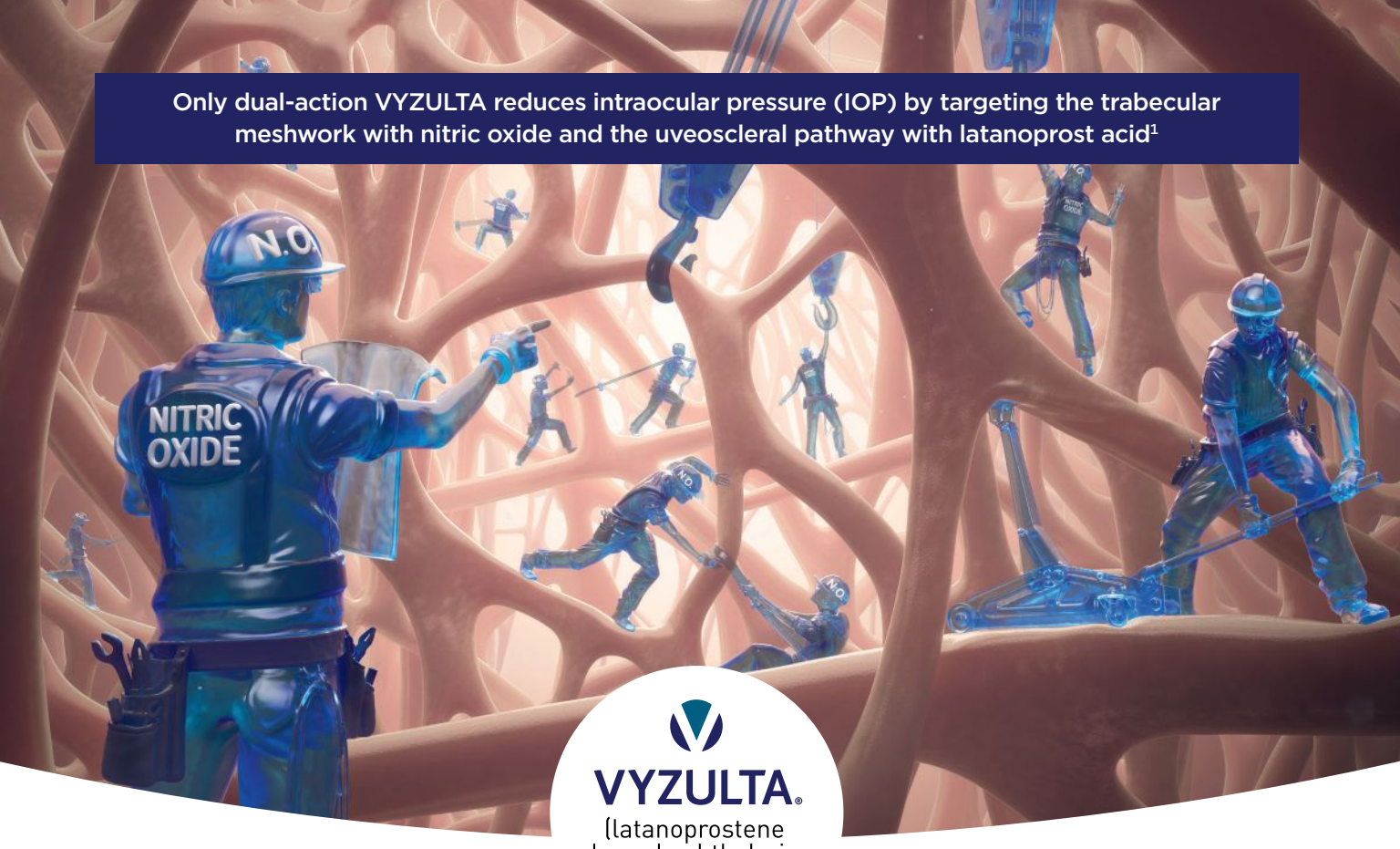

Only dual-action VYZULTA reduces intraocular pressure (IOP) by targeting the trabecular meshwork with nitric oxide and the uveoscleral pathway with latanoprost acid[1]

VYZULTA®
(latanoprostene bunod ophthalmic solution), 0.024%

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]

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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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BAUSCH + LOMB

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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IN THE NEWS

A third of **patients who undergo "eye lifts" with cosmetic facial fillers develop strabismus**, a new study finds—and surgery is only successful for patients without persistent ophthalmoplegia. The study looked at the records of 23 patients with ophthalmic artery occlusion after cosmetic facial filler injections. Five out of the six patients who had strabismus surgery showed initial ophthalmoplegia. Ultimately, successful outcomes were achieved in only the four patients without persistent ophthalmoplegia.

Yang H, Woo S, Kim S, Hwang J. Surgical outcomes of strabismus after iatrogenic ophthalmic artery occlusion caused by cosmetic filler injections. BMC Ophthalmol. December 16, 2019. [Epub ahead of print].

New research shows **fixed dosing with anti-VEGF eliminated disease activity**—absence of both leakage and retinal fluid—in most eyes with **neovascular AMD** over the course of 52 weeks. At baseline, 95.4% of eyes had both leakage and fluid. By week 52 of treatment, the number dropped to 6.0%.

Moshfeghi DM, Thompson D, Saroj N. Changes in neovascular activity following fixed dosing with an anti-vascular endothelial growth factor agent over 52 weeks in the phase III VIEW 1 and VIEW 2 studies. Br J Ophthalmol. December 11, 2019. [Epub ahead of print].

A recent study found that the **optical density of the post-lens fluid increases over time with miniscleral lens wear and negatively impacts low-contrast visual acuity (VA)**. The mean best-corrected high- and low-contrast VAs significantly improved with miniscleral lens use in 23 keratoconus patients. However, optical density significantly increased over time and low-contrast VA significantly decreased after two hours of lens wear.

Turhan SA, Yigit DD, Toker E. Impact of changes in the optical density of postlens fluid on the clinical performance of miniscleral lenses. Eye Cont Lens. November 29, 2019. [Epub ahead of print].

Birth Control Pills Alter the Retina

Women who took oral contraceptives for a year had a thinner RNFL, GCL and choroid.

By Jane Cole, Contributing Editor

Clinicians already know to keep an eye on dry eye, contact lens discomfort and corneal edema in their patients taking oral contraceptive pills, but new research suggests they need to watch the retina and macula as well. A study in *BMC Ophthalmology* suggests that, when taken for at least a year, birth control pills can cause significant changes in the retinal and choroidal thickness, and women who take them for longer periods may have further issues involving their central vision.

Researchers from Egypt used spectral-domain optical coherence tomography (OCT) to look at the effect oral contraceptive pills had on the macula, retinal nerve fiber layer (RNFL), ganglion cell layer (GCL) and choroid.

The study included 60 eyes of 30 healthy women who took monophasic oral contraceptive pills—Levora (0.03mg ethinylestradiol/0.15mg levonorgestrel, Mayne Pharma) for at least one year, and 60 eyes of 30 healthy women who did not take oral contraceptives. The investigators collected OCT measures of the retinal thickness in the follicular phase (day three) of the last menstrual cycle in all women. The study also took into account the body mass index (BMI) scores and age of each participant, but found no differences in BMI—or age—between the groups.

However, all macular parameters were considerably lower in the women who were taking oral contraceptives compared with the control group. And, the investigators reported that the women who took oral contraceptives had thinner RNFL, GCL and choroidal measurements.

The researchers suggested women who take birth control pills should have OCT imaging done on a routine basis, and additional long-term studies that investigate different types of oral contraceptives are warranted.

"It is important to find out when this thickness alterations can be clinically significant or symptomatic and if these changes are reversible or not," the researchers wrote in their paper.

Physicians should consider a patient's ocular history before recommending a contraceptive method and before prescribing birth control pills for reasons other than contraception, they added.

Shaaban YM, Badran TAF. The effect of oral contraceptive pills on the macula, the retinal nerve fiber layer, the ganglion cell layer and the choroidal thickness. BMC Ophthalmol. December 10, 2019. [Epub ahead of print].

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LWE Staining Reveals Lens-associated Insult

To better understand lid wiper epitheliopathy (LWE) from a cytological perspective, researchers conducted a study exploring the relationship between lid margin cell morphology, lid wiper epitheliopathy, contact lens wear and lens-related symptoms.

The team found that rigid contact lens wear was associated with significantly wider, more keratinized lid wiper conjunctival regions, as determined by histology. Rigid lens wear was also associated with higher lid wiper epitheliopathy grades compared with soft contact lens and non–lens wearers. The researchers believe these findings suggest a mechanical, lens-associated insult occurs at the lid margin, possibly linked to lens-related factors such as lens size, movement, material, edge design and modulus.

The study enrolled 20 habitual, symptomatic and 20 asymptomatic soft contact lens wearers, 18 rigid gas permeable wearers and 19 non–contact lens wearers. Participants were required to have a minimum of two years of continuous wear and a minimum wear schedule of three days per week. The upper lid wiper conjunctiva measured 424±171µm, 404±75µm, 667±219µm and 266±64µm in asymptomatic soft, symptomatic soft, rigid and non–contact lens wearers, respectively. The corresponding lower lid wiper conjunctivae measured 141±57µm, 232±150µm, 519±212µm and 225±102µm, which was significantly narrower than that of the upper eyelid in most cases.

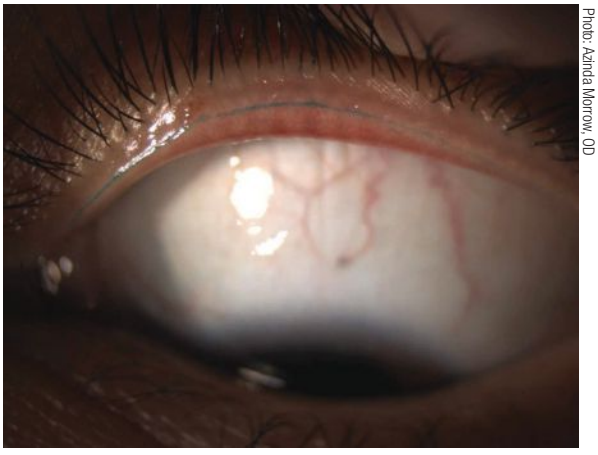

Photo: Azinda Morrow, OD

Staining shows lid wiper epitheliopathy present on the upper eyelid.

The participants' symptoms were not associated with any changes to the lid margin. Despite featuring prominent lid margin change, rigid lens wearers reported similar or better comfort than asymptomatic or even non-lens wearers. The researchers speculate that the apparent lack of correlation between friction-related insult and symptoms in rigid lens wearers might be masked by such mechanisms, thus preventing prediction of any association. Nevertheless, they note impression cytology offers a comprehensive view of the lid margin cytomorphology, allowing them to observe the effects of mechanical insult and to quantify the extent of vital staining lid wiper epitheliopathy grades.

Muntz A, Subbaraman LN, Craig JP, Jones L. Cytomorphological assessment of the lid margin in relation to symptoms, contact lens wear and lid wiper epitheliopathy. Ocul Surf. December 7, 2019. [Epub ahead of print].

Epithelial Thickness Unchanged in Daily CL Wear

Soft daily disposable contact lenses are often cited as the healthiest lens choice because of their lower risk of infection, but a new study reports they also don't appear to change corneal epithelial thickness. A team of Turkish researchers found that anterior corneal topographic readings rose and fluctuated naturally at times during the day, and the daily disposable lenses appeared to mask the steepening.

The study enrolled 32 healthy volunteers. At the first visit, researchers recorded keratometric measurements and corneal and epithelial thickness maps both in the morning and again eight hours later. The researchers then randomly fit each participant with one of four different brands of daily disposable lenses and on different days. All fitted lenses had a power of -3.00D. The investigators repeated the measurements prior to the fitting and again after eight hours of lens wear.

When patients weren't wearing lenses, anterior topographic readings showed significant steepening. Corneal thickness also decreased substantially in the central and temporal portion of the cornea in the afternoon, the researchers noted. No significant changes were found in the posterior topographical readings or corneal epithelial thickness.

When patients were wearing the daily disposable lenses, no significant change was seen in corneal and epithelial thickness or in the anterior and posterior curvatures during the day.

Additionally, the study found no major difference in epithelial thickness among the groups wearing the different contact lens types.

Turhan SA, Yigit DD, Toker E. Corneal epithelial thickness and corneal curvature changes during the day: The effects of daily disposable contact lens wear. Cont Lens Anterior Eye. December 10, 2019. [Epub ahead of print].

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Retinal Tear Repair Varies Based on Timing

Many surgical fields are impacted by fluctuating care on weekends, and a new study in *JAMA Ophthalmology* reports a similar trend for patients with retinal concerns.

Researchers from California found patients with rhegmatogenous retinal detachments who were treated on the weekend were more likely to undergo pneumatic retinopexy. Additionally, they reported patients who were treated on Sundays were more likely to require a second operation within 30 days, and those who were diagnosed on Fridays waited longer for surgery.

The claims-based study included 38,144 commercially insured patients in the United States with incident rhegmatogenous retinal detachment. All patients were treated within 14 days of diagnosis. The study assessed the patients' likelihood of repair with different procedures, and took into account the day of the week patients received the diagnosis or underwent retinal detachment repair.

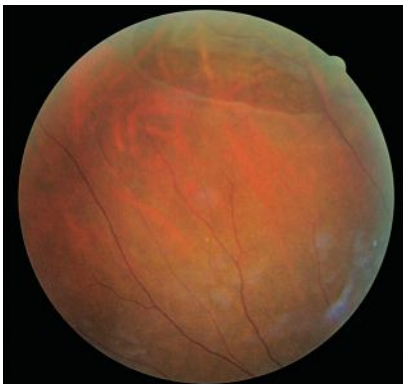

Photo: Diana Shechtman, OD

Patients such as this one with a large tear in the superior retina would be better served with surgical intervention on a weekday.

The researchers found pneumatic retinopexy was more likely to occur when patients received a diagnosis on Friday, Saturday or Sunday compared with a Wednesday diagnosis. The study also noted pneumatic retinopexy was the most common surgical procedure on Friday, Saturday, Sunday and Monday.

Patients who underwent pneumatic retinopexy on a Sunday were more likely to have a second procedure (repeat pneumatic retinopexy, scleral buckle or pars plana vitrectomy) within 30 days. The researchers found no link between the day of the week of the initial repair and the need for another procedure after scleral buckle or pars plana vitrectomy.

Another study highlight: patients who received a diagnosis on a Friday waited about 0.28 days longer for a repair than those who were diagnosed on a Wednesday.

Vail D, Pan C, Pershing S, Mruthyunjaya P. Association of rhegmatogenous retinal detachment and outcomes with the day of the week that patients undergo a repair or receive a diagnosis. JAMA Ophthalmol. December 19, 2019. [Epub ahead of print].

Dim the Lights—of Any Color

Intensity matters more than wavelength, study says.

Blue light has gotten a lot of negative press over the last decade. The popular understanding of its effect is that light on the blue spectrum—which has invaded our bedrooms by way of our omnipresent smartphones and tablets—specifically triggers the brain to stay awake. But researchers are reexamining that theory. A study recently published in *Current Biology* is suggesting that it's not so much the color of the light as much as its intensity. In fact, the study shows that yellow and white lights are linked to wakefulness moreso than blue light.[1]

The study suggests that the mammalian brain is conditioned to rest at the end of a light-to-dark cycle. In other words, as it gets darker, our brains prepare for sleep—whether that fading light is blue or not. To understand this, the researchers evaluated mice and their reactions to light brightness and color. They found that bright light of any color was stimulating, but when dimmed, blue light was actually more restful than yellow light.[1]

One of the researchers told the *BBC* that their research could mean that those "night mode" settings on smartphones and tablets aren't as helpful as advertised.

"Often what people are doing is adjusting the color of lighting or visual displays and making the screens more yellow," said Manchester University's Tim Brown, BSc, MRes, PhD. "Our prediction is that changing the color is having exactly the wrong effect. It's counteracting any benefit that you might get from also reducing the brightness of the screen."[2]

1. Mouland J, Martial F, Watson A, Lucas R, Brown T. Cones support alignment to an inconsistent world by suppressing mouse circadian responses to the blue colors associated with twilight. Curr Bio. 2019;29(12):4260-7.
2. Roberts M. What's the best colour lighting for sleep? BBC News. December 17, 2019.

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Reference: 1. Results from an in vitro laboratory study. TheraTears® SteriLid® Antimicrobial Eyelid Cleanser and Facial Wash showed efficacy in reduction of colony forming units for eight common eyelid organisms. Data was captured at 30 and 60 seconds.

M18-069-00

Ultrasound Lowers IOP in Glaucoma

For open-angle glaucoma patients with uncontrolled intraocular pressure (IOP) despite maximum medical therapy, high-intensity focused ultrasound may be a viable option. A study published in *Ophthalmology Glaucoma* found patients who underwent the ultrasound treatment had a 16% reduction in IOP and a decreased aqueous flow rate of 15% at three months post-treatment.

The comparative non-randomized interventional study enrolled 30 adults with either open-angle glaucoma or ocular hypertension who did not have adequate IOP control despite maximum medical treatment.

Patients underwent a comprehensive ophthalmic exam followed by fluorophotometry and tonography measurements of the aqueous humor. Patients then received six seconds of high-intensity focused ultrasound therapy. Aqueous humor dynamic measurements were repeated three months after the treatment.

Patients had a four-week washout from their glaucoma medication prior to the aqueous humor measurements at baseline and the three-month visit.

At the three-month visit, the approximate post-washout IOP was reduced by 16% (31.7±5.3mm Hg vs. 26.6±4.8mm Hg) while the aqueous flow rate was decreased by 15% (2.07±0.73µl/min vs. 1.77±0.55µl/min) from baseline without any significant effect on tonographic outflow facility and uveoscleral outflow.

The researchers noted a 20% risk of treatment failure, with six patients needing further surgical intervention within one month after the single ultrasound treatment.

Additionally, 80% of patients were able to undergo post-treatment washout measurements, and 26.6% of eyes achieved a greater than 20% IOP reduction at three months compared with baseline.

This is the first study that investigated aqueous humor dynamic effects using high-intensity focused ultrasound in patients with uncontrolled open-angle glaucoma on maximum tolerated medical therapy, the researchers said.

Alaghband P, Galvis E, Ramirez A, et al. The effect of high intensity focused ultrasound on aqueous humor dynamics in glaucoma patients. Ophthalmology Glaucoma. December 12, 2019. [Epub ahead of print].

Skip Steroids in Thygeson Patients

Topical tacrolimus is an aqueous suspension sometimes used in corneal healing and tear production.[1] In particular, volumes of research show its usefulness in dogs as an alternative to cyclosporine.[2] The hope—for humans—is that it can spare patients with any kind of ocular surface inflammation the potential complications of steroids. Now, research is showing that patients with Thygeson superficial punctate keratitis can dodge steroids using tacrolimus 0.02%.[3]

The study, published in *Cornea*, included the records of 10 patients—three males and seven females—all with Thygeson superficial punctate keratitis (TSPK). Seven of those patients were previously unresponsive when prescribed topical steroids or lubricants. All ten had bilateral involvement and were treated with topical tacrolimus 0.02% twice daily for an average of 10 weeks.[3]

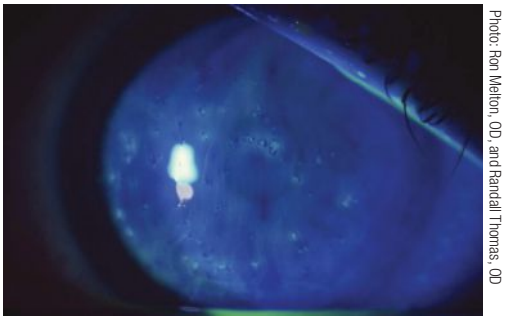

Photo: Ron Melton, OD, and Randall Thomas, OD

Standard TSPK presentation includes small, central epithelial opacities.

The investigators looked at how their symptoms improved, including tearing and photophobia, as well as structural signs. Notably, they examined the number, flattening and resolution of lesions and noted any decreases in staining.[3]

They found that all of the study patients experienced subjective improvement in symptoms such as tearing and photophobia and resolution of the superficial punctate keratitis in 72 hours after initiation of therapy. Tacrolimus was well tolerated in all patients, as well.[3] ■

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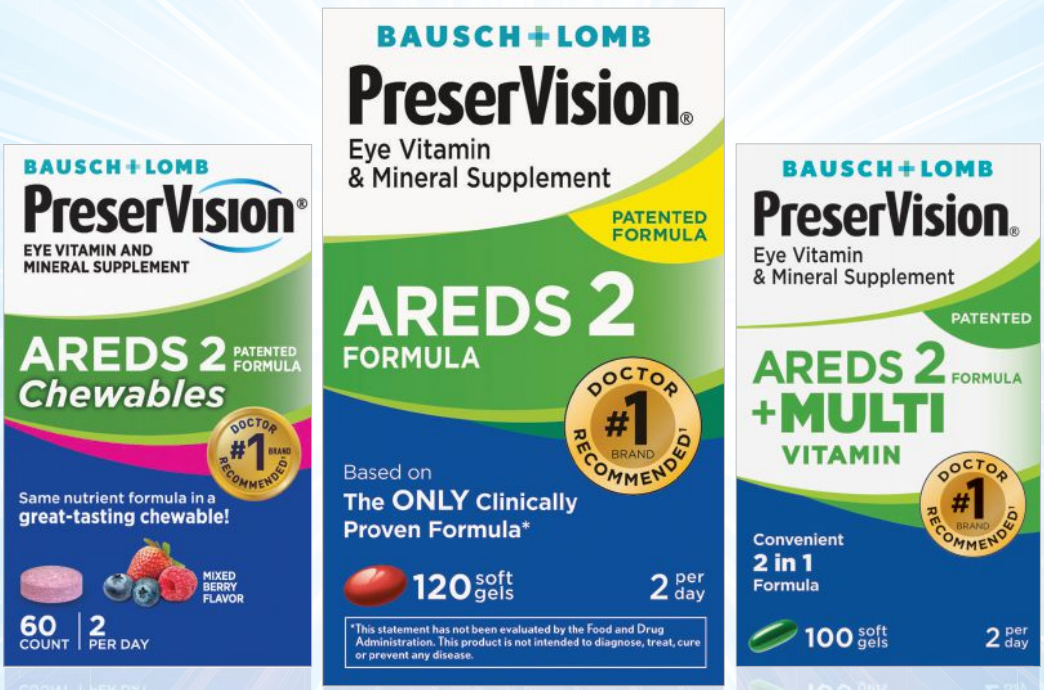

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Reference: 1. Age-Related Eye Disease Study 2 (AREDS2) Research Group. Lutein + zeaxanthin and omega-3 fatty acids for age-related macular degeneration: the Age-Related Eye Disease Study 2 (AREDS2) randomized clinical trial. *JAMA*. 2013;309(10):2005-2015.

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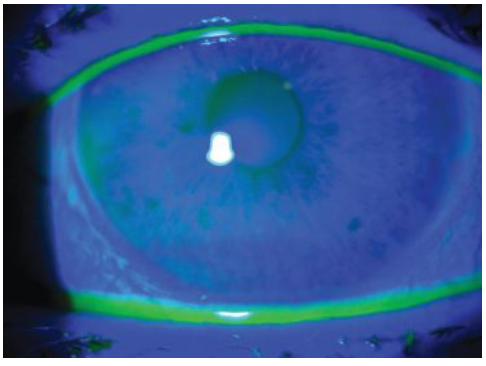

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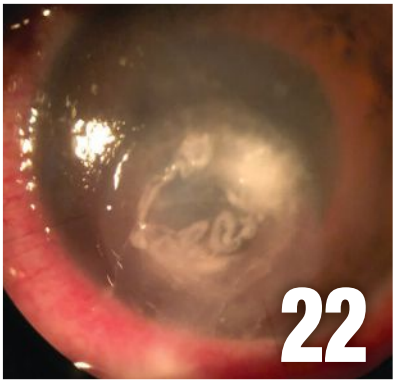

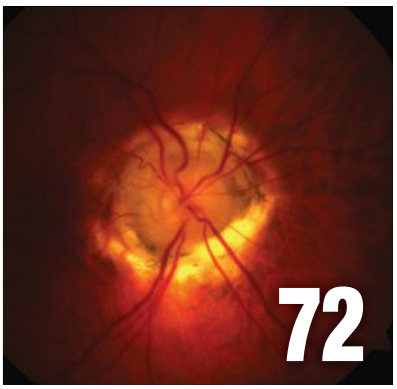

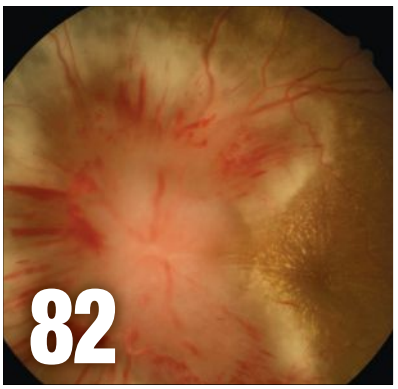

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1 McLaurin E, Cavet ME, Gomes PJ, Ciolino JB. Brimonidine ophthalmic solution 0.025% for reduction of ocular redness: A randomized clinical trial. Optom Vis Sci. 2018;95(3):264-271

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Outlook

By Jack Persico, Editor-in-Chief

Promises Worth Keeping

Let's get to work making good on your commitments to patients and opportunities for growth.

You're likely already tired of allusions to the connection between 2020 and 20/20, but please indulge us this month as we turn our attention to vision care for a special series of features entitled "The Promise of 2020." It seems like vision care—the bedrock of optometry—sometimes gets sidelined in favor of newer responsibilities in the realm of disease treatment and surgical comanagement.

You can see it everywhere. The keynote lectures at conferences, the prime real estate in exhibit halls, the heated online conversations and the cover stories in magazines like this one and others have all gravitated more toward the medical end of things. That's justified by the importance and relative newness of those responsibilities, and *Review* is proud to have been a leading voice for optometric scope expansion since at least the 1930s. This publication has helped move the profession forward with decades of advocacy and education, and will continue working hard to anticipate what comes next.

Still, I keep thinking back to a letter to the editor we received last fall from esteemed low vision expert Richard Shuldiner, OD. He took us to task for not impressing upon readers the importance of low vision. He wrote in part, "As optometrists, we must remember that all of the new technology for diagnosis and management we use, the nutritional and lifestyle changes the patient must make, the office visits, tests and injections into the eye they must endure are all done and suffered through for one reason: they want to see!"

Can't argue with that. We've been steadily bringing vision care topics back into *Review* and kick off the new year with a five-article series on any number of things than might keep a patient from seeing clearly enough to function well and enjoy life. Myopia control, acuity testing, binocular vision, presbyopia and, yes, low vision all get some well-deserved attention this month.

In this issue and all that's ahead for the year, our aim is to help you fulfill two senses of the word *promise*: as *pledge* and as *potential*.

