REVIEW OF OPTOMETRY • VOL. 160, NO. 11 • NOVEMBER 15, 2023 • High Myopes • Myopia Patient Questionnaire • Side Effects of Glaucoma Meds • Corneal Ulcers and Infiltrates • Autologous Serum Eye Drops • Managing Pterygium

How to Handle the High Myope, P. 36 • A Modern Tool to Assess Myopia Risk, P. 44

REVIEW of OPTOMETRY®

OCULAR SURFACE HEALTH ISSUE

November 15, 2023 • reviewofoptometry.com

Leadership in clinical care

Ocular Surface Side Effects of Glaucoma Meds

Here's a look at many possible iatrogenic complications—and what do to about them.

Page 66

Understanding Corneal Ulcers and Infiltrates

Page 50

Real-World Uses Of Autologous Serum Eye Drops

Page 58

EARN 2 CE CREDITS

Addressing Pterygium in Optometric Practice

Page 72

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.

Distributed by:

Bausch + Lomb, a division of

Bausch Health US, LLC

Bridgewater, NJ 08807 USA

Based on 9612403 (Folded), 9612303 (Flat) 5/2019

VYZ.0109.USA.20 Issued: 5/2020

VYZULTA®
(latanoprostene bunod ophthalmic solution), 0.024%

A BRANDED FIRST-LINE TREATMENT, RIGHT OUT OF THE GATE

IOP reduction for your open-angle glaucoma patients—with more horsepower

VYZULTA delivered up to **9.1 mmHg** mean IOP reduction from baseline—a greater reduction vs timolol—in pivotal studies[1,2]*

Excellent tolerability with <1% discontinuation rates due to ocular AEs[3,4]

Now with ~70% coverage for Medicare Part D and commercially insured patients nationwide†

LEARN MORE ABOUT VYZULTA HORSEPOWER AT VYZULTAHCP.COM

*Pivotal study designs: Two Phase 3, randomized, multicenter, parallel-group studies, APOLLO and LUNAR, evaluating noninferiority of once-daily VYZULTA vs twice-daily timolol maleate 0.5% in patients with open-angle glaucoma or ocular hypertension. Primary endpoint was IOP measured at 9 assessment time points in study eye. APOLLO (VYZULTA, n=284; timolol, n=133) and LUNAR (VYZULTA, n=278; timolol, n=136).[1,2]

†MMIT Analytics3, December 2022.

AE=adverse event; IOP=intraocular pressure.

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
- 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 full Prescribing Information on adjacent page.

References: 1. Weinreb RN, Scassellati Sforzolini B, Vittitow J, Liebmann J. Latanoprostene bunod 0.024% versus timolol maleate 0.5% in subjects with open-angle glaucoma or ocular hypertension: the APOLLO study. *Ophthalmology*. 2016;123(5):965-973. **2.** Medeiros FA, Martin KR, Peace J, Scassellati Sforzolini B, Vittitow JL, Weinreb RN. Comparison of latanoprostene bunod 0.024% and timolol maleate 0.5% in open-angle glaucoma or ocular hypertension: the LUNAR study. *Am J Ophthalmol*. 2016;168:250-259. **3.** VYZULTA Prescribing Information. Bausch & Lomb Incorporated. **4.** Weinreb RN, Liebmann JM, Martin KR, Kaufman PL, Vittitow JL. Latanoprostene bunod 0.024% in subjects with open-angle glaucoma or ocular hypertension: pooled phase 3 study findings. *J Glaucoma*. 2018;27(1):7-15.

BAUSCH + LOMB

Optometry Needed More in Urgent Referral Care

A decline in the workforce of the neuro-ophthalmology subspecialty inevitably means that ODs will see more patients who require prompt, accurate triaging.

Consistent with projections of an overall decline in the ophthalmology workforce, estimates at the level of individual subspecialties reveal insights into that profession's current readiness (or lack thereof) to meet demand. A new study on neuro-ophthalmology in the US paints a dispiriting picture.

Previous research indicates the need for neuro-ophthalmologists in the US to be approximately one expert per 1.2 million individuals. A recent survey estimated the current ratio level to be about 1.7 million individuals per neuro-ophthalmologist; only eight states reported numbers below the estimated threshold of 1.2 million.

In one new study in *Ophthalmology*, the current demographic and geographic distribution of neuro-ophthalmologists was recorded as of April 2023. It found a mean of 1.9 neuro-ophthalmologists per million US residents, but the range varied based on geographic location.[1]

Of the total 635 neuro-ophthalmologists identified, 68.7% were male and a strong majority (94.3%) graduated from an allopathic medical school; of the 85 physicians with a secondary graduate degree, 63.5% had a PhD. Interestingly, 25% of all neuro-ophthalmologists did a residency in neurology and 7.4% did a residency in ophthalmology and neurology, compared with the three-quarters that completed an ophthalmology residency. Almost one-third (30%) were trained in more than one fellowship, most commonly oculoplastics (12.3%) and pediatric (8.3%) ophthalmology.

Alarmingly, most of the current workforce is estimated to be in their late careers, with 60% in practice for 20 years or more. Comparatively low percentages were made up of mid-career neuro-ophthalmologists (18.9%, 10 to 19 years) and early career ones (21.1%, <10 years). Just as alarming, three states (Maine, South Dakota and Wyoming) had no neuro-ophthalmologists. Counties without a neuro-ophthalmologist displayed a lower median income, less vehicle access and lower health insurance rates.

Based on these rates, a projected 180 additional practicing neuro-ophthalmologists are needed to meet the demand of care in the US. This is especially limited by geography, as most currently practicing were located in metropolitan coastal areas and near academic institutions. Of the 30 counties with the greatest neuro-ophthalmologist numbers, 14 were unaccounted for in the top 30 populous counties.

The low number of neuro-ophthalmologists, especially in more remote areas, reflects recent research that found mean time from referral to consultation to be 34 days, peaking at one week for urgent care and 13 for routine. Without urgent access, this pushes patients to seek put emergency department (ED) visits, where expertise may be limited and unnecessary tests may take place.

Although more ophthalmology residents are seeking subspecialty training, this is not the case for neuro-ophthalmology, and the almost one-third in this study who trained in an additional fellowship may further exacerbate the shortage, as some did not list neuro-ophthalmology as their subspecialty on institutional home pages. However, an increase was observed in neurology-trained clinicians among early-career neuro-ophthalmologists, potentially alleviating some of the burden.

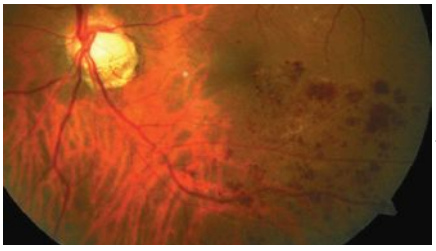


Photo: Bisant A. Labib, OD

CRAO is one condition that ODs can help in triaging to alleviate the burden on general ophthalmologists and neuro-ophthalmologists, ultimately resulting in better patient outcomes.

The study authors propose an immediate call-to-action to boost interest in neuro-ophthalmology as a subspecialty: "Potential strategies to incentivize residents to pursue neuro-ophthalmology could include modifying ophthalmology fellowships to offer extensive training in strabismus, orbital and cataract surgery, as well as temporal biopsy or Botox injection that could help generate more revenue," they wrote in their paper. "Another strategy is to require neuro-ophthalmology clinical rotation for neurology residents, especially early in their training. This can boost the number of neurology-trained neuro-ophthalmologists and help alleviate the shortage in this subspecialty."[1]

Optometric Role in CRAO

Another recent study, this one in *Journal of Neuro-Ophthalmology*, highlights just how optometrists can play an increasingly pivotal role in eye care in the wake of a dwindling neuro-ophthalmologist population. Its researchers surveyed the

US optometric community to determine current practice patterns in managing central retinal artery occlusion (CRAO), since they are often the first providers to evaluate patients with acute vision loss and diagnose the condition.

A total of 1,926 ODs responded to the survey, of which 98% had diagnosed fewer than five CRAOs in the prior year and 52% had not diagnosed a CRAO in the prior year. Of those who diagnosed at least one occurrence in the prior year, 71.7% evaluated patients more than four hours after initial vision loss, while only 13.6% evaluated patients within four hours. Those who diagnosed a CRAO primarily referred patients to an ED affiliated with a stroke center (44%), outpatient ophthalmology clinics (40%), an ED without a stroke center (13%), outpatient neurology clinics (1%) or other, mostly PCPs (56.4%).

The 56% of ODs who responded that did not specify they would refer an acute CRAO patient to an ED with a stroke center emphasizes the need for education in the optometric community. The 40% who would refer them to outpatient ophthalmology clinics sheds light onto the already burdened specialty, especially the subspecialty of neuro-ophthalmology. "Given the need to perform an urgent stroke evaluation in acute CRAO patients and the narrow thrombolysis treatment window, it is imperative that optometrists and ophthalmologists are educated to view acute retinal arterial ischemia as a stroke equivalent and establish appropriate networks to immediately refer patients with an acute CRAO to an ED affiliated with a stroke center, instead of referring to outpatient clinics," the authors wrote.[2]

They do suggest some solutions: "Education of optometrists on this topic should be pursued through established and new forums such as continued medical education courses, editorials and stroke awareness campaign advertisements in optometric journals and peer-to-peer education by academic optometric leaders to 'follow the guidelines.'"[2] But for neuro-ophthalmologists, who are greatly overburdened by the current US population, ODs will need to step up and properly manage these patients, referring them to the right type of care. To do so, perhaps optometrists would benefit from neuro-ophthalmologist educational outreach, describing proper protocol for certain conditions seen.

1. Pakravan P, Lai J, Cavuoto KM. Demographics, practice analysis and geographic distribution of neuro-ophthalmologists in the US in 2023. Ophthalmology. 2023;S0161-6420(23)00679-6.

2. Mileski KM, Biousse V, Newman NJ, et al. Optometric practice patterns for acute central and branch retinal artery occlusion. J Neuro-Ophthalmol. 2023;10.1097.

South Dakota ODs Can Now Perform IPL

In early August, the South Dakota Optometric Society (SDOS) submitted a petition to the state's Board of Examiners to allow trained optometrists in the state to perform intense pulsed light (IPL) treatment, a procedure that's becoming a more mainstream alternative for patients with dry eye—more specifically, meibomian gland dysfunction. When the Board met on August 28 to discuss the request, they arrived unanimously at their conclusion that IPL therapy is indeed within the scope of practice for ODs in South Dakota, and the ruling became effective less than two weeks later on September 9.

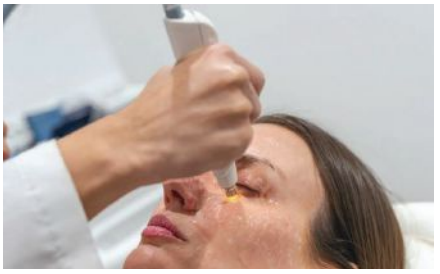


Photo: Hardeep Kataria, OD

Though the practice scope in South Dakota hasn't been updated in nearly 30 years, a new ruling will allow trained ODs to perform IPL therapy on patients with dry eye/MGD.

The official declaratory ruling states that the procedure is now approved for the nonsurgical treatment of dry eye disease "if the optometrist is educationally qualified and does not rely on laser technology or use any device setting that is outside the scope of practice in South Dakota." Additionally, it clarifies that patients may not be treated with IPL solely for cosmetic benefits or "after the optometric purpose for the treatment has been achieved." As goes for any other in-office procedure, the ruling also states that optometrists must be equipped to handle any complications that result from the treatment.

In typical anti-optometry fashion, the South Dakota Academy of Ophthalmology filed an appeal against the ruling in late September, posing the argument that IPL does not fall within the state's optometric scope of practice despite the Board's decision. The SDOS is in the process of determining its next steps for advocacy if the appeal is eventually granted.

While the news of this ruling is certainly a win for optometrists in the state, the scope of practice in South Dakota still lags far behind many other states, having not seen an update since 1994, when glaucoma drugs were added. In its most recent legal endeavor, the SDOS introduced a laser bill (SB 87) near the start of 2023 proposing to allow ODs to perform certain injections, chalazion and lid lesion removal, foreign body removal, YAG capsulotomy, LPI, SLT and corneal crosslinking. Though the legislation passed the state Senate with a vote of 26-9 in early February, it was ultimately killed once it reached the House Health and Human Services committee later that month. Despite the setback, ODs in the state are not prepared to let up on advocacy efforts any time soon.

The SDOS is now working with the Board and the AOA in preparation to reintroduce SB 87 in the 2024 session, with hopes that the legislature will finally recognize the need to update optometry's practice scope to better reflect the current training and skills of ODs in South Dakota.

Until then, trained ODs in the state can celebrate the recent ruling and take advantage of IPL to offer patients a more modern and targeted treatment for MGD.

Mass. Bill Aims to Revamp Optometry's Definition

While not a scope expansion play, the update would make it so every new OD enters at the same level of licensure. It would also allow the state's ODs to use the title "optometric physician."

The definition of optometry in Massachusetts was first established back in 1934, and shockingly—despite monumental change and advancements in medicine over the last century—the law has not been touched since. Eager to change this, the New England College of Optometry in association with the Massachusetts Society of Optometrists (MSO) and its advocates introduced a bill (HB 3608) in March proposing to modify certain aspects of the outdated document.

HB 3608 would allow every future OD who becomes licensed in Massachusetts to enter the profession at the same level.

To put into context how obsolete the state's definition of optometry is, Wayne Zahka, OD, past president and current executive director of MSO, notes that "it speaks of optometrists having a high school education, taking optics courses, it uses only male pronouns and it specifies that we can't be habitually drunk, along with a lot of other nonsense." The law also prohibits optometrists from referring to themselves as optometric physicians, which most other US states have allowed for many years.

HB 3608, currently residing in the state's Joint Committee on Public Health, has two primary objectives that will most profoundly affect the profession. The first: An updated definition would allow Massachusetts ODs to advertise and refer to themselves as optometric physicians. The second: Every OD who applies for licensure in the state would have to apply and qualify for the highest licensure, whereas now optometrists in Massachusetts possess one of four licenses depending on which courses and training they received in their schooling. The level of licensure dictates which procedures and services an OD is legally allowed to provide, regardless of scope laws in the state.

"In 1986, we passed a diagnostic bill, so with the way the current system works, anyone who received their license before 1986 and didn't take the course is not able to practice diagnostics," Dr. Zahka explains. The same rule applies to those who became licensed before therapeutics were added to the practice scope in 1993 or before glaucoma care was added in 2021. "We want to ultimately have one license level, with everyone practicing at the highest level," he says.

The bill would not change the level of licensure for practicing ODs in the state, but rather ensure that every optometrist who becomes licensed in the future would enter the profession at the same level. "All this bill is saying is that over time, the differing licenses are going to go away, which will make everything safer and easier," Dr. Zahka states.

Though HB 3608 is more of a housekeeping bill than a proposal for scope expansion, ophthalmology is still using its typical anti-optometry tactics to discourage its passage. However, the MSO is confident that with continued advocacy, the bill will ultimately make its way to the finish line.

A hearing was held on September 18 in the Massachusetts Joint Committee on Public Health, which has yet to decide the legislation's next steps. Since the state employs a two-year legislative cycle, the current session doesn't end until July. "Any time between now and then, we're hoping that the bill begins to move and gain some traction," says Dr. Zahka.

IN BRIEF

Dementia Risk Tied to Motor Neuropathy. A connection between dementia and ocular motor cranial neuropathy (OMCN) has long been speculated, as ocular motility dysfunction can occur when there's damage to cranial nerves III, IV and VI. To learn whether OMCN might be a predictor or independent risk factor for dementia, researchers in Korea recently conducted a nationwide cohort study. They found that **early-onset OMCN is a strong dementia predictor.**

The cohort included 19,243 patients and 96,215 matched controls without OMCN. Using the patients' health records from the Korean National Health Insurance Service, the researchers identified newly diagnosed OMCN by the first claim with a dementia diagnostic code and anti-dementia medications.

They reported that **patients with newly diagnosed OMCN had more metabolic comorbidities than non-OMCN patients.** Additionally, they found an association between new OMCN and an increased risk for all-cause dementia, Alzheimer's disease and vascular dementia. **Patients under 50 showed a stronger association between all-cause dementia and OMCN than older patients.**

The researchers explained in their *Ophthalmology* paper that the pathogenesis of OMCN isn't fully understood, but it's likely to result from a combination of factors, and **key mechanisms seem to include vascular damage, inflammation and neurodegeneration.**

"Our study presents new evidence indicating that **OMCN, particularly in younger patients, could serve as a strong predictor of cognitive decline, including the onset of Alzheimer's disease among the vast majority of the national population,"** the researchers concluded in their paper. They pointed out the **importance of conducting comprehensive neurological examinations in patients presenting with OMCN, including brain imaging and neuropsychological evaluation.**

Kim J, Han K, Jung J, et al. Early-onset ocular motor cranial neuropathy is a strong predictor of dementia: a nationwide, population-based cohort study. Ophthalmology 2023. [Epub ahead of print].

Higher Rate of Vascular Events & Death After RAO

With significantly increased risk, experts recommend systemic follow-up in these patients.

No proven therapy exists for vision loss following a retinal artery occlusion (RAO), but management involves reducing complications such as ischemia. Because of RAO's association with stroke, eye care providers refer these patients immediately for cardiovascular workup to a stroke center or emergency department, per the American Academy of Ophthalmology's Preferred Practice Pattern Guidelines. Experts say understanding secondary vascular events and identifying risk factors can help triage those at greatest risk as well as stratify management options. A study published recently in *JAMA Ophthalmology* added more risk data to the literature.

The researchers retrospectively identified 34,874 RAO patients' medical records with at least one year of follow-up, and a sex-, age- and comorbidities-matched cataract control cohort. At the time of the RAO event, patients were on average 66 years old. The researchers reported significantly higher rates of death, stroke and myocardial infarction (MI) after RAO compared with controls. Their findings are summarized in the table:

RETINAL ARTERY OCCLUSION VS. CONTROL POPULATION

(%)	2 weeks	30 days	1 year	5 years	10 years
Rate of death	0.14 vs. 0.06	0.29 vs. 0.14	3.51 vs. 1.99	22.74 vs. 17.82	57.86 vs. 55.38
Risk of stroke	1.72 vs. 0.08	2.48 vs. 0.18	5.89 vs. 1.13	10.85 vs. 4.86	14.59 vs. 9.18
Risk of MI	0.16 vs. 0.06	0.27 vs. 0.10	1.66 vs. 0.97	6.06 vs. 5	10.55 vs. 9.54

The researchers explained in their paper that after an RAO, there's an increased relative risk of vascular complications in the short term, compared with controls, though the absolute risk is relatively low. Long-term, the increased risk persists.

"We emphasize the potential need for multidisciplinary evaluation with long-term systemic follow-up of patients post-RAO," the researchers concluded in their paper.

Wai KM, Knapp A, Ludwig CA, et al. Risk of stroke, myocardial infarction, and death after retinal artery occlusion. JAMA Ophthalmol. October 26, 2023. [Epub ahead of print].

Tropicamide a Fine Alternative for Cycloplegic Refraction in Children

The drug was safe and effective for a non-strabismic population of three- to 16-year-olds regardless of refractive status, study shows.

Effective cycloplegia can be one of the most challenging aspects of a pediatric eye examination. Active accommodation in children is the primary source of error in measurements, and many studies on the pediatric population have shown that a lack of cycloplegia may result in an overestimation of myopia and an underestimation of hyperopia. The cycloplegic effect of the standard drug used, cyclopentolate, can continue for 24 hours—or even longer. Many propose that tropicamide would be an excellent alternative to cyclopentolate, given its favorable pharmacokinetics, but it has always been considered an ineffective cycloplegic despite its wide use as a mydriatic.

Researchers in Jordan recently compared the final cycloplegic refraction for the same patients using both cyclopentolate 1% and tropicamide 1% on two separate visits. Their study, published in *American Journal of Ophthalmology*, demonstrated that cyclopentolate gives final cycloplegic refraction that is more plus or less minus than tropicamide, which is concordant with the current belief and the few studies that compared the two agents.

A total of 185 eyes from 94 patients between the ages of three and 16 (average= 8.8; 54.3% female) were included. Out of the total sample, 44.9% eyes were obtained from young children (three to seven years old), 32.4% were older children (eight to 11) and 22.7% were teenagers (12 to 16). The study assessed the spherical equivalent (SE) change at the time of effective cycloplegia. All children had brown irises, as the researchers noted that eyes of this color were not as efficiently responding to cycloplegic agents as lighter-colored ones. All children were allocated to one of five subgroups according to the SE obtained after full cycloplegia. These subgroups were:

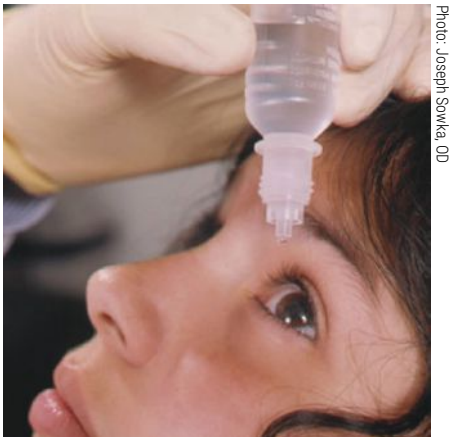


Photo: Joseph Sowka, OD

The time to effective cycloplegia for cyclopentolate is often considered to be between 30 to 60 minutes, and even shorter for light-colored irises.

STUDY SUBGROUPS

Refractive Category	Spherical Equivalent
high myopia	above -5.0
myopia	between -0.5 and -5.0
emmetropia	between -0.5 and +0.5
hyperopia	between +0.5 and +5.0
high hyperopia	above +5.0

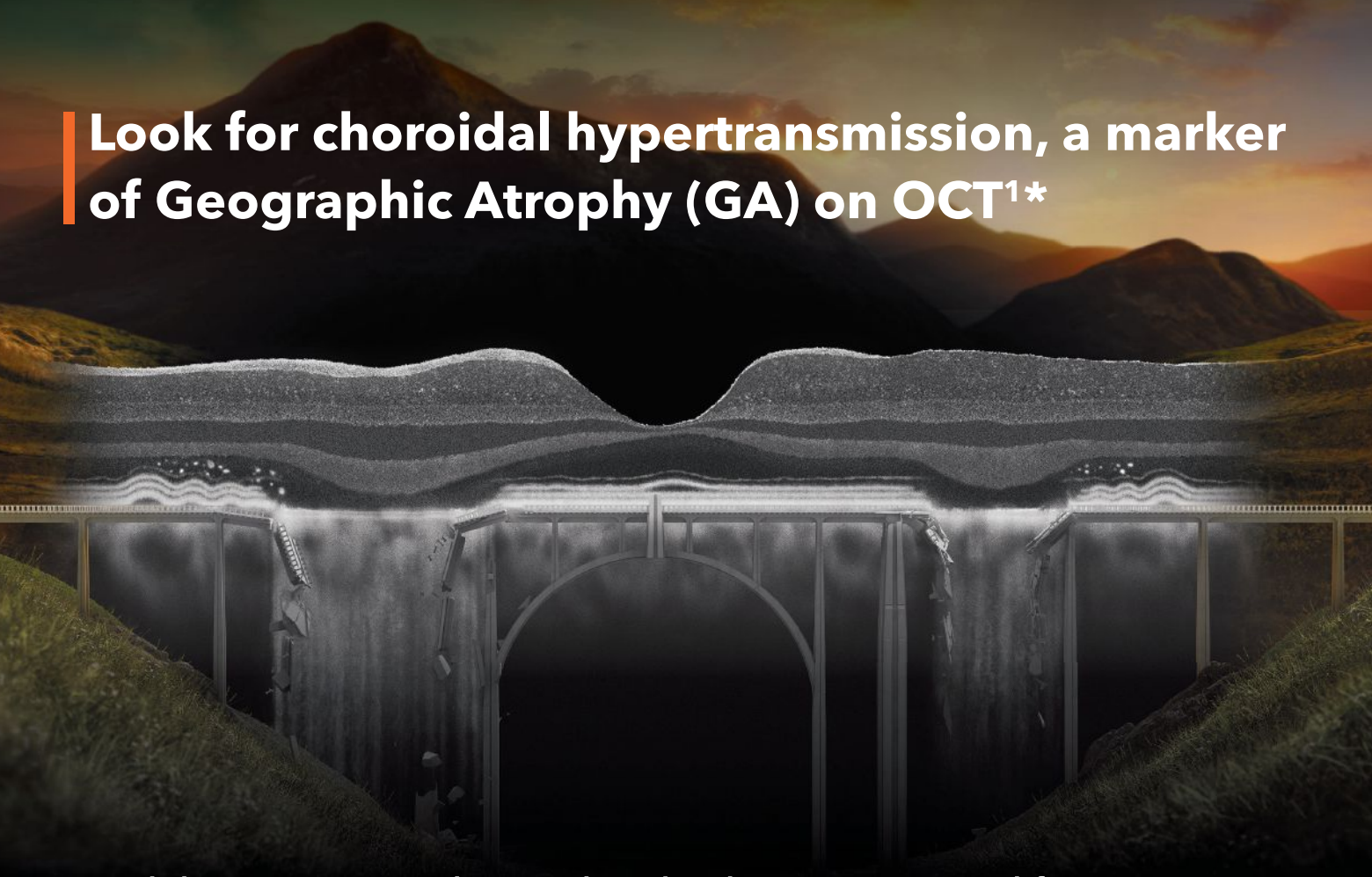
The average SE of both eyes before cycloplegia was -0.082D. The SE after instillation of cyclopentolate and tropicamide drops in both eyes was 1.07D and 0.96D respectively. The average change in SE after cycloplegia was 1.15D for cyclopentolate and 1.04D for tropicamide. The difference between change in SE of cyclopentolate and tropicamide was found statistically significant at 0.11D, however clinically insignificant. The change in SE between the two drops before and after cycloplegia in both eyes for all refractive error groups was clinically insignificant. The greatest effect of cyclopentolate and tropicamide was in hyperopic eyes with a change of SE of 1.54D and 1.39D respectively.

"Our study included the whole spectrum of refractive errors with age subgroup analysis," the researchers wrote in their paper. They also highlighted the reproducibility of their results within the different refractive and age subgroups made it even more valid.

"Tropicamide can be considered a reliable and effective substitute to cyclopentolate for cycloplegic refraction in non-strabismic children," the authors concluded. "We believe it can make a great relief for busy clinical practices, increase patient and parent satisfaction and have less effects on school attendance and performance."

Al-Thawabieh W, Al-Omari R, Abu-Hassan DW, et al. Tropicamide vs. cyclopentolate for cycloplegic refraction in pediatric patients with brown irises: a randomized clinical trial. Am J Ophthalmol. October 3, 2023. [Epub ahead of print].

Look for choroidal hypertransmission, a marker of Geographic Atrophy (GA) on OCT[1]*



- While BCVA is poorly correlated to lesion size, visual function continues to decline as lesions grow[2,3]
- It is critical to recognize GA and refer patients in a timely manner, as disease progression is relentless and irreversible[1,3-7]

Learn more about identifying GA at RecognizeAndReferGA.com

RECOGNIZE AND REFER

*GA is defined by atrophic lesions, resulting from loss of photoreceptors, RPE, and underlying choriocapillaris. This results in a choroidal hypertransmission defect on OCT.[1,8,9]
BCVA=best-corrected visual acuity; OCT=optical coherence tomography; RPE=retinal pigment epithelium.

References: 1. Fleckenstein M, Mitchell P, Freund KB, et al. The progression of geographic atrophy secondary to age-related macular degeneration. *Ophthalmology*. 2018;125(3):369-390. doi:10.1016/j.ophtha.2017.08.038. **2.** Heier JS, Pieramici D, Chakravarthy U, et al. Visual function decline resulting from geographic atrophy: results from the chroma and spectri phase 3 trials. *Ophthalmol Retina*. 2020;4(7):673-688. doi:10.1016/j.oret.2020.01.019. **3.** Sunness JS, Margalit E, Srikumaran D, et al. The long-term natural history of geographic atrophy from age-related macular degeneration: enlargement of atrophy and implications for interventional clinical trials. *Ophthalmology.* 2007;114(2):271-277. **4.** Boyer DS, Schmidt-Erfurth U, van Lookeren Campagne M, Henry EC, Brittain C. The pathophysiology of geographic atrophy secondary to age-related macular degeneration and the complement pathway as a therapeutic target. *Retina*. 2017;37(5):819-835. doi:10.1097/iae.0000000000001392. **5.** American Optometric Association. AOA Comprehensive adult eye and vision examination. *Quick Reference Guide: Evidence-Based Clinical Practice Guideline*. 1st ed. Accessed July 13, 2023. https//www.aoa.org/documents/EBO/Comprehensive_Adult_Eye_and_Vision_%20QRG.pdf. **6.** Holz FG, Strauss EC, Schmitz-Valckenberg S, van Lookeren Campagne M. Geographic atrophy: clinical features and potential therapeutic approaches. *Ophthalmology*. 2014;121(5):1079-1091. doi:10.1016/j.ophtha.2013.11.023. **7.** Lindblad AS, Lloyd PC, Clemons TE, et al; Age-Related Eye Disease Study Research Group. Change in area of geographic atrophy in the age-related eye disease study: AREDS report number 26. *Arch Ophthalmol*. 2009;127(9):1168-1174. doi:10.1001/archophthalmol.2009.198. **8.** van Lookeren Campagne M, LeCouter J, Yaspan BL, Ye W. Mechanisms of age-related macular degeneration and therapeutic opportunities. *J Pathol*. 2014;232(2):151-164. doi:10.1002/path.4266. **9.** Chakravarthy U, Bailey CC, Scanlon PH, et al. Progression from early/intermediate to advanced forms of age-related macular degeneration in a large UK cohort: rates and risk factors. *Ophthalmol Retina*. 2020;4(7):662-672.

Apellis

Visual Disorders More Common in Kids with ADHD

A growing body of research suggests a link between attention-deficit/hyperactivity disorder (ADHD) and various health problems, including certain ocular disorders, though the influence of medication regimens remains murky. A new study looked at the prevalence of 16 unique vision disorders among children and adolescents with ADHD compared to their non-ADHD peers. While the data did show a higher occurrence of visual disorders in the ADHD cohort, the authors concluded that neither medication use nor misdiagnosis appeared to confidently explain the association.

The large study included data on over one million individuals under age 22 (684,131 with ADHD and an equal number of matched controls). The prevalence of the following vision disorders was then compared between groups: strabismus, astigmatism, myopia, hypermetropia, anisometropia and aniseikonia, presbyopia, amblyopia, subjective visual disturbances, diplopia, visual field defects, color deficiencies, legal blindness, optic nerve disorders, glaucoma, non-age-related cataracts and nystagmus.

Those taking ADHD drugs were more likely to have 13 of the 16 visual disorders, with higher odds for those taking non-stimulants. Patients on stimulants had a significantly increased risk in seven of 16 outcomes, while those on non-stimulant medication had significantly higher rates of all measured disorders.

Photo: Getty Images

Patients with ADHD had an increased prevalence of 11 of 16 visual conditions, some of which included strabismus, nystagmus, myopia, astigmatism and subjective visual disturbances.

The researchers point out in their paper that this finding "supports other medication-based ADHD research into medical comorbidities, which suggest that stimulant medications tend to mitigate the impact of ADHD on certain disorders." They add that while non-stimulants are typically considered the "safer" medication for children with ADHD, "within the specific intersection of ADHD care and ophthalmology, our findings support the appropriate use of stimulant medication and indicate the need for further discussion into the comparative use of stimulant and non-stimulant ADHD medications."

Subgroup analysis, however, found the use of any ADHD med only mildly increased the likelihood of visual disorders, suggesting that this factor may not contribute to the increased prevalence of ocular comorbidities in ADHD patients.

The study data also contradicted the misdiagnosis hypothesis, which suggests that "some individuals with ADHD and visual disorders do not truly have ADHD, but rather experience some of the symptoms like inattention due to an inability to adequately see the object of attention," they wrote. They noted that this may be true in isolated cases; however, considering that this study found 50,000 more individuals with ADHD diagnosed with visual disorders than matched peers, it's unlikely that large of a patient population was misdiagnosed.

An important question surrounds the association between medication use and visual impairment in young ADHD patients. Because the evidence suggests it's unlikely the meds themselves increase the risk of visual disorders, that leaves a few alternative hypotheses on the table.

"Firstly, as individuals not requiring ADHD medications commonly experience less severe symptoms, it could be that their visual disorders are subclinical and less obvious than individuals requiring stimulant medications," the researchers explained in their paper. "Alternatively, the prescription of medications for ADHD requires regular contact with physicians and other providers, which may lead to an increased rate of visual disorder diagnosis even if the underlying prevalence is the same."

Choudhury RA, Adducci AJ, Sarwar H, Hale EW. Researching eyesight trends in ADHD (RETINA). Journal of Attention Disorders. October 21, 2023. [Epub ahead of print].

IN BRIEF

For Intracranial Hypertension, Monitor with OCT. Monitoring for papilledema development in patients with increased intracranial hypertension is critical, as this finding is a strong indicator of visual loss and impairment and may lead to optic nerve atrophy. Currently, experts say improvement in reliable and sensitive monitoring is needed. One possible option is using swept-source OCT and OCT angiography. Researchers in China used these modalities to study optic disc morphology and several structural and microvascular parameters. According to their study, published recently in *Ophthalmology and Therapy*, **patients with intracranial hypertension exhibit vascular abnormalities that correlate with clinical manifestations of the condition.**

The researchers found that **patients with intracranial hypertension (n=61) had significantly thicker peripapillary retinal nerve fiber layer and ganglion cell inner plexiform layer thickness with larger optic nerve head rim area than controls** (n=65). Additionally, they observed **significantly increased microvascular densities in the nerve fiber layer plexus and significantly reduced densities in the superficial vascular plexus, intermediate capillary plexus and deep capillary plexus vs. controls.**

Importantly, the researchers reported that structural thickness and microvascular densities correlated significantly with Frisen scores and intracranial pressure in patients with intracranial hypertension. This highlights "the potential clinical relevance of these parameters," the researchers wrote in their paper.

They concluded that **"patients with intracranial hypertension may benefit from monitoring optic nerve head structure and microvascular changes" with the OCT/OCT-A technology.**

Wang H, Cao L, Kwapong WR, et al. Optic nerve head changes measured by swept source optical coherence tomography and angiography in patients with intracranial hypertension. Ophthalmol Ther. October 4, 2023. [Epub ahead of print].

Atropine* PF

Now Available in 503B!

0.01%, 0.025%, and 0.05%

SCAN TO ORDER

100%

PRESERVATIVE-FREE.
BORIC ACID-FREE.

Still the same medication, but with no preservatives.

- Preservative-Free (no BAK)
- Patent-pending formulation
- $39 per bottle / $390 per box of 10
- 240 days expiration dating**

All three concentrations are also available to prescribe from our 503A Patient Specific Pharmacy.

Start prescribing to your patients today by scanning the QR code below. At atropine.com, you'll find EMR instructions, the MaxRX Prescriber Portal™ link, and our fax order form.

atropine.com

powered by imprimis Rx
A HARROW COMPANY

*For professional use only. ImprimisRx specializes in customizing medications to meet unique patient and practitioner needs. No compounded medication is reviewed by the FDA for safety and efficacy. ImprimisRx does not compound essential copies of commercially available products. These ingredients carry risks. Visit imprimisrx.com/productinformation for full product details.

**Stability studies conducted at controlled room temperature storage for up to 240 days.

Private Equity Managers Turn to ODs to Boost Efficiency

After acquisitions of ophthalmology practices, a recent analysis noted an increase of nearly one optometrist per clinic and a 24% expansion in patient volume by ODs.

An increasing number of physician practices have been acquired by private equity (PE) firms over the last decade, mainly due to the appeal of profitability and efficiency. ODs practicing in PE-acquired ophthalmology clinics are among the specialists benefiting from the switch, demonstrated by a study in *Ophthalmology*. The analysis compared service usage and Medicare spending between ophthalmology practices that have vs. have not been acquired by PE firms. While little to no effect was observed on utilization or total spending, the data did show that both the number of unique patients seen by optometrists, as well as the use of top-shelf Lucentis over Avastin, was greater in PE-acquired practices.

The study analyzed Medicare fee-for-service claims from 2012 to 2019 alongside a national database of PE acquisitions of ophthalmology practices. An event study framework was used to compare changes at a practice before and after PE acquisition to changes in practices that were never acquired. The main outcome measures included the number of beneficiaries seen, intravitreal injections and medications used for injections, along with spending on ophthalmologist and optometrist services, ancillary services and intravitreal injections.

Photo: Getty Images

This study noted that the number of ODs per practice increased by nearly one OD (89%) per practice after PE acquisition, while the number of ophthalmologists per practice increased by 52%.

By 2019, the analysis showed that the number of optometrists per practice increased by nearly one OD (89%) per practice after PE acquisition, while the number of ophthalmologists per practice increased by 52%. On average, optometrists in PE-acquired practices saw roughly 24% more beneficiaries per quarter than ODs in non-acquired practices, while for ophthalmologists, no increase was observed in the number of beneficiaries seen.

Total spending did not differ between PE-acquired and non-acquired practices, though the researchers noted a 5.5% increase in per-beneficiary per-quarter spending on MD services and a 4.6% decrease for ODs. Intravitreal injection spending also increased by 25%, due to greater use of Lucentis—an expensive medication—and a 12.9% decrease for Avastin, an inexpensive one.

Overall, this data validates the crucial role that ODs play in the efficiency of eyecare services, the demand for which is growing. The researchers noted in their paper that "these findings are consistent with the commonly stated hypothesis and empirical evidence that PE firms increase their use of non-physician clinicians, who are paid at lower rates."

Braun RT, Lelli GJ, Pandey A, et al. Association of private equity firm acquisition of ophthalmology practices with Medicare spending and utilization of ophthalmology services. Ophthalmology. 2023;S0161-6420(23)00707-8.