First, the pledge of 20/20. Patients rely on you to help them see because sight is utterly vital to life. A patient in the chair enters into an implicit compact with you: "Help me see the world to the best of my abilities, doc." You pledge to deliver on that every time you greet a patient.

Next, the potential of 2020. So many opportunities are yours for the taking. You can develop a subspecialty or remain a generalist. You can learn new skills, partner with MDs and evolve just as the profession at large is doing. Within the vast world of eye and vision care, you can chart the course that's right for *you*. No matter what, you'll undoubtedly improve the lives of thousands.

A final promise comes from us: to keep making *Review of Optometry* a trusted source of guidance to you in all your endeavors. We're humbled by your loyal readership and pledge to earn it, every month and every day, by helping you better understand tried-and-true vision topics, insights from the latest medical literature and everything in between. ■

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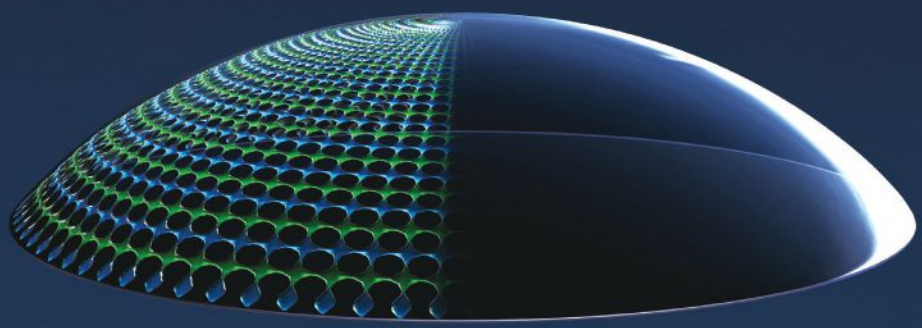

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The Year of Refraction

Innovative management approaches are in your office now or on the way.

By Paul M. Karpecki, OD, Chief Clinical Editor

You've heard a lot about myopia control, but it wasn't until a few months ago that we received the first FDA indication of a contact lens for it. Big changes are in the works for presbyopia management, too. It's shaping up to be a good year to be in the business of correcting refractive errors all across the lifespan.

On-label Myopia Control

In November 2019, the FDA approved CooperVision's MiSight 1 day contact lens to slow myopia progression for children between the ages of eight and 12.

The daily disposable soft lens is designed with center correction and peripheral defocus to reduce stimuli of myopia progression. In a three-year randomized controlled clinical trial of 135 children, the subjects were divided between MiSight and a conventional soft lens. For the full three-year period, progression of myopia in those wearing MiSight lenses was less than with conventional soft lenses. More importantly, subjects who used MiSight had lesser increases in axial length.[1]

Budget-friendly Tech

DGH Technology recently introduced an easy-to-use A-scan ultrasound with high-resolution—for less than $3,000. This technology provides A-scan tracking and myopia control reports. In addition to tracking myopia, ultrasound has relatively good reimbursement for other medical conditions, such as:

- Monitoring nevi every six or 12 months to rule out melanoma.
- Assessing posterior vitreous detachment in symptomatic patients.
- Differentiating buried drusen from papilledema.
- Imaging any conditions with a difficult view of the retina.

Adding Myopia Control

If 2020 is the year you tackle myopia control in your office, you'll need to purchase an ultrasound device to measure axial length. Sometimes refractive error can change significantly, but if the axial length remains the same, you must stay the course with your current myopia treatment.

If both axial length and the refraction are changing significantly, or the child's activities increase their risk of progression, consider adding low-dose atropine, which also works by creating peripheral retinal defocus. This once-a-day drop can significantly decrease myopia progression in children within a year.[2]

Researchers note that various concentrations reduce progression in a dose-dependent manner. All three concentrations—0.05%, 0.025% and 0.01%—are well tolerated and show no adverse events. The 0.05% concentration is the most effective in controlling progression of axial length and slowing progression of the myopic spherical equivalent.[2] Currently, 0.05% atropine drops require a compounding pharmacy such as Ocular Sciences or Imprimis.

Presbyopia in 2020

This will be a significant year for presbyopia correction with the potential approval of the VisAbility scleral insert (Refocus). Unlike clear corneal inlays, which are not without compromise, this micro-implant is placed in the sclera to create the space necessary to allow the lens zonules to return to their taught position. Current data of 20 presbyopes suggests they all can read J3 or newspaper print with the implant.

Over the next year, we'll also see ongoing research on drops to treat presbyopia, including various miotics that increase depth of focus and others that help return the crystalline lens to a more flexible state. Research into crystalline lens restoration shows that, as we age, the sulfhydryl bonds oxidize and progress to more rigid disulfide bonds. Thus, dihydrolipoic acid chemically reduces disulfide bonds and may work to reverse the rigidity of the human lens.

Optometry has many new opportunities in 2020 to better correct refractive errors. Adding any one of them to your daily routine can have significant effects on your patients and practice. ■

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

1. Chamberlain P, Peixoto-de-Matos S, Logan N, et al. A 3-year randomized clinical trial of MiSight lenses for myopia control. Optom Vis Sci. 2019;96(8):556-67.
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Survey Says…

Online polls can be fun, especially when you get to make up the questions.

By Montgomery Vickers, OD

It seems like I get an invitation to participate in at least one online survey per month to share how I feel about everything from buying frames to prescribing medications. With the constant upheaval in health care reimbursements throughout my career, I have found taking these surveys is the easiest way to make a couple bucks on a regular basis.

So, I decided to offer you, my colleagues, my own survey. Please answer each question thoughtfully. The honorarium? Uh, no.

1. What word most accurately describes you?

a. Optometrist.
b. Ophthalmologist.
c. Eye care provider.
d. Jimmy Buffett.

2. Which is the most important piece of technology in your office?

a. OCT.
b. Autorefractor.
c. Visual field analyzer.
d. Keg.

3. How many staff members work with you?

a. Three.
b. Four to six.
c. More than six.
d. At any given moment, maybe a couple of them.

4. Why should a patient choose your office?

a. We provide the finest in eyecare and eyewear.
b. We accept most insurances.
c. My team members are friendly.
d. If I go under, I'm taking you with me.

5. What is your specialty?

a. Contact lenses.
b. Dry eye treatment.
c. Pediatrics.
d. Star Trek.

6. What is your most common reason for making a referral to an ophthalmologist?

a. Cataracts.
b. Retinal concerns.
c. Oculoplastics.
d. The patient is my relative.

7. When was the last time you took a PD?

a. Last week.
b. Last month.
c. Last year.
d. A what?

8. When do you use handheld trial lenses?

a. To recheck refractions.
b. To show changes to a patient.
c. To refract myself.
d. To fry ants on the sidewalk.

9. How do you handle no-shows?

a. Try to reschedule them.
b. Let them know I am concerned they may have had an emergency.
c. Schedule all no-shows on Friday afternoons.
d. We are closed on Friday afternoons.

10. What is your success rate with multifocal contact lenses?

a. 50%.
b. 75%.
c. 90%.
d. 100% are successful in going back to glasses.

11. What is the number one reason a patient comes to see you?

a. Has a vision plan.
b. Referral from a friend.
c. Too many birthdays.
d. Heard that optometrists know how to party.

12. What would you do if they invented an eye drop that fixed every possible eye problem?

a. Retire.
b. Stick it in my own eye.
c. Charge $10,000 for the exam required to prescribe it.
d. No, I'd *really* just stick in it my own eye now that I think about it.

My answer to every question was d. How about you? ■

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On the Spot

Treating corneal ulcers and infiltrates starts with a careful understanding of their differences. **Edited by Paul C. Ajamian, OD**

Q I have a patient with a suspicious white spot in the cornea, with a history of contact lens overwear and poor compliance. How do I handle this case?

A "Deciding whether a patient has a corneal ulcer (bacterial infection) vs. a corneal infiltrate (sterile inflammation) can be one of the more challenging decisions we make," says Chris Cakanac, OD, of Your Family Eye Doctors in Murrysville, PA. While the two appear as whitish corneal lesions on a red eye, a closer look can offer clues, he notes. An ulcer is defined as a bacterial infection, often with an overlying epithelial defect and associated stromal infiltration. Ulcers tend to irritate the eye much more than an infiltrate. Expect severe diffuse conjunctival injection, often with a significant anterior chamber reaction or even hypopyon.

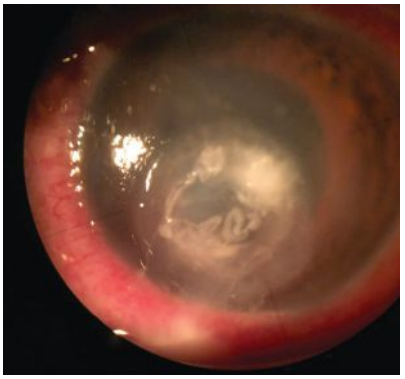
Infiltrates tend to have less injection and minimal anterior chamber reaction. "If there is no fluorescein staining (or just a trace), it is usually an indication you are dealing with a corneal infiltrate," Dr. Cakanac says.

Other differentiators include more pain in the infectious ulcer patient, as opposed to only light sensitivity and irritation in the infiltrate patient. A few other general characteristics, although there are always exceptions, include:

(1) Ulcers are single lesions more often than infiltrates, which can be multiple.

(2) Ulcers tend to be larger (2mm or more) while infiltrates are smaller.

(3) Infiltrates tend to accumulate along the limbus; a response to hypoxia from contact lenses or *Staph*. exotoxins in a blepharitis patient. Also look for blood vessel ingrowth.



Determining the nature of a white corneal lesion requires a closer look.

"So, poor contact lens compliance related to overwear and poor hygiene, along with chronic *Staph*. lid disease, are often the culprits behind both ulcers and infiltrates," Dr. Cakanac adds.

Treatment Protocols

In days gone by, the standard of care for a corneal ulcer was to obtain a culture and sensitivity on every one, according to Dr. Cakanac. As our therapeutic agents have dramatically improved, cultures and sensitivities are now reserved for cases threatening the visual axis or not responding to treatment.

"If you're a practitioner who likes rules, consider the '1-2-3 rule'—culture any ulcer within 1mm of the visual axis, any ulcer with two or more infiltrates or any ulcer with a larger than 3mm epithelial defect," Dr. Cakanac says. And you may want to culture the contact lens case as well.

Successfully treating an ulcer (infection) requires an antibiotic. By contrast, an infiltrate (sterile inflammation) requires a steroid. When in doubt, it is always safer to begin with a topical antibiotic. The steroid can always be added later. For early lesions, a commercially available fluoroquinolone is usually adequate. For more serious ulcers, the standard is still the combination of either cephazolin fortified to 50mg/ml or vancomycin fortified to 25mg/ml to cover gram-positive organisms, as well as tobramycin fortified to 14mg/ml to cover gram-negative strains.

"Know where your nearest compounding pharmacy is and what their hours are, so that in an emergency you can get drops made up," Dr. Cakanac advises.

Once considered a contraindication, adding a topical steroid to antibiotic therapy for an ulcer can decrease overall ocular inflammation, pain and possibly scarring, many experts now believe. The Steroids for Corneal Ulcers Trial showed that while adding a steroid did not statistically improve visual outcomes, there was no increased risk of corneal perforation.[1]

Corneal infiltrates usually respond to most topical steroids in standard doses. "If the diagnosis is in question, use a concurrent topical antibiotic," Dr. Cakanac notes. ■

1. Jacob MK. Idiopathic orbital inflammatory disease. Oman J Ophthalm. 2012;5(2):124-5.

Passionate about patient experience?

"MY PATIENTS CAN DEFINITELY TELL I AM."

Multitasker **Lisa Genovese**, **OD**, co-owner of **Insight Eye Care's** multiple locations, talks about using technology to efficiently juggle being a full-time optometrist, a full-time entrepreneur, and a full-time parent. By using the most advanced Phoroptor®, **Phoroptor® VRx**, and the pixel-perfect **ClearChart® 4** Digital Acuity System, she's brought balance to her practice and personal life.

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Accommodation in Peril

More patients are struggling with their near vision these days. Here's why and how you can help. **By Bisant A. Labib, OD**

As use of technology skyrockets, so too does the incidence of near vision complaints. To provide the proper diagnosis and treatment, practitioners must be familiar with the diagnostic possibilities of near work–induced asthenopia. In children, these symptoms are often due to an underlying accommodative or binocular vision disorder. In the more advanced-age population, it can be as simple as presbyopia. However, in the pre-presbyopic population, near vision complaints may be due to accommodative dysfunction.

The ability to accommodate requires a change in the dioptric power of the eye through the increase of lens thickness and curvature. This is achieved through the contraction of the ciliary muscle and relaxation of the lens zonules. These changes are necessary to view objects and images clearly at near.[1] Accommodation testing offers the practitioner crucial information about a patient's focusing capacity.

Out of Focus

Accommodation decreases with increasing age and the loss of lens elasticity. Other causes of decreased accommodation can include head trauma, midbrain diseases and encephalitis.[1] In pre-presbyopes, this is termed *accommodative insufficiency*. The exact underlying mechanism for accommodative insufficiency in healthy pre-presbyopic subjects is not well understood. However, evidence suggests the presence of an inhibitory accommodative control system regulated by the autonomic nervous system, specifically the sympathetic branch.[2]

Accommodative dysfunction is a term that encompasses accommodative insufficiency, ill-sustained accommodation, accommodative excess and accommodative infacility (*Table 1*). Of these subtypes, insufficient accommodation is the most commonly encountered condition, representing 55% to 84% of cases.[3-5] It also accounts for the most common cause of asthenopia in children ages eight to 15, highlighting the importance of proper diagnosis and management.[6]

Those with accommodative insufficiency often present with difficulty performing near tasks. Symptoms can include visual discomfort, eyestrain, fatigue, blurred vision, headache, diplopia and difficulty focusing from one distance to another.[2,7,8] These can interfere with a student's academic progress because avoiding work at near relieves the visual demand.[2,7]

Accommodative insufficiency is often misdiagnosed in young children and must be differentiated from dyslexia or other binocular vision disorders.[9]

A Focus on Anatomy

The accommodative pathway is mostly innervated by the parasympathetic system and begins in the midbrain. Stimulation arises via the near triad, which encompasses miosis, convergence and accommodation. There is projection to the Edinger-Westphal nucleus, where the fibers travel to the ciliary ganglion, synapse and, ultimately, continue to the ciliary body and iris sphincter.[1]

1. Ruskell GL. Accommodation and the nerve pathway to the ciliary muscle: a review. Ophthalmic Physiol Opt. 1990;10(3):239-42.

Diagnostic Know-how

Clinicians can test accommodative amplitudes using push up to blur monocularly and comparing it with the relative age-based expectations, determined through use of Hofstetter's formula to calculate the minimum amplitude, as follows:[8]

15 – (patient age x 0.25)

If the measured value falls two or more diopters below the minimum, the patient has insufficient accommodation.[6,10,11] However, research that compared this subjective push up test with more objective methods such as minus lens stimulation or techniques employing a proximal stimulus found the subjective measure substantially overestimates amplitudes in young children.[10]

Table 1. Accommodative Dysfunction Subtypes

Accommodative insufficiency	Insufficient amplitude of accommodation relative to age-based expectations
Ill-sustained accommodation	Normal amplitude of accommodation that deteriorates over time
Accommodative excess or spasm	Accommodative system inappropriately over-accommodates for a stimulus
Accommodative infacility	Difficulty focusing/blurred vision at distance after prolonged near viewing, or vice versa

Additional diagnostic criteria for accommodative insufficiency include a score of ≤3 cycles per minute (cpm) on binocular accommodative facility (BAF) testing and ≤6cpm in each eye on monocular accommodative facility (MAF), with trouble clearing the -2.00D lens on each test (*Table 2*). Negative relative accommodation (NRA) is normal, but positive relative accommodation (PRA) values are often less than -1.25D. Finally, monocular estimated method (MEM) testing would reveal a lag of accommodation and is often ≥+0.75D. Many suggest that a combination of two abnormal test values is required to make the diagnosis.[6,11] In addition to reduced amplitudes, failing minus on monocular accommodative facility testing is the most associated diagnostic finding with accommodative insufficiency.[12]

Bring Things Back into Focus

Treatment includes the use of plus lenses for reading as well as in-office or home-based vision therapy to train accommodative facility, with cure rates ranging from 80% to 100% of cases.[6,13] The use of plus lenses at near serves as an aid to reduce the blur secondary to the patients accommodative system and obtain a clear retinal image.[6]

The optimal amount of plus has yet to be determined and may range from patient to patient. Many studies support the use of a +1.00D add power, especially compared with +2.00D lenses. In such studies, +1.00D alleviated symptoms by providing minimal aid with near focus, which allows the accommodative system to relax while still engaging during near tasks. With +2.00D lenses at near, the patient's accommodative system is not stimulated and the lenses serve as a crutch, minimizing the potential for long-term improvement in accommodative amplitudes.[6] Several studies conclude that a statistically significant improvement in the near point of accommodation was measured in patients using +1.00D lenses at near after several weeks of treatment.[2,6,14] One study also showed a significant improvement in accommodative amplitudes and reading velocity after eight weeks.[2]

Vision therapy for accommodative insufficiency emphasizes the manipulation of blur, disparity and target proximity.[7] Tasks are designed to improve accommodative amplitudes and facility, as well as reduce latency. The sequence of office-based vision therapy begins with normalizing and balancing the accommodative responses in each eye, followed by binocular accommodative therapy. Programs consist of weekly 60-minute sessions for 12 weeks, with periods of re-evaluation.[15] Often, office-based therapy is reinforced with home-based exercises for 15 minutes per day, with a focus on accommodative rock.[15]

Overall, while there is a statistically significant improvement in accommodative amplitudes using both plus lenses at near and vision therapy, greater and more long-term improvements are seen with compliance with vision therapy regimens.[14]

Table 2. Accommodative Insufficiency Testing

Diagnostic Test	Expected Value
Accommodative amplitude (AA)	2.00D or more of a decrease based on Hofstetter's formula for minimum AA
BAF	≤3cpm
MAF	≤6cpm
NRA/PRA	PRA of less than -1.25D, normal NRA
MEM	Lag of accommodation (≥+0.75D)

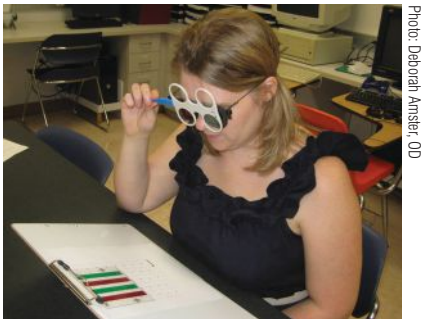

Photo: Deborah Amster, OD

Vision training activities, such as accommodative flippers, can help to improve accommodation.

Up to 100% of accommodation insufficiency cases are curable but, if left unmanaged, can deter students from performing well academically. Understanding the various diagnostic elements of accommodation can ensure you catch these cases early and treat appropriately. ■

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12. Cacho-Martinez P, García A, Lara F, Seguí MM. Diagnostic signs of accommodative insufficiency. Optom Vis Sci. 2002;79(9):614-20.
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It's Time For a Reboot

The new year is the best time to make sure your medical record-keeping practices have a solid foundation. **By John Rumpakis, OD, MBA, Clinical Coding Editor**

As we usher in a new year, the timing is perfect to look back to ensure that good processes are in place and use our future time wisely to prepare for upcoming coding changes.

A Good Foundation

Your medical record is the cornerstone of your practice and the only legal record of patient care delivered. Medical record compliance is paramount for everyone in your practice. Make sure you maintain a thorough, well-documented and accurate medical record, as it is the key to providing the best care to the patient and to defending what you have been paid, should you be called upon to do so. The foundational elements should always contain:

1. Reason for visit (ideally captured when the patient made the appointment)
2. Chief complaint
3. Delineation of any standing orders (routine testing or non-medically necessary services)
4. Medical necessity clearly established for: type of visit (920XX vs. 992XX vs. S062X), level of visit, any additional testing or procedures performed
5. Clear record keeping and patient signature if an advanced beneficiary notice (ABN) is used
6. Clearly written assessment and plan—always include what you want the patient to do, why and when it should be done.

The Coding Triad

To thrive in a third-party paid world, you must understand the "coding triad": *coding*, *coverage* and *reimbursement*. Each of these has a specific function and meaning.

Coding. This is the only legal way to describe what happened during the physician/tech/office/patient encounter. Each code has a specific definition and set of characteristics you must know before you use it. Coding properly isn't only for insurance companies. You must code properly for every patient, irrespective of who is paying.

Coverage. When a patient has a form of payment assistance (insurance, medical savings plans, etc.), the third party generally has policies dictating if payment assistance will be provided and the conditions necessary for them to provide it. Coverage policies usually provide a clear explanation of the indications and limitations with respect to coverage and medical necessity for the coverage to exist and be allowed.

Reimbursement. This is calculated by different methods depending on the third-party payer. Managed vision care plans generally provide a predetermined contract rate based on internal supply/demand/use/profit calculations. Medical carriers usually follow the Resource Based Relative Value System where each CPT code has a total relative value unit and is further modified by your geographic location and dollar-based conversion factor. There are a couple of considerations with reimbursement:

a. Before you join the plan, know how they calculate reimbursements.

b. Keep current on the maximum allowables for each service, procedure and materials you provide. The total payment is often the sum of the patient copay and carrier payment.

c. For maximum profitability, analyze your fees quarterly to ensure you are charging properly considering your carrier's maximum allowable values.

d. If you don't like your carrier's reimbursement rates, you don't have to be a member of the plan. If renegotiating your reimbursements isn't successful, you always have the option to not participate.

e. One crucial pointer: you must charge everyone equally for the services you provide. You must have one fee per CPT code, no matter who is paying. For example, if you charge $175 for a 92004, you must charge $175 to every patient who gets a 92004, whether they have payment assistance or are paying out-of-pocket.

A firm grasp of these coding triad and medical record compliance concepts is critical for everyone in your office providing patient care. The medical record is really a reflection on your clinical thought process in managing the patients care within your local standard of care. Practice and perfect these skills and you, your practice and your patients will all win. ■

Send your coding questions to rocodingconnection@gmail.com.

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PEER • REVIEWED PRA ARTICLE

Myopia Control: Decisions and Discussions

Follow along with a hypothetical case to learn how to better navigate the options with patients and parents. By Andrew Pucker, OD, PhD

Eight-year-old Olivia reports to your clinic for the first time with her 6-year-old sister and her mother. Her referring doctor's letter explains that her refractive error was -2.50DS OD/OS. He also indicates that the patient had no binocular vision or ocular health issues.

You begin your myopia management consult by giving your patient and her family an in-depth overview of your services while you walk them through your consent form. You specifically start by defining myopia as a condition that typically results from the eye being too long for its refractive components, which is known as axial myopia.

Myopia is less commonly refractive in nature, though refractive myopia can occur and if it does it typically results from the corneal power or lenticular power being too strong for the eye.[1] This refractive status typically results in distance blur because a distance image is focused in front of the retina. While describing the condition—commonly known as nearsightedness—you make use of an eye model and ensure that everyone understands the anatomical basics.

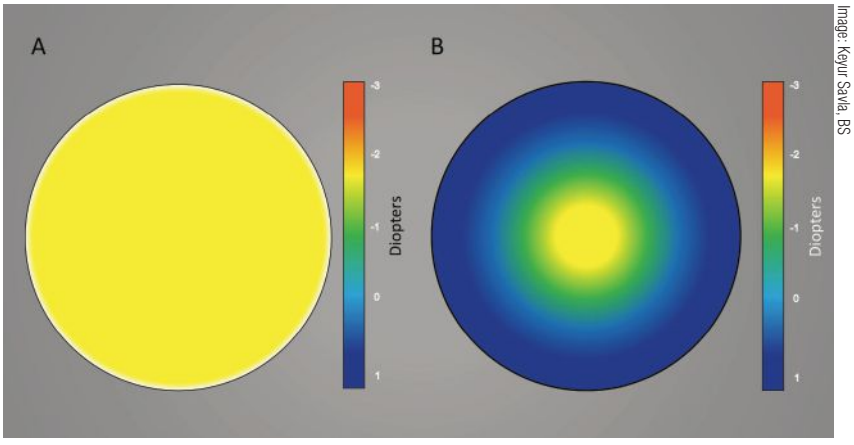


Image: Keyur Savla, BS

This graphic shows representations of (A) a spherical contact lens and (B) a center-distance multifocal contact lens.

You elaborate, explaining that myopia affects approximately one third of Americans and that the condition is likely caused by a mix of genetic, lifestyle, and environmental factors.[2-4] You also clearly tell your young patient that anyone has a chance of becoming myopic and that she should not at all feel bad about the need to wear glasses.

You notice that Olivia's mother was also wearing glasses, and you ask if her father wears does, too. Olivia's mother says no. You explain that anyone has a chance of becoming myopic, even children without myopic parents. However, having one myopic parent makes a child approximately twice as likely to develop myopia and those with two myopic parents are approximately five times more likely.[5] You also explain that the prevalence of myopia has increased in recent years and that this is likely because

of environmental factors such as people spending less time outdoors.[5,6]

At this point, Olivia's mother asks if there is anything that she can do to help prevent her younger daughter from developing myopia. While research shows that approximately two hours per day outdoors may be able to stave off myopia development in at-risk patients, outdoor time has minimal effect on patients who have already developed myopia.[7]

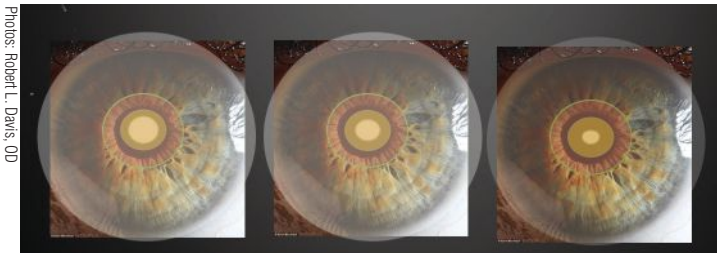
However, you have good news for Olivia's mother. You happen to provide special interventional techniques—namely low-dose atropine, overnight orthokeratology and multifocal soft contact lenses.[1] These treatments are designed to slow the progression of myopia. By reducing Olivia's overall refractive error, you hope to not only decrease her dependence on glasses and contact lenses, but also lower her risk of conditions such as glaucoma or a retinal detachment.[8]

These three techniques represent some of the latest developments in slowing myopia progression.

Atropine

Meta-analysis data indicates that 1% atropine can safely treat amblyopia and is also likely safe for myopia management.[9] Atropine has also been used to slow myopia progression for years, though habitual use of 1% atropine results in photophobia and reduced accommodative ability.[10]

More recent research found that 0.01% atropine is able to slow myopia progression with minimal accommodative or photophobic side effects.[10] They specifically found that when 0.01% atropine was compared with 1.0% atropine for slowing myopia progression that 1.0% atropine was able to slow refractive error progression to a greater degree than 0.01% atropine; however, when subjects stopped drops, the 1.0% atropine group's eye growth rebounded, negating the majority of its treatment effect while the 0.01% atropine group had limited rebound, which resulted in an effective myopia management method (slowed refractive error progression by 59%).[10,11]



Photos: Robert L. Davis, OD

This series shows various multifocal zone sizes within a pupil.

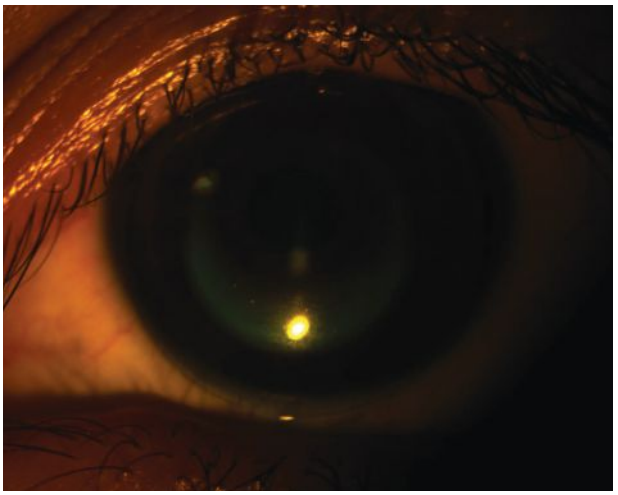
This seminal study has since been criticized for using a historical control group and for having minimal effect on axial length progression in the low dose atropine group.[11] Nevertheless, another recent study shows that 0.025% and 0.05% atropine appear to have a clinically meaningful effect on both axial length and refractive error.[12] While research shows the side effects with low-dose atropine are minimal, administering the drops before bed could further mitigate any potential side effects.[10]

The mechanism by which atropine slows eye growth is currently unknown. In the United States, low-dose atropine can only be obtained from a compounding pharmacy. Atropine can be used on even your youngest patients because parents can apply the drops.

Orthokeratology

This technology was developed to mitigate daytime myopic refractive error. The lenses are worn while sleeping. When they are removed, the patient, ideally, should be able to see clearly at distance after corneal reshaping has taken full effect.[1] Many patients can achieve full correction within about one week, though this does vary by the patient's starting refractive error.[1] Since the patient will have a refractive error that progressively decreases during the initial adaption period, patients should be given a series of daily disposable contact lenses with lessening powers to make up the refractive error difference. Daily disposable power should be selected based upon the patient's refractive error after one night's wear. Orthokeratology is now commonly used to slow myopia progression and researchers believe that it works by reducing the patient's amount of peripheral hyperopic defocus.[1]

Our understanding of orthokeratology's mechanism is largely based upon researchers who first laser ablated the fovea of the right eyes of Rhesus monkey while at the same time not damaging their left eyes.[13,14] They then applied a myopia stimulus to each eye (experiment one used form deprivation/cloudy lenses while experiment two used minus lenses), and found they were still able to induce myopia in both eyes.[13,14] These experiments subsequently suggested that the fovea was not essential for regulating refractive error development and that the peripheral retina may be more important for regulating emmetropization.



This patient demonstrates a well-fit orthokeratology lens.

Investigators now believe orthokeratology can slow myopia progression by approximately 50%.[15-17] However, only a limited range of refractive errors are approved by the FDA for the correction of myopia (typically better than -6.00D of sphere power and 1.50D of cylinder power). Patients need to be mature enough to apply contact lenses to use orthokeratology, though these lenses are typically worn in the home, so parents can help with this technology.

Multifocal Soft Contact Lenses

Multifocal contact lenses were originally designed for correcting presbyopia, though soft multifocal lenses are now commonly used to manage myopia progression. Researchers believe center-distance, or extended depth-of-focus multifocal contact lenses, can slow myopia progression much like orthokeratology lenses, by reducing peripheral hyperopic defocus.[18,19]

The efficacy of multifocal contact lenses varies greatly by study, though the data again suggest that these soft contact lenses are able to slow myopia progression by approximately 50%.[20,21]

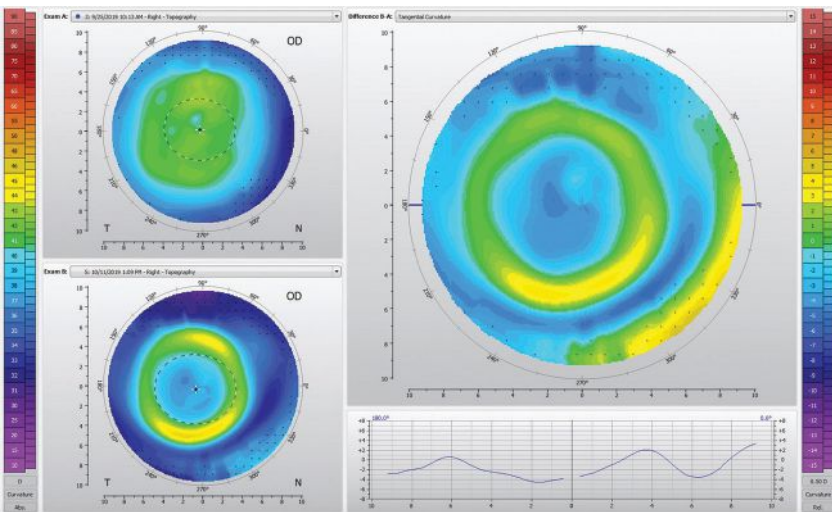
Multifocal contact lenses formally studied have been limited to spherical designs; however, in my experience, many people who have clinically meaningful astigmatism are still interested in trying contact lens-based myopia management. I've found that patients can be successfully fit in custom soft, multifocal, toric contact lenses.

Children who use soft contact lenses need to show an elevated level of responsibility and be able to fully care for the contact lenses outside the home. Parents are frequently concerned that contact lenses are unsafe for young children, but research actually suggests that this younger age group is at a lower risk of developing a contact lens complication compared with college age adults, and both groups may find social benefit from wearing contact lenses.[22]

Work Up

After discussing all of the options with Olivia and her mother, you indicate that you will not be able to fully determine what treatment option will work for Olivia until after you complete your myopia management evaluation. They agree to complete the evaluation, and you talk to Olivia to understand her visual needs. During this discussion, Olivia tells you she is an avid swimmer. You also evaluate her visual acuity, cover test at distance and near, accommodative amplitudes, pupil size, cycloplegic refractive error, corneal topography with a horizontal visual iris diameter measurement and axial length with non-contact biometry.

Binocular vision testing can help monitor atropine side effects and determine if a near add may cause multifocal contact lens wearers to decompensate. Refractive error and axial length testing are intended to monitor the patient's myopia progression, and topography is necessary to order specialty contact lenses.[23]



This topography shows a well-fit orthokeratology lens.

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A Historical Perspective on Myopia "Control"

By Paul Harris, OD

Since the early days of A.M. Skeffington and the Optometric Extension Program, optometry had in its grasp a systematic examination and analysis system for understanding how function alters structure over time. Only now, through modern research, are the actual physiological mechanisms being revealed. However, the observations and associations, and in particular the clinical experience of seeing results of patients over many years of follow-up, at least suggested that myopia could be controlled. In those days, the term, "myopia control" referred to the application of lenses, at both distance and near, to guide the development of future refractive changes to either being stable (no new myopia added on over time) or to reduce the need for minus sphere powers at distance to restore standard visual acuity.

Every optometrist who followed these guidelines took the time to take the extended data, reviewed patterns in the findings and performed some form of near-point retinoscopy, were then able to prescribe lenses that afforded a degree of myopia control. These same optometrists knew when they had little leeway to prescribe something other than what they measured, and then knew that the only way to stabilize progressive, or as it was called then "school myopia," was to institute vision therapy, with emphasis in the areas of accommodation.

This approach was fundamental to the teaching of Skeffington, Leo Manas, Nat Flax, Bill Ludlam and many other optometric luminaries over the years. While newer treatment methods such as low-dose atropine, orthokeratology lenses and soft multifocal contact lenses certainly show where optometry can go, it would do all a service to continue to include techniques which are a part of our heritage, and that many optometrists in the United States and worldwide continue to provide.

When I teach about this more basic, fundamental approach at Southern College of Optometry, I call it "refractive engineering." It seems to garner more interest when spoken about that way. The newer usage of the term "myopia control" seems to not be evolutionary, because the older methods all still work. Those new methods are here to supplement, not replace.

At worst, I'm concerned that overreliance on today's conception of myopia control could, one day, lead to a lack of exposure to the evidence base of traditional lens prescribing. My appeal to the profession is for us to remember our roots and not to cease to promulgate the knowledge and clinical acumen on which these advancements were built.

After fully evaluating Olivia, you conclude that she could be a good candidate for all three myopia management options. Since she is motivated to wear contact lenses and because she is a swimmer, you determine that orthokeratology may be the best option for her lifestyle (lower risk of developing an eye infection compared to soft contact lenses).

You thoughtfully explain that Olivia will need to use her selected myopia intervention for several years to obtain clinically meaningful results. You prep her to anticipate the natural fall-off in motivation she'll experience at some point, as the effort doesn't "fix" her myopia—only helps slow it down. You let her know you and her parents are in this for the long haul with her. No one knows when myopia progression will stop, though I recommend using myopia management for as long as possible since research shows some patients' eyes continue to grow into their 20s.[24]

When Olivia's family decides to move forward with orthokeratology, you schedule Olivia for a dispense visit. There, you perform a normal orthokeratology lens evaluation, and you find that each lens yields a perfect bull's eye pattern with 20/20 acuity OD/OS. You next fully educate Olivia and her mother on how to apply, remove and care for the lenses and you see her the following morning. At the next morning visit, Olivia presents without the lenses on with 20/30 visual acuity OD/OS and a -1.00 refraction OD/OS. The lenses also appeared well-centered via topography. You then provide Olivia with a set of -1.00DS and -0.50DS daily disposable soft contact lenses. You evaluate the lenses, and you send her home with the lenses after teaching her how to use them.

You next see Olivia again at one week, and you find that she is plano DS OD/OS at the end of the work day and that she has 20/20 visual acuity OD/OS with well-centered lenses as evaluated with topography. You subsequently find the same positive outcomes at one month and six months, and you find at six months when you repeat your full myopia management work up that Olivia has had minimal refractive error or axial length progression.

You then recommend at this point that Olivia should be monitored every six months with lens adjustments only made as needed. You also indicate that if Olivia shows signs of progression that you would consider adding atropine to the treatment plan because it has been found to provide additional slowing in a recent randomized clinical trial.[25]

Applying these myopia control techniques can be rewarding

because you have the potential to preserve the quality of a patient's vision. However, it is also challenging because myopia management is new to many regions of the United States. Therefore, it may be best to begin offering these services by recruiting patients from your own practice. The ideal patient is one who is getting their first pair of glasses because such a patient has potential to gain the most cumulative benefit. ■

Dr. Pucker is an assistant professor at the University of Alabama at Birmingham.

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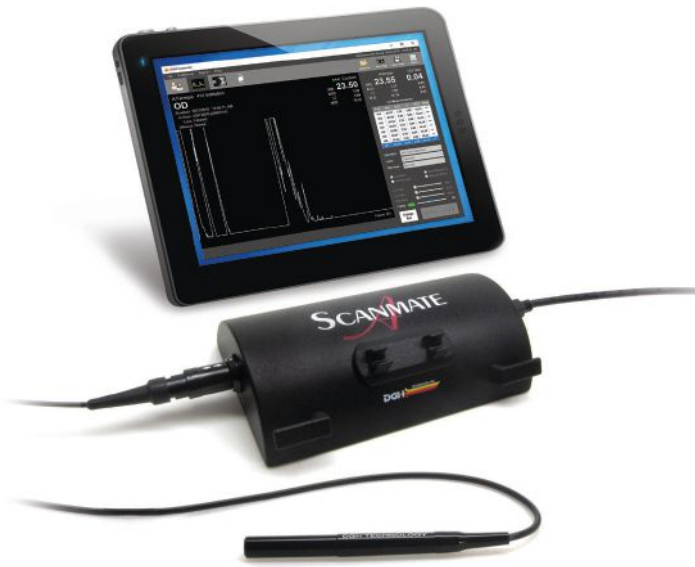
Are axial length measurements part of your myopia management program?



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PEER • REVIEWED PRA ARTICLE

Clinical Refraction Tips and Tricks

Here's what I've learned through years of hands-on experience. **By Paul Harris, OD**

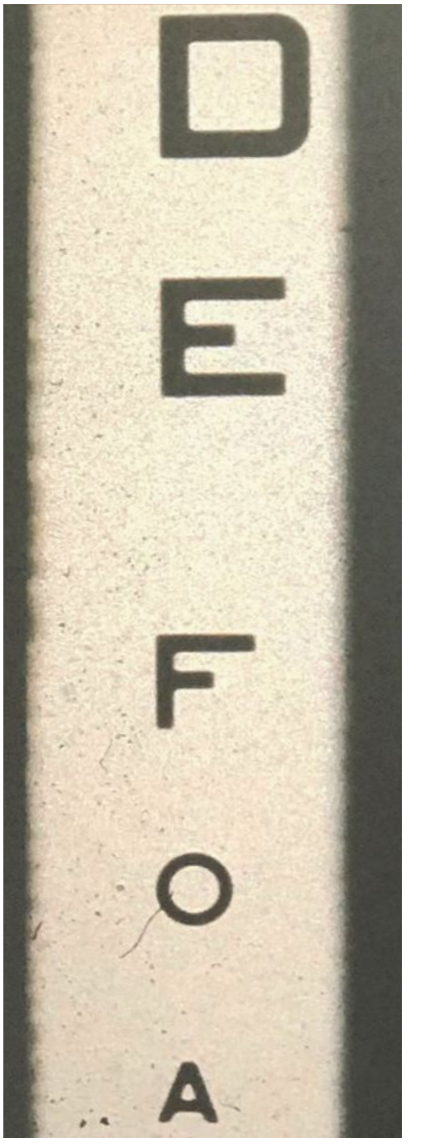
For well over a century now, our profession has mainly been associated with one of the many critically important things we provide for our patients: prescriptions that translate into glasses and/or contact lenses. Eyewear dispensed from these scripts is what the public usually sees as the end goal of going to the optometrist's office. This article will explore tips, tricks and techniques I've developed over 40 years of both performing and teaching refraction to aid patients in obtaining clear, single, binocular vision when possible and to help them accomplish all the things they wish to do in their lives.

Work With a Range

I once believed only one prescription should emerge from each examination. However, in nearly all instances, a range of potential lenses could be prescribed to a patient, all of which would help meet their needs. We must ditch the mindset that comes with working with one prescription and look for the range of lenses available for any given patient. It's up to us to help patients understand that there is no one perfect lens.

We can look at prescribing as a negotiation between the doctor and the patient. If we end up with a single lens to present our patient with, the negotiation is simple and not much of a negotiation at that. Asking whether or not it is satisfactory yields a yes or a no. If we have a range of lenses, the patient has a choice to make. Do they want maximum visual acuity at distance even if it impacts their reading speed or comprehension level when used at near? Or maybe they want to be able to do a specific task, such as playing a musical instrument or competing in a sport. The better we understand a patient's wants, needs and priorities and the more options we're able to give them, the higher the chance we'll be able to work together to narrow in on the best solution. Approaching the situation in this way could lead to multiple prescribing opportunities. This is a win-win scenario—happier patients help your practice grow, both financially and patient-wise.

A case-in-point of multiple prescriptions is my own vision. I have a general-purpose pair of Trivex Transitions for everyday use. However, I can't use these glasses while fulfilling my clinical teaching duties, so I have an occupational pair of Trivex trifocals, which allow me to clearly see my dual screen setup and my patients' faces during case presentations from five to six feet away without having to tilt my head back. I have another pair I wear while playing my bass trombone that are single vision to match the intermediate of



This old projector chart shows a single column of letters.

my occupational glasses. I also have a pair of polarized multifocal lenses for driving and enjoying the outdoors. When I get a new prescription, I get four new pairs of glasses.

Get In, Get Out… Efficiently

Patients have limited attention spans as is, and that's before taking into account the fact that they're sitting in an optometrist's office when they could be literally anywhere else. This doesn't mean we should cut corners during our exams. It does, however, mean that we should be efficient and use our time wisely before we lose the patient.

This open chart from 20/70 to 20/40 shows half of the letters in red and half in green.

An example of saving time while not negatively affecting outcomes has to do with taking visual acuities. We all know that deciding whether a letter on the chart is a "C," an "O" or a "G" can be difficult and time-consuming for some patients. All we really need is a quick way to know if something has changed between appointments. Getting acquainted with computerized visual acuity measuring systems and developing a testing methodology that goes from non-seeing to seeing allowed me to obtain visual acuities far quicker and with more precision than I ever could before. Instead of getting the generalized 20/25+, I could get 20/23 in about half the time. By focusing on what our patients are seeing and how we're showing it, we can shave time off our testing sequence without sacrificing our precision.

Another example of efficiency in action involves our refraction routine. As taught, we typically do a nearly complete monocular refraction of the right eye and then the left eye before moving to the binocular balance. This includes finding the sphere power we have in place for our cylinder testing.

After retinoscopy, I recommend using an open chart from 20/70 to 20/40 or so depending on your chart options, with half of the letters shown in red and half in green, and asking the patient which side is blackest or clearest. With one or two clicks, you can find where the change is occurring and proceed with cylinder testing. To do this efficiently, I test the right eye first and then move to the left eye. With most patients, I then go to a single 20/40 line to do my cylinder testing and switch between eyes. Minimal chart changes and eye rotations are efficient ways to save time.

Take the Pressure Off

"Which is better, one or two?" is the part of the eye exam comedians seem to gravitate toward when they do routines about going to the optometrist. One of our patients' greatest fears is that they will get the wrong pair of glasses if they give us one wrong answer. I realized early on that if I let the patient dictate how this part of the testing should go, they end up asking me to repeat the slides any number of times. So, I emphasize that they should give me their first impression and, even if they start to second-guess themselves, we will end up where we need to be.

It doesn't help when we flip the lenses from one choice to another too quickly during an exam. The patient is given very little time in between to focus on what they're seeing and decide where it ranks. This necessitates many flips and leaves patients feeling certain they made a mistake. I have found that staying on each choice for about three seconds leads to a definite selection after only one flip the majority of the time.

Don't Take Shortcuts

Some believe that after a certain age, since accommodation might be considered non-functioning or functioning to such a small degree, we only need to perform monocular refractions. This, however, could cause visual problems later on. Obtaining the binocular balance (most plus or least minus to the first good 20/20) gets us one end of the range when prescribing. Even though this number is usually not included in the final prescription, it's nice to have it, especially if we are concerned about progressive myopia or accommodative esotropia. We also use it to step down binocularly and remove plus or add minus to get to our best visual acuity lens. This is the other end of the range, from which our prescription options emerge.

Find the Right Tools

For some of our colleagues, the near point rod for the phoropter might be used more as a back scratcher than as something that holds the near point card. But, I'll assume you do near point testing, at least some of the time.

I purchased the Rotochart (Ametek Ultra Precision Technologies, Reichert Technologies) as an optometry student and have used it my entire career. The device has 12 different charts, six per side, that the user can easily rotate through. I've watched countless times as your typical cards get misplaced. The Rotochart, and others like it, has helped solve this problem for me.

I use chart 11, an 8x8 block of 20/20-sized letters, most often for near phoria testing to obtain the positive and negative relative accommodations. I've learned to check in with my patients to make sure they understand what I'm asking for. As I move to lens powers that I know should create some blur and patients still report the letters as clear, it tells me that they don't. When I ask them to read a specific letter further down on the chart and they can't, it shows that we're on different pages.

What I assume is happening is that they are continuing to look at the first line rather than being on the lookout for any changes happening as a whole as I switch the lenses. So, I specify what I'm looking for and then reduce the lens power until the patient can first see the letters clearly. Whatever tool you pick for your arsenal may bring some hiccups, but finding what works best for you and educating the patient accordingly makes a world of difference in obtaining efficient, accurate results.

Make Every Measurement Count

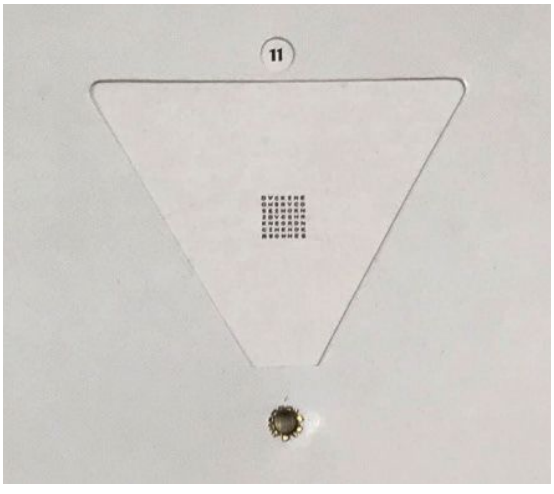
Phoria measurement is another one of those probes we all learned in school but may have stopped performing along the way, mostly because the data culled from the test never seems to be used in altering the prescription or treatment plan given to the patient. In reality, this finding helps predict the degree to which a patient will be able to use the lenses we prescribe.

I was taught to always perform a pair of phoria measures at each distance but with different lenses in place. I take a phoria through my refraction and another through plano, which is called the habitual. Be as consistent as possible during the testing by delivering the set the same way, using the same target and lighting, moving the prism at the same speed and conducting the two phoria tests as close together in time as possible. The key is to find the difference between the two measures, and taking all of these factors into consideration will give you the best shot.

For example, a new myope comes in and we find -0.50 yields a sharp, comfortable 20/20 OD, OS and OU. At that point, I take the phoria measure with the -0.50 in place and record it. Then, I immediately remove the -0.50 to get back to the habitual and take the phoria again. Often, the change in the phorias, or lack thereof, is more a measure of the choices the patient makes at the moment they look at the target. They may fixate on one point, shifting the phoria toward less exo or more eso. Or, they may focus on the bigger picture and take it all in equally and at once, showing more exo or less eso.

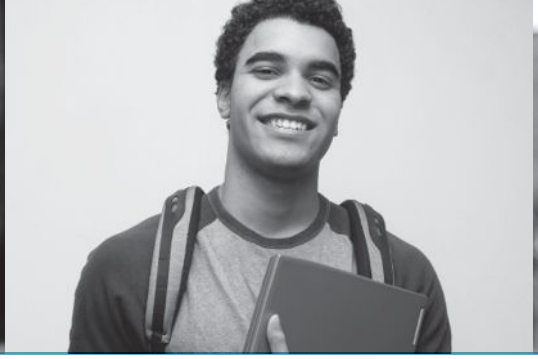
In general, I like to see more variability in each pair of phorias measured with different lenses because that signifies the patient is more flexible. When working with a patient where there is little to no fluctuation, I need to be more careful in prescribing to make sure that any change I make is truly warranted, else the patient might return far too soon for an encore refraction.

Refraction remains a core service—an art—provided by optometrists. Directed by science, but guided by a series of principles to encourage efficiency and accuracy, it allows today's optometrists to serve the prescribing needs of patients far beyond what any automated system is capable of. ■



This is chart 11 of the Rotochart.

Dr. Harris teaches amblyopia, strabismus and pediatrics at the Southern College of Optometry. Clinically, he practices vision therapy, vision rehabilitation and hospital-based care for ABI/TBI, pediatrics and electrodiagnostics. He is actively involved in research looking into new ways to measure stereo acuity and visual acuity and how color can help patients who suffer from ABIs/TBIs, migraines and seizure disorders.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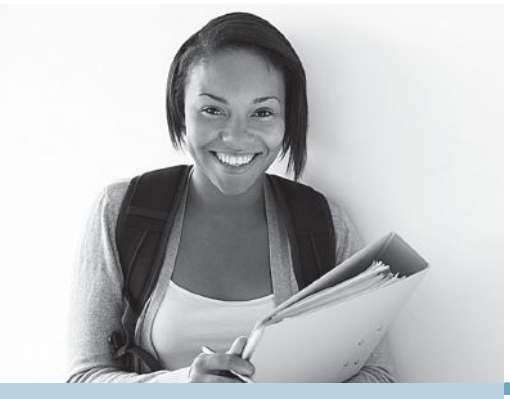

About Rick

Rick Bay served as the publisher of The *Review* Group for more than 20 years.

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PEER • REVIEWED PRA ARTICLE

New Thinking on Binocular Vision Problems

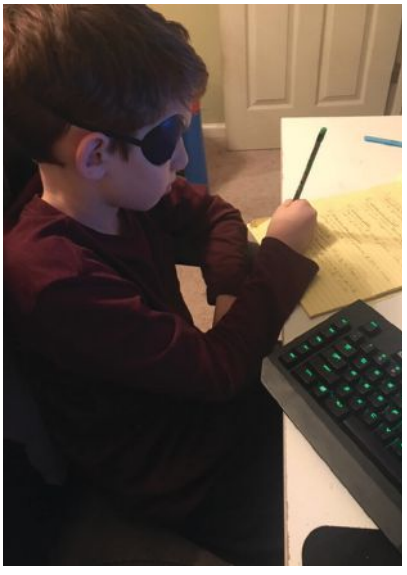
The latest research clarifies how optometrists can treat these patients most effectively.

By Marie Bodack, OD, and Erin Jenewein, OD

Binocular vision problems should not frighten optometrists—many of these conditions are relatively easy to diagnose and manage. We know more about treating these conditions today than we did 20 years ago thanks, in part, to an increase in binocular vision research.

In particular, the Pediatric Eye Disease Investigator Group's (PEDIG) Amblyopia Treatment Study (ATS) and Convergence Insufficiency Treatment Trial (CITT) have helped optometrists develop a diversity of treatment options for patients with binocular vision conditions.

These patients are likely to present to your office as children whose parents bring them to an eye exam. They'll explain that "His teacher thinks he needs an eye exam because he has problems reading," or, "She failed a screening. They said she has a lazy eye." They may also present as adults who complain that a new job sits them in front of their computers all day. They're likely to tell you, "By the end of the day, I can't read, I have a splitting headache and I'm seeing double."



Here, a young patient is seen patched and performing monocular oculomotor activity using the Home Therapy System (Vision Therapy System).

All of these patients can be evaluated and managed in your optometric practice, and as optometrists we have the unique ability to change patient's lives by treating these visual conditions.

More Than Reading Problems

Reading in school-aged children between kindergarten and third grade usually involves learning how to read; learning the names and sounds of the letters and then putting them together to make simple words and sentences. Once the child has mastered how to read, they begin to read to learn. This process begins in fourth grade and continues through adulthood. As classes become more advanced, books feature fewer images, the font size gets smaller and words get longer. Reading assignments take longer to complete and are more demanding on the visual system.