Minerals Ca, K and Mg All Key in Glaucoma Prevention

Certain vitamins and nutrients have been linked to decreased risk of ocular disease, such as glaucoma, though conflicting data surrounds this point. A new cross-sectional study focused its gaze on three important macroelements—calcium, potassium and magnesium—to examine which might influence glaucoma risk. It found that sufficient dietary consumption of all three is likely necessary to protect against glaucoma, though each seemed to influence its development in a distinctive way.

Data from 7,042 adults aged 40 or older who completed glaucoma exams were obtained from a large database from 2005 to 2008. Regression models were used to explore the association between dietary Ca, K, and Mg intake (based on a 24-hour dietary recall) and glaucoma.

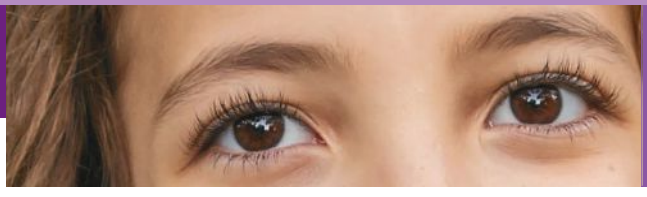
Slightly more than 8% of the cohort had glaucoma. After covariate adjustment, the researchers noted that enough dietary Ca consumption (>800 mg/day) resulted in a decreased risk of glaucoma in both patients with and without hypertension, as well as in those with visual field defect (OR: 0.59). Specifically in non-hypertension patients without visual field defect, they found that potassium intake (4.7g/day recommended) may protect against glaucoma (OR: 0.41).

When they evaluated the association between glaucoma and Mg intake, the authors found that when intake reached the recommended level (400mg/day for males aged 19 to 30; 420mg/day for males >30; 310mg/day for females aged 19 to 30; 320mg/day for females >30), the risk of glaucoma decreased in hypertension patients (OR: 0.05).

While each nutrient brings a unique benefit to the table, the researchers advise that adequate intake of all three is necessary to hinder the development or progression of glaucoma. They concluded in their paper that "hypertension/non-hypertension persons aged <65 years old and with or without VF defect should all pay attention to getting enough dietary supplement of Ca, K and Mg."

Zhang Y, Zhao Z, Ma Q, Li K, Zhao X, Jia Z. Association between dietary calcium, potassium, and magnesium consumption and glaucoma. PLoS ONE.

MAKE CHILDREN'S SIGHT



YOUR FIGHT™.

Protect their vision from getting worse as they grow.

Meet MiSight® 1 day: the only dual purpose contact lens to both **correct vision and control myopia.**§1

Through early intervention, **you have the power** to protect their vision from worsening with the **first and only*** FDA approved† product proven to slow the progression of myopia in children, aged 8-12 at the initiation of treatment.§1 MiSight®, for the love of sight.

SEE MORE

CooperVision® | MiSight® 1 day for daily wear

* Only FDA approved soft contact lens designed for myopia control in the U.S.

† Indications for Use: MiSight® 1 day (omafilcon A) soft (hydrophilic) contact lenses for daily wear are indicated for the correction of myopic ametropia and for slowing the progression of myopia in children with non-diseased eyes, who at the initiation of treatment are 8-12 years of age and have a refraction of -0.75 to 4.00 diopters (spherical equivalent) with ≤ 0.75 diopters of astigmatism. The lens is to be discarded after each removal.

§ Compared to a single vision 1 day lens over a 3-year period.

1. Chamberlain P et al. A 3-year Randomized Clinical Trial of MiSight® Lenses for Myopia Control. Optom Vis Sci. 2019;96(8):556-567

FEATURES

REVIEW OF OPTOMETRY • Vol. 160, No. 11 • NOVEMBER 15, 2023

Could it be KC (KERATOCONUS)?

KC File #1: The Patient Who Corrects to 20/20

Mitch "Private Eye" Ibach OD, FAAO, Vance Thompson Vision

A 29-year-old patient came to our office for a LASIK consult because she was unhappy with fluctuating vision in her contact lenses. The patient had ocular allergies but had no other ocular diagnoses.

Her entering glasses prescription was a modest one and we were able to refract her to 20/20. However, the refraction in the right eye was our first clue that something was not quite right.

Not only is >2.00 D of refractive cylinder a warning signal for keratoconus, but the oblique axis is also unusual. About 90% of young corneas have with-the-rule (WTR) astigmatism.[1] The change in myopic spherical equivalent (SE) from baseline (the glasses prescription) was not what we would expect to see in an adult patient, either.

Refraction and exam findings

	RIGHT EYE	BCVA	LEFT EYE	BCVA
Lensometry	-0.50 -1.50 x31	20/30	-1.50 -0.50 x172	20/20-
Refraction at Phoropter	-0.75 -2.25 x34	20/20	-1.75 -0.75 x160	20/20+
Pachymetry	478 µm		483 µm	
Autokeratometry	45.5 / 47.50 x 112		44.9 / 46.75 x80	

Autokeratometry from her referring optometrist was on the steeper side of normal, and our pachymetry measurements showed that both eyes had borderline thin corneas. Upon further questioning, the patient recalled that her sister had keratoconus. Having a first-degree relative (a parent, sibling, or child) with keratoconus increases the risk of developing the disease by 15- to 67-fold.[2]

At this point, we have some risk factors, but not a clear diagnosis. A closer look at topography, tomography, and anterior segment OCT epithelial mapping provided further information to make a decisive diagnosis of progressive keratoconus in the right eye.

This case illustrates that patients who see 20/20 at the phoropter can still have keratoconus. At 29, our patient was at an age where there is greater risk of progression,[3] and her ocular allergies and family history elevate that risk. She was fortunate to be diagnosed and treated early in the course of her disease, while she was still correctible to 20/20. **Simply by following the KC clues that are hiding in plain sight, you can help patients like this one preserve their vision by referring them to a corneal specialist. If further testing confirms the patient has progressive KC, iLink® cross-linking could slow or halt its progression. Visit iDetectives.com to learn more.**

KC File #1: THE CLUES

- Large change in refraction from lensometer to phoropter
- High astigmatism (-2.25 D) with an oblique axis
- Borderline thin corneas (478/483 µm)
- Relatively steep auto Ks (47.5)

REFERENCES:
1. Kojima T, et al. *Am J Ophthalmol* 2020;215:127-34, **2.** Wang Y, et al. *Am J Med Genet* 2000;93(5):403-9. **3.** Ferdi AC, et al. *Ophthalmology* 2019;126(7):935-45.

#FollowTheClues

iDetective
Following the clues for early KC detection

DEPARTMENTS

REVIEW OF OPTOMETRY • NOVEMBER 15, 2023

VISIT US ON SOCIAL MEDIA

Facebook: revoptom
Twitter: revoptom
Instagram: revoptom
Threads: revoptom
LinkedIn: company/review-of-optometry

REVIEW OF OPTOMETRY (ISSN 0147-7633) IS PUBLISHED MONTHLY, 12 TIMES A YEAR BY JOBSON MEDICAL INFORMATION LLC/WebMD, 283-299 MARKET STREET, 2 GATEWAY CENTER, 4TH FLOOR, NEWARK, NJ 07102. PERIODICALS POSTAGE PAID AT NEWARK, NJ AND ADDITIONAL MAILING OFFICES. POSTMASTER: SEND ADDRESS CHANGES TO REVIEW OF OPTOMETRY, PO BOX 81, CONGERS, NY 10920-0081. SUBSCRIPTION PRICES: US: ONE YEAR $56; TWO YEARS $97, CANADA: ONE YEAR $88, TWO YEARS $160, INT'L: ONE YEAR $209, TWO YEARS $299. FOR SUBSCRIPTION INFORMATION CALL TOLL-FREE (877) 529-1746 (USA); OUTSIDE USA, CALL (845) 267-3065. OR EMAIL US AT REVOPTOMETRY@CAMBEYWEST.COM. PUBLICATIONS MAIL AGREEMENT NO: 40612608. CANADA RETURNS TO BE SENT TO BLEUCHIP INTERNATIONAL, P.O. BOX 25542, LONDON, ON N6C 6B2.

NOW AVAILABLE TO PRESCRIBE

Learn more at XDEMVYHCP.com

xdemvy™
(lotilaner ophthalmic solution) 0.25%

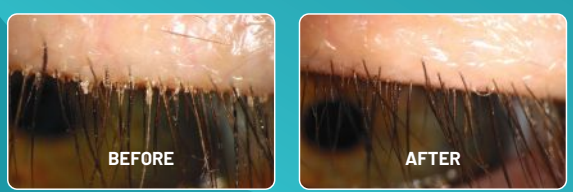
Might over mites

in just 6 weeks

1st & only

FDA-APPROVED TREATMENT FOR *DEMODEX* BLEPHARITIS (DB)

Real results



44% and 55% of patients taking XDEMVY in SATURN-1 (N=209) and SATURN-2 (N=193), respectively, achieved a significant improvement in their eyelids (reduction of collarettes to no more than 2 collarettes per upper lid) at Day 43 vs 7% (N=204) and 12% (N=200) of patients taking vehicle (P<0.01 in each trial).*

All images are of actual patients who participated in clinical trials for Tarsus Pharmaceuticals.

INDICATIONS AND USAGE

XDEMVY (lotilaner ophthalmic solution) 0.25% is indicated for the treatment of *Demodex* blepharitis.

IMPORTANT SAFETY INFORMATION:

WARNINGS AND PRECAUTIONS

Risk of Contamination: Do not allow the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to minimize contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

Use with Contact Lenses: XDEMVY contains potassium sorbate, which may discolor soft contact lenses. Contact lenses should be removed prior to instillation of XDEMVY and may be reinserted 15 minutes following its administration.

ADVERSE REACTIONS: The most common adverse reaction with XDEMVY was instillation site stinging and burning which was reported in 10% of patients. Other ocular adverse reactions reported in less than 2% of patients were chalazion/hordeolum and punctate keratitis.

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

Reference: XDEMVY [prescribing information]. Tarsus Pharmaceuticals, Inc; 2023.

*The safety and efficacy of XDEMVY for the treatment of DB were evaluated in a total of 833 patients (415 of whom received XDEMVY) in two 6-week, randomized, multicenter, double-masked, vehicle-controlled studies (SATURN-1 and SATURN-2). Patients were randomized to either XDEMVY or vehicle at a 1:1 ratio, dosed twice daily in each eye for 6 weeks. All patients enrolled were diagnosed with DB. The primary efficacy endpoint was defined as the proportion of patients with collarette reduction to no more than 2 collarettes per upper eyelid at Day 43 (SATURN-1: XDEMVY N=209, vehicle N=204, P<0.01; SATURN-2: XDEMVY N=193, vehicle N=200, P<0.01).

tarsus

XDEMVY™ (lotilaner ophthalmic solution) 0.25%, for topical ophthalmic use

BRIEF SUMMARY OF PRESCRIBING INFORMATION
Please see the XDEMVY™ package insert for full Prescribing Information.

INDICATIONS AND USAGE
XDEMVY is indicated for the treatment of *Demodex* blepharitis.

CONTRAINDICATIONS
None.

WARNINGS AND PRECAUTIONS
Risk of Contamination Do not allow the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to minimize contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

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

ADVERSE REACTIONS
Because clinical studies 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.

XDEMVY was evaluated in 833 patients with *Demodex* blepharitis in two randomized, double-masked, vehicle-controlled studies (Saturn-1 and Saturn-2) with 42 days of treatment. The most common ocular adverse reaction observed in controlled clinical studies with XDEMVY was instillation site stinging and burning which was reported in 10% of patients. Other ocular adverse reactions reported in less than 2% of patients were chalazion/hordeolum and punctate keratitis.

USE IN SPECIFIC POPULATIONS
Pregnancy: Risk Summary There are no available data on XDEMVY use in pregnant women to inform any drug associated risk; however, systemic exposure to lotilaner from ocular administration is low. In animal reproduction studies, lotilaner did not produce malformations at clinically relevant doses.

Data *Animal Data* In an oral embryofetal developmental study in pregnant rats dosed during organogenesis from gestation days 6-19, increased post-implantation loss, reduced fetal pup weight, and incomplete skeletal ossification were observed at 50 mg/kg/day (approximately 1390 times the recommended human ophthalmic dose (RHOD) on a body surface area basis) in the presence of maternal toxicity (i.e., decreased body weight and food consumption). A rare malformation of situs inversus of the thoracic and abdominal viscera occurred in 1 fetus from a pregnant rat receiving 50 mg/kg/day; whether this finding was treatment-related could not be excluded. No maternal or embryofetal toxicity was observed at 18 mg/kg/day (approximately 501 times the RHOD on a body surface area basis). In an oral embryofetal development study in pregnant rabbits dosed during organogenesis from gestation days 7-19, no embryofetal toxicity or teratogenic findings were observed at 20 mg/kg/day (approximately 580-times the RHOD on an AUC basis), even in the presence of maternal toxicity (i.e., decreased food consumption and body weight).

In an oral two-generation reproductive toxicity study, F0 male and female rats were administered lotilaner at doses up to 40 mg/kg/day for 10 weeks before pairing and during the 2-week pairing period (3 weeks for males). Dosing for F0 females continued through lactation day 22. F1 male and female rats were administered lotilaner at 1 and 5 mg/kg/day post-weaning from day 23 for 10 weeks before pairing and during the 2-week pairing period (3 weeks for males). Dosing for F1 parenteral females continued through lactation day 22. There were no clear adverse effects on the F1 generation, and a slightly lower mean body weight during lactation was noted for F2 pups at 5 mg/kg/day. The no observed adverse effect level (NOAEL) was determined to be 5 mg/kg/day (approximately 139 times the RHOD on a body surface area basis).

Lactation: Risk Summary There are no data on the presence of XDEMVY in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lotilaner following 6 weeks of topical ocular administration is low and is >99% plasma protein bound, thus it is not known whether measurable levels of lotilaner would be present in maternal milk following topical ocular administration. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for XDEMVY and any potential adverse effects on the breast-fed child from XDEMVY.

Pediatric Use: Safety and effectiveness in pediatric patients below the age of 18 years have not been established.

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

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis Long-term studies in animals have not been performed to evaluate the carcinogenic potential of lotilaner.

Mutagenesis Lotilaner was not genotoxic in the following assays: Ames assay for bacterial gene mutation, *in vitro* chromosomal aberration assay in cultured human peripheral blood lymphocytes, and *in vivo* rat micronucleus test.

Impairment of fertility In a two-generation study of reproductive performance in rats, F0 male and female rats were administered lotilaner at oral doses of 40 mg/kg/day for 80 days reduced to 20 mg/kg/day for 47-50 supplementary days. Reduced pregnancy rates and decreased implantation rates were observed in F0 females at doses 20 mg/kg/day) (approximately 556 times the RHOD on a body surface area basis), which were also associated with maternal toxicity (i.e., decreased body weight and food consumption). No effects on fertility were observed in F0 females at the dose of 5 mg/kg/day (approximately 139 times the MRHOD on a body surface area basis). No effects on fertility were observed in F0 males at the oral dose of 20 mg/kg/day (approximately 556 times the RHOD on a body surface area basis), and no effects on fertility were observed in F1 males and females at the oral dose of 5 mg/kg/day (approximately 139 times the RHOD on a body surface area basis).

PATIENT COUNSELING INFORMATION
Handling the Container Instruct patients to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to minimize contamination of the solution. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

When to Seek Physician Advice Advise patients that if they develop an intercurrent ocular condition (e.g., trauma or infection), have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice concerning the continued use of XDEMVY.

Use with Contact Lenses Advise patients that XDEMVY contains potassium sorbate, which may discolor soft contact lenses. Contact lenses should be removed prior to instillation of XDEMVY and may be reinserted 15 minutes following its administration.

Use with Other Ophthalmic Drugs Advise patients that if more than one topical ophthalmic drug is being used, the drugs should be administered at least 5 minutes between applications.

Missed Dose Advise patients that if one dose is missed, treatment should continue with the next dose.

RX only

US--2300345 9/23

REVIEW of OPTOMETRY

Founded 1891

Editorial Offices

19 Campus Blvd., Suite 101• Newtown Square, PA 19073

Jobson Medical Information/WebMD
283-299 Market Street, 2 Gateway Center, 4th Floor
Newark, NJ 07102

Subscription inquiries: (877) 529-1746
Continuing Education inquiries: (800) 825-4696

Printed in USA

BY JACK PERSICO
EDITOR-IN-CHIEF
OUTLOOK

Leaving New York

Vision Expo East's move to Orlando closes the curtain on a long run of prominence for the city in the optometric landscape.

It's not an exaggeration to say that optometry was invented in New York. Charles Prentice, the closest thing optometry has to a George Washington, was an influential—some would say infamous—practitioner from New York who, among other things, worked with Columbia University to begin the first university-affiliated optometric education curriculum. Prentice's friend and fellow New Yorker Andrew Cross wrote seminal texts on retinoscopy. Another friend, Frederick Boger, founded this very publication in New York in 1891, where it was published for many decades. Boger was vociferous in lobbying for the formation of a national organization, and worked with Prentice, Cross and Charles Lembke to establish what came to be known as American Optometric Association, which also operated out of New York for decades.

Countless other prominent doctors kept New York the epicenter of the optometry profession for at least another half century. Even as late as 1968, the city's cadre of influential optometrists held sufficient clout as to host a transformative meeting at LaGuardia airport wherein the power brokers of optometry decided to move the profession into the world of medical care and pharmaceutical prescribing.

In time, most of the big optometric institutions moved away from New York, lured to other locations for a variety of reasons, and the city lost its preeminence in the profession—or rather, New York became just one power center among many across America that helped optometry flex its collective muscles.

Sadly, another optometric institution is about to say farewell to the Big Apple, as the Vision Council recently announced that Vision Expo East will move to Orlando in 2025.

Legendary optometric writer and educator Irv Bennett launched a precursor to Vision Expo called OptiFair in 1978. It was an overnight sensation, drawing a crowd of 6,511 to the New York Hilton for that first meeting. OptiFair, and later Vision Expo East, created an early template for how to run a successful event that somehow managed to combine a high-minded educational conference with the wheeling and dealing of a retail trade show.

I don't begrudge the Vision Council for its decision. Clearly, they believe the new venue will be better equipped to host such a massive event than Manhattan's aging Jacob Javits Center, and the new city a bigger drawing card for ODs in the bustling Southeast than the prospect of a trip to chilly New York in mid-March. But I'll be one of many old-timers (my first Vision Expo East was in 1992) who'll feel a twinge of sadness next spring as the New York era draws to a close for the conference and, increasingly, the wider profession. I do wonder what will come of the retail and fashion side of things at VEE. Will those vendors and buyers follow the meeting south? Orlando is many things, but a fashion mecca it is not.

I guess the positive way to look at this move, and optometry's larger exodus from New York, is that the profession's success elsewhere validates its core concepts and business model. Optometry started as the province of a handful of eccentric "refracting opticians" in New York, who built a new profession that suited their aims and ideas. But the model they created works—everywhere. Even in Orlando. ■

BY MONTGOMERY VICKERS, OD

CHAIRSIDE

What's Your Policy?

If something happened with a patient but isn't written on their chart, it didn't happen.

My hobby over the past 43 years has been trying to figure out which is better: number one or two. Somebody needs to know, because so many patients have no idea. But, my profession is songwriting. Yes, I have an album on iTunes. It's been there since around 2008. It has not gone platinum, but I did sell four copies that I know of, so I'm on my way, thanks to my mom, kids and some dude from Milwaukee.