Treating a patient with these reading problems starts with a detailed history. The phrase "reading problems" itself can mean different things to different people. By asking more specific questions, you can better streamline your exam and testing.

Reading problems can be broken into two main classifications: visual efficiency problems and visual processing or perceptual

problems. Each of these groups experiences different symptoms. Visual efficiency problems manifest as signs of discomfort when reading, such as double vision, headaches, words moving on the page, words blurring and loss of place when reading. These can indicate a problem with refractive error, binocularity, accommodation or oculomotor skills. These symptoms are more common for patients in that "reading to learn" phase, when reading becomes more demanding.

In contrast, visual processing problems manifest as more cognitive/academic type symptoms. These include poor comprehension, letter and word or number reversals, difficulty remembering what was read, struggling to recognize words and problems sounding out words. Visual processing problems come into play more in that earlier phase—when a child is learning how to read. These problems can be classified according to the visual skill affected: spatial skills, memory, analysis and visual auditory integration (*Table 1*).

Evaluation

The history should include questions on recent changes to health if the symptoms are acute. Patients on certain medications—particularly for attention problems and depression—may have accommodative problems, patients who have had a traumatic brain injury (TBI) or concussion may also have binocular problems (See '*Five Additional Causes for Binocular and Accommodative Problems*').

As with any patient, the most important thing is to first determine an adequate refractive prescription. Because pediatric patients can accommodate large amounts during retinoscopy, a cycloplegic refraction should be considered if the child has moderate to high hyperopia, amblyopia, esotropia or if the retinoscopic reflex is unstable.[1] Additionally, a cycloplegic refraction is strongly recommended if the patient is not correctable to 20/20. With patients who are myopic, a full cycloplegic refraction is not generally indicated; refraction with tropicamide can be adequate.[1]

If visual acuity is reduced at distance or near, this reduced acuity may adversely impact the patient's ability to read. However, even if visual acuity is adequate, and the refractive error is minimal, a patient complaining of asthenopic symptoms when reading requires a thorough binocular and accommodative work-up. Basic techniques such as stereopsis, cover test and near point of convergence can provide significant information regarding a patient's binocular status. Keep in mind, issues with binocular vision can manifest at distance as well. Additional tests, including vergence ranges, particularly at near, can also be helpful in determining a diagnosis (*Table 2*).

Finally, in all cases, a thorough health assessment is necessary to rule out pathology. Findings such as a visual field defect, relative afferent pupillary defect, optic nerve edema or atrophy or retinal pathology indicate a nonfunctional cause for the defect and must be treated appropriately.

Lessons from the Literature

One of the most common conditions that can affect a patient's near binocular status is convergence insufficiency (CI).[2,3] This is generally classified by the triad of exophoria at near, receded near point of convergence and reduced positive fusional vergence ranges (base out) at near.

The CITT was a randomized clinical trial looking at vision therapy as a treatment for CI in children ages nine to 18 years.[2] Twelve weeks of office-based vision therapy were compared with office-based placebo therapy as well as home-based pencil push-up therapy and home-based computer therapy plus pencil push-ups. It found that patients in the office-based vision therapy group had lower scores on the Convergence Insufficiency Symptom Survey (CISS), a survey used to quantify symptoms in children with CI, as well as near-point of convergence (NPC) and positive fusional vergence (PFV) values that had improved significantly more than the other treatment groups.

Five Additional Causes for Binocular and Accommodative Problems

- **Concussion** – a recent study found that 49% of children and adolescents had CI after a concussion.[1]
- **ADHD** – a retrospective review found that 9.8% of children with CI had a diagnosis of ADHD; and 15.9% with a diagnosis of ADHD had a diagnosis of CI.[2]
- **Lyme disease** – a retrospective review of pediatric and adult patients with Lyme disease found that 53% had CI.[3]
- **Stimulant medications** (methylphenidate, dexmethylphendate, dextroamphetamine) – package inserts report "Difficulites with accommodation" or "blurring of vision."
- **SSRIs** (fluoxetine, sertraline, paroxetine, escitalopram, fluvoxamine, citalopram) – package inserts report risk of blurred vision.

1. Master CL, Scheiman M, Gallaway M, Goodman A, et al. Vision diagnoses are common after concussion in adolescents. Clin Pediatric 2016;55:260-7.
2. Granet D, Gomi CF, Ventura R, Miller-Scholte A. The relationship between convergence insufficiency and ADHD. Strabismus 2005;13:163-8.
3. Matta NA, Singman EL, McCarus C. Lyme disease and convergence insufficiency: is it a near fit? Am Orthiot J 2006;56:147-50.

Table 1. Visual Processing Problem Classifications

Efficiency	Processing
Acuity Hyperopia Myopia Astigmatism	Spatial skills Laterality Directionality
Binocularity CI CE	Visual memory Sequential Simultaneous
Accommodation Infacility Insufficiency Excess	Visual analysis (form perception, discrimination, figure ground)
Oculomotor Saccades	Visual auditory integration

Subsequent research found that most of the children who were asymptomatic after the 12 weeks of therapy, maintained those improvements for at least a year after therapy.[3] From the many papers that arose from the work of the CITT study, clinicians now have better evidence for the testing/treatment of this condition including a validated symptom survey, criteria for diagnosis and treatment options.[2,3]

For instance, the CITT study helped identify the signs and symptoms important to determine patient selection as well as gauge if treatment is successful.[2,3] We learned that office-based vision therapy is the most successful treatment for CI patients. Many optometrists now incorporate the CISS as a screening tool for school-aged patients.[4] The CISS has been validated for children ages nine to 18. Investigators say a score of 16 or greater is the cutoff for distinguishing children with symptomatic CI from those with normal binocular vision.[4]

For adult patients, a score of 21 or greater indicates symptoms of CI.[5] Recently, published work by the CITT study group, found that after 16 weeks of office based vision therapy vs. office based placebo therapy, signs of CI such as NPC and PFV improved, but the CISS scores were not statistically significantly different between the two groups.[6] The authors cautioned that the CISS may not be the best metric to use alone to determine whether or not treatment is successful in children.[6]

Although, to date, no large-scale randomized clinical trials of vision therapy for CI in adults are available, smaller scale studies show some success.[5-8] One such study on adult males found that 62% of patients who received in-office plus home therapy and 30% of patients who received only home therapy were successfully treated with vision therapy.[8] Many of the therapy techniques used in this study were the same used by the CITT group.

The vision therapy protocol in the CITT study focused on accommodation, voluntary convergence and fusional vergence.[2] Although many techniques can be accomplished with traditional methods, more sophisticated and equipment intensive therapy techniques such as vectograms, aperture rule and computerized orthoptics were also included in CITT.[2]

When conducting vision therapy, assess the patient's signs and symptoms at regular intervals.[2] Although the CITT used 12 weeks of 60-minute therapy sessions for the study, in practice, sessions may be closer to 30 or 45 minutes.[2]

In the same way that research has improved our understanding of CI, the PEDIG ATS studies have helped optometry deepen its understanding of amblyopia treatment.[9,10] From these studies, we know that when seeing a patient with amblyopia, the recommended treatment is to prescribe glasses and then monitor the patient's visual acuity every six to eight weeks.[9,10] That research shows that, in patients with isoametropic amblyopia, 73% obtained 20/25 visual acuity (VA) in one year with glasses alone.[9]

In patients with anisometropic amblyopia, approximately one-third showed resolution of the amblyopia with refractive correction alone and more than 75% of patients improved two lines or more in visual acuity.[10]

Similarly, in patients with strabismic and combined mechanism amblyopia, 75% improved two or more lines of visual acuity with spectacle correction alone, with resolution of amblyopia occurring in more than a third of patients.[11] Treating patients with spectacles first can help improve visual acuity, which can make penalization therapy easier for a patient.

Patching

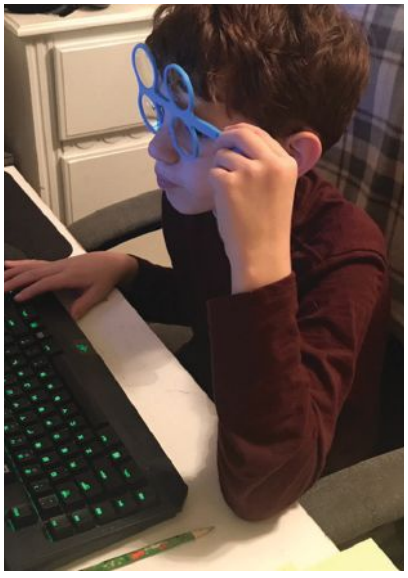
If patients do not show acuity improvement with spectacle correction alone, or if visual acuity plateaus for two consecutive visits, additional amblyopia treatment should be initiated.

Currently, penalization therapy is a mainstay of amblyopia treatment. For patients with moderate amblyopia (20/80 acuity or better), two hours of daily patching is recommended, based on data from the ATS.[12,13]

Research suggested that a weekend atropine regimen was as effective as daily atropine for amblyopia treatment, and that Bangerter filters can be used as an alternative to patching as a treatment for patients with amblyopia.[14,15]

Patients can purchase a variety of adhesive patches from a pharmacy, but you may also want to order cloth patches meant to fit over glasses and cover not only the eye itself but also above, below and to the side of the glasses.

Prior to the ATS studies, research had no information on potential treatment for children older than seven with amblyopia. The ATS studies found that, among children seven to 12 years old, more than half with amblyopia responded to treatment.[16] In an older group, children between 13 and 17 years old, only 25% responded to treatment; however, among patients who had not previously been treated for amblyopia, 47% of patients responded to treatment.[16]



Here, a patient is seen partaking in a binocular accommodative activity using a computerized therapy system. Research is now showing that these types of treatments can have a lasting impact.

One of the major criticisms of amblyopia treatment is that treating children and teenagers with patching can be difficult for both patient and parent. Children do not like to wear a patch and may try to remove it, frustrating parents. If the patch is placed on the glasses, the child may refuse to wear the glasses.

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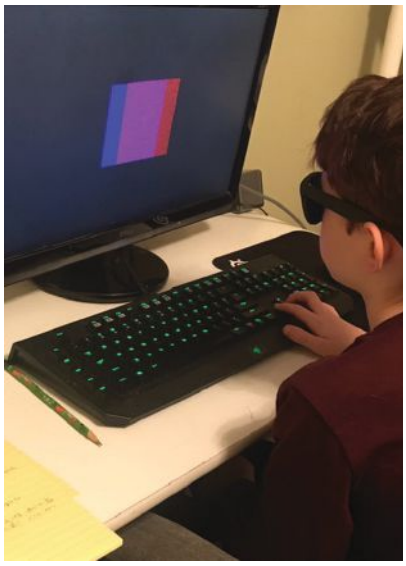
The latest ATS studies are evaluating newer binocular treatments for amblyopia. These treatments often use games or tasks that employ dichoptic stimuli, which use red/green glasses to form a binocular percept, showing different images to each eye. The image presented to the sound eye has reduced contrast, which allows patients that are normally unable to fuse images the ability to use their eyes together. As the patient plays the game successfully, the contrast increases until they are able to fuse the images with 100% contrast in each eye.

PEDIG first evaluated a binocular treatment using the Hess Falling Blocks, a game similar to Tetris. In a study of five to seven year olds using this treatment for 16 weeks, researchers found that the amblyopic eye acuity improved with patching and video game play; however, the improvement was not as good in the video game group as in the patching group.[17] Surprisingly, compliance was actually better in the patching group.[17] In an older cohort aged 13 to 16 years, amblyopic patients had a minimal response to the therapy.[17,18]

Other technologies have employed the use of dichoptic movies instead of video games for amblyopia. One study found that eight children, ages four to 10, with amblyopia who viewed 3D movies for two weeks showed an improvement in visual acuity of two lines.[20]

Bringing It To Your Clinic

When a practitioner encounters a patient with reading problems, or symptoms of double vision or headaches when reading, doing an NPC, near phoria and near PFV ranges can provide a lot of information and help with the diagnosis of CI. The patient's findings can be compared with the norms from the literature.



This patient is performing a vergence activity with computerized vision therapy system.

The treatment of a CI can employ brock string for convergence work, monocular accommodative facility or near far hart chart for accommodation, and distance hart chart for saccades. The therapy can advance to vectograms, aperture rule and lifesaver cards for convergence. The practitioner should reevaluate the patient after eight or 10 sessions. If the patient is not showing any improvement in signs or symptoms, another etiology for the condition might need to be explored.

If the patient does not tolerate a patch, atropine is another option, starting with 1% atropine on weekends. If prescribing atropine, be sure to educate the patients on pupillary dilation and blur. Atropine with a full distance prescription causes penalization at near only, so if it is during the school year make sure that your patient is able to easily read age-appropriate font with the amblyopic eye. If near print is blurry, you may have to consider a bifocal for schoolwork. Although the incidence of side effects with 1% atropine in the ATS trials was very low, doctors must educate patients and parents on all potential side effects. These can include facial flushing, increased heart rate and dry mouth.

Keep in mind, that although atropine is an effective treatment for amblyopia, it might not be the best option for a patient with light eyes, as these children will develop one dilated large black pupil and one noticeably light eye. If cosmesis is a concern, other treatment options—such as patching—may be appropriate for these patients. Additionally, if your patient will be spending time outdoors, make sure that they are wearing sunglasses or photochromatic lenses to decrease sensitivity to bright sunlight.

For patching, atropine or Bangerter filters, patients should be monitored every eight weeks for VA improvement. If the VA is improving, the penalization method can continue until vision is stable. If improvement is minimal or if acuity plateaus, increasing the hours of patching from two to six, or changing the treatment method is acceptable.[21] Patients should be monitored for a year after treatment is discontinued, as research shows a quarter of patients may show a regression in VA.[22]

Binocular Options

If you would like to incorporate bi-ocular or binocular therapy into your practice, you can use basic red/green targets for your patient. Commercially available matching games, playing cards and other activities that patients with amblyopia can use to incorporate

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Table 2. Binocular Vision Tests

Test	Normal Values
Near Cover Test	Ortho to 6XP
NPC	5cm/7cm accommodative 7cm/10cm non-accommodative
Positive fusional vergence Smooth	17/21/11
Negative fusional vergence Smooth	13/21/13
Amplitude of accommodation	15-1/4age +/-2
Lag of accommodation	+0.25 to +0.75
Negative relative accommodation	+2.00 (+/-0.50)
Positive relative accommodation	-2.37 (+/-1.00)
Vergence Facility 3BI/12BO	15 cycles per minute

binocular therapy into their treatment plan. Practitioners can also make worksheets using red and green text that the patient reads with red-green glasses and a filter but pay attention to the cancellation. Monocular fixation in a binocular field (MFBF) therapy is another method that can be used treat amblyopia. The patient wears a red filter over the sound eye with no filter over the amblyopic eye and completes activities using a red pen or pencil that can be seen by the amblyopic eye only.

These bi-ocular and binocular therapy techniques are most appropriate for patients with refractive amblyopia or patients with particularly small angles of strabismus. Patients with large angles of strabismus are generally not best managed with binocular techniques unless there is a mechanism to correct for their angle of strabismus.

If you want to try binocular therapy instead of penalization, or if the visual acuity plateaus, numerous options are available. Many companies have their own binocular therapies, although none have been studied in a large randomized clinical trial. One such company, Vivid Vision, employs the use of virtual reality goggles with their platform to treat amblyopia, strabismus and vergence disorders. Their protocol involves having the patient wear virtual reality goggles and play interactive games that have the patient stop oncoming targets with their hands, pop targets with their fingers or aim their eyes to look at a target.

A Few Helpful Pointers

Children with binocular problems can present with symptoms that span across a spectrum that ranges from asymptomatic/avoider, to avoider to symptomatic. A child with reading trouble who persists in trying to read and but gets headaches is symptomatic. When children are too uncomfortable to even try reading, they are avoiders. Children who adapt by covering an eye when reading, or holding things farther away, can be considered asymptomatic/avoiders.

Similarly, when examining a child with amblyopia, particularly if it is anisometropic and the parent had no concerns prior to the child's failing a school screening, it is important to realize that child may not complain that one eye does not see. A child with amblyopia does not realize they could be seeing things differently.

Children with learning disabilities may have refractive errors or problems with binocular/accommodative skills. A study, looking at 50 children on Individual Education Plans (IEPs) compared with age-matched controls and did full binocular work ups. The children with the IEPs had various types of learning disabilities, many of which were specific to reading. The study found that "there are significant associations between reading speed, refractive error and vergence facility."

The authors did not claim that the sole cause of the children's reading difficulties was visual or binocular, as these problems can be multifactorial. However, they did recommend that students being considered for an IEP should have a full eye examination, including binocular vision testing.[23] Vision is a piece of the pie when dealing with reading problems.

The next time you encounter a patient whose history is suggestive of a binocular problem—including amblyopia—approach the exam in a sequential pattern using history to guide your testing. Incorporate basic binocular testing into your evaluation and remember to first rule out any potential pathology.

Regarding your treatment of these patients, at the very least, educate your patients about these conditions and make some perti-

nent and educated recommendations. Refer the patient to a vision therapy provider for treatment or do it yourself if this is a treatment modality you are comfortable providing. ■

Dr. Bodack is an associate professor and chief of the Pediatric Primary Care Service at Southern College of Optometry

Dr. Jenewein is an assistant professor at Salus University and its principal site investigator for the Pediatric Eye Disease Investigator Group,

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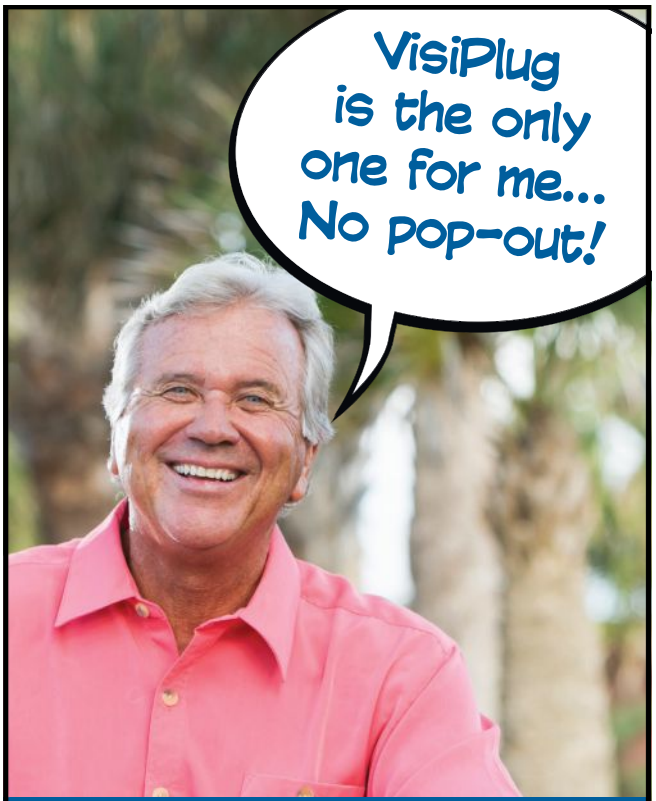

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PEER • REVIEWED PRA ARTICLE

The Crowded Landscape of Presbyopia Correction

Today's patients have different visual needs, and you have new tools at your disposal to help—with more on the way. **By David Geffen, OD**

Uncompromised presbyopia correction seems to be as elusive as ever, despite a growing population seeking these therapies. The global number of patients with presbyopia is expected to be approximately 1.4 billion by now, and many remain unsatisfied with the currently available options.[1,2] Researchers, innovators and manufacturers are forging ahead with a number of new technologies for every form of correction, including spectacles, contact lenses, intraocular lenses (IOLs), surgical treatments and pharmaceuticals. Here's a look at what's new in your armamentarium and what might be available in the future.

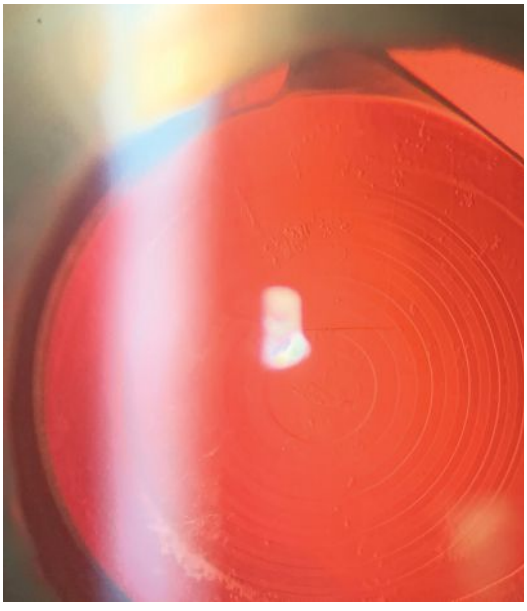


Photo: Cecelia Koetting, OD

So far, patients seem to like the range of vision provided by the new trifocal PanOptix IOL.

New Angle, Age-old Problem

Today's US presbyopic population is significantly different from 20 years ago. The Baby Boomer generation (ages 52 to 70) wants to feel and look more youthful and is working much later in life. In addition, digital devices are creating new visual demands we need to address. The majority of these patients, 63.9%, report symptoms of digital eye strain.[3] Even among Generation Xers (ages 36 to 51), 65% spend more than five hours per day on digital devices, with 66% experiencing symptoms of digital eye strain.[3] This phenomenon may partially explain why we are seeing presbyopic symptoms at younger ages.

Many presbyopes are grappling with the psychological effects of getting older and struggling with their vision, possibly more so than in the past as a result of the ubiquitous presence of digital devices. One study found that presbyopia was associated with worse vision-related quality of life than emmetropia in younger individuals.[4]

As such, presbyopes face a host of issues when they visit our offices looking for a solution—and we need to be ready to meet the demand with new and creative solutions.

Currently, we employ several means of correcting presbyopia: spectacles, monovision and multifocal contact lenses, IOLs with reading glasses, monovision and multifocal IOLs and corneal inlays. Despite ever-improving multifocal

options, monovision is still the most common way doctors treat their patients to correct presbyopia.[5] For contact lenses, only about 12% of presbyopic fits are with a multifocal design. As for IOLs, only about 8% of surgeries are done with a presbyopia-correcting lens.[6] Some feel multifocal and trifocal designs take up too much chair time, while others do not feel they provide adequate vision for the patients.[7] Many just can't break longstanding habits. However, doctors should recommend these options with regularity, as they can provide significant benefits to the right patients.

Contact Lenses of Today

Multifocal contact lens designs continue to evolve. We now have several designs that allow our patients the freedom of spectacle-free vision most of the time. For example, Bausch + Lomb recently introduced the first off-the-shelf toric multifocal, Ultra Multifocal for Astigmatism, for patients who are presbyopic with astigmatism.

Most of the current multifocal contact lens designs use aspheric optics to achieve near acuity, making lens centration critical to allow the optics to work properly. While these designs do work, they are not ideal for every patient, as they require some optical compromise. Several new designs are in early development, but little information is available currently.

Some innovative designs under investigation include a water gradient lens to simulate an accommodative effect, thus allowing the patient more natural vision with a true full range. Another lens uses microelectrodes to allow for variable vision. Many of the larger contact lens companies have started to partner with tech companies to help them develop new designs.

IOLs in the Works

In addition to recommending an IOL during cataract surgery, clinicians can consider clear lens extraction for patients, usually older than 55, looking for a refractive surgery option. Although many of these patients come into the office for a LASIK consultation, the lens changes that will occur over the next decade make a clear lens exchange a reasonable alternative. During a clear lens exchange, the surgeon removes the crystalline lens prior to cataract formation.

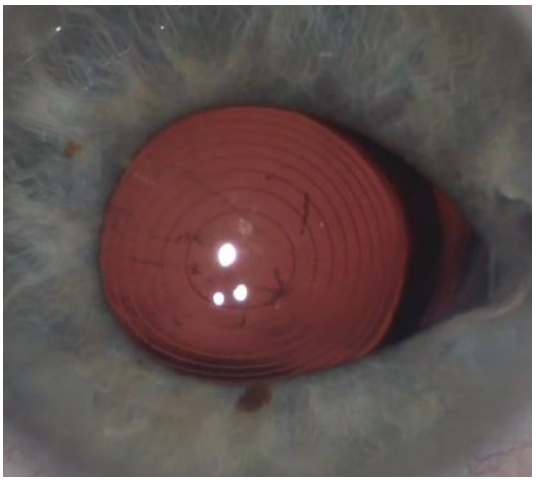


Photo: Derek Cunningham, OD, and Walter Whitley, OD

The Symfony IOL uses refractive echelettes that appear similar to the concentric rings of a multifocal but diffract rather than split the light entering the eye.

Patients considering an IOL have several presbyopia correction options: they can obtain the best distance vision possible and use readers for near, implant an IOL focused at near for monovision or choose an advanced technology IOL, whether accommodative or multifocal.

Though many patients could benefit from a presbyopia-correcting IOL, only about 12% of IOLs implanted are of the advanced technology type (including toric IOLs).[6] Surgeons have been slow to embrace this technology, and referring ODs have been equally hesitant to recommend them—whether out of habit or because they question the lens's performance.

However, optometry plays a vital role in this decision. We typically have a longstanding relationship with the patient and know their visual needs. For example, a patient corrected with multifocal contact lenses will likely do well with a multifocal IOL and may not be happy with a single-vision IOL. We need to be more proactive in our recommendations to give the patient all their options.

The approved IOLs for presbyopia can be either accommodative or multifocal. The only approved accommodative IOL is the Crystalens (Bausch + Lomb), which remains relatively less popular due to its unpredictable near vision. Two multifocal IOLs approved in the United States include the Tecnis Symfony (Johnson & Johnson Vision) and the Restor (Alcon). These IOLs come in a variety of add powers and have had good success with some side effects, the most common being halo and glare with limited range of clear vision.

The newest IOL in the United States is Alcon's AcrySof IQ PanOptix. This trifocal lens, designed to provide near, intermediate and distance vision, has been used successfully outside the United States for a few years. So far, the reports are quite encouraging for this lens, as patients say they like the range of vision and have little glare.

Several new IOLs are potentially coming to the US market soon:

The ***RxSight light adjustable IOL*** has been approved in the United

States but has yet to hit the overall market. It should be widely available early this year. The lens is a 6mm silicone optic with a PMMA haptic. The IOL material is modifiable until it is "fixed" by ultraviolet (UV) light, meaning the doctor can adjust the prescription to meet the patient's needs after the initial implantation. The lens can also be modified to change the amount of asphericity, thereby creating a multifocal effect. If near vision is not adequate or the patient doesn't like the vision it initially provides, you can modify it. The patient needs to avoid UV exposure until the final Rx is established, so they must wear UV-blocking glasses until then.

The ***AT Lisa (Zeiss)*** refractive-diffractive hybrid lens has both toric and nontoric versions and a 3.75D add.[8] It directs light to one focal point for near and another for distance, and uses simultaneous images to which the patient needs to neuroadapt. This lens splits the light by using 65% for distance and 35% for near. The design uses concentric diffractive rings that are rounded to reduce halo and glare. The lens has 0.11µm of negative spherical aberration. The lens gets good reports

Scleral Multifocal Contact Lenses: The Search For Comfort

By Nitya Murthy, MS

Many patients with presbyopia are looking to rid themselves of glasses for convenience and cosmetic reasons. Contact lenses are a great option, and for those already wearing contact lenses, multifocal contact lenses are a no-brainer.

However, issues of comfort and quality of vision can thwart contact lens success in this population. In particular, symptoms of dryness, which increase with age, are the most challenging aspect of adapting to multifocal soft contact lens wear.[1] This is where the resurgence of scleral contact lenses can be a valuable asset in our toolbox.

Scleral multifocals are generally dismissed as opportunities for presbyopic patients for several reasons:

- They are commonly reserved for corneal irregularities.
- They require more chair time and skill to fit.
- Billing for medically necessary contact lenses for patients with normal corneas can be challenging.

However, newer options have addressed most of these concerns. For example, various scleral lenses are now designed for normal corneas, with standard base curves and diameters that are compatible with most normal eyes. As for billing, insurance companies provide varying degrees of coverage. CPT code 92071 or V2627 may be covered by the patient's insurance, while other vision insurance contact lens material fees may be used toward the cost of a scleral lens.[2]

The Pros

The advanced optics coupled with improved comfort and dry eye relief make scleral contact lenses a compelling option. To make them more user-friendly, many companies have developed new lens designs that maximize the optics while cutting down on chair time.[3] Lenses generally come in simultaneous designs and use lid anatomy and pupil size to center and anchor the lenses.[4]

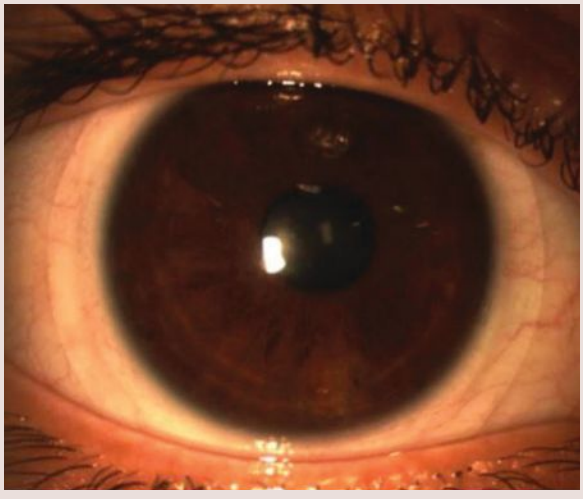
Several common variations in fitting philosophies exist:

Aspheric vs. concentric. Aspheric lenses have smooth power transitions throughout the lens between distance, intermediate and near powers and are a good option for presbyopes with low adds.[4] Concentric designs have designated distance and near rings that alternate moving from the center to the periphery.

Center-near vs. center-distance. These fall under the umbrella of concentric designs and perform as they are named. Generally, center-near designs are more common, given the prevalent demand for near-work at mobile device distances. However, center-distance designs are more appropriate for emerging presbyopes and those who prefer to have better distance acuity.[4]

Practitioners can choose the best lens design based on the patient's lifestyle needs. Most scleral lens manufacturers offer myriad variations in these designs and include fitting guides to help align the power zones with the patient's pupil.

Scleral lenses provide many invaluable advantages, and fitting them is easier than ever before. We must offer our presbyopic patients all lens options so they can choose the lens that best suits them—which just might be a scleral.



Scleral lenses could help address presbyopia and dry eye.

Ms. Murthy is a 4th year student at Kentucky College of Optometry (KYCO) and president of the KYCO Contact Lens Society.

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for distance and near vision but may lack in the intermediate area.[9]

The ***Lentis Mplus (Oculentis)*** is a one-piece zonal refractive lens with plate haptic and two refractive segments. The design has a large aspheric distance-vision zone and a sector-shaped zone with 3.00D of near add embedded on the posterior surface.[10] The big advantage of this bifocal IOL is that it provides good distance vision.[11] A large distance optic zone ensures good contrast sensitivity and reduced glare and halos. Some patients may notice ghost images, as the design also uses simultaneous vision.[12,13] Patients can read with this lens in any direction of gaze and do not need to look down as with bifocal spectacles. Some patients do not achieve the near vision they expect, and the intermediate vision may not be good enough for some patients.[11]

The ***Fine Vision (PhysIOL)*** is a trifocal diffractive IOL that uses constructive interference to capture light energy that other diffractive lenses lose. The lens has 3.50D power for near and 1.75D for intermediate vision. Its main advantage is that it can provide intermediate acuity, which is especially useful for digital device use. The lens surface is microlathed in an alternating pattern from the center to periphery. The lens uses constructive interference to increase the amount of light used for each focal point.[10] The lens has not had a lot of market tests yet, but early results have been positive.

With the ***FluidVision IOL (PowerVision)***, silicone fluid is stored in the soft haptics and accommodative effort forces the fluid to move into the central fluid chambers. This changes the shape of the anterior optic and shifts the eye's focus to near. Still in early studies, this lens could provide as much as 5.00D of accommodation.[14]

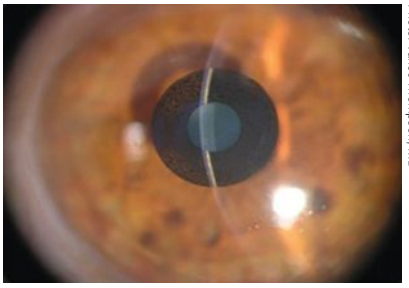


Photo: Vance Thompson, MD

The Kamra inlay requires distance vision near plano before surgery.

The ***Dynacurve IOL (NuLens)*** is implanted in front of the collapsed capsular bag. The capsule exerts pressure from the ciliary muscle to move the fluid and modify the shape of the optic to cause an accommodative effect. In theory, the researchers say this lens could provide up to 12.00D of accommodation.[15]

Perfect Lens is not a lens per se but rather a technology designed to modify nearly any pre-existing *in situ* IOL using a femtosecond laser. The laser can create a multifocal effect of bifocal or trifocal design. If necessary, the lens can be changed several times to achieve the best vision.[16]

The ***Gemini Refractive Capsule (Omega Ophthalmics)*** is not an IOL but a capsular ring that, when inserted into the capsular bag, maintains the original size and shape of the bag. This ensures the proper lens position. This design controls the x/y plane of the eye and helps control the z plane. The ring allows the surgeon to implant most any IOL into it to achieve the best refractive result. Because this ring keeps the capsule bag intact, you should be able to replace the IOL if a better lens becomes available.

The ***IC-8 small aperture IOL (Acufocus)*** is another option currently approved in Europe. The lens is designed to extend the eye's depth of focus by combining a small aperture with a monofocal lens. A retrospective case series conducted in Australia found more than 90% of healthy participants achieved uncorrected distance, intermediate and near visual acuity of 6/12 or better in the corrected eye. The researchers noted that more than half remained spectacle-free for all distances at final follow-up, and those who used spectacles did so only for certain needs such as near-vision tasks and reading in poor lighting.[17]

Other Surgical Corrections

Several surgical approaches can address a presbyope's needs:

Monovision with LASIK or photorefractive keratectomy has been employed for years, and we are well aware of the limitations of this technique. Presby-LASIK has fallen out of favor in the United States due to regression and unpredictability.

Likewise, conductive keratoplasty is rarely used due to regression.

Corneal inlays are an additive technology that can be removed in the event of patient dissatisfaction. The procedure does not remove any tissue, providing an opportunity to potentially employ future technologies.[18] Although three companies went through FDA trials to get these devices to market, two have since gone out of business. The third device, the Kamra inlay (CorneaGen), is still a viable option. With this monovision technique, the inlay is placed in the nondominant eye, creating a pinhole pupil to increase the near eye's depth of focus. The eye's distance vision needs to be close to plano before the procedure. The inlay has not found a strong following and relatively few procedures are being done.

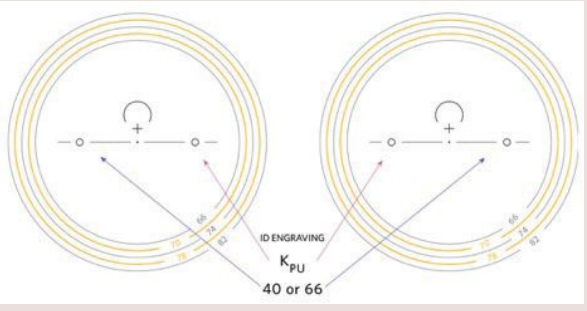
The other two inlays were the Raindrop (Revision Optics), which changed the corneal shape to create the near effect, and the Flexivue

Spectacle Lenses for Presbyopia: Shifting Focus

Glasses are still the go-to option for most presbyopes. It's a mature field, technologically, but that doesn't mean patients won't have some futuristic options in the coming years. Here are just a few on the market or under development:

Signet Armorlite recently released a new ophthalmic lens called Kodak PowerUp, which the company claims can partially acclimate patients to progressive addition lenses before they need them. The company says the product is particularly suited to the visual tasks of a digital, device-centric world by helping patients achieve prolonged, comfortable reading up close. Kodak PowerUp lenses offer two levels of power in the reading area: 0.40D and 0.66D.[1]

Researchers at Stanford have created what they are calling "auto-focals"—eyewear that uses eye tracking technology to identify what the wearer is looking at and then adjust the focus accordingly. The device (the prototype of which looks like a bulky VR headset) incorporates fluid-filled lenses that bulge and thin when the field of vision changes, identified with eye-tracking sensors.[2] All 56 presbyopes who used the device during preliminary testing were surprised at how well it performed with reading and other tasks.[2]



Kodak's PowerUp lens provide two add powers for reading.

Adjustable focus spectacles are already available from several companies, including Adlens and Eyejusters.[3-5] These ophthalmic lenses use dials on the sides of the frames to change the lens prescriptions based on the user's needs. Adlens incorporates two thin lenses that slide by each other when the wearer shifts the knob, thus changing the power.[3,5] Eyejusters have a range of +0.50D to +4.00D and allow users to change the power of each lens independently, providing more options for those with varying prescriptions in each eye.[5]

The 2005 startup PixelOptics may have filed for bankruptcy in 2013, but its Empower electronic lenses are still a hot topic in many forums as recently as September 2018.[6,7] These battery-powered glasses used a liquid crystal reading segment that was activated based on head tilt or with a swipe of a hand. Little information exists on the product's current availability.

Several augmented reality options show promise in helping to correct presbyopia, although none are ready for the consumer market.[8]

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Microlens (Presbia), which provides distance vision through a central plano zone surrounded by one or more rings of varying powers for intermediate and near vision.[19]

The VisAbility insert (Refocus Group) is placed in four quadrants outside the visual axis in scleral tunnels. The bands are inserted in both eyes to create an increase in accommodative effect by allowing the ciliary muscle to exert more pressure on the lens. Studies show about a 1.50D increase in accommodation. The device is awaiting FDA approval and should be available in 2020. This technique will not have an effect on future cataract surgery.

Drops on the Way

A pharmaceutical presbyopia management option might prove to be the Holy Grail clinicians and researchers have been looking for. Several are in the pipeline:

Yolia's True Vision Treatment combines customized contact lenses and specially formulated eye drops to provide a noninvasive, binocular treatment for presbyopia. The drops soften the cornea to allow the rigid lenses to reshape the eye and then stabilize the new shape. This treatment adds asphericity to the corneal surface, creating a multifocal effect. The company is now doing clinicals in Mexico and the United States.

Novartis's UNR-844 (formerly EV06) lipoic acid choline ester 1.5% is a prodrug that penetrates through the cornea and metabolizes into choline and lipoic acid. Enzymes within the lens fiber cells chemically reduce the lipoic acid to its active form dihydrolipoic acid. This chemically reduces disulfide bonds, ensuring the lens fibers remain flexible to allow for continued accommodation. This treatment is in early trials and not much data is available at this time.

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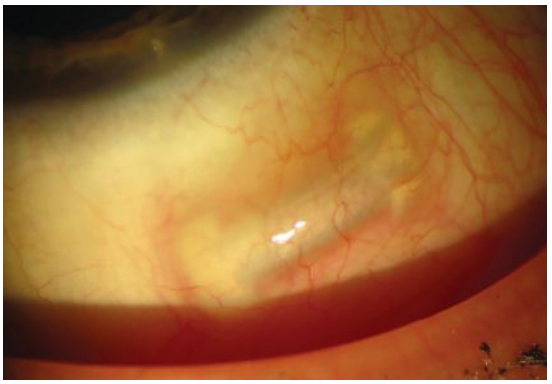

Photo: Refocus Group

The VisAbility scleral inserts represent a new concept in presbyopic surgery currently undergoing FDA trials.

The ***Liquid Vision (PRX-100, Presbyopia Therapies)*** drop contains aceclidine and low-dose tropicamide to create a miotic pupil without the accommodative effect. This results in a pinhole effect to increase the eye's depth of focus. The drop is used once a day in the nondominant eye.

The ***CSF-1 drop (Orasis)*** is a parasympathomimetic agent with a nonsteroidal anti-inflammatory in an oil-based formulation that also causes a miotic pupil and increases the eye's depth of focus. This option is currently in Phase II trials.

FOV Tears, currently available in Colombia, is a combination of a parasympathetic, alpha agonists 1 and 2, an anti-cholinesterase and an NSAID, according to Colombian researcher Felipe Vejarano, MD, a lead investigator for the drug. The drop affects the ciliary muscle, which causes a physiological accommodation and a dynamic pseudo-accommodation. Initial study results suggest the drop has a cumulative effect, lasting four to five hours initially, but can last up to eight hours with continual use.[20] More recent data shows the drops improved near vision by one or more lines in 92.3% of the patients two hours after instillation, with a greater effect in the youngest patients compared with the oldest.[21] The drop remains under investigation in Colombia and Spain.

Allergan's AGN-199201 and AGN-190584, both miotic-based drops that work as pupil constrictor agents, remain in development. Early research found 70.6% of participants who first received one drop of AGN-190584 ophthalmic solution and one drop of the AGN-199201 vehicle in the nondominant eye and then two drops of AGN-199201 vehicle in the dominant eye experienced a two line or more improvement.[22]

Researchers have also investigated a ***combination of carbachol 3% and brimonidine 0.2%*** to create a miotic effect to improve vision in presbyopia. A pilot study of 10 naturally emmetropic and presbyopic subjects shows the monocular treatment with one drop a day of carbachol/brimonidine in the nondominant eye provided statistically significant improvement in mean near visual acuity for all patients. The improved depth of focus caused a statistically significant improvement in near visual acuity, with no change in binocular distance vision, the study found.[23]

Many presbyopia correction options are under investigation, and some are more promising than others. No doubt the coming years will see new management strategies for this growing population in need, as we are embarking on entirely novel ways to treat this condition. ■

Dr. Geffen is the director of Optometric and Refractive Services at the Gordon Schanzlin New Vision Institute of TLC Laser Eye Centers in San Diego, CA. He is the immediate past president for the Optometric Cornea and Cataract Refractive Society.

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PEER • REVIEWED PRA ARTICLE

Low Vision: Why and When to Recommend

Decreased visual acuity is just one of many reasons to refer patients. Here's a look at who else might benefit. **By David Lewerenz, OD**

Low vision care is a crucial part of our profession. It's endorsed by many key organizations, including the American Academy of Optometry, the American Optometric Association, the American Academy of Ophthalmology, the National Eye Institute and the World Health Organization. The American Academy of Ophthalmology's CEO, David Parke, MD, even claimed in a recent video that "vision rehabilitation is now the standard of care for patients who are losing their vision."[1] This is a strong message: if you're not referring for low vision care, you're not practicing at an acceptable standard.

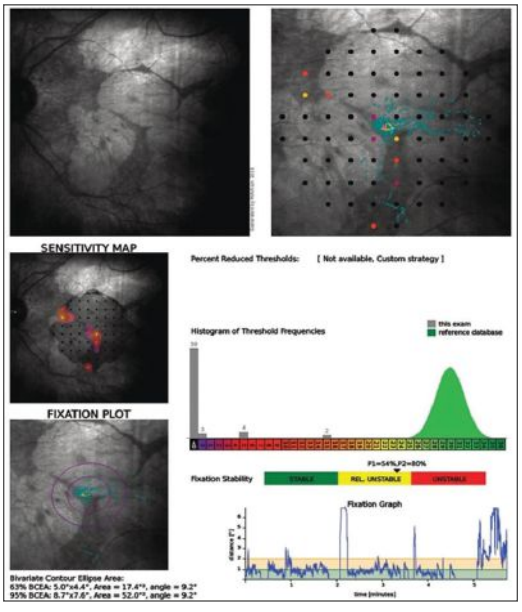

Fig. 1. This microperimetry readout shows a case of a spared channel of central vision in a patient with macular telangiectasia.

Most optometrists eventually refer patients in need of low vision services, but the process for determining when to refer is often up for debate. The most common approach is to set a visual acuity threshold; many refer for low vision care when best-corrected visual acuity in the better-seeing eye reaches 20/40, 20/60 or 20/70. Some educational and vocational programs even set a visual acuity threshold for admission.

However, basing your low vision referral on visual acuity alone is insufficient and ignores many other visual complications that decrease patients' visual functioning and quality of life. For example, visual acuity may be minimally affected, but a deficiency in contrast sensitivity, visual field, ability to handle glare or see at night, color vision, stereopsis or binocularity can affect a patient's functioning equal to that of visual acuity loss.

So, if you can't depend on visual acuity to guide your referral decision, what can you base it on? My preferred definition of low vision comes from the National Eye Institute: "Low vision is a vision problem that makes it hard to do everyday activities. It can't be fixed with glasses, contact lenses or other standard treatments like medicine or surgery."[2] So, when a patient's life is impacted by vision, it's time to refer, regardless of visual acuity.

This article provides a more comprehensive approach to low vision referrals with the help of several case examples. The cases, although incomplete, provide vignettes of relevant information to highlight the many different patient populations

that could benefit from low vision services—and it's more than you might have realized.

Foveal Sparing

Some patients with age-related macular degeneration (AMD), especially those with central geographic atrophy from non-exudative AMD, develop a large central scotoma with a tiny island of vision at the center. These types of patients may have 20/30 vision when reading letter-by-letter on a visual acuity chart, but that does not reflect their visual function. When reading in a real-world environment, they may function more like a patient with visual acuity ten times worse.

Testing near vision with a well-designed continuous text chart, such as the MNRead or the SK Read is often quite revealing, as these tests can expose a much deeper level of visual impairment than a visual acuity chart. Inability to fluently read a 1.0M sentence with ordinary glasses is an indication that referral might be beneficial.

Another important sign of foveal sparing is the paradoxical situation of greater ease with reading smaller rather than larger print, because the small island of central vision is incapable of taking in more than a letter or two at a time when the text is large.

Bright illumination can be an effective tool in managing patients with foveal sparing, as the portions of relative scotoma will begin to contribute to the visual process if lighting is sufficient, effectively limiting the size and scope of the ring scotoma.

A sure sign of a patient with foveal sparing is the patient who describes walking outside into bright sunlight to read print or keeping a portable flashlight with them everywhere they go.

Microperimetry can be another useful tool for investigating foveal sparing. *Figure 1* shows a patient with macular telangiectasia and reveals a narrow corridor of dim vision just a few degrees wide, surrounded by a large area of blindness nearly 20 degrees in diameter. She was able to register 20/50 on an ETDRS visual acuity chart, although this, in no way, represents how she functions in the real world. She benefitted from bright illumination

Contrast Sensitivity

For adults, the Pelli-Robson or Mars tests are quick and convenient ways to evaluate contrast sensitivity. Although only one spatial frequency is evaluated, they provide useful data and a great opportunity to educate patients. The Hiding Heidi test is remarkable in assessing pediatric patients as young as two years.

Functional problems become evident when contrast sensitivity reaches the moderate or severe level of reduction from normal.

Contrast Sensitivity Testing

Level	Levels of Impairment With Mars or Pelli-Robson tests (Weber contrast calculation)	Percent of impairment using Hiding Heidi (Michelson contrast calculation)
Profound reduction	0.00 log CS to 0.60 log CS	25%
Severe reduction	0.75 log CS to 0.90 log CS	10%
Moderate reduction	1.05 log CS to 1.20 log CS	5%
Mild reduction	1.35 log CS to 1.65 log CS	2.5%
Normal	1.80+ log CS	1.25%

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Contrast Sensitivity Loss

Contrast sensitivity is extremely important in determining how a person functions. It's critical in distinguishing the flesh tones we use to identify a face and in determining where a sidewalk meets a curb or a step when walking. For a person with very poor contrast sensitivity, seeing rice on a white plate or coffee in a black cup becomes nearly impossible.

The level of contrast sensitivity loss is not predicable based on visual acuity. Consider these real-life examples, in which the patient's contrast sensitivity loss is not at all proportionate to their visual acuity deficit:

- A 90-year-old female with AMD had visual acuity of 20/80 but log contrast sensitivity of 0.45, which is considered profound loss
- An 84-year-old male with AMD had visual acuity of 20/400 and log contrast sensitivity of 1.50, which is only mild loss
- An 83-year-old female with AMD had visual acuity of 20/40 and log contrast sensitivity of 0.75, which is severe loss

As these examples illustrate, contrast sensitivity testing can reveal a level of vision loss that would not be predicted by visual acuity alone.

The 90-year-old female described above was an avid mahjong player but had to stop playing due to her vision loss. She was able to resume playing after I fit her with a 3x Ocutech Mini variable focus telescope, mounted to use in slight downgaze and in good illumination (*Figure 2*).

Visual Field Loss

A patient can have 20/20 visual acuity alongside many conditions that cause visual field loss such as: homonymous hemianopia, bitemporal hemianopia, concentric loss, paracentral scotoma, ceco-central scotoma and altitudinal loss.

Due to this variety of visual field loss, it is impossible to provide a specific criterion on which to base a low vision referral. Rather, if your patient has visual field loss, refer for low vision care if the loss interferes with their daily activities. Scanning training, reverse telescopes, Peli prisms and improved illumination can assist patients with problems related to visual field loss. Depending on their vision and their personal needs, we may refer the patient for orientation and mobility training and, where appropriate, behind-the-wheel driving rehabilitation services.

Diplopia

Many conditions can cause double vision; for example, it is a sequela of glaucoma drainage device implantation in about one in four cases.[3,4] Diplopia and the resulting binocular confusion can be difficult problems for both the patient and the clinician. One reason is that suppression rarely provides relief for adult patients, given their relatively lower level of neuroplasticity and ability to suppress compared with children. Prism glasses, referral for strabismus surgery and a wide spectrum of options for occlusion exist to assist patients with diplopia. Consider these two patient examples:

An 80-year-old female had experienced extremely frustrating constant diplopia for more than two years

20/Unhappy

In my experience, referral sources sometimes send patients who are not technically low vision, yet they are unhappy with their vision. By far the most common type of referral in this category is from cataract surgeons, who have completed a cataract extraction with intraocular lens (IOL) implantation, and the patient is unhappy with their vision despite registering normal visual acuity of 20/20 or 20/25 on standard visual acuity tests. This is more common with, but not limited to, the use of multifocal IOLs. A significant number of multifocal IOL patients have more higher-order aberrations and slightly reduced contrast sensitivity compared with patients with monofocal IOLs.[1,2] Dissatisfaction with multifocal IOLs is somewhat dependent on personality type.[3] Here is a recent example:

A 71-year-old retired accountant was referred by her cataract surgeon. She had received Tecnis Symfony (Johnson & Johnson Vision) multifocal IOLs with her cataract surgery six months previously. She was dissatisfied with her vision for reading and night driving. I was given a tall order from the cataract surgeon: come up with a plan to improve her vision without prescribing glasses because she didn't want them (hence the multifocal IOLs). Her left eye was strongly dominant. She refracted to 20/15 in each eye with plano -0.50 x 040 in the right eye and +0.25D sphere in the left. My recommendation, which the cataract surgeon carried out, was to perform PRK on the right eye to leave it at -0.75D sphere and use brimonidine drops OU when driving at night to slightly reduce pupil size. These changes were successful, but she did finally consent to wearing glasses with -0.75D sphere for the right eye when driving at night.

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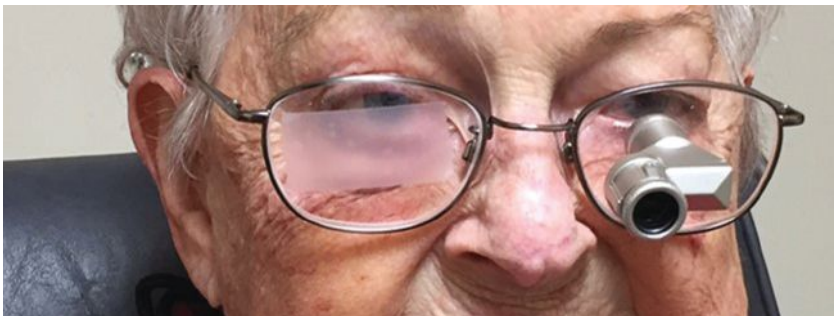

Fig. 2. We used a 3x Ocutech mini variable focus telescope to help this patient see when playing mahjong.

secondary to thyroid eye disease with orbital decompression surgery. Her visual acuity was corrected to 20/32 in the right eye and 20/40 in the left. She had a 14Δ left hypertropia that increased significantly in left gaze. She was fit with progressive addition lenses with +3.00D add and prism of 6Δ base-up in the right eye and 6Δ base-down in the left. She was thrilled to have her diplopia controlled with the glasses in all but far left gaze.

Sometimes, one pair of glasses can't solve all of a patient's problems. A 38-year-old female presented with Kearns-Sayre syndrome, a mitochondrial condition that can cause symptoms similar to retinitis pigmentosa, such as nyctalopia and mid-peripheral visual field loss. Another common sign of this syndrome, experienced by this patient, was external ophthalmoplegia. She was orthophoric at distance and had the accommodation expected of someone her age but had no ability to converge. Single vision computer glasses were provided with +0.50D add and a total of 7Δ base-in. For reading, she received a +1.25D add with a total of 13Δ base-in, also in single vision lenses.

Acute Monocular Vision Loss

An estimated two to four in 100,000 people per year will experience enucleation or evisceration of one eye, and one study found 2% of US veterans in a polytrauma center were monocular.[5-8]

Adjusting to acute vision loss in one eye can be a monumental task, and it is especially helpful to refer when the loss is recent and occurred suddenly, as in a case of ocular injury or enucleation from ocular malignant neoplasm.[9,10] Any type of vision rehabilitation program, including those in private practices, academic institutions, non-profit clinics and the Veterans Administration, can help patients adapt to acute monocular vision loss. The following cases illustrate the benefits these programs provide:

A 46-year-old marketing specialist had her left eye enucleated due to malignant melanoma. The right eye had normal visual acuity, visual field, contrast sensitivity and color vision. She was quite symptomatic from the loss of the temporal crescent of visual field in the left eye and reported mobility difficulties.