> **The problem with policies is this: As soon as you make what you think is a good policy, a better reason to change it suddenly appears.**

One of my songs—not on the album—is titled, "What's Your Policy?" This song has absolutely nothing to do with optometry, but in optometric practice, we spend a lot of time working on our policies, don't we? In fact, we may spend more time developing policies than on any single other part of our day when we are not griping on Facebook or X (what used to be known as Twitter).

A patient no-shows. What's your policy? Mine is to reschedule them on days we are closed.

A patient wants to "borrow" a couple pairs of contact lenses to hold him over until his next exam. What's your policy? I don't know… has he been seen within the past six years?

A staff member wants to take off every other Wednesday afternoon. What's your policy? If they're not gushing blood from their ears every other Wednesday afternoon, why?

It goes on and on. The problem with policies is this: As soon as you make what you think is a good policy, a better reason to change it suddenly appears. New policy? New reason it needs to change.

But, policies can help everyone in the office stay on the same page, in total agreement. In total agreement that you, the policymaker, are as dumb as stone.

So, we decide that the staff members should have a voice and your policy is that you will back them up when they have to, on the fly, adjust and amend some policy you gave them so the staffer can appear to be nice and fair, and give your time and materials away rather than explain to the patient what the "real" policy is, such as, "patients have to pay for stuff in this office."

Often, policies start to harden into impenetrable walls. My wife, Renee, who ran my office for over 38 years, finally convinced me that if something happens with a patient but is not written on their chart, it means that it did not happen after all. What if nobody bothers to scribble into the EHR the contact lenses we dispensed… you know, the ones they love, love, love, or perhaps the ones they hate, hate, hate?

Well, this means no matter what the doctor and patient may remember, that no contact lenses were dispensed at all. Don't believe me? Ask your lawyer. The patient could state that you dispensed two shiny new pennies for him to wear and that's why he's suing you for that big ol' central corneal scar. Prove you didn't.

So, I became very serious about putting every little thing on the chart.

Now, I do not own an optometric practice anymore. I am a mere junior associate, so what do I know, anyway?

But, shouldn't the policy be that the patient's final contact lens Rx is found on the their chart? Why should I have to rifle through digital "invoices" to see what contact lenses this gal is wearing when she comes in for her next appointment?

How about a policy that when you dispense something to a patient, such as sample drops or a trial contact lens, it states this was done on the chart?

Why not? Because that's never been the policy.

What's your policy? It shouldn't just be a song. ■

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

From the makers of the #1-prescribed dry eye brand in Europe*

Covering the spectrum of Dry Eye Relief

Over-the-counter iVIZIA® lubricant eye drops deliver a unique combination of immediate and long-lasting relief and ocular surface protection in a **preservative-free** formulation.

- Advanced formulation offers a combination of povidone (active), hyaluronic acid (HA), and trehalose
- HA and trehalose increased tear film thickness for up to 240 minutes
- Proprietary, **multi-dose bottle**

Chronic Dry Eye Patient Usage Study†:

Up to 8 hours of relief

as well as improved comfort during computer work, reading, and driving[1]

84%

of users reported iVIZIA worked better than their previous eye drops[1]

Recommend iVIZIA and request samples by visiting iVIZIA.com/ECP.

Scan here.

*Prescription market data, Dec. 2022 – S01K without cyclosporine.

†In a chronic dry eye patient usage study, participants from a variety of socioeconomic backgrounds answered questions about iVIZIA. There were 203 chronic dry eye patients, ranging from ages 28-80, who used their current eye drops before switching to iVIZIA for 30 days.[1]

‡To limit blurriness when using contact lenses, remove contacts, apply drops, then insert contacts.

Reference: 1. Data on file.

Made by Théa let's open our eyes | Distributed by Similasan® EVIDENCE-BASED EYE CARE

BY PAUL M. KARPECKI, OD
CHIEF CLINICAL EDITOR

Show Up for OSD

Recent FDA approvals make it easier to treat your patients.

Ocular surface disease (OSD) is right in front of us. Perhaps you have to express meibomian glands and have patients look down so you can scan their eyelids and instill fluorescein dye, but that's less complex than managing other ocular diseases, and new therapeutics have made the task even easier. Now is the time to "show up" to manage OSD patients and challenge yourself by taking your practice to another level.

New FDA Approvals

Here are recently developed therapeutic agents that target unmet OSD needs:

• ***Miebo*** (perfluorohexyloctane 100%, Bausch + Lomb). This is the first dry eye treatment that targets evaporation; it has been shown to inhibit evaporation four times more than healthy meibum can.[1] It works best when patients have MGD but are not completely lipid deficient—meaning, avoid the evaporative dry eye train wrecks with severe meibomian gland atrophy. Fortunately, these types are extremely rare, but Miebo requires some lipid secretions, even dysfunctional, to anchor the alkanes that make up a key part of the drug chemistry. Miebo was shown to create a monolayer barrier for up to six hours.[2]

Although listed as QID, most of my patients are experiencing impressive results, including corneal staining clearing, symptom resolution and improved vision with either BID or TID dosing. Miebo has almost no side effects except slight blur upon instillation (then super-clear vision minutes later) or patients stating they can't feel the drop upon instillation. This could be because there are no preservatives, as it's a single agent drop and each is only 11µL compared to the 30µL to 50µL typical for most drops.

> **Miebo is the first dry eye treatment that targets evaporation and has been shown to inhibit evaporation four times more than healthy meibum can.**

• ***Xdemvy*** (lotilaner 0.25%, Tarsus Pharmaceuticals). This is the first and only drug approved for *Demodex* blepharitis, a condition that is likely present in at least 20 million people, with few effective treatments available.[3] Patients suffering from itching, dry, gritty or red eyes are often treated with dry eye therapies when they actually had *Demodex* blepharitis, most likely due to doctors not having patients look down while at the slit lamp and scanning the upper eyelid margins for collarettes, which are composed of mite waste products and is a sign of *Demodex* blepharitis.

Xdemvy is dosed BID for six weeks. I've found complete resolution of collarettes in as little as one week by having patients instill the drop and then rub the excess liquid into their lashes and adnexa. But, six weeks of treatment is required because the life cycle of the mites is roughly 16 to 18 days and the mites and eggs will have another potential 18 days. The drop is generally comfortable, with less than 10% of patients in the clinical trials stating burning upon instillation, although I haven't had a patient express these symptoms.

• ***Vevye*** (0.1% cyclosporine A, Novaliq). As we've seen with Cequa (0.9%), higher concentrations of cyclosporine with novel vehicles do much better. The unique vehicle for Vevye is another semi-fluorinated alkane, perfluorobutylpentane. While this doesn't have the extended duration on the ocular surface as Miebo, it will increase bioavailability and comfort, and is also water- and preservative-free.

Don't Forget Glaucoma Patients

As much as we think patients are compliant with their meds, prostaglandin analogs and preservatives are toxic and inflammatory and some patients with OSD stop using their glaucoma drug due to pain and discomfort. New products like Iyuzeh, a preservative-free latanoprost, or Zioptan (tafluprost) are needed. Other options include selective laser trabeculoplasty as a first-line therapy and the most effective PGAs, like Vyzulta (latanoprostene bunod), which can minimize the need for two medications. Preservative-free Simple Drops from Imprimis Pharmaceuticals offer a triple drop (timolol, bromonidine, dorzolamide) and a quad drop (timolol, brimonidine, dorzolamide, latanoprost), both of which allow patients to avoid multiple meds and preservatives.

It's an exciting time for OSD management, and these new innovations have made it well worth showing up! ■

1. Krösser S, Spencer E, Grillenberger R, et al. Ocular and systemic distribution of ^{14}-C perfluorohexyloctane following topical ocular administration to rabbits. Invest Ophthalmol Vis Sci. 2018;59:2656.

2. Sheppard JD, Nichols KK. Dry eye disease associated with meibomian gland dysfunction: focus on tear film characteristics and the therapeutic landscape. Ophthalmol Ther. 2023;12(3):1397-418.

3. Schaumberg DA, Nicholas JJ, Papas EB, et al. The international workshop on MGD: report of the subcommittee on the epidemiology of and associated risk factors for MGD. Invest Ophthalmol Vis Sci. 2011;52(4):1994-2005.

About Dr. Karpecki

Dr. Karpecki is the director of Cornea and External Disease for Kentucky Eye Institute and an associate professor at KYCO. He is the Chief Clinical Editor for Review of Optometry and chair of the New Technologies & Treatments conferences. A fixture in optometric clinical education, he consults for a wide array of ophthalmic clients, including ones discussed in this article. Dr. Karpecki's full disclosure list can be found in the online version of this article at www.reviewofoptometry.com.

iyuzeh™

(latanoprost ophthalmic solution) 0.005%

Transform how you lower IOP.

POWER WITHOUT PRESERVATIVES.

We owe it to our patients with elevated intraocular pressure, with open-angle glaucoma or ocular hypertension to provide a new evidence-based approach. It is an extremely exciting time to prescribe IYUZEH™ for my patients.

Monique M. Barbour, MD, MHA, FAAO

INDICATIONS AND USAGE

IYUZEH™ is a prostaglandin analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Known hypersensitivity to latanoprost or any other ingredients in this product.

WARNINGS AND PRECAUTIONS

Pigmentation: Topical latanoprost ophthalmic products, including IYUZEH™ have been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as latanoprost 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 latanoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

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

Eyelash Changes: Latanoprost ophthalmic products, including IYUZEH™ may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation: IYUZEH™ 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 because inflammation may be exacerbated.

Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with latanoprost ophthalmic products, including IYUZEH™. IYUZEH™ 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.

Herpetic Keratitis: Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. IYUZEH™ should be used with caution in patients with a history of herpetic keratitis. IYUZEH™ should be avoided in cases of active herpes simplex keratitis because inflammation may be exacerbated.

Contact Lens Use: Contact lenses should be removed prior to the administration of IYUZEH™ and may be reinserted 15 minutes after administration.

ADVERSE REACTIONS

The following adverse reactions have been reported with the use of topical latanoprost products: iris pigmentation changes, eyelid skin darkening, eyelash changes (increased length, thickness, pigmentation, and number of lashes), intraocular inflammation (iritis/uveitis), and macular edema, including cystoid macular edema.

DRUG INTERACTIONS

The combined use of two or more prostaglandins, or prostaglandin analogs including IYUZEH™ is not recommended. It has been shown that administration of these prostaglandin drug products more than once daily may decrease the IOP lowering effect or cause paradoxical elevations in IOP.

Please see full Prescribing Information at www.iyuzeh.com and Brief Summary on the next page.

Explore the power of preservative-free latanoprost at iyuzeh.com

Théa
let's open our eyes

iyuzeh™

(latanoprost ophthalmic solution) 0.005%

HIGHLIGHTS OF PRESCRIBING INFORMATION

This brief summary does not include all the information needed to use IYUZEH safely and effectively. See full prescribing information for IYUZEH.

Initial U.S. Approval: 2022

----------INDICATIONS AND USAGE----------

IYUZEH is a prostaglandin F2α analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

----------CONTRAINDICATIONS----------

Known hypersensitivity to latanoprost or any other ingredients in this product.

----------WARNINGS AND PRECAUTIONS----------

Pigmentation: Topical latanoprost ophthalmic products, including IYUZEH have been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as latanoprost 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 latanoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

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

Eyelash Changes: Latanoprost ophthalmic products, including IYUZEH may gradually change eyelashes and vellus hair in the treated eye; these changes include increased length, thickness, pigmentation, the number of lashes or hairs, and misdirected growth of eyelashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation: IYUZEH 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 because inflammation may be exacerbated.

Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with latanoprost ophthalmic products, including IYUZEH. IYUZEH should be used with caution in aphakic patients, pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Herpetic Keratitis: Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. IYUZEH should be used with caution in patients with a history of herpetic keratitis and should be avoided in cases of active herpes simplex keratitis because inflammation may be exacerbated.

Contact Lens Use: Contact lenses should be removed prior to the administration of IYUZEH and may be reinserted 15 minutes after administration.

----------ADVERSE REACTIONS----------

The following adverse reactions have been reported with the use of topical latanoprost products and are discussed in greater detail in the prescribing information:

- Iris pigmentation changes
- Eyelid skin darkening
- Eyelash changes (increased length, thickness, pigmentation, and number of lashes)
- Intraocular inflammation (iritis/uveitis)
- Macular edema, including cystoid macular edema

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.

In the two clinical trials conducted with IYUZEH (latanoprost ophthalmic solution) 0.005% comparing it to XALATAN the preserved 0.005% latanoprost reference product, the most frequently reported ocular adverse reactions were conjunctival hyperemia and eye irritation (Table 1).

Table 1. Adverse Reactions

	Adverse Reactions [n (%)]	
Symptom/Finding	**IYUZEH (n=378)**	**XALATAN (n=358)**
Conjunctival hyperemia	129 (34)	133 (37)
Eye irritation	72 (19)	112 (31)
Eye pruritus	57 (15)	58 (16)
Abnormal sensation in eyes	51 (14)	52 (15)
Foreign body sensation in eyes	44 (12)	36 (10)
Vision blurred	28 (7)	30 (8)
Lacrimation increased	19 (5)	14 (4)
Photophobia	13 (3)	17 (5)

----------POSTMARKETING EXPERIENCE----------

The following adverse reactions have been identified during post-approval use of topical latanoprost products. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to ophthalmic latanoprost products, or a combination of these factors, include:

- Nervous System Disorders: Dizziness; headache; toxic epidermal necrolysis
- Eye Disorders: Eyelash and vellus hair changes of the eyelid (increased length, thickness, pigmentation, and number of eyelashes); keratitis; corneal edema and erosions; intraocular inflammation (iritis/uveitis); macular edema, including cystoid macular edema; trichiasis; periorbital and lid changes resulting in deepening of the eyelid sulcus; iris cyst; eyelid skin darkening; localized skin reaction on the eyelids; conjunctivitis; pseudopemphigoid of the ocular conjunctiva.
- Respiratory, Thoracic and Mediastinal Disorders: Asthma and exacerbation of asthma; dyspnea
- Skin and Subcutaneous Tissue Disorders: Pruritis
- Infections and Infestations: Herpes keratitis
- Cardiac Disorders: Angina; palpitations; angina unstable
- General Disorders and Administration Site Conditions: Chest pain

----------DRUG INTERACTIONS----------

The combined use of two or more prostaglandins, or prostaglandin analogs including IYUZEH is not recommended, and administration of these prostaglandin drug products more than once daily may decrease the IOP lowering effect or cause paradoxical IOP elevations.

----------USE IN SPECIFIC POPULATIONS----------

Pregnancy: There are no adequate and well-controlled studies of IYUZEH administration in pregnant women to inform drug-associated risks.

Lactation: It is not known whether this drug or its metabolites are excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when IYUZEH is administered to a nursing woman. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IYUZEH and any potential adverse effects on the breastfed child from IYUZEH.

Pediatric Use: The safety and effectiveness of IYUZEH have not been established in pediatric patients.

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

----------OVERDOSAGE----------

Intravenous infusion of up to 3 mcg/kg of latanoprost in healthy volunteers produced mean plasma concentrations 200 times higher than during clinical treatment with latanoprost ophthalmic solution and no adverse reactions were observed. IV dosages of 5.5 to 10 mcg/kg caused abdominal pain, dizziness, fatigue, hot flushes, nausea, and sweating.

----------HANDLING THE CONTAINER----------

IYUZEH is a sterile solution that does not contain a preservative supplied in a single-dose container. The solution from one individual container is to be used immediately after opening for administration to one or both eyes. Since sterility cannot be maintained after the individual container is opened, the remaining contents should be discarded immediately after administration. Open a new single-dose container every time you use IYUZEH.

Manufactured for: Thea Pharma Inc. Waltham, MA.

U.S. Patent N°. 8,637,054.
Revised: 04/2023

A Nose for News

An exam of the adnexa and face can help identify possible tumors.

Q A patient presented for a cataract evaluation, but the most glaring finding was a large lesion on his nose. How do I approach this?

A "A few questions come to mind when a patient has a lesion on their face," says Blair Lonsberry, OD, professor of optometry at Pacific University College of Optometry. "When did it appear? Location? Is it pigmented? Has it changed recently? Ulceration? Race of the patient? Age of the patient?"

This patient's race (Caucasian), age (over 60) and location (sun-exposed skin) would lead one to think of a basal cell carcinoma (BCC) or squamous cell carcinoma (SCC). The most frequent (over 75%) skin malignancy in humans is BCC, which arises from stem cells associated with hair follicles, and chronic sun exposure is the most important factor in their development.

"The average lifetime risk for Caucasian individuals to develop BCC is approximately 30%," Dr. Lonsberry says. "The typical patient demographic is fair-skinned individuals, typically older (peak incidence is at 80 years old), and the lesions most commonly arise on the forehead, top of the ears, neck and shoulders (sun-exposed areas)."

Skin-deep Foes

BCC most commonly presents as a slow-growing, skin-colored nodule with a pearly, shiny appearance. "Blood vessels are typically noted 'feeding' or visible on the tumor surface, with larger tumors showing central ulceration," Dr. Lonsberry notes. "The central ulceration happens as the tumor increases in size and the supportive feeder blood vessels supply the active growing tumor on the periphery. With no 'normal' blood vessels feeding the central portion of the tumor, it begins to ulcerate."

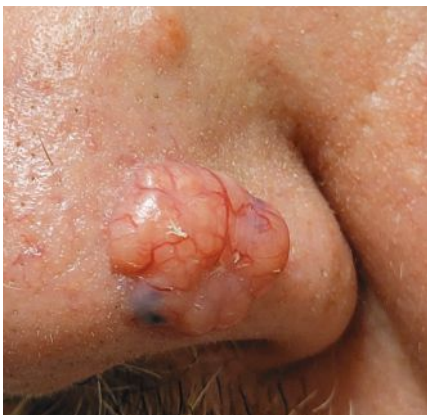


Fig. 1. SCC discovered during outine exam.

The classic BCC presentation is a tumor with "pearly borders with ulceration in the middle." Metastasis is rare (<1% of cases), but it can progress to large, locally advanced and often deeply infiltrating tumors if not detected early, or if mismanaged or neglected.[1,2] This lesion (*Figure 1*) doesn't have the typical presentation but rather a thickened (hyperkeratotic), plaque-like appearance with telangiectatic vessels over the top.

Squamous cell carcinoma is the second-most common skin malignancy after BCC. "SCC most commonly appears after the age of 50 in areas of past sun exposure and typically occurs in light-skinned and light-eyed males who have a history of UV solar radiation exposure," Dr. Lonsberry says. "It typically has a precursor lesion called actinic or solar keratosis, which then can exhibit tumor progression and has the potential to metastasize in the body."