The level of difficulty from the loss of visual field is often disproportionate to the amount of actual visual field loss from monocularity in many patients. Other symptoms also difficult to explain include the need for more light, photophobia and fatigue with visually intense tasks. As expected, this patient also suffered a complete loss of stereopsis and had difficulty with hand-eye

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tasks such as activities involving reach-and-grasp ability and pouring liquids from a pitcher.

Following her low vision evaluation, we referred her to our occupational therapist, who helped her adapt with new strategies for daily tasks, such as hand-eye activities and training to develop a method for scanning to her left when walking.

Partial monocular vision loss also causes troublesome rivalry symptoms for some patients. A 78-year-old retired physician and professor had significant visual field loss and reduced contrast sensitivity in the left (formerly dominant) eye due to glaucoma. His symptoms were so severe he told me he felt his vision would be better if he lost the left eye entirely, and he often closed the left eye when performing visually intense tasks. His visual acuity was correctable to 20/32 in the right eye and 20/50 in the left.

After several visits, we determined different levels of occlusion would help for different tasks. For some activities he required total occlusion of the left eye, but for others he preferred partial occlusion, which we provided with Bangerter foil. We prescribed single vision lenses for mobility with 0.2 Bangerter foil over the entire left lens. For reading, we placed 0.2 Bangerter foil over the bifocal portion only of his left lens and included a +3.00D bifocal add in the right lens. For computer use, he required total occlusion, achieved with a left lens painted black and a single vision lens for the right eye with a +1.50D add.

Night Blindness

Nyctalopia occurs most famously in retinitis pigmentosa, which affects nearly 100,000 people in the United States, but it can occur with other conditions as well.[11] Again, visual acuity may not be bad enough to trigger a referral, but a person can be significantly impaired from night blindness and could benefit from low vision care.

For many of our retinitis pigmentosa patients, we recommend a high-end flashlight, such as the MT 14 by LED Lenser. At 1,000 lumens, it is extremely bright, has a uniform, adjustable wide field of illumination, is rechargeable and maintains full brightness as the battery discharges. It might seem excessive to spend more than $100 for a flashlight, but it's significantly better than what is often purchased in a hardware or discount store. Many of our patients report that they frequently use the flashlight on their smart phone, but this provides 100 lumens or less, and the light is diffuse rather than focused. The difference between the phone flashlight and the MT 14 is easy to appreciate for almost all of our patients with nyctalopia.

Photophobia

Cone dystrophies, achromatopsia, aniridia, oculocutaneous and ocular albinism are just some of the conditions that can result in extreme photophobia. In many cases, these patients would qualify for a low vision referral based on visual acuity, but addressing the photophobia by selectively attenuating light with filters can greatly assist these patients. For reasons we only partially understand, patients with cone dystrophies and achromatopsia frequently report far less photophobia and greater visual comfort and ability to see detail when using filters in the red portion of the spectrum.[12] Red-tinted contact lenses are a viable and more discreet option for these patients.[13-15] This patient's experience illustrates the benefits of many different low vision strategies, including management of photophobia:

A 20-year-old computer science student presented with incomplete achromatopsia, left esotropia and amblyopia. He was referred for a host of vision related challenges, including extreme photophobia. His best-corrected visual acuity was 20/60 in the right eye and 20/80 in the left. He showed moderate con-

Low Vision Metrics

If you're determined to attach numbers to the decision-making process, I suggest following the 40-20-1 rule from Roy Cole, OD, now retired and one of the most respected and beloved people in low vision. Dr. Cole likes to say a person should be referred for low vision care if:

- Visual acuity is 20/40 or worse, or
- Visual field is 20 degrees or less, or
- The patient has one or more functional complaints related to decreased vision

Dr. Cole also developed an eight-question screening protocol to help identify patients in need of low vision services. I have added an item to Dr. Cole's list (#7 below) that is far more relevant today.

Do you have trouble doing what you want to do because of your vision? For example, do you have difficulty:

1. Reading your mail?
2. Watching television?
3. Recognizing people?
4. Paying your bills?
5. Signing your name?
6. Walking stairs, curbs, crossing the street or driving?
7. Reading the screen on your cell phone?

During the past month, have you, due to your loss of vision:

8. Been feeling down, depressed or hopeless?
9. Had little interest or pleasure in doing things?

If the patient answers yes to any of these questions and refractive, medical or surgical strategies cannot help, it's time to refer for low vision.[1]

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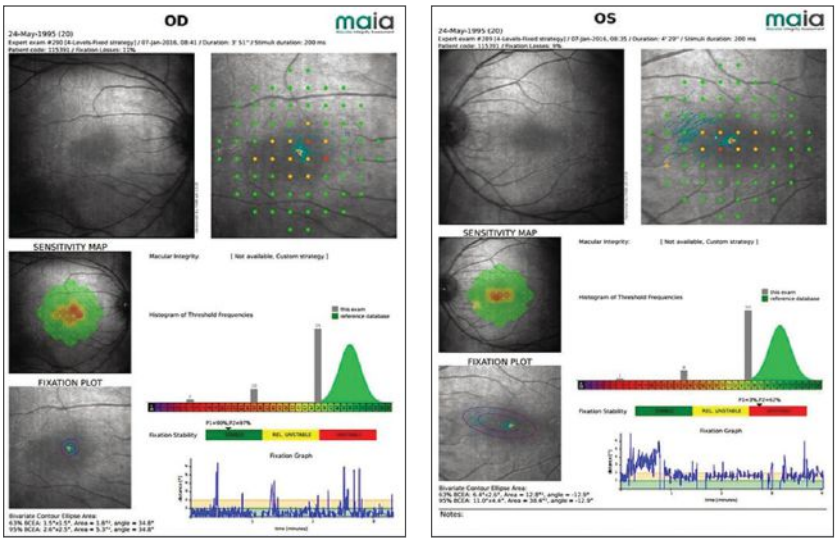

Fig. 3. Microperimetry of a 20-year-old patient with partial achromatopsia reveals small central scotomas that affect his vision.

trast sensitivity loss and suppression of the left eye on Worth four-dot test. Microperimetry indicated small central scotomas (*Figure 3*). He was provided with a pocket magnifier and single vision glasses with a 35% transmission red tint. Happy with the results, he later returned for a 2.2x bioptic telescope with the same red tint in both the carrier lens and the telescope.

The breadth of cases we work with in low vision rehabilitation is quite remarkable. Rather than depending on a specific level of visual acuity loss to guide your decision about referral, simply talk to your patients and find out if they're experiencing functional problems due to their vision. If so, referral to a low vision rehabilitation specialist might be helpful. Your patients will thank you when they return for ongoing care. ■

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Dry Eye Epidemiology in Practice

Understand who gets dry eye, and why, to help you better diagnose and manage these patients. **By Michelle Hessen, OD**

Keratoconjunctivitis sicca, referred to as dry eye disease (DED), is a growing public health concern affecting as many as 17% of women and 11.1% of men in the United States.[1] This is likely an underestimation, considering the number of self-treating patients and mild/periodic cases with intermittent symptoms.

The Tear Film and Ocular Surface Society's Dry Eye Workshop II (DEWS II) defined DED as a "multifactorial disease of the ocular surface characterized by a loss of homeostasis of the tear film, and accompanied by ocular symptoms, in which tear film instability and hyperosmolarity, ocular surface inflammation and damage, and neurosensory abnormalities play etiologic roles."[2] This definition adds "a loss of homeostasis" as a disease characterization, which is the "unifying characteristic describing the fundamental process in the development of dry eye disease."[2] An additional change in definition is the generalization of ocular symptoms. DEWS I includes discomfort and visual disturbance, while the new definition describes DED as "accompanied by ocular symptoms."[2] This change encompasses all symptoms that are now used to describe dry eye. Both DEWS I and DEWS II definitions state that DED is a multifactorial disease.

DEWS II also recognized three subgroups based on etiopathogenesis: aqueous deficient, evaporative and mixed, as the lines between aqueous deficient and evaporative have become less distinct.

Dry Eye By the Numbers

DED prevalence varies considerably due to different definitions and study parameters, something DEWS II

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- Discuss the epidemiology of dry eye.
- Describe the clinically relevant definition of dry eye.
- Identify dry eye patients in their practice.
- Recognize the long-term prognosis of dry eye as a diagnosis.

Target Audience: This activity is intended for optometrists engaged in the care of patients with secondary glaucomas.
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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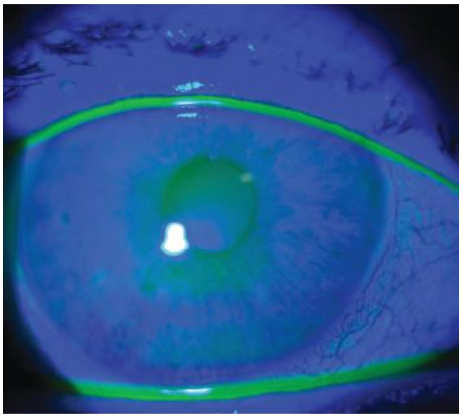

Fig. 1. fluorescein tear break-up time assessment.

aims to improve. A population-based study of DED in Melbourne, Australia, reported that of the 926 participants aged 40 to 97 years, 16.3% had a low Schirmer test (≤8mm) and 10.8% had a high rose bengal score (≥4mm).[3] The prevalence of self-reported dry eye in 3,722 participants of the Beaver Dam (Wisconsin) Eye Study varied from 8.4% of subjects younger than 60 to 19.0% of those older than 80, with an overall prevalence of 14.4%.[1]

Influencing factors remain constant despite diagnostic criteria used, and include sex, age and geographic location.[4] Prevalence increases linearly with age, and females are more affected according to the report.[4] Prevalence appears higher in Asian than in Caucasian populations, though studies have not been conducted in all major geographic regions. Peri- and postmenopausal females seem to be particularly at a higher risk. In addition, hormonal studies demonstrate that sex hormones influence ocular surface conditions through their effects on aqueous tear secretion, meibomian gland function and conjunctival goblet cell density.[5,6]

Thus, an altered hormonal state (e.g., following menopause) may be an underlying cause of dry eye. Diabetes and other systemic conditions, such as connective tissue diseases, Sjögren's syndrome (SS) and thyroid disease have also been associated with DED prevalence.

Several other external factors are also known to precipitate and exacerbate dry eye, including long-term contact lens wear, refractive laser surgery, smoking and extended visual tasks such as computer use, television watching and prolonged reading.[7-9] Worsening of dry eye may also be attributed to low relative humidity conditions that are common in office environments, air-conditioned cars, airplane cabins and extreme hot or cold weather.[10]

Dry eye may be caused by systemic medications such as antihistamines, antidepressants, anticholinergics, isotretinoin, anxiolytics, diuretics and beta-blockers.[4,11] Frequent instillation (more than four to six times daily) of preserved eye drops, particularly with benzalkonium chloride (e.g., for glaucoma), may also contribute to DED because of their well-established ocular surface toxicity.[2] Another important etiology is neuropathic pain due to a lesion or disease in the somatosensory system, in which ocular pain symptoms of dry eye disproportionally outweigh clinical signs, possibly with no ocular surface staining.

Irrespective of the presence of any identifiable underlying local or systemic inflammatory disorder, DED seems to be invariably associated with chronic inflammation of the ocular surface, although it is not known whether the local inflammation is causative or simply occurs as a consequence of ocular dryness. One of the major challenges in the area of dry eye, a multifactorial condition, is proper assessment.

Diagnostic Testing

There is a notoriously poor correlation between dry eye symptoms and signs. The DEWS II Diagnostic Methodology report asserts that the first step in a dry eye workup should include gathering a comprehensive patient history via one of the available patient questionnaires.[12] Those listed below all help clinicians quantify a patient's experience of their condition in a systematic fashion and provide early signals to pursue:

- Ocular Surface Disease Index
- Dry Eye Questionnaire
- Impact of Dry Eye on Everyday Living
- Visual Function Questionnaire
- Dry Eye-related Quality-of-life Score
- Computer Vision Symptom Scale

Because routine diagnostic testing of the ocular surface is often variable, the diagnosis of DED should be based on a combination of symptoms and objective, repeatable diagnostic clinical tests—any one of them alone may miss a number of patients with the disease.

Eyelid and tear film evaluation. Slit lamp examination begins with the evaluation of the eyelid positioning relative to the globe as well as evaluation of the meibomian glands. Meibomian gland dysfunction (MGD) is often diagnosed through clinical exam of the lid margin to assess the degree of inspissation and telangiectasia, as well as the assessment of meibomian gland expressibility and meibum quality. Commercially available meibography imaging systems can help to assess meibomian gland atrophy.

It is also important to evaluate the blink cycle: are the spontaneous blinks complete and at an appropriate rate? The tear film lipid layer is formed in the upstroke of each blink, when lipid from the lower meibomian reservoir spreads upward over the aqueous subphase of the preocular tear film.[13] Blink rates vary considerably in normal adults, which likely reflects individual variation

and influence of environmental conditions. Blink rates can be influenced by mental state, attention, activity, exposure of the ocular surface and environmental conditions. In controlled environments (about 22° C with humidity of 40%), the blink rate in normal adults ranges between 15 and 20 blinks per minute.[14-16] Blink rate increases in dry eye, where it is thought to be compensatory. Blink rate falls during a number of common tasks requiring visual concentration, such as visual display use, reading and driving, and the increased evaporative loss may act as a trigger for DED.[14]

The tear meniscus is a strip of fluid lying at the junction of the lid margin and the globe formed by surface tension forces as the lid margin separates from one another in the upstroke of a blink.[17] The volume of the menisci is directly related to the total volume of the tear fluid and indirectly to the lacrimal secretory rate.[18,19] For this reason the height and radius of curvature of the tear menisci are reduced in aqueous-deficient DED and their measurement in the lower meniscus is used in dry eye diagnosis.[20-24]

Anterior segment optical coherence tomography as well as some other ocular surface imaging systems that deliver interferometry, provide a noninvasive measure of the tear volume by quantifying the meniscus height. In clinical practice, a tear meniscus below 0.2mm is regarded as pathological. A foamy tear meniscus is an indicator of altered lipid layer in patients with MGD.

Tear film stability. Assessed as fluorescein tear break-up time (TBUT), this is determined by instilling fluorescein dye from a strip moistened with sterile non-preserved saline in the inferior culde-sac then evaluating stability of the precorneal tear film. TBUT is a test to determine the homeostasis of the tear film. It is subjective and may be influenced by fluorescein volume at the slit lamp with a cobalt blue filter (*Figure 1*). Values below 10 seconds are definitively pathological. TBUT may be best measured noninvasively, as fluorescein can reduce the stability of the tear film, compromising the accuracy of the measurements.

Noninvasive topography-based imaging systems, such as the keratograph (Oculus), CA-800 (Topcon) and the HD analyzer (Visiometrics) also provide an automated measurement of TBUT using the distortion of the mires reflected from the precorneal tear layer.[25] Recurrent tear break-up in the same area may be an indication of localized anterior basement membrane abnormalities.

Ocular surface staining. Vital dye staining has been the mainstay of clinical diagnosis and a significant component of DED severity grading. The two most commonly used dyes in clinical practice are sodium fluorescein for highlighting corneal defects and lissamine green for conjunctival staining (*Figures 2 and 3*). It is recommended to wait one to three minutes to assess fluorescein staining after instillation of the dye.[26]

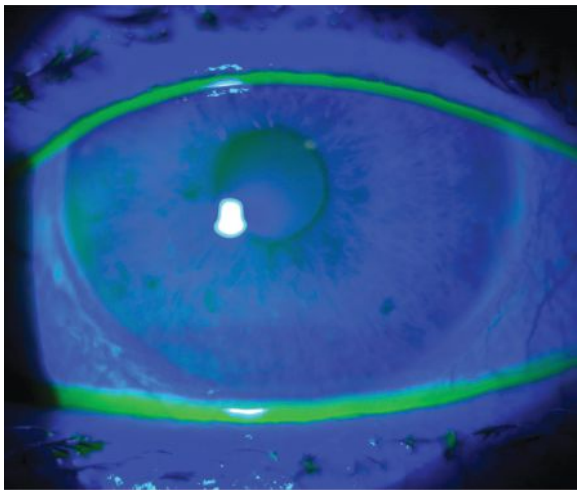

Fig. 2. Corneal punctate epithelial erosions viewed with sodium fluorescein and cobalt blue filter.

Corneal punctate staining is actually a small area of pooled dye in a space where a cell is missing; hence, the term punctate epithelial erosion.[27] However, several studies show that even under normal conditions, some corneal epithelial cells actually take up the dye and are stained.[28,29] Researchers suggest that corneal epithelial cells that are in the process of sloughing (those with damaged cell membranes or an altered glycocalx) can take up fluorescein dye.[27] Both cellular uptake and intercellular dye diffusion may occur with damage or stress to the corneal epithelium.

Diffuse corneal and conjunctival staining is commonly seen in viral keratoconjunctivitis and medicamentosa.[30,31] Staining of the inferior cornea and bulbar conjunctiva is typically observed in patients with staphylococcal blepharitis, MGD, lagophthalmos and exposure, whereas staining of the superior bulbar conjunctiva is typically seen in superior limbic keratoconjunctivitis.[30,31] A pattern of exposure-zone (interpalpebral) corneal and bulbar conjunctival staining is typically seen with aqueous tear deficiency.[30,31]

Lissamine green penetrates membrane-damaged conjunctival cells to stain the nucleus.[27] Lissamine staining of the conjunctiva should be assessed one to four minutes after instilling the dye using a drop from a strip inside the far lower temporal lid in upgaze with the lower eyelid pulled slightly temporally to avoid damage to the conjunctival or lid wiper tissue.[12,32,33] Lissamine green stains epithelial cells only if the cell membrane is damaged. Corneal and conjunctival staining are informative markers of disease severity in severe DED; however, staining of

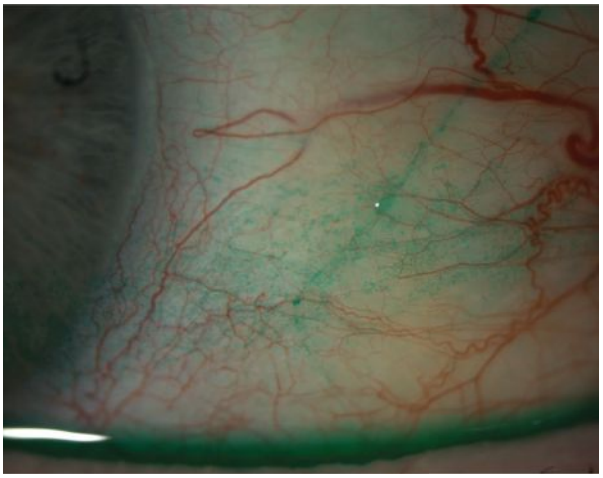

Fig. 3. Conjunctival staining with lissamine green.

the ocular surface in mild-moderate DED shows poor correlation with disease severity.[34]

Tear film osmolarity. This test uses a micro-electrode to measure the number of charged particles in a tear sample (~0.2µl); the electrode is designed to reduce potential reflex tearing as it avoids direct contact with the ocular surface and collects the tear fluid by passive capillary reaction.[35] The accuracy differs by only 2mOsm/L in both normal and dry eye patients.[35] The instant result also minimizes the level of tear evaporation.[35,36]

Tear osmolarity threshold values vary from 305mOsm/L to 316mOsm/L.[36,37] One study reported that using tear osmolarity threshold of 305mOsm/L gave a 98.4% positive predictive value.[37] Other studies suggest using a threshold of 316mOsm/L to 317mOsm/L provides a sensitivity that varied from 59% to 81%, specificity from 78% to 94%, a positive predictive value of 85% and a negative predictive value of 74%.[35,38,39] Tear osmolarity can be influenced by, and correlated with, disease severity.[35,38]

Currently, the 316mOsm/L threshold is believed to better discriminate between mild and moderate/severe DED, while 308mOsm/L is now considered the accepted threshold.[36] One study found 308mOsm/L was most sensitive for discriminating between normal eyes and those presenting with early stages of DED; it correctly diagnosed severe dry eye and normal tear film 90.7% and 81.3% of the time, respectively.[38]

Reliability studies determined diagnostic performance and revealed a sensitivity of 81% and a specificity of 80% of the threshold value of 308mOsm/L.[40] Another study reported the coefficient of reproducibility was 39mOsml/L and the coefficient of repeatability was 33mOsm/L.[41] Researchers show that a variation of 35mOsml/L in consecutive tear osmolarity readings in an individual and three consecutive readings are required with the osmometer to obtain a reliable measure of tear osmolarity.[42]

Tear osmolarity variability can also be diagnostic of dry eye; variability between the two eyes in normal, mild or moderate DED patients and severe dry eye patients was 6.9±5.9mOsm/L, 11.7±10.9mOsm/L and 26.5±22.7mOsm/L, respectively.[38] Variability also increases with the severity of dry eye both in inter-eye measurements as well as repeat measurements in the same eye. In contrast to patients with normal tear film, tear osmolarity has good repeatability with no significant difference in osmolarity values when using up to four readings taken one to 15 minutes apart.[37,43]

Matrix metalloproteinase (MMP-9) testing. This commercially available point-of-care test can also be used as an aid in the diagnosis of dry eye. MMP-9 is an effector molecule that participates in the inflammatory DED cycle by disrupting the epithelial layers by cleaving tight junctions.[44] Researchers report that conjunctival expression of MMP-9 was significantly higher in subjects with SS DED and MGD than in a control group; furthermore, the expression was significantly higher in the SS DED than the MGD group.[45] The qualitative nature of this test may be used to assess change in the disease state. Although the test does not differentiate dry eye from other inflammatory ocular surface diseases, it can be helpful in the management as it marks the presence of inflammation despite lack of staining.[46]

Schirmer testing. This measures the secretions of the lacrimal gland by using calibrated filter paper strips placed in the conjunctival sac of the temporal third of the lower eyelid with the patient's eyes closed for a five-minute period of time. Schirmer I testing is performed without anesthesia, whereas the Jones basal secretion test is performed after instillation of a topical anesthetic. In theory, the latter measures only the basal secretion, without reflex tearing. A value of 10mm or less is considered abnormal.[47,48]

Dry Eye Forecast

A five-year natural history study was performed on patients with mild-moderate DED to explore the hypothesis that dry eye is a progressive condition that has substantive and measurable impacts not only on the ocular surface, but on quality of life and visual functioning.[49] Patients were using artificial tears as needed. A striking disease burden is observed with regard to blurred vision, productivity and visits to eye care practitioners in mild to moderate DED patients compared with normal subjects of similar ages and genders.[49]

Treatment Approaches for Dry Eye

Managing dry eye can be frustrating at times, but with new treatment options you can help the patient overcome the signs and symptoms of their condition. Patient education is crucial for successful treatment, as proper explanation of possible causative factors helps the patient understand the condition and aids in setting realistic expectations. Therapy recommendations are related to the severity of both the signs and symptoms.

Clinicians should discuss lifestyle and environmental modifications, regardless of disease severity. Humidifiers, smoking cessation, essential fatty acid supplementation and the use of non-preserved ocular lubricants and lid hygiene may all be beneficial. For MGD management, in-office eyelid procedures such as Lipiflow (Johnson & Johnson Vision), iLux (Alcon) or intense pulsed light may be options. Punctal occlusion can help to increase tear volume. Therapeutic contact lenses (soft bandage contact lenses and scleral lenses) are often helpful in managing DED. Dehydrated and cryopreserved amniotic membranes are also available for the treatment of severe ocular surface disease. One study showed sustained improvement for four months in DED subjects who wore Prokera Slim (Bio-tissue) for approximately five days.[50] The authors also reported reduced corneal and conjunctival staining and improved visual acuity.

Anti-inflammatories

Because inflammation has a significant role in the etiopathogenesis of dry eye, promoting ocular surface disruption and symptoms of irritation, a number of anti-inflammatory and immunomodulating agents are available:

Corticosteroids. Through several mechanisms of action, these topical agents help reduce ocular inflammation. In the context of DED therapy, topical steroids are used for a short course to avoid possible unwanted side effects such as raised intraocular pressure and cataract formation.[51] Randomized controlled clinical studies show that unpreserved corticosteroid eye drops, instilled for two to four weeks, improve the symptoms and clinical signs of moderate to severe DED.[51,52] After two weeks of treatment, symptoms regressed moderately (43%) or completely (57%), while corneal fluorescein staining reduced significantly. Patient discomfort and clinical signs remained reduced for several weeks after therapy ceased.[51,52]

Similarly, a retrospective review of 31 patients treated with preservative-free 0.01% topical dexamethasone showed a significant subjective improvement in symptoms in 84% of the subjects with chronic ocular surface irritation and/or tearing, refractory to various preserved topical steroids, including 0.2% loteprednol, 0.1% fluorometholone and 1% prednisolone.[53]

Cyclosporine A. This is a mainstay medication for DED. As an immunosuppressant, it inhibits the calcineurin–phosphatase pathway by complex formation with cyclophilin, reducing the transcription of T-cell–activating cytokines such as interleukin-2.[54] When used to treat DED, it can improve OSDI scores, TBUT, Schirmer I scores, corneal fluorescein staining and goblet cell density.[55]

Lifitegrast. This pharmaceutical agent blocks the binding of the surface proteins lymphocyte function-associated antigen-1 and intercellular adhesion molecule-1, thereby reducing inflammation in DED.[56] One study shows lifitegrast ophthalmic solution 5.0% reduced corneal fluorescein and conjunctival lissamine staining and improved symptoms of ocular discomfort and eye dryness compared with placebo when administered twice daily.[56]

Tetracycline derivatives. Oral tetracycline derivatives uniquely possess antibacterial as well as anti-inflammatory properties. Doxycycline inhibits c-Jun N-terminal kinase and extracellular signal-related kinase mitogen-activated protein kinase signaling in epithelial cells of the ocular surface exposed to hyperosmolar stress, down-regulating the expression of CXCL8 and proinflammatory cytokines IL-1 and TNF.[57] Doxycycline inhibits MMP-9 activity and supports ocular surface integrity.[58,59] Additionally, studies demonstrate that minocycline inhibits expression of cell-associated proinflammatory molecules, including major histocompatibility complex class II.[60] Doxycycline can be effective in patients with ocular rosacea by reducing irritation symptoms, improving tear film stability, and decreasing the severity of ocular surface disease.[61-63] In addition, doxycycline is useful in the treatment of corneal erosions.[64,65]

Azithromycin

This is a broad-spectrum macrolide antibiotic, used both topically and orally, with anti-inflammatory properties. Azithromycin can block the activation of NF-kB, leading to decreased inflammatory cytokine levels such as interleukin-6 and interleukin-8.[66] It also suppresses the production of proinflammatory mediators by inhibiting cultured human corneal epithelial cells.[67] Topical azithromycin is FDA approved for the treatment of bacterial conjunctivitis; however, it may be used as off-label therapy for clinical control or relief of symptoms and signs of MGD, as well as improvement in lipid behaviors of meibomian gland secretion.[68]

Two studies compare the efficacy of doxycycline and azithromycin for the management of MGD.[69,70] A five-day oral azithromycin regimen was compared with one month of doxycycline 200mg in one study.[69] Although both treatments significantly improved clinical scores and symptoms, azithromycin was more effective in improving clinical signs. In the second study, both topical 1% azithromycin for four weeks and twice daily 100mg oral doxycycline for two months significantly decreased the clinical signs of MGD. Oral doxycycline treatment was slightly less effective in improving foreign body sensation and the signs of plugging and secretion than topical azithromycin.[70]

Autologous Serum

Serum contains several anti-inflammatory factors that have the capability to inhibit soluble mediators of the ocular surface inflammatory cascade of DED. These include inhibitors of inflammatory cytokines and MMP inhibitors.[71-73] Clinical trials show autologous serum drops can improve ocular irritation symptoms and conjunctival and corneal dye staining in SS DED.[74-76]

With the evolution of anti-inflammatory based therapies for dry eye, it is a reasonable expectation that ocular surface disruption can be controlled and patient symptoms may be substantially minimized, thus reducing the impact of this condition on their quality of life. It is important nonetheless to educate DED patients on potential increased risks of dry eye associated with refractive surgery, multifocal cataract surgery and other anterior segment surgical procedures. Comanaging with other medical professionals is essential for successful treatment in cases with underlying systemic conditions. Clinicians must help patients understand the chronicity of DED and the goals of management to lay the groundwork for realistic expectations. ■

Dr. Hessen is an assistant professor at the Wilmer Eye Institute's Ocular Surface Diseases and Dry Eye Clinic at Johns Hopkins School of Medicine, where she specializes in ocular surface disease.

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OSC QUIZ

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1. According to DEWS II, which is not a common finding in multifactorial dry eye disease?
a. Symptoms of discomfort.
b. Microcystic corneal edema.
c. Visual disturbance.
d. Tear film instability.

2. What is the most common risk factor for dry eye?
a. Older age.
b. Alcohol consumption.
c. Female sex.
d. a and c.

3. Which factor is known to precipitate and exacerbate dry eye?
a. Altered hormonal state (menopause).
b. Refractive laser surgery.
c. Long-term contact lens wear.
d. All of the above.

4. What type of medications have been linked with causing dry eye?
a. Statins (HMG-CoA reductase inhibitors).
b. Antihistamines.
c. Cholinergic agonists.
d. None of the above.

5. It is well understood that which eye drop preservative causes ocular surface toxicity?
a. Benzalkonium chloride.
b. Purite.
c. Thimerosol.
d. Silver sulphate.

6. Which osmolarity value is most sensitive for discriminating between normal eyes and those with early dry eye?
a. 325mOsm/L.
b. 250mOsm/L.
c. 308mOsm/L.
d. 278mOsm/L.

7. Which value for a Schirmer testing result would indicate dry eye?
a. 8.
b. 13.
c. 17.
d. a and b.

8. Dry eye evaluation should include all of the following testing, except:
a. Blink rate.
b. Tear break-up time.
c. Color vision.
d. Sodium fluorescein staining of the ocular surface.

9. What lifestyle modification may be helpful in a patient with dry eye?
a. Humidifier.
b. Smoking cessation.
c. Essential fatty acids.
d. All of the above.

10. Which medication for the treatment of dry eye inhibits the calcineurin-phosphatase pathway by complex formation with cyclophilin, thus reducing the transcription of T-cell–activating cytokines?
a. Loteprednol 0.5%.
b. Azithromycin.
c. Cyclosporine A.
d. Lifitegrast.

11. What daily dosing of lifitegrast ophthalmic solution 5% reduces corneal fluorescein and conjunctival lissamine staining and improves symptoms of ocular discomfort and eye dryness?
a. Once daily.
b. Two times daily.
c. Three times daily.
d. Four times daily.

12. Doxycycline is effective in the treatment of which condition?
a. Ocular rosacea.
b. Fuchs' corneal dystrophy.
c. Recurrent corneal erosions.
d. a and c.

13. When treating patients with dry eye, it is important to understand that all of the following may be impacted, except:
a. Visual function.
b. Economic burden of eye drops.
c. Productivity.
d. Color vision.

14. It is imperative to caution dry eye patients that they may have worsening of their condition after which of the following:
a. LASIK surgery.
b. Lipiflow.
c. Intense pulsed light treatment.
d. Punctal plugs.

15. Diffuse corneal staining noted after adding a new preserved eye drop would be associated with what condition?
a. Aqueous tear deficiency.
b. Incomplete blink.
c. Staphylococcal blepharitis.
d. Medicamentosa.

16. Which of these is a commercially available point-of-care test used to aid in the diagnosis of dry eye?
a. Matrix metalloproteinase-9 test.
b. IL-2 test.
c. T-cell test.
d. All of the above.

17. To obtain an accurate osmolarity reading, you should do all of the following, except:
a. Perform osmolarity testing before vital dye staining.
b. Collect sample after two hours of any eye drop instillation.
c. Instill one drop of topical anesthetic.
d. Collect from outermost area of eyelid to reduce potential reflex tearing.

18. Dry eye is most common in which types of patients?
a. Women.
b. Men.
c. Children.
d. Teenagers.

19. Which antibiotic may be used both orally and topically for an anti-inflammatory effect in patients with dry eye/MGD?
a. Doxycycline.
b. Azithromycin.
c. Lifitegrast.
d. Cyclosporine A.

20. Clinicians should only use a short course of topical steroids to minimize the possibility of which of the below unwanted side effects?
a. Increased intraocular pressure.
b. Cataract formation.
c. Increased osmolarity.
d. a and b.

Examination Answer Sheet

Dry Eye Epidemiology in Practice

Valid for credit through January 15, 2023

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Answers to CE exam:

1. Ⓐ Ⓑ Ⓒ Ⓓ
2. Ⓐ Ⓑ Ⓒ Ⓓ
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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. Discuss the epidemiology of dry eye. ① ② ③ ④ ⑤
22. Describe the clinically relevant definition of dry eye. ① ② ③ ④ ⑤
23. Identify dry eye patients in your practice. ① ② ③ ④ ⑤
24. Recognize the long-term prognosis of dry eye as a diagnosis. 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:

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The following is your: ☐ Home Address ☐ Business Address

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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 119118 RO-OSC-0120

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

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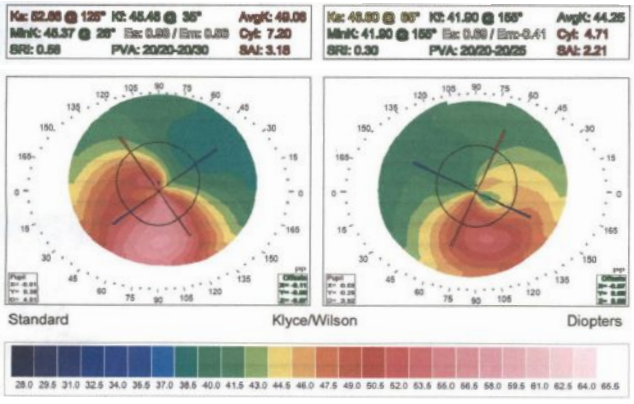
Sun Salutation

An alternate approach to CXL using natural light could be in the works.

Edited by Joseph P. Shovlin, OD

Q I recently received a referral from a cornea specialist to fit a keratoconus patient with contact lenses. The patient is taking 400mg of riboflavin, which the specialist states has helped stabilize the cornea. Is the referring doctor expecting ultraviolet (UV) exposure to help stabilize the cornea similar to a corneal crosslinking (CXL) procedure?



The corneal topography of a 20-year-old who has undergone CXL shows irregular inferior steepening consistent with keratoconus in the right eye more so than the left. Data collected annually will continue to assess for corneal stability vs. progression.

A Until recently, there was no treatment or intervention that could successfully alter the progressive nature of keratoconus, according to Nurit Wilkins, OD, clinical instructor at the University of Maryland School of Medicine. Management included visual correction with corneal and scleral gas permeable contact lenses and corneal transplantation in cases of advanced disease. Now, the FDA-approved CXL procedure can halt the progression of the condition by applying topical riboflavin (vitamin B2) to the cornea and immediately exposing it to UV light emitted by an approved device.

The process stimulates the formation of new crosslinks between the collagen fibers of the cornea, causing the fibers to become shorter and thicker and the cornea to stiffen. This in turn strengthens and stabilizes the corneal stroma and prevents progressive thinning, scarring and bulging that are seen in keratoconus.

Bridge the Gap

While CXL has been effective in delaying the progression of keratoconus and sequelae of the condition, Dr. Wilkins says there are several limitations of this treatment, including lack of availability and high cost.

Recently, some clinicians reported that they might have found a solution, suggesting that high doses of oral riboflavin combined with sunlight can stabilize the cornea similarly to treatment with CXL. One study evaluated topographic corneal changes in three individual cases of patients ingesting 400mg to 800mg of riboflavin supplements daily.[1] Researchers observed corneal flattening and improved visual acuity in each case—similar outcomes to CXL.[1]

In a small, unpublished study, all seven participants taking dietary riboflavin achieved corneal stabilization and/or flattening.[2] The investigator is studying this further through an IRB-approved trial overseeing patients who ingest 400mg of vitamin B2 and spend 15 minutes outside each day without sunglasses.[2]

If the combination of oral riboflavin and sunlight does indeed have mechanisms that are similar to CXL, Dr. Wilkins notes that corneal stabilization could be offered to more patients and at a lower cost. The current state of research is preliminary, however, she emphasizes.

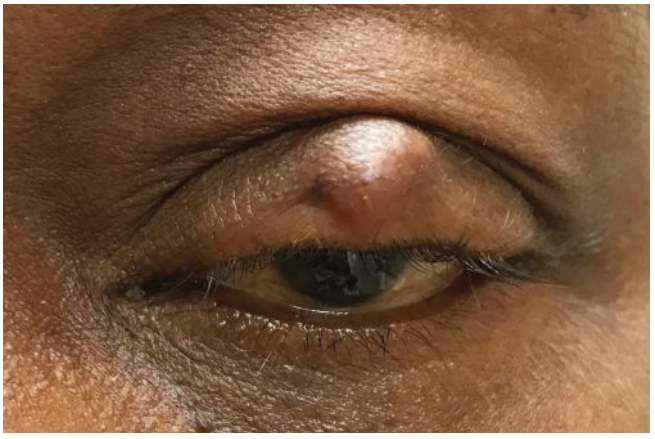
While current case reports are exciting and promising, Dr. Wilkins concludes that, in the absence of evidence-based clinical trials supporting the practice of prescribing dietary riboflavin supplementation for the treatment of keratoconus, clinicians should exercise caution when discussing this with patients. She looks forward to seeing the results of ongoing and future clinical trials. ■

1. Schaeffer K, Jarstad J, Schaeffer A, et al. Topographic corneal changes induced by oral riboflavin in the treatment of corneal ectasia. Invest Ophthalmol Vis Sci. 2018;59:9.
2. Dietary riboflavin (vitamin B2) and cornea crosslinking. NIH Clinical Trials. clinicaltrials.gov/ct2/show/NCT03095235. March 29, 2017. Accessed December 19, 2019.

Three Pillars of Chalazia Management

From a conservative approach to steroid use to surgery, dealing with these pesky lumps is all about savvy patient selection. **By Joseph W. Sowka, OD**

A 66-year-old woman presented complaining of a large, painless lump in her left upper lid that developed rather rapidly over several days beginning two months earlier. Though the lesion was painless now, she did experience some moderate pain while it was developing. She had been putting hot water on it to no avail.



A lid lump like this patient's may resolve with conservative therapy, but if it doesn't, steroids and surgery are options.

Evaluation

Her best-corrected visual acuity was 20/20 in each eye. The remainder of her examination was normal, except for biomicroscopically visible crusting about the eyelashes, blocked meibomian glands and a grossly visible, painless, hard, focal lump in her left upper eyelid. Based upon appearance and history, it was clear that she had developed a chalazion, most likely secondary to chronic blepharitis. There are several options for treating this patient and virtually every doctor has a "favored" approach to managing chalazia. However, does the science support any or any of these "can't-miss" treatments?

Conservative Therapies

Chalazion is a common inflammatory condition of the eyelid. Two patterns of granulomatous inflammation represent the spectrum of changes in its clinical course. Mixed-cell granulomas consisting of neutrophils, lymphocytes, plasma cells, macrophages, giant cells and granulation tissue may be present.[1,2] Additionally, you may see suppurating granulomas characterized by epithelioid cell granulomas with numerous neutrophils in a proteinaceous background.[1,2] The cells involved in these lesions are steroid sensitive.[1,2]

Chalazia (plural of chalazion) are typically caused by blockage of the meibomian glands and chronic lipogranulomatous inflammation. It can affect patients of any age, race or gender. Common complaints are poor cosmesis, local irritation and, in cases of large lesions, mechanical ptosis and corneal astigmatism.[3]

Conservative management can include lid scrubs (either with baby shampoo or commercially prepared scrubs), hot compresses with or without digital massage, topical antibiotic solutions and ointments, oral antibiotics or a combination of antibiotic or steroid solutions and ointments.[4-6] However, the effects of these approaches aren't always clear. One study shows simple lid hygiene resulted in clinical chalazia cure in 80% of cases.[6] Another shows hot compresses and lid hygiene together had a 43% cure rate.[5] In a 2006 investigation hot compresses, lid hygiene and antibiotic ointment QID, shows a 58% cure rate.[4]

More recent research looked at 149 patients with one or more chalazia on separate eyelids and randomized them to receive therapy involving hot compresses only, hot compresses plus tobramycin drops and ointments, and hot compresses plus tobramycin/dexamethasone drops and ointment over four to six weeks. Treated with hot compress alone, 21% saw complete lesion resolution. Adding tobramycin drops and ointments to hot compresses worked out for 16% of subjects and hot compresses plus tobramycin/dexamethasone drops and ointments helped 18% achieve resolution.[7]

None of these differences in treatment could be considered significant. Lesions that completely

resolved had a statistically significant lower pretreatment duration of 1.5 months compared with lesions that did not completely resolve with lesions present over 2.2 months. This report shows that hot compresses alone or in combination with tobramycin or tobramycin/dexamethasone drops and ointment are all effective first-line treatments; however, lesions present longer than two months are less likely to resolve with these conservative therapies alone.[7]

While "conservative" therapies are non-invasive and exceedingly safe, they clearly do not work for every patient.

Steroids

The inflammatory cells that comprise chalazia are steroid sensitive, which is why some research is considering intralesional steroid injection as a management option.[2-11] Intralesional injection involves the injection of 0.1ml to 0.3ml of triamcinolone actetonide (5mg/ml to 40mg/ml) from a conjunctival approach.[3,4,8] Like conservative therapies, no clear delineations as to the optimal amount and concentration of steroid exist. However, the success rates for this management modality is typically higher than for conservative therapy.[4-9] A 2006 study saw a 94% cure rate (vs. 58% for conservative therapy) with intralesional injection of triamcinolone.[4] Another investigations achieved an 80% success rate after two injections.[9]

While intralesional injection of triamcinolone is generally safe, significant complications can occur. Skin depigmentation is a common occurrence following intralesional injection in dark-skinned patients.[4,9,11] Also, inadvertent globe perforation is a possibility.[12] Rarely, microembolization by steroid particles can result in retinal and choroidal infarction with subsequent permanent vision loss.[12]

Surgery

Incision and curettage remains an option. The lesion can be surgically removed, typically through a palpebral conjunctival approach, with the use of scalpel and chalazion clamp following an injection of anesthetic. Thermal cautery is often performed immediately following surgical excision, but this is typically the surgeon's choice, as it does not appear to reduce recurrence rate.[13] Cure rates with surgical excision are between 90% and 100%, though more than one surgery may be necessary.[8,9] Surgical excision is typically the recommended procedure for lesions that are larger than 11mm and chronic (lasting more than eight months).[2]

While highly successful, surgical excision also has potential complications. If excision goes through the dermis, scarring is possible. Further, inadvertent globe perforation may occur during chalazion excision.[14] Surgical excision remains an option if conservative or intralesional injection fail to resolve the condition.

Comparing intralesional steroid injection to surgical curettage in a meta-analysis, researchers found that for a single procedure, surgical curettage was more successful than steroid injection at achieving resolution.[15] If multiple procedures were necessary, then the difference in success between steroid injection and surgical curettage was reduced.[15]

Intralesional steroid injection and surgical curettage shows similar results.[16] A single triamcinolone acetonide injection followed by lid massage is almost as effective as incision and curettage.[17] A study of chronic chalazia that were unresponsive to medical treatment, noted that lesions responded well to both steroid injection and surgical curettage.

In our case, conservative therapy with hot compresses alone was recommended. Due to her skin pigmentation, steroid injection was not advocated. Ultimately, conservative therapy did not result in any significant improvement and she underwent successful surgical excision. ■

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Edited By Carlo J. Pelino, OD, and Joseph J. Pizzimenti, OD

Flower in the Eye, Smoke in the Brain

The appearance of a characteristic optic nerve may signify systemic or intracranial vascular abnormalities. **By Nevi Hehar, OD**

Congenital anomalies of the optic disc may occur in isolation or as part of a larger systemic syndrome. These malformations include optic nerve hypoplasia, optic pit, coloboma, morning glory disc anomaly (MGDA), tilted disc, peripapillary staphyloma, megalopapilla and optic nerve drusen.[1-3] Visual impairment is one of many side effects these patients could experience. Concurrent neurologic and systemic features help identify and predict possible outcomes, which may be life-threatening.

Case Report

A 58-year-old Caucasian female presented with complaints of bilateral blur, worse at near, in each eye. Her health history was positive for Moyamoya disease (MMD) and related cerebrovascular accident. Distance acuities with correction measured 20/20-2 OD and OS. Dilated fundus examination revealed MGDA with an enlarged nerve head, retinal excavation, glial tissue and anomalous retinal vessels, all in the right eye. Fundus examination of the left eye was unremarkable.

Central retinal photography and OCT results were consistent with MGDA in the right eye. The patient was informed on the importance of continued care and scheduled for a return visit to undergo central threshold perimetry. Her ocular status will continue to be monitored on a biannual basis with appropriate refractive, structural and functional ophthalmic evaluation.

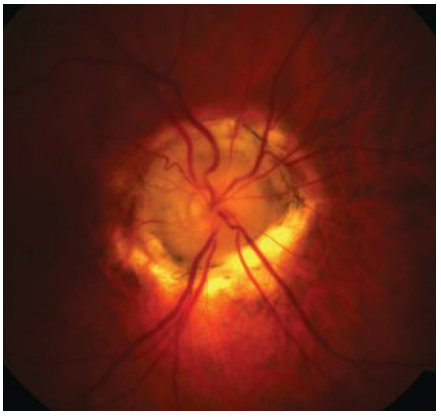

Fig. 1. Enlarged, excavated optic nerve with glial tissue and anomalous retinal vessels.

Flowery Fundus

Named for its resemblance to the morning glory flower, MGDA is an uncommon optic disc anomaly (*Figure 1*). An embryonic developmental alteration of the lamina cribrosa and posterior sclera causes this defect.[1-4]

MGDA may present on its own or in association with systemic or intracranial vasculapathies, such as MMD, which occurs in up to 50% of patients with the anomaly.[2-4] It appears as a large optic disc with funnel-shaped excavation of the surrounding retina, annular pigmentation around the nerve head, a characteristic glial tuft and an abnormal retinal vascular pattern that presents in a spoke-like fashion around the disc (*Figure 2*). MGDA is usually sporadic and hasn't been linked to a specific genetic defect.

Hand-in-hand Vasculopathy

MMD was first described in Japan in 1957.[5] It predominantly affects people of Asian descent—the highest incidence falls among Japanese and Korean patients.[5,6] The annual incidence of MMD is 0.086 per 100,000 people in the United States compared with 3.16 to 10.5 per 100,000 people in Japan.[6,7] Although the etiology of MMD is unknown, the East-West ethnicity discrepancy suggests a strong genetic predisposition.[7]

The age of onset follows a bimodal distribution, with an initial peak occurring in children between

Table 1. Suzuki Classification of Angiographic Grades in MMD[8,9]

Grades	Definition
I	Narrowing of the Carotid Fork—stenosis of the terminal portion of the ICA
II	Initiation of the Moyamoya—stenosis of all terminal branches of the ICA and appearance of deep Moyamoya vessels
III	Intensification of the Moyamoya—progression of vessels with "puff of smoke" appearance on MRA
IV	Minimization of the Moyamoya—regression of deep Moyamoya vessels and appearance of transdural collaterals from the external carotid artery (ECA)
V	Reduction of the Moyamoya—continued reduction of vessels and progression of transdural collaterals
VI	Disappearance of the Moyamoya—disappearance of deep Moyamoya vessels, complete occlusion of the ICA (blood supply is now derived mainly from the ECA)

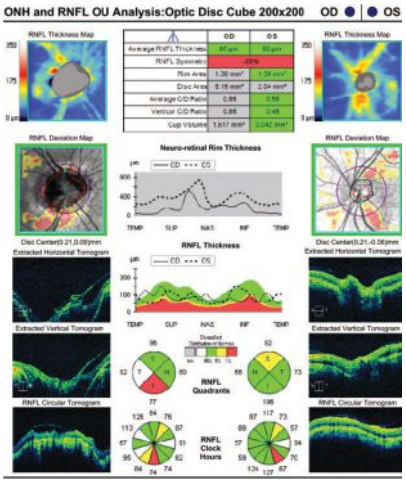

Fig. 2. OCT revealing enlarged disc area of the right optic nerve and excavation.

five and 10 years of age and a second peak affecting adults in their fourth or fifth decade of life.[6]

The clinical presentation of MMD differs between children and adults. Children mainly exhibit ischemic symptoms, the most common being a transient ischemic attack (TIA), which is usually recurrent.[6,8] Adults usually present due to an ischemic stroke or an intracranial hemorrhage secondary to fragile collateral vessel rupture, which can ultimately result in acute transient or permanent symptoms secondary to brain ischemia.[5,6,9] Patients report symptoms that include headaches, seizures, hemiparesis, sensory impairment and aphasia/dysarthria and may experience severe disability or even mortality.[7,9,10]

Moyamoya angiopathy typically presents with various cerebrovascular manifestations that include TIA, ischemic stroke, hemorrhagic stroke, seizures and headaches.[10,11] The angiopathy can present as the sole manifestation of MMD or exist in association with other factors, such as Down syndrome, autosomal-dominant thoracic aortic aneurysm, head tumor radiotherapy, sickle cell disease and neurofibromatosis, in which case it is referred to as Moyamoya syndrome.[8,10,11] It can result in progressive stenosis and occlusion of the internal carotid artery (ICA) and/or the proximal portion of the anterior cerebral and middle cerebral arteries.

Moyamoya, a Japanese word that translates to "puff of smoke," refers to a network of abnormal, thin, fragile collateral vessels that are evident on cerebral angiography and resemble a smoke cloud.[5,6,10] These vessels develop at the base of the brain, adjacent to the site of occlusion secondary to chronic brain ischemia.[1,6,10,11]

Make the Diagnosis

Diagnosing MMD requires visualization of at least one ICA and/or its branches as well as the network of collateral vessels.[6,7] Radiologic assessment, therefore, is an important factor in detecting MMD. MRI/MRA may be sufficient to diagnose the disease when findings are bilateral; however, unilateral cases require catheter angiography.[7,9,12]

Treat and Manage

The course of MMD spans from clinical silence for several years to rapid progression.[5,7] Its severity can be classified into six stages based on Suzuki's classification, which highlights the angiographic evolution of the disease (*Table 1*).[8,9] A management plan is decided accordingly.

There is no curative treatment for arterial occlusion regression or Moyamoya vessel prevention. Due to the more progressive nature of the disease in the pediatric population, treatment is geared toward preventing irreversible brain damage.[8,12] Treatment is strongly recommended for symptomatic adults since the stroke rate is estimated at 10% to 15% per year compared with 3% in asymptomatic patients.[7,9,11,12]

The mainstay of treatment in symptomatic patients with ischemic MMD is surgical revascularization.[9,12] The goal is to improve cerebral blood flow and prevent infarction. Direct or indirect bypass has been shown to improve blood flow and decrease ischemic events postoperatively.[12] Post-op complications may include permanent neurologic deficits secondary to ischemic or hemorrhagic stroke. These can be caused by several factors, largely depending on the patient's hemodynamic status.[7,12] Treating hemorrhagic MMD is more controversial and remains unspecified.

Patients who present with MGDA or another optic nerve anomaly may have other neurological signs and symptoms that a fastidious history can help reveal. When these signs and symptoms are present, the clinician should order neuroimaging to assess the vascular and structural integrity of the brain and work hand-in-hand with neurology and neurosurgery specialists to decrease the risk of mortality from potential cerebrovascular events. ■

Dr. Hehar is an instructor at the Pennsylvania College of Optometry.

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Crisis Management

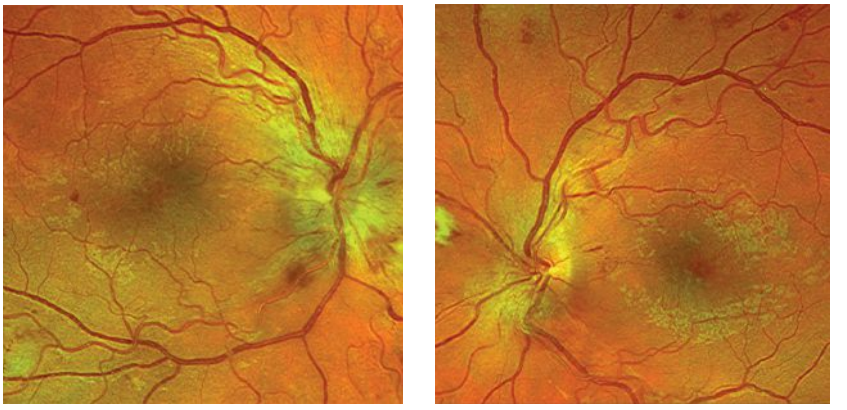
When a patient with end-stage kidney disease develops visual symptoms, you may have an emergency on your hands. **By Eric Dillinger, OD, and Mark T. Dunbar, OD**

A 34-year-old male presented with complaints of blurred vision in both eyes and headaches over the past few weeks. He reported that he never had vision problems before.

His systemic history was significant for Type 2 diabetes and end-stage kidney disease. While awaiting a kidney transplant he was hospitalized for 10 days with related complications. He just got out of the hospital the day he visited our clinic. He reported his hemoglobin A1c was 6.8 and his blood sugar two days earlier was 94. He also had high blood pressure for which he was medicated.