The most common areas for SCC are the face, nose, neck, bald scalp, extensor forearms, dorsal hands and shins. The typical presentation is a hyperkeratotic plaque with color varying from flesh-toned to erythematous with variable degrees of scale, crusting and ulceration. Another common finding is telangiectasias with or without active bleeding.[3,4]

Take a Sample

Conclusive diagnosis requires a biopsy with histopathology to determine the type of cells present as well as the staging and surgical borders. The most common surgical procedure for both BCC and SCC is Mohs micrographic surgery or resection with peripheral and deep exhaustive margin assessment. Mohs is recommended to achieve local control for high-risk and very-high-risk cutaneous squamous-cell carcinoma with very low rates of local recurrence.[1,4]

Our patient, who had never seen a dermatologist, was encouraged to see one immediately—and we booked it for him. Biopsy confirmed SCC. A Mohs procedure was scheduled. During the full-body exam, malignant melanoma was also found on his back, the detection of which could potentially save his life.

"Do not ignore non-ocular lesions on the face and other exposed skin," Dr. Lonsberry advises. "We have the tools to look closely at skin abnormalities in the normal course of our eye exams." Don't leave appointments to chance, he advises. Make the appointments for them! ■

1. Fagan J, Brooks J, Ramsey ML. Basal cell cancer. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. www.ncbi.nlm.nih.gov/books/NBK470301/. Updated April 14, 2023. Accessed September 22, 2023.

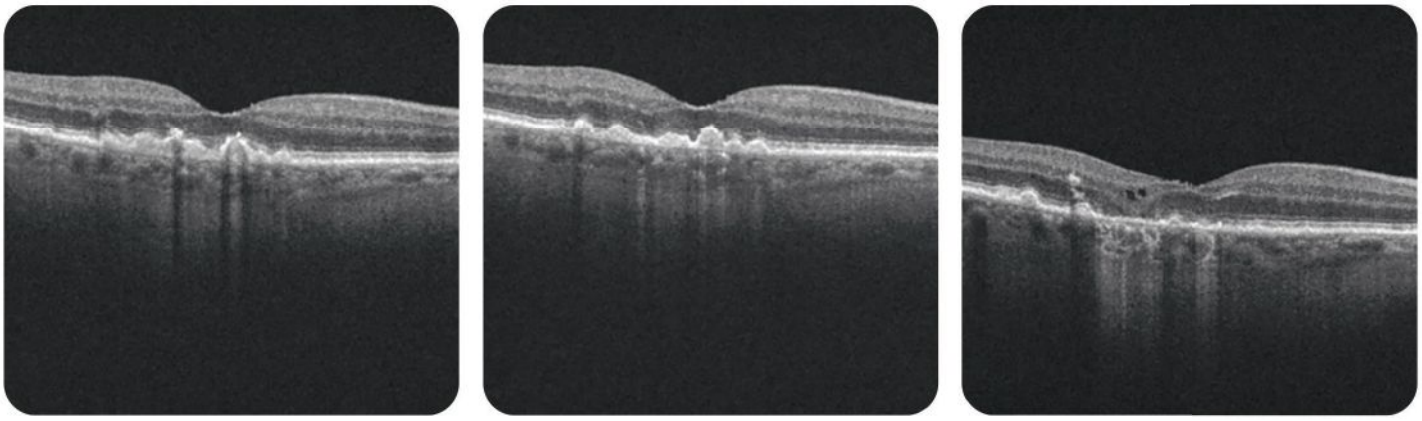
2. Peris K, Fargnoli MC, Kaufmann R, et al. European consensus-based interdisciplinary guideline for diagnosis and treatment of basal cell carcinoma–update 2023. Eur J Cancer. 2023;192:113254.

3. Howell JY, Ramsey ML. Squamous cell skin cancer. [In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. www.ncbi.nlm.nih.gov/books/NBK441939/. Updated July 31, 2023. Accessed September 22, 2023.

4. Wysong A. Squamous-cell carcinoma of the skin. N Engl J Med. 2023;388(24):2262-73.

About Dr. Ajamian **Dr. Ajamian** is board certified by the American Board of Optometry and serves as Center Director of Omni Eye Services of Atlanta. He is vice president of the Georgia State Board of Optometry and general CE chairman of SECO International. He has no financial interests to disclose.

GEOGRAPHIC ATROPHY (GA) CAN PROGRESS FASTER THAN YOU THINK[1]



Baseline **Month 3** **Month 6**

1. Boyer D, Schmidt-Erfurth U, van Lookeren Campagne M, et al. The pathophysiology of geographic atrophy secondary to age-related macular degeneration and the complement pathway as a therapeutic target. *Retina*. 2017;37(5);819-835.

INDICATION

IZERVAY™ (avacincaptad pegol intravitreal solution) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD)

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

IZERVAY is contraindicated in patients with ocular or periocular infections and in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments

Intravitreal injections, including those with IZERVAY, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.

EVERY MONTH MATTERS WHEN TREATING GA

iZERVAY™
(avacincaptad pegol intravitreal solution) 2 mg

Learn more at IZERVAYecp.com

Neovascular AMD

In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

Increase in Intraocular Pressure

Transient increases in intraocular pressure (IOP) may occur after any intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed appropriately.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥5%) reported in patients receiving IZERVAY were conjunctival hemorrhage, increased IOP, blurred vision, and neovascular agerelated macular degeneration.

Please see full Prescribing Information for more information.

IVERIC BIO
An Astellas Company

IZERVAY™ (avacincaptad pegol intravitreal solution)
Rx only

Brief Summary: This information is not comprehensive. Visit IZERVAYecp.com to obtain the FDA-approved product labeling or call 609-474-6755.

1 INDICATIONS AND USAGE

IZERVAY is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

2 DOSAGE AND ADMINISTRATION

2.1 General Dosing Information

IZERVAY must be administered by a qualifed physician.

2.2 Recommended Dosage

The recommended dose for IZERVAY is 2 mg (0.1 mL of 20 mg/mL solution) administered by intravitreal injection to each affected eye once monthly (approximately every 28 ± 7 days) for up to 12 months.

2.4 Injection Procedure

Only 0.1 mL (2 mg) should be administered to deliver a single dose. Any excess volume should be disposed.

Prior to the intravitreal injection, patients should be monitored for elevated intraocular pressure (IOP) using tonometry. If necessary, ocular hypotensive medication can be given to lower the IOP.

The intravitreal injection procedure must be carried out under controlled aseptic conditions, which includes the use of surgical hand disinfection, sterile gloves, a sterile drape, and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad-spectrum topical microbicide should be given prior to the injection.

Inject slowly until the rubber stopper reaches the end of the syringe to deliver the volume of 0.1 mL. Confrm delivery of the full dose by checking that the rubber stopper has reached the end of the syringe barrel.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure (IOP). Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry.

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis (e.g., eye pain, redness of the eye, photophobia, blurring of vision) without delay.

Each vial and syringe should only be used for the treatment of a single eye. If the contralateral eye requires treatment, a new vial and syringe should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, filter needle, and injection needle should be changed before IZERVAY is administered to the other eye. Repeat the same procedure steps as above.

Any unused medicinal product or waste material should be disposed of in accordance with local regulations.

3 DOSAGE FORMS AND STRENGTHS

Intravitreal solution: 20 mg/mL clear to slightly opalescent, colorless to slightly yellow solution in a single-dose vial.

4 CONTRAINDICATIONS

4.1 Ocular or Periocular Infections

IZERVAY is contraindicated in patients with ocular or periocular infections.

4.2 Active Intraocular Inflammation

IZERVAY is contraindicated in patients with active intraocular inflammation.

5 WARNINGS AND PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments

Intravitreal injections may be associated with endophthalmitis and retinal detachments. Proper aseptic injection techniques must always be used when administering IZERVAY in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay, to permit prompt and appropriate management.

5.2 Neovascular AMD

In clinical trials, use of IZERVAY was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (7% when administered monthly and 4% in the sham group) by Month 12. Patients receiving IZERVAY should be monitored for signs of neovascular AMD.

5.3 Increase in Intraocular Pressure

Transient increases in intraocular pressure (IOP) have been observed after an intravitreal injection, including with IZERVAY. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

6 ADVERSE REACTIONS

The following potentially serious adverse reactions are described elsewhere in the labeling:

- Ocular and periocular infections
- Active intraocular inflammation
- Endophthalmitis and retinal detachments
- Neovascular AMD
- Increase in intraocular pressure

6.1 Clinical Trials Experience

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

The safety of avacincaptad pegol was evaluated in 733 patients with AMD in two sham-controlled studies (GATHER1 and GATHER2). Of these patients, 292 were treated with intravitreal IZERVAY 2 mg (0.1 mL of 20 mg/mL solution). Three hundred thirty-two (332) patients were assigned to sham.

Adverse reactions reported in ≥2% of patients who received treatment with IZERVAY pooled across GATHER1 and GATHER2, are listed below in Table 1.

Table 1: Common Ocular Adverse Reactions (≥2%) and greater than Sham in Study Eye

Adverse Drug Reactions	IZERVAY N = 292	Sham N = 332
Conjunctival hemmorhage	13%	9%
Increased IOP	9%	1%
Choroidal neovascularization	7%	4%
Blurred vision*	8%	5%
Eye pain	4%	3%
Vitreous floaters	2%	<1%
Blepharitis	2%	<1%

* Blurred vision includes visual impairement, vision blurred, visual acuity reduced, visual acuity reduced transiently.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no adequate and well-controlled studies of IZERVAY administration in pregnant women. The use of IZERVAY may be considered following an assessment of the risks and benefits.

Administration of avacincaptad pegol to pregnant rats and rabbits throughout the period of organogenesis resulted in no evidence of adverse effects to the fetus or pregnant female at intravenous (IV) doses 5.1 times and 3.2 times the human exposure (based on AUC) at the maximum recommended human dose (MRHD) of 2 mg once monthly, respectively.

In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15%-20%, respectively.

Animal Data

An embryo fetal developmental toxicity study was conducted with pregnant rats. Pregnant rats received daily intravenous (IV) injections of avacincaptad pegol from day 6 to day 17 of gestation at 0.1, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. An increase in the incidence of a non-adverse skeletal variation, described as short thoracolumbar (ossification site without distal cartilage) supernumerary ribs, was observed at all doses evaluated. The clinical relevance of this finding is unknown. Plasma exposures at the high dose were 5.1 times the MRHD, based on Area Under the Curve (AUC).

An embryo fetal developmental toxicity study was conducted with pregnant rabbits. Pregnant rabbits received daily IV injections of avacincaptad pegol from day 7 to day 19 of gestation at 0.12, 0.4, 1.2 mg/kg/day. No maternal or embryofetal adverse effects were observed at any dose evaluated. Plasma exposure in pregnant rabbits at the highest dose of 1.2 mg/kg/day was 3.2 times the human exposure at the MRHD, based on AUC.

8.2 Lactation

There is no information regarding the presence of avacincaptad pegol in human milk, the effects of the drug on the breastfed infant or on milk production.

The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for IZERVAY and any potential adverse effects on the breastfed infant from IZERVAY.

8.4 Pediatric Use

Safety and effectiveness of IZERVAY in pediatric patients have not been established.

8.5 Geriatric Use

Of the total number of patients who received IZERVAY in the two clinical trials, 90% (263/292) were ≥65 years and 61% (178/292) were ≥75 years of age. No significant differences in efficacy or safety of avacincaptad pegol were seen with increasing age in these studies. No dose adjustment is required in patients 65 years and above.

17 PATIENT COUNSELING INFORMATION

Advise patients that following IZERVAY administration, patients are at risk of developing neovascular AMD, endophthalmitis, elevated intraocular pressure and retinal detachments. If the eye becomes red, sensitive to light, painful, or if a patient develops a change in vision, instruct the patient to seek immediate care from an ophthalmologist.

Patients may experience temporary visual disturbances and blurring after an intravitreal injection with IZERVAY and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

Manufactured by:
IVERIC bio, Inc., An Astellas Company. Parsippany, NJ 07054

BY BISANT A. LABIB, OD

Elastin Expansion

Differentiating secondary glaucoma types like pseudoexfoliative syndrome is crucial in providing proper care.

Whenever encountering glaucoma in practice, we immediately strive to employ an effective treatment regimen to preserve visual function. This is a critical and necessary goal, but, as primary care practitioners, there is often more to the story. Determining the cause of glaucoma, for example, may alter your overall management approach. Specifically, secondary glaucomas such as pseudoexfoliative are important to distinguish from other forms because it further requires systemic evaluation. To understand why, we must visit the pathogenesis of this systemic syndrome.

Genetic Considerations

Pseudoexfoliative syndrome (PEX) is a systemic disorder that manifests primarily in the eye, particularly in structures of the anterior segment. It is distinct from true exfoliation, which is a result of infrared damage affecting the anterior lens capsule. One well-established link for the development of PEX is the LOXL-1 gene at locus 15q22. This gene codes specifically for elastic fiber constituents of the extracellular matrix.[1]

To understand the impact of this alteration, we have to revisit the function of elastic fibers. Elastin is an extracellular matrix connective tissue protein responsible for the elasticity and recoil of various structures and organs throughout the body. Included in its effects are large arteries, the heart, pulmonary structures, skin and eyes. Under normal and healthy conditions, this complex structure slowly degrades over time, with a half-life of 70 years due to its intricate network of crosslinked components. Tropoelastin is a soluble precursor for elastic fibers, responsible for promoting the attachment and migration of various molecules such as fibroblasts, endothelial cells and others. It is the most elastic protein molecule, with the ability to stretch eight times its original length, and is bridged and crosslinked by the enzyme lysyl oxidase (LOX) to form a mature fiber. This explains the relationship between extracellular matrix elastin and tropoelastin as well as the role of LOX—all of which are mechanisms implicated in the pathophysiology of PEX.[2]

Elastin is abundant throughout the body in elastic structures. This includes, but is not limited to, the aorta and major blood vessels such as large arteries, the lungs, elastic ligaments, tendons, the skin, liver and eyes.[2] As such, PEX is not an ocular condition but a systemic one. However, it does predominantly affect the structures of the eye and can be diagnosed through an ocular examination. As mentioned, this is likely due to elastic fibers being integral in maintenance of ocular structures. In fact, elastin is present throughout many ocular structures, such as the conjunctiva, muscle tendons, sclera, choroid and meninges. Most importantly, it is densest in the sclera surrounding the peripapillary optic nerve head. One can surmise the relationship between PEX and glaucoma from this anatomic information alone.[3]

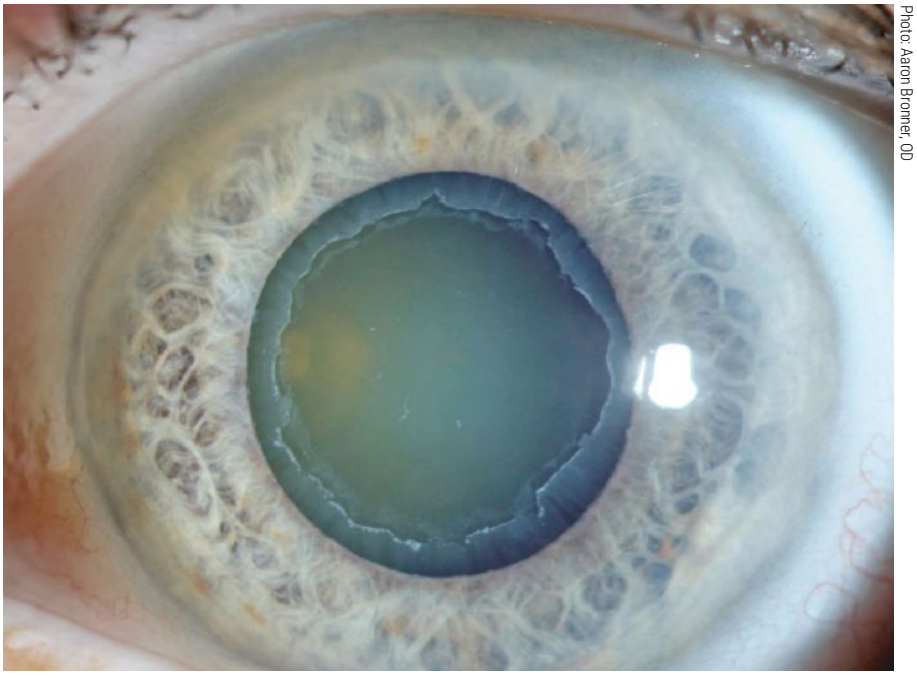


Photo: Aaron Bronner, OD

PEX can cause notable effects to the cornea and iris.

About Dr. Labib

Dr. Labib graduated from Pennsylvania College of Optometry, where she now works as an associate professor. She completed her residency in primary care/ocular disease and is a fellow of the American Academy of Optometry and a diplomate in the Comprehensive Eye Care section. She has no financial interests to disclose.

TABLE 1. SUMMARY OF CLINICAL FINDINGS ASSOCIATED WITH PEX

Anterior Segment Structure	Clinical Manifestation of PEX
Lens	· Two rings on the anterior capsule separated by a clear zone · Phacodonesis or dislocation from weakened zonules
Angle	· More pigmented trabecular meshwork · Sampaolesi's line
Cornea	· Endothelial deposits · Endothelial cell dysfunction · Increased central corneal thickness
IOP	· Raised IOP · Increased IOP post-dilation due to pigment liberation
Optic nerve	· Glaucomatous optic neuropathy due to raised IOP and weakened elastin surrounding the peripapillary sclera

Clinical Ramifications

A defect in the elastin and lysyl oxidase relationship yields the production of aggregated protein deposits, or exfoliative material, in tissues that synthesize elastin fibers. As this relates to the eye, these depositions accumulate in the ciliary body, anterior lens capsule, iris and trabecular meshwork. All these areas are necessary for aqueous production, circulation and drainage to prevent an increase in intraocular pressure (IOP) and subsequent development of glaucoma. Clinical findings on ocular examination may include the following structures:

• ***Lens.*** Easily the most common diagnostic feature is the deposition of material on the anterior surface of the lens, comprising three zones. The first is a central ring corresponding to the diameter of the patient's normal pupil size. The outermost ring is a granular, layered peripheral margin. Separating these two areas is a third clear zone. The lens can also become weakened over time from damage to the zonules, called phacodonesis. This not only can cause lens dislocation but also can complicate cataract surgery techniques.

• ***Iris.*** Findings of this structure can overlap with a different type of secondary glaucoma—pigmentary dispersion glaucoma (PDS). In PEX, exfoliative material can accumulate around the pupillary border. There is also loss of pigment around the sphincter, leading to iris transillumination defects. Iris blood vessels are also narrowed to a greater degree or destroyed.

> **Studies have identified a correlation between patients who have ocular manifestations of PEX, including glaucoma, and a positive association with hypertension, myocardial infarction, stroke, angina and aortic aneurysms.**

• ***Trabecular meshwork.*** Also overlapping with PDS, there is often increased pigmentation of the trabecular meshwork with PEX, as well as pigmented Schwalbe or Sampaolesi line.

• ***Cornea.*** Evidence of PEX can also be found on the cornea in the form of exfoliative buildup on the central corneal endothelium. The endothelium also often exhibits cellular dysfunction because of cellular loss, leading to an increase in corneal thickness.

• ***IOP.*** The marked increase in IOP is what makes PEX patients significantly more susceptible to developing glaucoma. The material deposited into the trabecular meshwork prohibits the free flow of aqueous. Oftentimes, there will be an increase in post-dilation IOP due to additional pigment liberation from dilation.[1,3,4]

Holistic Care

The astute clinician can readily recognize PEX and knows to look for evidence of it, either treating the patient for glaucoma or to monitor them for their increased susceptibility in its development upon PEX manifestation. Keep in mind, though, that the eye is not the only site of pathology, as elastic fibers are present at various sites throughout the body. Several well-known studies have identified a correlation between patients who have ocular manifestations of PEX, including glaucoma, and a positive association with hypertension, myocardial infarction, stroke, angina and aortic aneurysms. Elevated homocysteine levels, which are implicated in cardiovascular diseases, is another potential correlation. The vast number of elastic fibers in the structures of the heart is key in substantiating these claims.[4]

Though the mechanism of PEX is extremely complex and multifaceted, this oversimplification of its pathophysiology is helpful in being able to appropriately manage your patient. Because of PEX's primarily ocular manifestations, the eyecare provider is key in diagnosing the syndrome, monitoring and treating the ocular sequelae and in corresponding with the patient's primary care and other providers to manage systemic risks. ■

1. Ariga M, Nivean M, Utkarsha P. Pseudoexfoliation syndrome. J Curr Glaucoma Pract. 2013;7(3):118-20.

2. Wang K, Meng X, Guo Z. Elastin structure, synthesis, regulatory mechanism and relationship with cardiovascular diseases. Front Cell Dev Biol. 2021;9:596702.

3. Gelman S, Cone FE, Pease ME, et al. The presence and distribution of elastin in the posterior and retrobulbar regions of the mouse eye. Exp Eye Res. 2010;90(2):210-5.

4. Vardhan AS, Haripriya A, Ratukondla B, et al. Association of pseudoexfoliation with systemic vascular diseases in a South Indian population. JAMA Ophthalmol. 2017;135(4):348-54.

IZERVAY™
(avacincaptad pegol intravitreal solution) 2 mg

Join us for a collaborative discussion on how IZERVAY™ may benefit your patients

Webinar Event

December 12, 2023

For your convenience, this program will be broadcast twice

6:00 PM - 7:00 PM ET (60 minutes)

9:00 PM - 10:00 PM ET (60 minutes)

You will learn:

- How to detect the imaging biomarkers
- Efficacy and safety for IZERVAY
- Treatment considerations for patients

Presenters

Diana Shechtman OD, FAAO
Consultative Optometrist
Eye Centers of South Florida
Miami, FL

Priya Vakharia MD
Retina Specialist
Retina Vitreous Associates of Florida
Tampa, FL

REGISTER NOW

Scan this QR code to register
or visit https://mngh.co/AEB47D

This presentation is from Iveric Bio, an Astellas Company, and Drs. Shechtman and Vakharia are being compensated by Iveric for their time. Continuing medical education credits are not available in connection with this program.

IVERIC bio, Inc., An Astellas Company
8 Campus Drive Parsippany-Troy Hills, NJ 07054

REVIEW of OPTOMETRY | IVERIC BIO An Astellas Company

BY JEROME SHERMAN, OD, AND SHERRY BASS, OD

YOU BE THE JUDGE

Diagnose Amblyopia with Caution

Reduced monocular vision without an amblyogenic factor should not be ignored.

Amblyopia is the most common reason for vision loss in kids and reported at 1% to 5% in various population studies.[1,2] Most clinicians and experts consider amblyopia as monocular reduction of best-corrected visual acuity in the absence of any observable pathology. The two most common amblyogenic factors are constant unilateral strabismus and/or significant anisometropia. Without such an amblyogenic factor, the clinician must consider a series of less than obvious disorders such as subtle corneal involvement, a maculopathy not easily observable with ophthalmoscopy and, most problematic of all, an optic nerve or visual pathway disorder that could result in blindness or even death.

Case

A 13-year-old Caucasian girl presented with her mother for her first eye exam complaining of blurred vision in her right eye. Her ocular and general health history were unremarkable, and no family history of unusual visual problems were reported to the technician who obtained the history. Unaided visual acuity (VA) was 20/40 OD and 20/20 OS. The external exam performed by the optometrist—pupils, color vision, motility, cover test, confrontation visual fields—were recorded as normal. A refraction yielded no significant refractive error and pinhole did not improve the VA in the right eye. Goldmann IOPs were measured as normal, and a dilated fundus exam (DFE) was unremarkable. Routine fundus photos were taken of the posterior pole OU.

The doctor diagnosed amblyopia and suggested no intervention such as glasses, patching or eye exercises. According to the patient and her mother, the doctor told her she would likely "grow out of" the lazy-eye condition and recommended a follow-up in one year.

The teenager went on with her busy schedule—school, sports, friends and a boyfriend—without any noticeable change. She had an occasional headache, which was relieved by Tylenol (acetaminophen, Johnson & Johnson). However 50 weeks later, she experienced flashing lights in class in her right eye only, followed by a further loss of vision several minutes later. Panicked, her mom scheduled an emergency appointment with the same doctor the next morning. VA on this second visit was now 10/400 in the right eye but remained at 20/20 in the left. The external exam revealed an afferent pupillary defect OD compared with normal pupils on the first exam. The fundus exam on this occasion revealed a slightly pale disc in the right eye only.

A series of referrals resulted in an MRI and arterial angiography later that same day. The imaging revealed a 3.5cm prechiasmal mass on the right side that compressed part of the chiasm. The patient was then referred to a highly rated pediatric neurosurgeon associated with a prestigious children's hospital.

You Be the Judge

In light of the facts presented thus far, consider the following questions:

- Since confrontation visual fields and the DFE were both normal on the first visit, was the diagnosis of amblyopia justified?
- Since the doctor did not find a constant unilateral strabismus or significant anisometropia, should the doctor have considered other possible diagnoses?
- Was the doctor correct when he stated to the patient and the parent that she would likely "grow out of" the lazy-eye condition?
- Do normal confrontation visual fields give both the doctor and patient a false sense of security?
- Is the doctor not culpable of malpractice because both confrontation visual fields and a DFE were both normal?

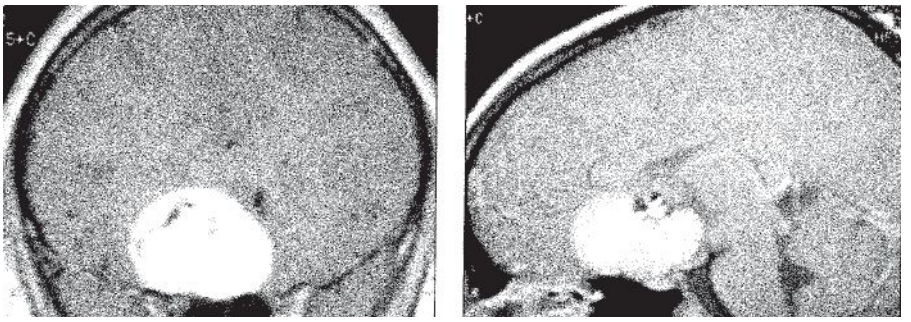
Follow-Up

The patient and her parents listened carefully as a team of pediatric neurosurgeons discussed the risks and benefits of surgery to remove the brain tumor. No other options, such as gamma knife radiation, were recommended because the tumor was just too large to be treated successfully. The family was told that death, paralysis, loss of smell and blindness were possible as consequences of the major surgical procedure. But if all went well, the surgical intervention would perhaps result in normal VA and a near normal field in the left eye.

The parents consented and surgery was scheduled for the next morning. By all indications, the surgeon performed flawlessly. But two hours after surgery,

About Drs. Sherman and Bass

Dr. Sherman is a Distinguished Teaching Professor at the SUNY State College of Optometry and editor-in-chief of *Retina Revealed* at www.retinarevealed.com. During his 53 years at SUNY, Dr. Sherman has published about 750 various manuscripts. He has also served as an expert witness in 400 malpractice cases, approximately equally split between plaintiff and defendant. Dr. Sherman has received support for *Retina Revealed* from Carl Zeiss Meditec, MacuHealth and Konan. **Dr. Bass** is a Distinguished Teaching Professor at the SUNY College of Optometry and is an attending in the Retina Clinic of the University Eye Center. She has served as an expert witness in a significant number of malpractice cases, the majority in support of the defendant. She serves as a consultant for ProQR Therapeutics.



A coronal (left) and mid-sagittal (right) MRI. Several experts testified that a year earlier, the tumor would have been far smaller and treatable with gamma knife radiation.

marked complications arose, most notably elevated intracranial pressure. After noninvasive medical intervention failed, a shunt was inserted to relieve the pressure build-up but also failed. With informed consent from the parents, removal of part of the frontal lobe was performed and proved successful.

The patient woke up the next morning after two surgical procedures, both with general anesthesia, opened both eyes and saw nothing—not a thing again except for vague light perception. Her boyfriend visited her in the hospital, was told that his girlfriend will likely be blind forever and never returned. Her girlfriends did better and lasted about a month. The distraught parents were very supportive but realized everything had changed forever. They soon found a highly regarded law firm and began working with a young, sympathetic but aggressive attorney.

I (JS) was contacted because of previous publications about the diagnosis and misdiagnosis of amblyopia. I reviewed all the information available, including the depositions of the eye doctor and the technician who took the original history and from the mother and the patient. Of particular interest, the doctor testified that he did perform confrontation visual fields and both the patient and the mother supported this assertion. The doctor then testified that with normal confrontation visual fields, there was no reason to perform an automated visual field, a device he did have in his office. He also stated that he performed color vision testing, which was normal. However, under oath he was forced to admit that he performed the color vision test with both eyes open and hence did not compare the "affected" eye to the "normal" eye. Note that color vision loss does not occur in amblyopia and hence monocular color vision could be diagnostic.

The patient and mother testified that they told the technician that the vision loss in the right eye was rather recent—information that the technician did not note on the record. Also, the doctor never independently inquired about this critical point from the patient and mom during the exam. Recognize that doctors hold responsibility for their technicians and other office personnel via the legal doctrine of vicarious liability. Not surprisingly, a review of school records indicated that VA in the past was always normal.

The Outcome

Unlike most malpractice cases, this case did go to a jury trial, and the verdict of culpability was reached on a Friday afternoon. Several local newspapers published the story over the weekend and the name of the culpable doctor was revealed. The doctor had two kids in the same high school as the blind patient and within days everyone at school knew whose father was responsible for their blind classmate. The final verdict was $9.2 million, believed to be the largest ever against an optometrist.

Our Opinion

This landmark case occurred a quarter of a century ago. If modern day technology were used, many subtle abnormalities could have been detected. For example, OCT (not widely available at the time) can detect photoreceptor disorders invisible to ophthalmoscopy and, more importantly, a reduction in the retinal nerve fiber layer (RNFL) and ganglion cell complex that may be secondary to a brain tumor compressing the optic nerve. Reliance on confrontation visual fields has proven disastrous in a series of well-publicized malpractice cases. Automated visual fields, even a screening visual field, should be performed when there is no explanation for a patient's symptoms or reduction in best-corrected VA, in all patients regardless of age. In the June 2023 installment of *You Be the Judge,* a pituitary adenoma in a middle-aged male was missed on four visits over eight years and resulted in death. The minor reduction in VA to 20/25 in each eye was attributed to mild cataracts but automated visual fields were never performed.

Silver Lining

This unfortunate case was widely distributed in the optometric press at the time and included the names of the optometrist and the expert witnesses. I (JS) had numerous lectures canceled, but far more importantly, a handful of clinicians in the years following contacted me and reported that knowledge of this case changed their professional behavior and some young "amblyopic" patients were demonstrated to have brain tumors.

Earlier diagnosis and appropriate treatment generally result in better outcomes. As a neurosurgeon once testified, "It is far easier to remove a grape from the brain than a grapefruit." Learning from the mistakes of others can avoid such disasters. ■

1. Meng Z, Fu J, Chen W, et al. Prevalence of Amblyopia and associated risk factors in Tibetan grade one children. Ophthalmic Res. 2021;64(2):280-9.

2. Kuwera E. Lazy eye (amplyopia). Johns Hopkins Medicine. www.hopkinsmedicine.org/health/conditions-and-diseases/lazy-eye-amblyopia. Accessed September 29, 2023.

NOTE: This article is one of a series based on actual lawsuits in which the author served as an expert witness or rendered an expert opinion. These cases are factual, but some details have been altered to preserve confidentiality. The article represents the authors' opinion of acceptable standards of care and do not give legal or medical advice. Laws, standards and the outcome of cases can vary from place to place. Others' opinions may differ; we welcome yours.

Tyrvaya® is not another drop
It's an **ocular surface-sparing** nasal spray.[2]

Activates real, basal tears
Tyrvaya® is believed to work by activating the trigeminal parasympathetic pathway resulting in **basal tear production**.[2]*

Real tears, real fast
In 2 clinical trials with **mild, moderate, and severe** dry eye disease patients, Tyrvaya increased tear production from baseline by **≥10 mm in Schirmer's Test Score (STS) in nearly 50% of patients at week 4**, with increased tears seen as early as the first dose and over 12 weeks.[2-8]†

SEE WHAT TYRVAYA CAN DO

*The exact mechanism of action is unknown.
†Tyrvaya was evaluated across 3 randomized, vehicle-controlled, double-masked studies in which adults aged ≥22 years diagnosed with dry eye disease received 1 spray of either active drug or vehicle in each nostril twice daily. Primary endpoint: % of patients with mean change from baseline in STS of ≥10 mm at week 4 in ONSET-1: 52% with Tyrvaya (n=48) vs 14% with vehicle (n=43) and in ONSET-2: 47% with Tyrvaya (n=260) vs 28% with vehicle (n=252). Onset of action: mean change from baseline in STS ~5 minutes after first dose (not a prespecified endpoint) in ONSET-1 was 17.2 mm with Tyrvaya (n=48) vs 4.0 mm with vehicle (n=43) and in ONSET-2 was 16.5 mm with Tyrvaya (n=260) vs 6.9 mm with vehicle (n=251). Observed data. On Day 1 in clinical studies, a baseline anesthetized Schirmer's test was performed. Tyrvaya was then administered concurrently with Schirmer's test. Schirmer's test results were measured at ~5 minutes. Mean change from baseline in STS at week 12 in the MYSTIC study was 10.8 mm with Tyrvaya vs 6.0 mm with vehicle. Limitations: Ex-US, single-center study. All subjects were Hispanic or Latino. Tyrvaya group mean baseline STS 5.5 mm (n=41); vehicle group mean baseline STS 5.3 mm (n=41). All randomized and treated patients were included in the analysis and missing data were imputed using last-available data. [2-8]
See references on next page.

Indication
Tyrvaya® (varenicline solution) nasal spray is indicated for the treatment of the signs and symptoms of dry eye disease.

Important Safety Information
The most common adverse reaction reported in 82% of patients was sneezing. Events that were reported in 5-16% of patients were cough, throat irritation, and instillation-site (nose) irritation.

Please see Brief Summary of Prescribing Information on the next page and the full Prescribing Information at Tyrvaya-pro.com.

tyrvaya®
(varenicline solution)
nasal spray 0.03 mg

BRIEF SUMMARY: Consult the full Prescribing Information for complete product information available at www.tyrvaya-pro.com.

INDICATIONS AND USAGE

TYRVAYA® (varenicline solution) nasal spray is a cholinergic agonist indicated for the treatment of the signs and symptoms of dry eye disease.

ADVERSE REACTIONS

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.

In three clinical trials of dry eye disease conducted with varenicline solution nasal spray, 349 patients received at least 1 dose of TYRVAYA. The majority of patients had 31 days of treatment exposure, with a maximum exposure of 105 days.

The most common adverse reactions reported in 82% of TYRVAYA treated patients was sneezing. Other common adverse reactions that were reported in >5% of patients include cough (16%), throat irritation (13%), and instillation-site (nose) irritation (8%).

USE IN SPECIFIC POPULATIONS

Pregnancy: Risk Summary: There are no available data on TYRVAYA use in pregnant women to inform any drug associated risks. In animal reproduction studies, varenicline did not produce malformations at clinically relevant doses.

All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data: *Animal Data*: Pregnant rats and rabbits received varenicline succinate during organogenesis at oral doses up to 15 and 30 mg/kg/day, respectively. While no fetal structural abnormalities occurred in either species, maternal toxicity, characterized by reduced body weight gain, and reduced fetal weights occurred in rabbits at the highest dose (4864 times the MRHD on a mg/m^2 basis).

In a pre- and postnatal development study, pregnant rats received up to 15 mg/kg/day of oral varenicline succinate from organogenesis through lactation. Maternal toxicity, characterized by a decrease in body weight gain, was observed at 15 mg/kg/day (1216 times the MRHD on a mg/m^2 basis). Decreased fertility and increased auditory startle response occurred in offspring at the highest maternal dose of 15 mg/kg/day.

Lactation: Risk summary: There are no data on the presence of varenicline in human milk, the effects on the breastfed infant, or the effects on milk production. In animal studies varenicline was present in milk of lactating rats. However, due to species-specific differences in lactation physiology, animal data may not reliably predict drug levels in human milk.

The lack of clinical data during lactation precludes a clear determination of the risk of TYRVAYA to an infant during lactation; however, the developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for TYRVAYA and any potential adverse effects on the breastfed child from TYRVAYA.

Pediatric Use: Safety and efficacy of TYRVAYA in pediatric patients have not been established.

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

References: 1. Jones L, Downie LE, Korb D, et al. *Ocul Surf*. 2017;15(3):575-628. **2.** Tyrvaya. Prescribing Information. Oyster Point Pharma; 2021. **3.** Oyster Point Pharma. Data on file. OPP-002 (ONSET-1) Clinical Study Report. August 4, 2019. **4.** Oyster Point Pharma. Data on file. OPP-101 (ONSET-2) Interim Clinical Study Report. October 13, 2020. **5.** Quiroz-Mercado H, Hernandez-Quintela E, Chiu KH, Henry E, Nau JA. *Ocul Surf*. 2022;24:15-21. **6.** Wirta D, Torkildsen GL, Boehmer B, et al. *Cornea*. 2022;4(10):1207-1216. **7.** Wirta D, Vollmer P, Paauw J, et al. *Ophthalmology*. 2021;0(0):379-387. **8.** Oyster Point Pharma. Data on file. OPP-004 (MYSTIC) Clinical Study Report. March 19, 2020.

VIATRIS™

Manufactured for Oyster Point Pharma, Inc. 202 Carnegie Center, Suite 106, Princeton NJ 08540. For more information, visit www.tyrvaya-pro.com. To report an adverse event, contact 1-877-EYE-0123.

HOW TO HANDLE THE HIGH MYOPE

Anticipate the following issues during the long-term management of these patients' ocular health.

JESSICA STEEN, OD
FORT LAUDERDALE, FL

In recent years, the eyecare community has done an admirable job of raising awareness to the dangers wrought by myopia and reframing the condition as a disease amenable to intervention. Once passed off as an inconvenience to be remedied with glasses, myopia poses ocular health risks that may not manifest for decades. Patient-centered care of highly myopic individuals relies on understanding the risk of development of this ocular pathology as well as knowing the long-term potential complications related to any past procedures. Let's dive into the vulnerabilities related to high myopia through addressing chronic pathology, with a focus on patient-driven concerns related to long-term prognosis.