On examination, his best-corrected visual acuity was 20/50 OD and 20/30 OS. Extraocular motility testing was normal. Confrontation fields were full-to-careful finger counting OU. His pupils were equally round and reactive to light, with no afferent pupillary defect (APD). His anterior segment exam was unremarkable OU. His intraocular pressure (IOP) measured 14mm Hg OU.

Dilated fundus exam revealed changes as seen in the fundus photos. An OCT was performed and is available for review.



What structural changes can these images of the right (at left) and left fundus reveal, and can it help explain this kidney disease patient's visual presentation?

Take the Retina Quiz

1. What additional testing would be most helpful in making a diagnosis?
a. Fluorescein angiography.
b. MRI scan.
c. Blood pressure.
d. Erythrocyte sedimentation rate and C-reactive protein.

2. How would you characterize the optic nerves in this patient?
a. Physiologic.
b. Neovascularization of the disc.
c. Bilateral disc swelling.
b. Ischemic.

3. How would you characterize the retinal findings?
a. Mild microvascular retinal changes.
b. Moderate-to-severe retinal vascular changes.
c. Severe retinal ischemia.
d. Proliferative disease.

4. What is the most likely diagnosis?
a. HTN retinopathy.
b. NPDR with center-involved DME.
c. Combined HTN retinopathy and NPDR.
d. CRVO OU.

5. How should this patient be managed?
a. Referral for consideration of anti-VEGF therapy.
b. Visual field and neuro-ophthalmology consult.
c. Lumbar puncture and MRI.
d. Immediate referral to the emergency department for blood pressure control.

For answers, see page 82.

Diagnosis

Optic nerve swelling was evident in both eyes, as were scattered cotton-wool spots as well as retinal hemorrhages. On further questioning, our patient said that when he was admitted to the hospital, his blood pressure was 220/190. Based on the guidelines established by the Joint National Committee (JNC) on Prevention, Detection, Evalua-

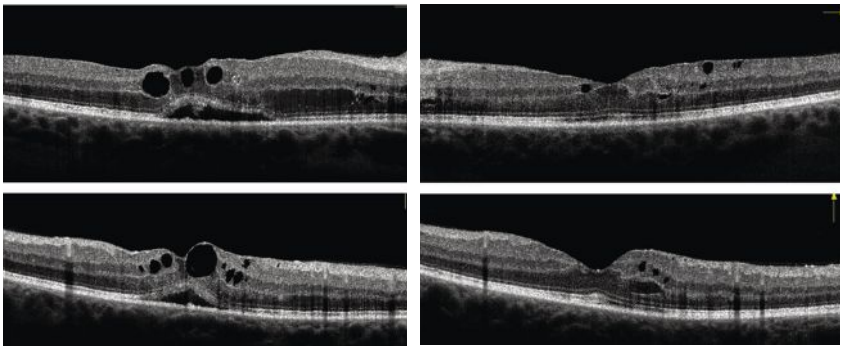
tion and Treatment of High Blood Pressure, our patient was clearly having a hypertensive emergency. The disc swelling we saw was likely a sequela from this hypertensive event. Fortunately, they were able to get his blood pressure under control. By the time he came to us, it was 135/070.

Based on the JNC guidelines systolic blood pressure (SBP) >179mm Hg or diastolic blood pressure (DBP) >109mm Hg is classified as "hypertensive crisis." Hypertensive crisis can be further categorized as either hypertensive emergency or hypertensive urgency.[1]

End-organ damage in the presence of significantly elevated blood pressure is classified as hypertensive emergency whereas hypertensive crisis occurs in the absence of end organ damage. Then it is classified as hypertensive urgency. End-organ damage may manifest in the central nervous system, eye, heart (left ventricular dysfunction) and kidney.

However, not everything on his retinal exam resulted from high blood pressure. His diabetes also played a role. He had scattered retinal hemorrhages, exudate and fluid in each macula. This fluid in the macula is easily visualized on the SD-OCT scan where several large retinal cysts, as well as puddle of subretinal fluid, were visible in the right eye. The left eye also had fluid, but not as much. The macular edema was a bit confounding. Did it arise from the diabetes or the disc swelling associated with the hypertensive crisis?

Our impression was that it was more likely from his diabetic retinopathy (DR). The DR seems worse in his right eye as there were scattered retinal hemorrhages in four quadrants, which puts him at a level of severe non-proliferative diabetic retinopathy (NPDR). The left eye was not as bad. We only noted a moderate case of NPDR.



Can these OCT images of the right (at left) and left eyes reveal our 34-year-old patient's diagnosis?

Discussion

The combination of uncontrolled blood pressure and diabetes does not bode well for our patient. Unfortunately, he's not alone. Approximately 75 million Americans, or about one in three, have hypertension and only 54% control their blood pressure.[2] The combination of hypertension and diabetes is also common, affecting 30% of patients with younger onset diabetes and 75% of people with older-onset.[3] To make matters worse, in many of these patients, blood pressure is poorly controlled. In those with younger-onset diabetes only 60% of patients have their blood pressure controlled; in older-onset diabetes, it's even worse with only 42% achieving blood pressure control.[3] This combination puts patients at a higher risk of cardiovascular disease, nephropathy and amputation.

Our patient already has kidney failure and is awaiting a transplant. The current American Diabetes Association guidelines recommend a treatment goal of SBP <140mm Hg and DBP <90mm Hg for most patients with diabetes. Lower systolic and diastolic blood pressure targets, such as <130/80mm Hg, may be appropriate for individuals at high risk of cardiovascular disease, if they can be achieved without undue treatment burden.[4] Our patient at this point seems to have achieved this goal.

Our patient was referred to a retina specialist to evaluate his macular edema. The specialist elected to observe the patient closely to see if the edema would resolve with better blood pressure and blood sugar control. No doubt the optic nerve swelling will slowly resolve, but it would have been interesting to see the extent and severity when he presented to the hospital 10 days earlier. Hopefully, he has turned the corner for the better and he will get the necessary care that is required to maintain good vision and a good quality of life. ■

Dr. Dillinger practices at Horizon EyeCare in Owatonna, MN.

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Failure is Not an Option

When a corneal graft is compromised, you need to take swift action to save this vulnerable tissue from total loss. **By Christian Corzo, OD, and Richard Mangan, OD**

A 45-year-old Hispanic male presented to clinic with a chief complaint of progressive blurry vision that started approximately four days earlier in his right eye. Accompanying symptoms included light sensitivity and ocular irritation. The patient denied any ocular discharge, ocular trauma or recent illness.

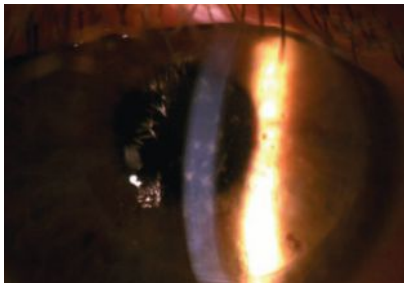
The patient's ocular history was remarkable for penetrating keratoplasty (PK), which was performed 25 to 30 years ago in both eyes. At this visit, the patient denied using a topical steroid for maintenance therapy. His best-corrected visual acuity (BCVA) was 20/70 OD, 20/50 OS. His anterior segment findings are provided (*Figure 1*). We observed no palpable preauricular node (PAN) at that visit. The rest of the exam was unremarkable.

Given the patient's presentation of unilateral subepithelial infiltrates (SEIs) and temporal graft edema, with a chief complaint of acute progressive blurry vision, we considered diagnoses of corneal graft rejection, herpes simplex keratitis (HSK), epidemic keratoconjunctivitis (EKC) and corneal graft failure (CGF).

Differential Diagnosis

The patient denied any previous history of herpes simplex treatment or previous episodes of HSK. The exam showed stromal edema. It was non-centralized and did not appear disc-formed. In addition, an anterior chamber reaction was absent.

In a patient with a corneal graft rejection, the presence of scattered



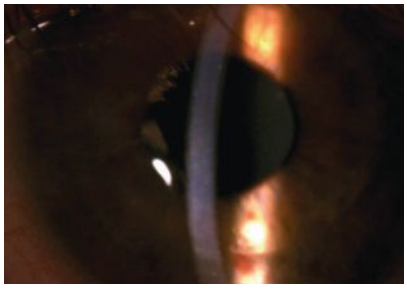


Fig. 1. At top, upon presentation, scattered SEIs were noted throughout the right corneal graft along with temporal graft edema. Below, the left corneal graft was remarkable for scattered SPK; no SEIs or graft edema were noted.

SEIs can mimic EKC. In addition, the absence of EKC characteristics, such as conjunctival follicles, pseudomembranes or PANs, were noted. Though SEIs were present, they were limited strictly to the graft cornea. Unlike this case, EKC does not present with corneal edema. Though treatment for EKC and epithelial/stromal corneal graft rejection would be similar (moderate to aggressive use of topical steroids), corneal graft rejection seemed likely due to the presence of graft edema and SEIs that were limited to the graft cornea in the absence of any pseudomembranes or PANs.

CGF is the result of any loss of graft structural integrity, which leads to irreparable vision loss. Classically, graft failure presents as gradual onset of graft edema in the absence of inflammation or keratic precipitates.[1] In this case, though graft edema was evident, inflammation was noted in the form of SEIs. Because the patient's findings were attributed to active inflammation and because the integrity of the corneal graft did look adequate, we attributed the findings to corneal graft rejection, not graft failure. Since graft rejection could lead to failure, timely action was required.

Assessment and Plan

Based on the clinical presentation, we suspected either a combined form of graft rejection; specifically, chronic stromal rejection with possible endothelial graft rejection or endothelial graft rejection.

Scattered SEIs limited to the corneal graft are typical of chronic stromal rejection, but corneal edema is not characteristic of this form of rejection. The presence of corneal edema in an eye with a previously clear and quite graft should raise suspicions of endothelial graft rejection regardless of the presence of an endothelial rejection line.

When handling combined forms of rejection (or endothelial graft rejection), administer a systemic steroid. Given that the PK in this eye was 30 years old and, most likely would require systemic steroids, we consulted with a cornea specialist and scheduled the patient for a next day consultation.

Presentation

Corneal graft rejection is an immune mediated process wherein a graft that has been clear for at least two weeks suddenly succumbs to graft edema in addition to anterior segment inflammatory signs.[2] Early symptoms include blurry vision, mild discomfort, redness, photophobia and ocular irritation; late-stage symptoms include markedly deceased vision, irritation, ocular pain and tearing.

Corneal graft rejection can present with a combination of signs and is classified into four subcategories: epithelial graft rejection, chronic stromal rejection, hyperacute stromal rejection and endothelial graft rejection (See *Corneal Graft Rejection Categories*).[2]

Therapeutics

Treatment must be individualized. In cases of isolated epithelial or chronic stromal rejection, both of which have a higher rate of reversibility, topical prednisolone acetate 1% can be dosed up to six times per day with a tapering schedule that extends six to eight weeks.[6]

A more aggressive approach must be taken when handling endothelial, acute stromal or combined forms of corneal graft rejection. In these cases, use topical corticosteroids in conjunction with systemic therapy—prednisone acetate 1% Q1hr (or difluprednate 0.05% Q2hrs) in combination with either, with 40mg to 80mg of oral prednisone daily or a single (or three) IV dose of methylprednisolone 500mg.[6] This may be given in conjunction with subconjunctival betamethasone 3mg in 0.5ml. Topical antibiotics and cyloplegics should be prescribed for prophylactic coverage and if there is an iritis present, respectfully.[7]

Regardless of the type of corneal transplant surgery a patient undergoes, the patient should be placed on a daily topical steroid (such as loteprednol or fluorometholone) for life to decrease the risk of rejection; patients demonstrating a steroid response should be treated accordingly with IOP-lowering medications.

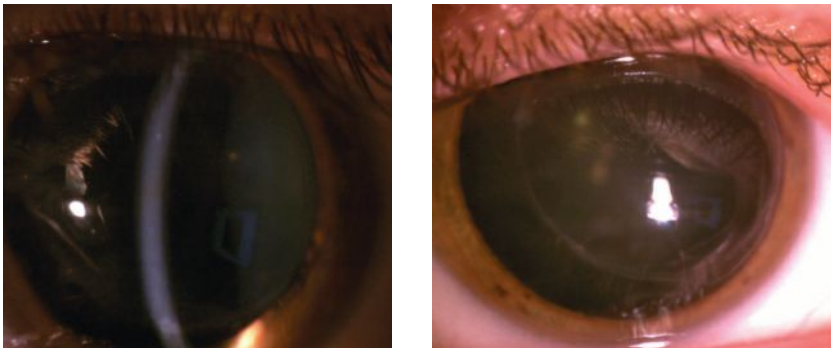


Fig. 2. At left, after aggressive steroid use and several visits with ophthalmology, this right corneal graft was finally clear. Though the left graft did not undergo rejection throughout this case, a photo of the left eye was provided for contrast.

In addition, our care expands beyond the scope of managing active cases of graft rejection: we are tasked with helping to mitigate the

Corneal Graft Rejection Categories

1. Epithelial graft rejection – In these cases, patients are typically asymptomatic with mild inflammation. Clinically, it presents as an elevated, undulating line that stains with sodium fluorescein or rose bengal. This linear pattern presents in the graft periphery (near the graft-host junction) and progresses toward the center of the graft epithelium. The epithelium behind the rejection line will presents a hazy and irregular.[2,3] The average onset of an epithelial rejection line is three months.[2] One manifestation which bears little clinical significance is the presence of Kaye's dots: punctate epithelial opacities located anterior to the suture line of the corneal graft. Although this form of rejection is self-limiting, prompt treatment is required due to its approximately 74% association with other forms of rejection.[2]

2. Chronic stromal rejection – This form of rejection presents with scattered SEIs, which are limited to the donor graft tissue. The presence of scattered SEIs can mimic EKC in a patient who presents with an episode of graft rejection. One way to differentiate the two would be based on the amount of conjunctival injection noted and the presence (or absence) of a PAN. Chronic stromal rejection will present with mild injection without a PAN. Although this form of rejection would unlikely lead to graft failure, the presence of SEI indicates that the host tissue is sensitized to the donor tissue and endothelial rejection may be impending.[2]

3. Hyperacute stromal rejection – This is typically seen in conjunction with or immediately following endothelial rejection. Early signs include ciliary congestion and engorgement of the corneal vessels. It presents as sudden onset of peripheral full-thickness haze in a previously clear corneal graft that spreads to the corneal center of the graft within 24 to 48 hours.[2]

4. Endothelial graft rejection – In terms of severity, endothelial graft rejection is the most symptomatic and ruinous type of rejection. Endothelial rejection is more commonly seen in younger patients and is directly correlated to the degree of corneal vascularization prior to transplantation. These patients will present with pain, redness and decreased vision. Findings will include Khodadoust line (a chain-like configuration limited to the donor endothelium which consist of white blood cells), stromal edema, keratic precipitates limited to the donor tissue and an anterior chamber reaction. In addition, endothelial graft rejection is classified into the three following categories: possible, probable and definite.[2] Such a form of rejection requires immediate emergency treatment.[2-4] The rate of reversal for severe endothelial rejection in a patient who underwent PKP is as high as 63% when proper timely treatment is initiated.[5]

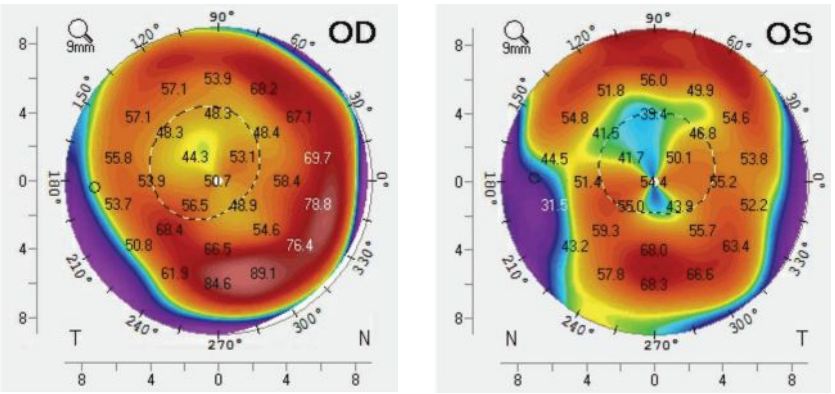


Fig. 3. These tangential curvature maps show our patient's corneal topography.

risk factors that can lead to episodes of rejection. For example, consider placing patient on a prophylactic antiviral (such as acyclovir) if the patient has previously reported an incidence of HSK and is currently not on oral antivirals. Lid disease compounded by ocular surface disease (such as severe dry eye) can incite epithelial damage and could trigger inflammation. Other conditions that should be treated accordingly include, but are not limited to; exposed/loose sutures, poorly fitting post-surgical contact lenses, trichiasis and entropion. Managing such comorbidities will prevent possible episodes of corneal graft rejection.

Our patient was diagnosed with early epithelial/stromal rejection and placed in the following treatment regimen: Durezol (difluprednate 0.05%, Novartis) Q1hr OD, Besivance (besifloxacin, Bausch + Lomb) TID OD, and one Medrol (methylprednisolone, Pfizer) pack PO as direct and scheduled for a next-day follow up. After three more visits with the cornea specialist, the graft rejection had resolved (*Figure 2*).

Endothelial Rejection Severity

Possible: Graft edema only.

Probable: Edema, cells/flare, keratic precipitates on donor button.

Definite: Edema, cells/flare, keratic precipitates on donor button, Khodadoust line.

When a patient presents with graft rejection, proper classification and prompt initiation of treatment is crucial. In most cases, failure to reverse rejection results from delayed treatment. This can lead to significant donor endothelial cell loss, which can in turn lead to permanent graft damage and loss of recoverable vision.[8] Patients who undergo corneal transplantation, regardless of procedure type, require daily maintenance with immunosuppressive therapy to prevent graft rejection, hence the importance of routine exams to evaluate patient compliance with medications. Patients should be evaluated and treated for any comorbidities to decrease risk of an episode of rejection. ■

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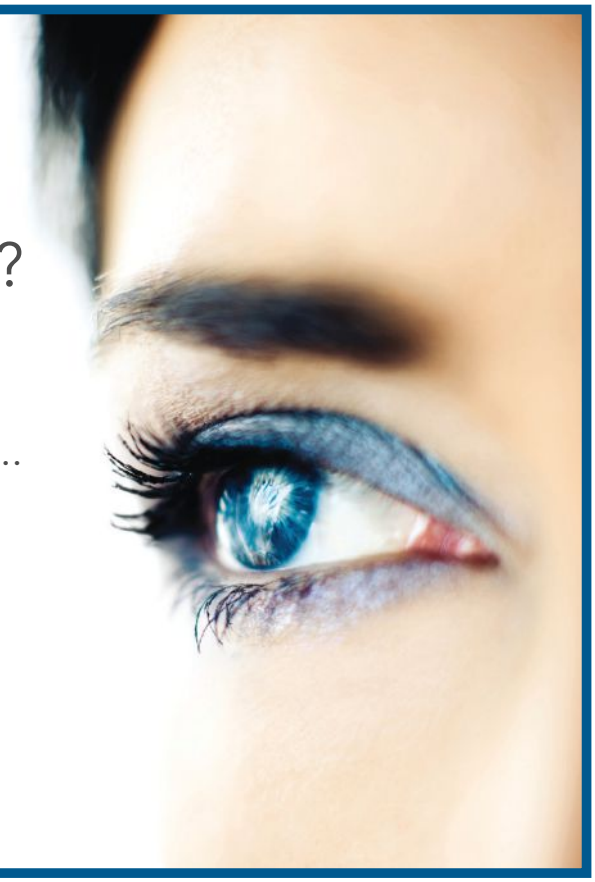


Diagnostic **Quiz**

The Pressure is On

A young patient's eyes might explain his headaches. **By Andrew S. Gurwood, OD**

History

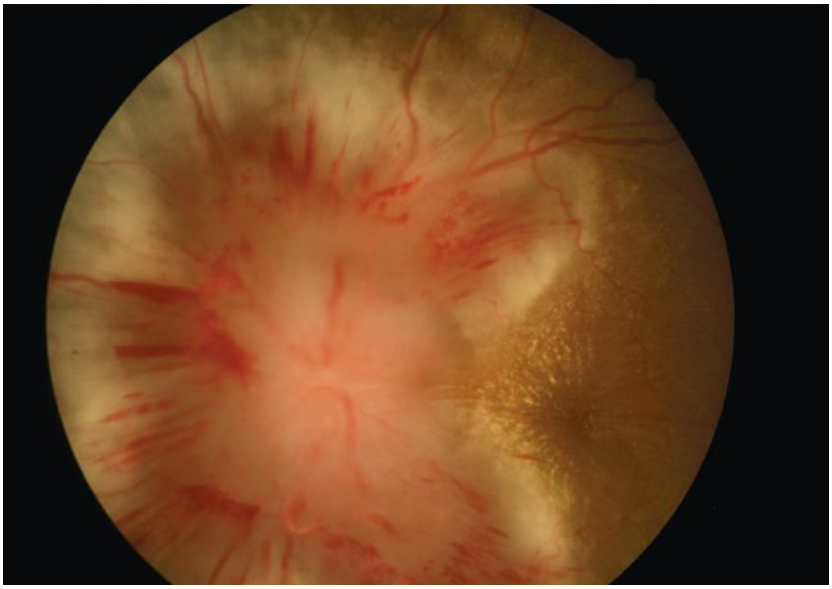
A 37-year-old man presented to the office with a chief complaint of headache via the emergency department. He explained that his vision was also poor in both eyes for the previous seven days. His ocular history was non-contributory. His systemic history was positive for hypertension, diabetes and hypercholesterolemia. He admitted to poor medical compliance. He denied trauma or allergies of any kind.

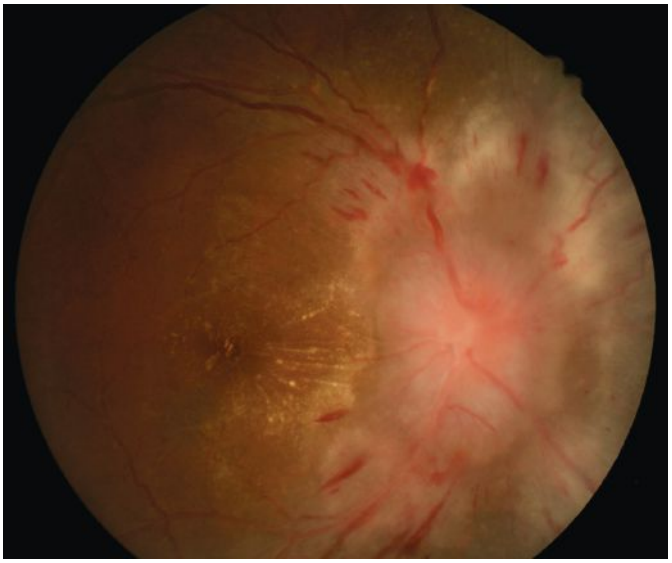
Diagnostic Data

His best-corrected entering visual acuities were 20/70 OD and 20/100 OS at distance and near. His external examination was normal with the exception of facial Amsler distortion OU. There was no afferent pupillary defect. His anterior segment findings were normal. Goldmann applanation tonometry measured 17mm Hg OU. The pertinent dilated fundus examination findings are demonstrated in the photographs.

Your Diagnosis

Does the case presented require any additional tests, history or information? Based on the information provided, what would be your diagnosis? To find out, visit www.reviewofoptometry.com. ■





These fundus images show a patient's left (above) and right eyes. Can these images explain his headaches and poor vision?

Retina Quiz Answers *(from page 74):* 1) c; 2) c; 3) b; 4) c; 5) a .

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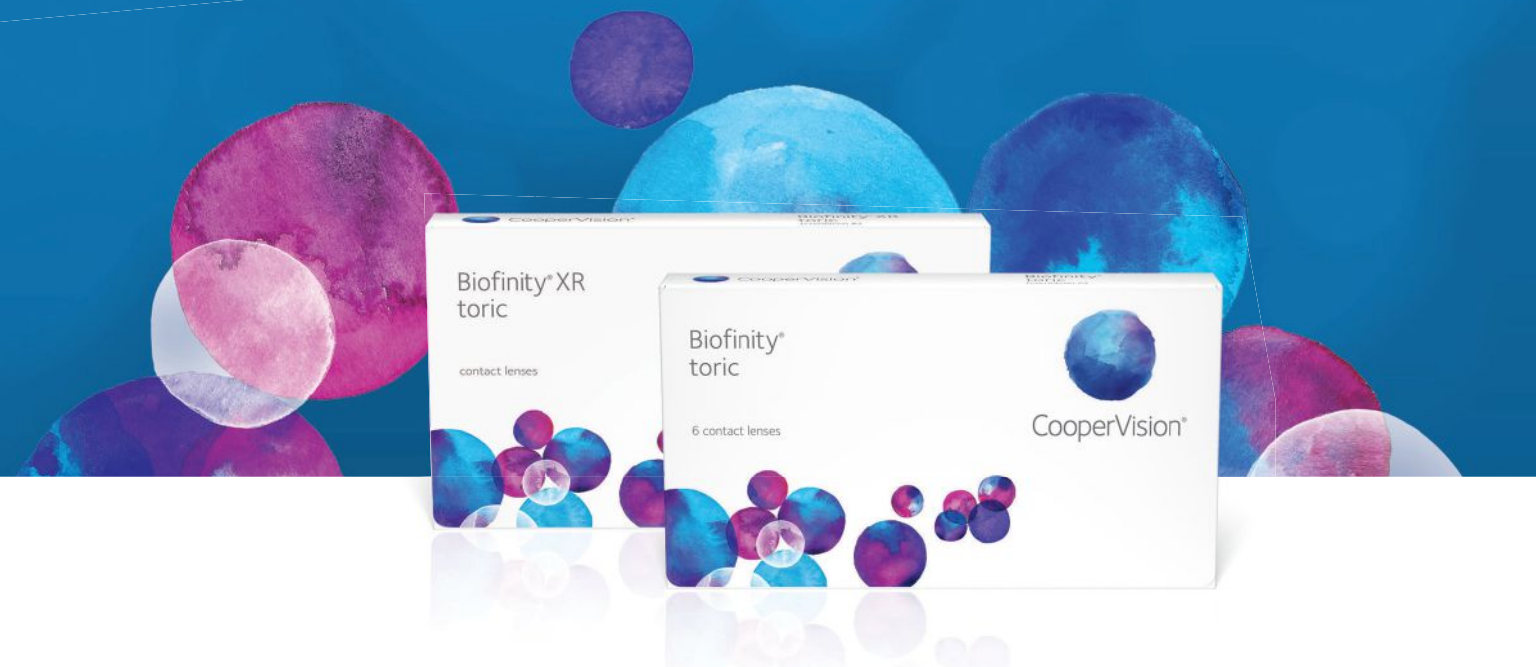

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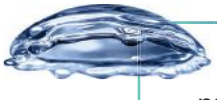

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