While local and global projections related to myopia, high-myopia and associated visual impairment hold steady in their expected impact on visual function and ocular health, they reflect the necessary role of managing providers for prevention, early intervention, continued care and education that begins in the exam room.[1,2] Changes in pediatric myopia management and addressing early pediatric myopia clinical ideas are meaningful in altering the potential course of the disease, associated pathology and visual dysfunction in adulthood. However, we still must be ready to meet the needs of our growing population of highly myopic adult patients.

What's in a Name?

"Degenerative" myopia, "pathologic" myopia, "malignant" myopia or just "myopia"? Difficulty in labeling of this condition often stems from the variability in literature and absence of a comprehensive, globally accepted definition of high myopia and its associated pathologies. In speaking about high myopia, most commonly we refer to refractive error (spherical equivalent) of -6.00D or higher or axial length at least 26.0mm or 26.5mm; however, there is no clear scientific rationale for how these threshold values were determined.[3-5] Importantly, high myopia does not imply pathologic myopia. The latter is an umbrella term that includes a host of clinical diagnoses that may affect the optic nerve, neurosensory retina, Bruch's membrane, choroid and sclera, which are specifically related to posterior staphyloma formation and variability in three-dimensional globe-shape.[3-6]

Back to Square One

Factors leading to myopia development are complex, with a basis in genetics and significant environmental impact on its development and progression.[1,7-10] While the physiological mechanisms behind myopia development are still being investigated, animal models have demonstrated that, in response to retinal defocus, a signaling cascade beginning in the neurosensory retina leads to biochemical changes in the retinal pigment epithelium (RPE), choroid and sclera that result in collagen remodeling and increased axial length.[7] Near work activities, light levels and time outdoors have been proposed to contribute to myopia development and progression, and epidemiological research continues to explore additional environmental factors that may be implicated.[7] Data from twin studies have reported high heritability (90%) of myopia; however, a recent meta-analysis estimated the heritability of myopia to be only 18.4%.[8,9]

Based on that, the ability to predict the development of myopia based on genetics alone falls half-way between chance and perfect prediction (area under the curve = 0.75).[9] Early and regular comprehensive eye examinations, including cycloplegic refraction in line with clinical practice guidelines, are more practical to identify those who are progressing towards myopia, or those who have myopia, in order to employ meaningful early intervention with the goal of slowing future progression than genetics alone.[11]

About the author

Dr. Steen is an associate professor at Nova Southeastern University College of Optometry where she serves as director of the Glaucoma Service, coordinator of the Primary Care with Emphasis in Ocular Disease Residency and teaches courses in glaucoma and ocular pharmacology. Her financial disclosures include Bausch + Lomb, Santen, Iveric Bio, Alcon, Viatris, Ocuphire, Ocuterra, Allergan, Thea Pharma, Ocuphire and Carl Zeiss Meditec.

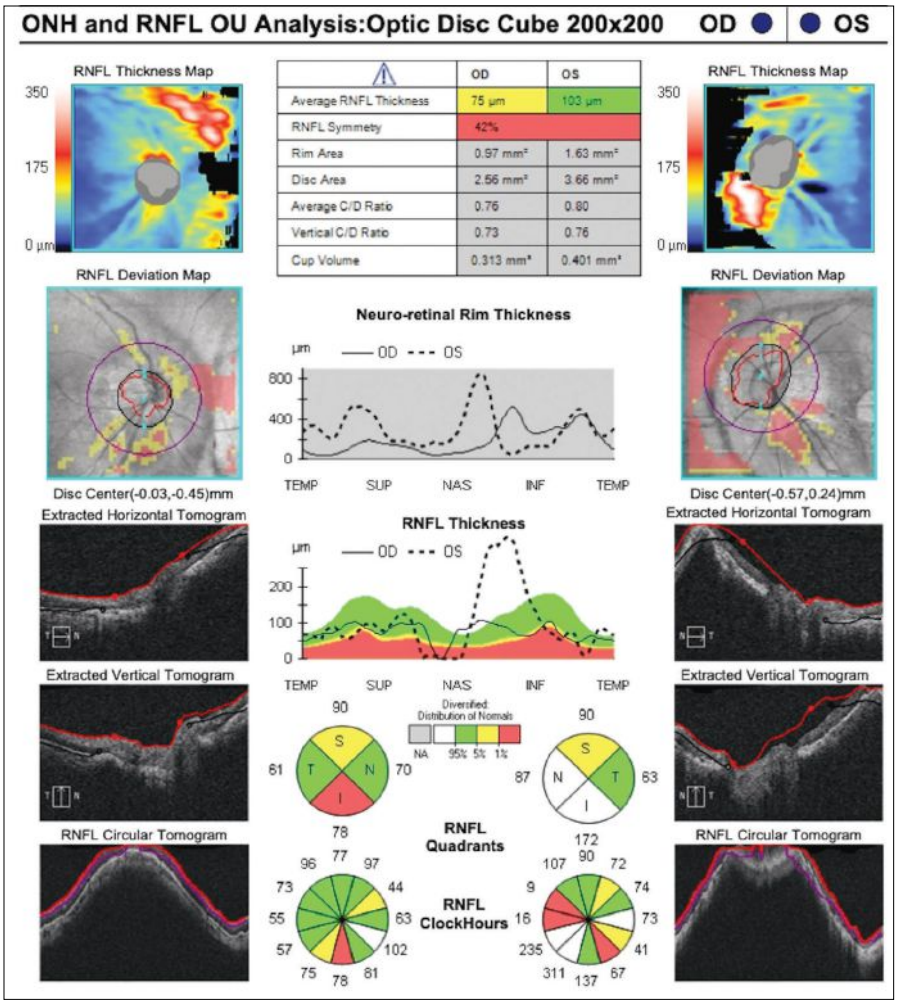
Sight-threatening Sequelae

Vision loss due to pathology associated with high myopia is a substantial source of global visual impairment.[2] With a 6mm increase in axial length (24mm to 30mm), the distance between the optic disc and ora serrata has been described to increase by 4.3mm.[12] Being aware of this sets the stage for a deeper understanding of the wide variety of potential peripheral retinal, macular and optic nerve pathology that encompasses pathologic myopia. While peripheral retinal pathologies leading to retinal tear or retinal detachment are significant complications associated with high myopia, here we focus on the chronic ocular conditions that have a high disease burden due to chronic progressive vision loss.

Cataract Development and Treatment

Visually significant nuclear sclerosis occurs at a younger age in high myopes, and myopic individuals have been shown to have an increased likelihood of developing posterior subcapsular cataract.[4,12,13] Meeting the high visual expectations of younger, highly myopic individuals who undergo cataract surgery often involves a goal of contact lens or spectacle independence; however, for those with the macular pathology or axial length greater than 28mm, the use of multifocal intraocular lenses is controversial.[14,15] High myopes are more likely to experience intraocular lens tilt and intraocular lens decentration inducing defocus, as well as coma-like aberration (possibly due to larger capsular bag in myopic eyes), compared with standardized diameters of intraocular lenses or zonular weakness.[14] Following cataract surgery, high myopia has also been determined to be an additional risk factor for the development of visually significant posterior capsular opacification.[16]

Retinal tear and retinal detachment are established postsurgical complications with an increased risk amongst high myopes (axial length > 26mm) and those with lattice degeneration.[17] Retinal tear or detachment is most likely to occur within the first six months following cataract surgery, with a median time of approximately 4.5 months following the procedure.[17] Identifying highly myopic patients who have additional risk of specific postoperative complications, along with patient education and a plan set with office triage staff to best manage emergency concerns when they arise, can lead to early detection and referral for treatment.



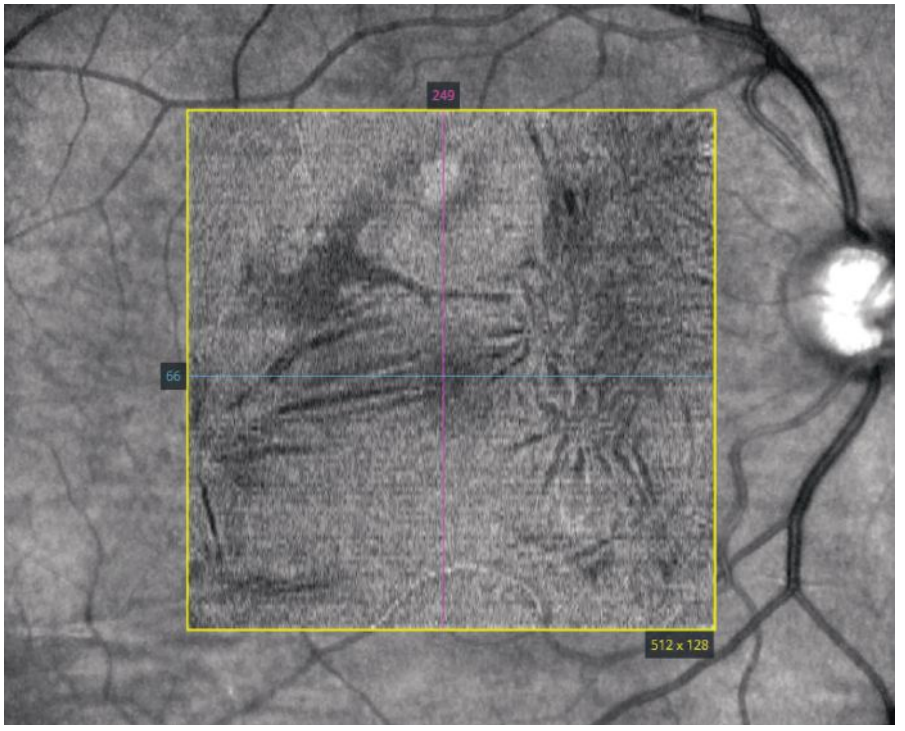
Macular posterior staphyloma with severe choroidal thinning and RPE disruption on spectral domain OCT.

Myopic Maculopathy

This term is a general descriptor for the neovascular, atrophic and tractional conditions that affect the macula in high myopes. While classification systems have been developed with the goal of consistent description and standardization among clinical trials and epidemiological studies, they are not commonly used in a clinical environment.[3,5,18]

Posterior staphyloma, a scleral outpouching with increased curvature, is an important feature of pathologic myopia and a primary feature that leads to macular pathology. Posterior staphyloma may occur in nonmyopic eyes, and therefore does not necessarily rule in the diagnosis of pathologic myopia.[5,10] As axial length increases, the retina, choroid and sclera become thin, which may lead to foveoschisis, myopic macular atrophy, macular neovascularization or serous retinal detachment associated with dome-shaped macula.[4,5,10]

Vitreous liquefaction and posterior vitreous detachment occur in younger myopic eyes, and the development of epiretinal membrane is common and found in up to 45.7% of highly myopic individuals.[5,19] Myopic tractional maculopathy, which includes vitreomacular



Epiretinal membrane following barrier laser photocoagulation of retinal break en face.

traction, foveoschisis and macular hole, is primarily due to the presence of posterior staphyloma and the inability of the retina to match the curvature of the more curved underlying sclera.[5,10] Generally, myopic tractional maculopathy progresses slowly. Observation is recommended until best-corrected visual acuity declines in line with anatomic worsening determined by OCT, where surgery will be considered.[5,10]

Chorioretinal degeneration leading to atrophic myopic maculopathy is a visually devastating end-stage disease following development and treatment of macular neovascularization. It can be a primary outcome of myopic choroidopathy with similar visual consequences to geographic atrophy occurring in age-related macular degeneration, despite having a different underlying pathogenesis.[5,10] Myopic chorioretinal degeneration begins in the posterior pole as patchy areas of RPE and choroid loss, often with RPE hyperplasia at the edge of the lesion, and increases over time to form large atrophic lesions. In addition to fundus images for documentation, OCT and fundus autofluorescence are valuable to monitor progression of atrophy.[4,5,10,20,21] While recent therapeutic advancements for the treatment of geographic atrophy secondary to age-related macular degeneration are available to slow disease progression, no therapeutic strategies are currently approved for the treatment of myopic macular atrophy.

The development of macular choroidal neovascularization is associated with the presence of lacquer cracks, or linear defect of the RPE-Bruch's membrane complex in high myopes.[4,5,10] Macular neovascularization in high myopia tends to be highly responsive to anti-VEGF therapy when treated promptly.[5,10]

Glaucoma Risk

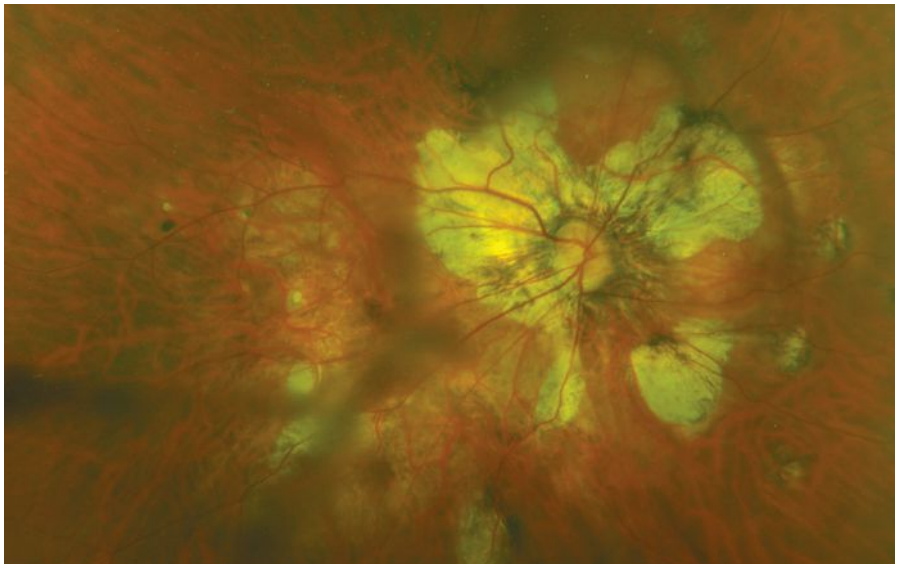
Our understanding of the risk factors related to the development of primary open-angle glaucoma continues to evolve. Recently published 10-year follow up data of the Beijing Eye Study identified high myopia (≤-6.00D) to be associated with a 7.3-fold increased risk for the development of open-angle glaucoma compared with emmetropic eyes.[22] As myopia increases, the risk of open-angle glaucoma increases, with a meta-analysis describing a 20% increase in the risk of development of glaucoma with every one diopter increase in myopia.[23] The risk profile increases with spherical equivalent higher than -6.00D and increases further from -8.00D.[23]

The presumed reason for increased risk of glaucoma in myopic individuals has been related to a thinner, stretched sclera and reduced scleral rigidity compared with emmetropic eyes.[22,24] The lamina cribrosa also stretches and thins with increased axial elongation, increasing the shearing stress on the pores of the lamina cribrosa and the axons that pass through them.[25] Ischemic stress to the lamina cribrosa may be increased in highly myopic eyes due to an increase in the distance between the lamina and its vascular supply.[25] Increased oxidative stress driving cell death as a result of RPE and choroidal atrophy in highly myopic eyes has also been proposed to be a potential contributing mechanism to increased glaucoma risk in highly myopic eyes.[26]

Nonglaucomatous optic neuropathy due to high myopia may be challenging to differentiate from open-angle glaucoma.[25] Axial elongation and increased temporal parapapillary atrophy can cause physical stretching of ganglion cell axons between the fovea and optic disc, resulting in parafoveal visual field defect in the absence of glaucomatous optic disc appearance.[25,27] The prevalence of nonglaucomatous optic neuropathy due to high myopia was recently described to be 29.3% in a Russian population of individuals over the age of 40 with increased likelihood of optic neuropathy with increased axial length.[27]

Long-Term

After surgical management of a retinal tear or detachment, it may be difficult to distinguish the subtleties between expected findings associated with treatment and those that may prompt re-referral. The purpose of barrier laser photocoagulation in retinal tear or detachment treatment is to create adherence between the retina and choroid to prevent liquefied vitreous from entering the subretinal space.[28] Considering the induced traction caused by photocoagulation at the boundary of detached and attached retina, patients who are critical observers



Patchy chorioretinal atrophy in a high myope with posterior staphyloma.

may continue to have symptoms of localized photopsia in the treatment area.

Epiretinal membrane (ERM) formation following laser photocoagulation or pars plana vitrectomy may also occur. While some ERMs may develop and progress quickly, asymptomatic or minimally symptomatic development following retinal laser may also occur.[28] This typically happens in younger myopic patients who have undergone pars plana vitrectomy, which may present as a form of form-fruste proliferative vitreoretinopathy. Asymptomatic or the minimally symptomatic development of epiretinal membrane following retinal laser may also occur. If a patient becomes visually symptomatic, re-referral for surgical evaluation is warranted.[28]

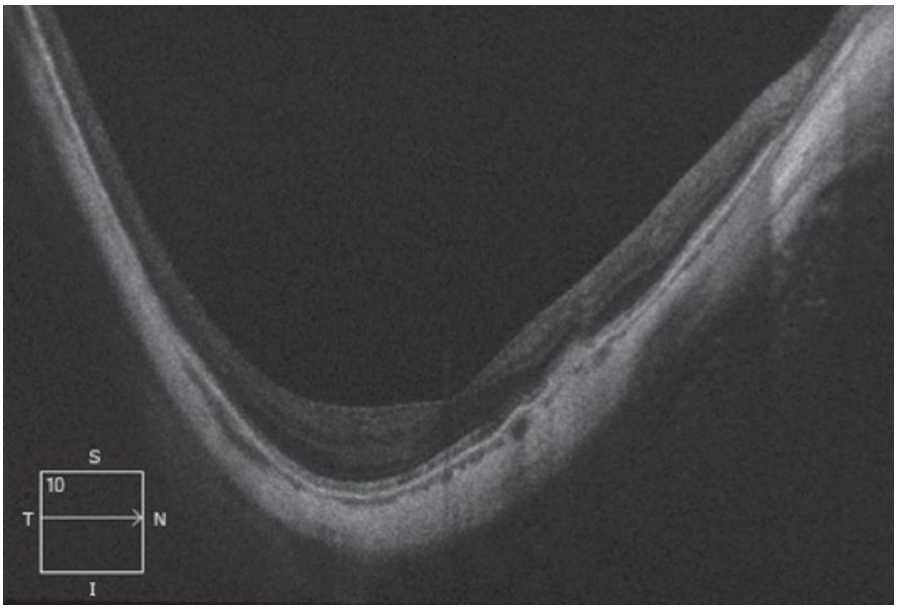
Tamponade agents are surgical adjuncts used in retinal detachment repair procedures that encourage chorioretinal adherence. While gas tamponade (*i.e.*, SF_3 or C_3F_8) is preferred from a patient perspective due to its ability to resorb, long-term silicone oil tamponade may be used in cases of complex retinal detachment repair, including cases with history of proliferative vitreoretinopathy, ocular trauma or severe diabetic retinopathy.[29] While silicone oil is generally removed three to six months after insertion at the discretion of the operating surgeon, it may be left indefinitely, depending on patient risk factors.[29] Silicone oil emulsification generally begins within the first year following injection. While emulsification alone is not a reason for removal, it may lead to complications including corneal endothelial dysfunction and corneal decompensation, intraocular inflammation and open-angle glaucoma.[29,30]

Clinically, early emulsification is observed as small bubbles in the vitreous cavity. Silicone oil can migrate into the anterior chamber and result in "reverse hypopyon" with emulsified silicone oil particles, which are lighter than the aqueous, settling superiorly in the anterior chamber, which is best observed with gonioscopy in early cases.[30] Silicone oil present in the anterior chamber can result in corneal endothelial cell loss and may enter and clog the trabecular meshwork.[30]

The resulting reduction in aqueous outflow can lead to elevated intraocular pressure (IOP), which has been described to occur in as many as 56% of eyes, and open-angle glaucoma.[29,31] Any patient with silicone oil in the vitreous cavity should remain under the care of a retinal surgeon, in addition to a comanging provider's care for periodic evaluation for known potential ocular complications, including elevated IOP that may require IOP-lowering therapy or necessitate oil removal.

High Myopia and Imaging

OCT is an important tool for structural evaluation of the optic nerve and macula, which, due to the increased curvature of a posterior staphyloma, can make imaging retinal pathology challenging. Reference databases comparisons of nerve fiber layer thickness, optic disc parameters and ganglion-cell or ganglion-cell complex parameters of commercially available OCT systems in the United States have traditionally excluded eyes with refractive error greater than -6.00D.



Segmentation error and imaging acquisition error due to parapapillary staphyloma.

Menicon

Unique never felt so good.

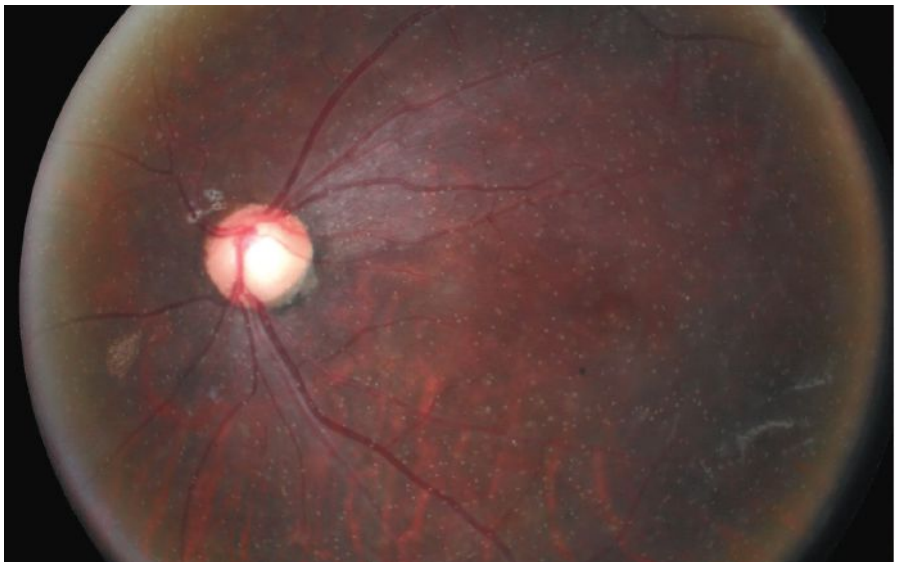
Unique pH™ is a highly effective multipurpose solution for gas permeable contact lenses that cleans, conditions, and disinfects in one bottle.

Unique pH™ conditions lenses by adjusting to the eye's natural tear pH to enhance the wettability and comfort of gas permeable contact lenses on insertion. The formula is designed to provide a soothing effect during lens wear.

ORDER ONLINE
www.meniconwebstore.com

Complimentary starter kits available!

meniconamerica.com



Silicone oil emulsification following pars plana vitrectomy for treatment of rhegmatogenous retinal detachment.

Reference database parameters should be made with a reflection of the individual, their ocular feature and whether they may or may not be represented within the reference database.

With increased axial length, transverse magnification of the imaging area of the OCT is reduced, which results in a larger retinal area imaged compared with an eye of average axial length.[32] This may lead to an underestimation of peripheral macular thickness due to inclusion of additional retinal area being imaged in a high axial length eye, which would otherwise not be included in an eye of average axial length, or an underestimated of RNFL thickness due to the lower density of axons further from the optic disc imaged by the induced larger scan area.[32] OCT-based optic disc parameters, including neuroretinal rim thickness, rely on accurate determination of Bruch's membrane opening, which may not be discernible in highly myopic eyes, especially in the presence of significant parapapillary atrophy impacting reproducibility and software-based segmentation.[33]

Takeaways

Strategies employed during childhood aimed to delay, reduce or prevent the development high myopia are key to disrupting the rapidly rising trend of this condition and its associated ocular pathology. An understanding of the chronic ocular pathology associated with increased axial length and its early identification, along with individualized monitoring schedules, retinal surgical referral when indicated and comanagement with other providers, is central for maximizing long-term visual outcomes and the unique needs of highly myopic individuals. ■

1. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology. 2016;123(5):1036-42.

2. Fricke TR, Jong M, Naidoo KS, et al. Global prevalence of visual impairment associated with myopic macular degeneration and temporal trends from 2000 through 2050: systematic review, meta-analysis and modelling. Br J Ophthalmol. 2018;102(7):855-62.

3. Flitcroft DI, He M, Jonas JB, et al. IMI - defining and classifying myopia: a proposed set of standards for clinical and epidemiologic studies. Invest Ophthalmol Vis Sci. 2019;60(3):M20-30.

4. Haarman AEG, Enthoven CA, Tideman JWL, et al. The complications of myopia: a review and meta-analysis. Invest Ophthalmol Vis Sci. 2020;61(4):49.

5. Ruiz-Medrano J, Montero JA, Flores-Moreno I, et al. Myopic maculopathy: current status and proposal for a new classification and grading system (ATN). Prog Retin Eye Res. 2019;69:80-115.

6. Moriyama M, Ohno-Matsui K, Modegi T, et al. Quantitative analyses of high-resolution 3D MR images of highly myopic eyes to determine their shapes. Invest Ophthalmol Vis Sci 2012;53(8):4510-8.

7. Chakraborty R, Read SA, Vincent SJ. Understanding myopia: pathogenesis and mechanisms. In: Ang M, Wong T, eds. Updates on Myopia. Singapore, Springer, 2020.

8. Hammond CJ, Snieder H, Gilbert CE, Spector TD. Genes and environment in refractive error: the twin eye study. Invest Ophthalmol Vis Sci. 2001;42(6):1232-6.

9. Hysi PG, Choquet H, Khawaja AP, et al. Meta-analysis of 542,934 subjects of European ancestry identifies new genes and mechanisms predisposing to refractive error and myopia. Nat Genet. 2020;52(4):401-7.

10. Ohno-Matsui K, Wu PC, Yamashiro K, et al. IMI pathologic myopia. Invest Ophthalmol Vis Sci. 2021;62(5):5.

11. American Optometric Association. Evidence-Based Clinical Practice Guideline: comprehensive pediatric eye and vision examination aoa comprehensive pediatric and vision examination. 2017. www.aoa.org/aoa/documents/practice management/clinical guidelines/ebo guidelines/comprehensive pediatric eye and vision exam.pdf. Accessed August 31, 2023.

12. Panda-Jonas S, Auffarth GU, Jonas JB, Jonas RA. Elongation of the retina and ciliary body in dependence of the sagittal eye diameter. Invest Ophthalmol Vis Sci. 2022;63(10):18.

13. Pan CW, Cheng CY, Saw SM, et al. Myopia and age-related cataract: a systematic review and meta-analysis. Am J Ophthalmol. 2013;156(5):1021-33.e1.

14. Wang L, Jin G, Zhang J, et al. Clinically significant intraocular lens decentration and tilt in highly myopic eyes: a swept-source optical coherence tomography study. Am J Ophthalmol. 2022;235:46-55.

15. Grzybowski A, Kanclerz P, Tuuminen R. Multifocal intraocular lenses and retinal diseases. Graefes Arch Clin Exp Ophthalmol. 2020;258(4):805-13.

16. Donachie PHJ, Barnes BL, Olaitan M, et al. The Royal College of Ophthalmologists' National Ophthalmology Database study of cataract surgery: report 9, risk factors for posterior capsule opacification. Eye (Lond). 2023;37(8):1633-9.

17. Morano MJ, Khan MA, Zhang Q, et al. Incidence and risk factors for retinal detachment and retinal tear after cataract surgery: IRIS Registry (Intelligent Research in Sight) analysis. Ophthalmol Sci. 2023;3(4):100314.

18. Ohno-Matsui K, Kawasaki R, Jonas JB, et al. International photographic classification and grading system for myopic maculopathy. Am J Ophthalmol. 2015;159(5):877-83.e7.

19. Ripandelli G, Rossi T, Scarinci F, et al. Macular vitreoretinal interface abnormalities in highly myopic eyes with posterior staphyloma: five-year follow-up. Retina. 2012;32(8):1531-8.

20. Ang M, Wong CW, Hoang QV, et al. Imaging in myopia: potential biomarkers, current challenges and future developments. Br J Ophthalmol. 2019;103(6):855-62.

21. Itoi M, Hieda O, Kusada N, et al. Progression of myopic maculopathy: a systematic review and meta-analysis. Eye Contact Lens. 2023;49(2):83-7.

22. Wang YX, Yang H, Wei CC, et al. High myopia as risk factor for the 10-year incidence of open-angle glaucoma in the Beijing Eye Study. Br J Ophthalmol. 2023;107(7):935-40.

23. Ha A, Kim CY, Shim SR, et al. Degree of myopia and glaucoma risk: a dose-response meta-analysis. Am J Ophthalmol. 2022;236:107-19.

24. Sergienko NM, Shargorogska I. The scleral rigidity of eyes with different refractions. Graefes Arch Clin Exp Ophthalmol. 2012;250(7):1009-12.

25. Jonas JB, Wang YX, Dong L, Panda-Jonas S. High myopia and glaucoma-like optic neuropathy. Asia Pac J Ophthalmol (Phila). 2020;9(3):234-8.

26. Francisco BM, Salvador M, Amparo N. Oxidative stress in myopia. Oxid Med Cell Longev. 2015;2015:750637.

27. Bikbov MM, Iakupova EM, Gilmanshin TR, et al. Prevalence and associations of nonglaucomatous optic nerve atrophy in high myopia: the Ural Eye and Medical Study. Ophthalmology. July 17, 2023. [Epub ahead of print].

28. Israilevich R, Salabati M, Mahmoudzadeh R, et al. Secondary epiretinal membrane after laser retinopexy for retinal tear or localized retinal detachment: surgical outcomes and optical coherence tomography structural analysis. Retina. 2022;42(1):38-45.

29. Toklu Y, Cakmak HB, Ergun SB, et al. Time course of silicone oil emulsification. Retina. 2012;32(10):2039-44.

30. Shimmura-Tomita M, Takano H, Tanaka Y, et al. Status of corneal endothelial cells in the presence of silicone oil in the anterior chamber. Sci Rep. 2021;11(1):14055.

31. de Corral LR, Cohen SB, Peyman GA. Effect of intravitreal silicone oil on intraocular pressure. Ophthalmic Surg. 1987;18(6):446-9.

32. Niyazmand H, Lingham G, Sanfilippo PG, et al. The effect of transverse ocular magnification adjustment on macular thickness profile in different refractive errors in community-based adults. PLoS One. 2022;17(4):e0266909.

33. Zheng F, Wu Z, Leung CKS. Detection of Bruch's membrane opening in healthy individuals and glaucoma patients with and without high myopia. Ophthalmology. 2018;125(10):1537-46.

Treating Itchy Eyes in Allergy Sufferers

by John Hovanesian, MD
Harvard Eye Associates in Laguna Hills, CA

sponsored by Alcon

Ocular allergy symptoms, including itchy, watery eyes, often accompany nasal congestion in seasonal allergy suffers. Ocular symptoms, however, are often overlooked by allergists, pediatricians, and primary care physicians because patients may be more bothered by the nasal symptoms and neglect to mention having itchy eyes.[1] Patients often self-treat with over-the-counter oral non-sedating antihistamines and nasal corticosteroid sprays to relieve both ocular and nasal symptoms, but treatment dissatisfaction can be high due to incomplete relief, slow onset of action, or short duration of relief.[1]

Olopatadine 0.7% (Pataday Once Daily Relief *Extra Strength*) is a dual action agent that blocks histamine receptors and stabilizes mast cell membranes, thereby inhibiting the release of chemical mediators from conjunctival mast cells. Application of anti-allergy drugs directly to the ocular tissues can offer rapid onset of action, and less systemic involvement. Pataday *Extra Strength* has been shown to work faster and provide more ocular allergy itch relief at 24 hours compared to both Flonase Allergy Relief Nasal Spray and Claritin 24-Hour Tablets (Figures 1 and 2).[2†] Therefore, while oral antihistamines and nasal corticosteroids can offer allergy relief, these results offer strong evidence for recommending Pataday *Extra Strength* for fast and long-lasting ocular itch relief.

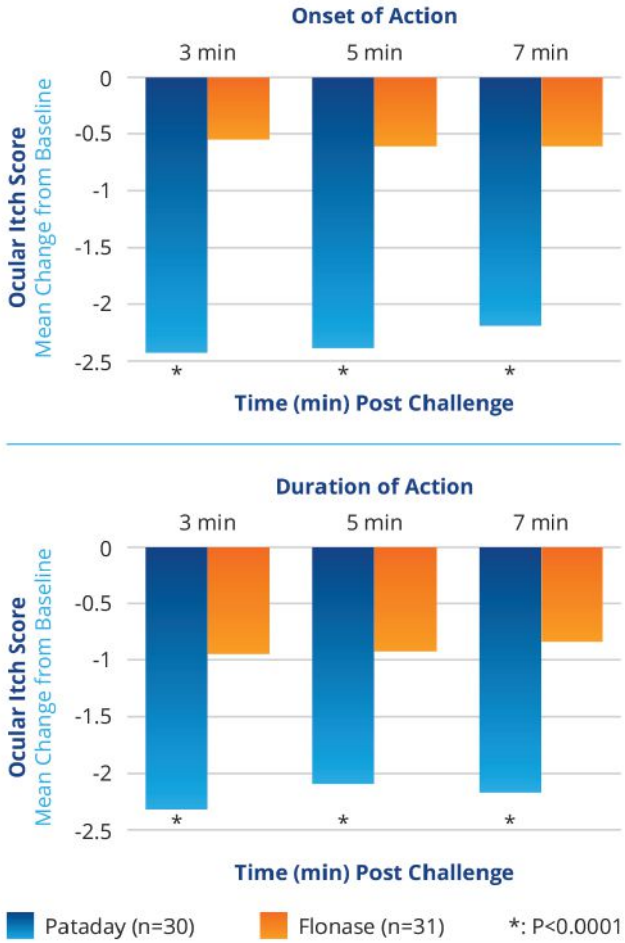


Figure 1: OLOPATADINE 0.7% VERSUS STEROID NASAL SPRAY. Participants were treated with either Pataday (n = 30) or Flonase (n = 31), then exposed to allergens 15 minutes later. At 3, 5, and 7 minutes after allergen exposure, Pataday group had significantly lower eye itch scores compared to the Flonase group. After 2 weeks of at-home treatment, similar results were seen at all post-allergen exposure timepoints 24 hours after treatment.

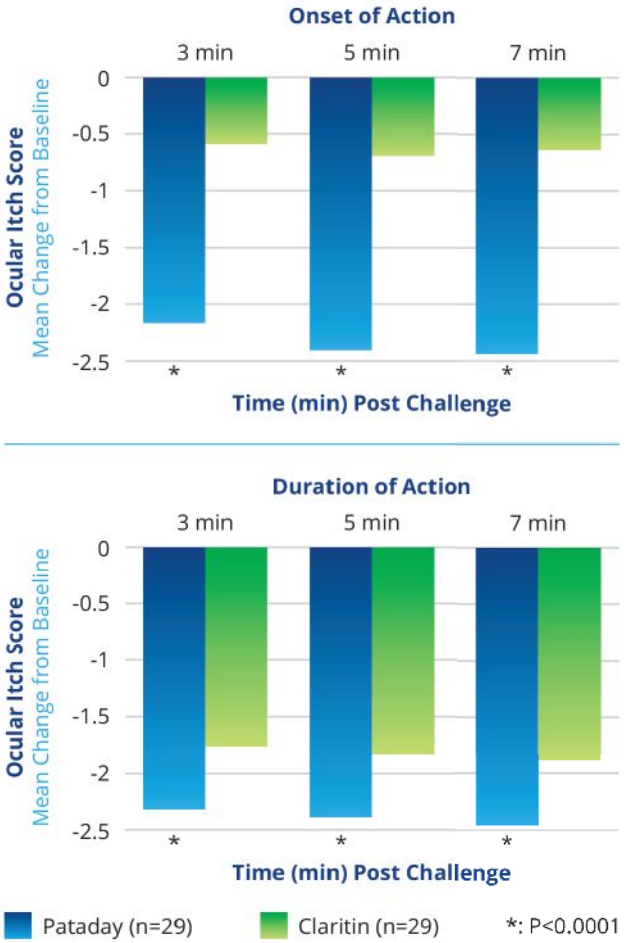


Figure 2: OLOPATADINE 0.7% VERSUS ORAL ANTIHISTAMINE. Pataday group (n = 29) reported significantly lower eye allergy itch scores compared to those in the Claritin group (n = 29) approximately 15 minutes after treatment. Two weeks after self-treating at home, the Pataday group reported statistically significantly lower itch scores compared to the Claritin group 24 hours after treatment.

†Based on the Conjunctival Allergen Challenge model

References 1. Meltzer EO, Farrar JR, Sennett C. Findings from an online survey assessing the burden and management of seasonal allergic rhinoconjunctivitis in US patients. *The Journal of Allergy and Clinical Immunology: In Practice*. 2017 May 1;5(3):779-89. **2.** Alcon data on file, 2022.

A MODERN TOOL TO ASSESS MYOPIA RISK

The newly developed UH NEAR survey offers clinicians and researchers a practical way to gather data on health and lifestyle factors to personalize patient care.

BY LISA OSTRIN, OD, PhD
HOUSTON

Whether you are a clinician assessing your patients' risk for myopia or a researcher studying myopia etiology and epidemiology, patient questionnaires can provide insightful data to inform treatment and management decisions, as well as save precious chair time. One recently developed myopia survey called UH NEAR—University of Houston Near work, Environment, Activity and Refraction—can be a valuable tool to systematically collect information about children's demographics, ocular history and visual activity.[1] The survey was designed for parents of children ages five to 17 years to answer on behalf of their child to collect myopia risk factor data. It takes into account the numerous aspects of heredity, demographics and visual environment to aid clinicians and researchers in compiling relevant information that has been linked to myopia in the recent literature.

As myopia increases in prevalence and options to control the condition become more widely available, it is nearing the standard of care to discuss myopia risk, progression and management with young patients and their parents. Studies have shown that any degree of myopia increases the risk for associated potentially blinding ocular pathologies, including myopic macular degeneration, choroidal neovascularization, posterior subcapsular and nuclear cataracts and primary open-angle glaucoma.[2]

Family history and genetics play a significant role in the pathogenesis of myopia. One of the strongest predictors is a child's number of myopic parents.[3] However, the prevalence of myopia is increasing faster than genetics alone can account for, suggesting that generational changes in the social and visual environment may also play a role.[4]

While numerous environmental and behavioral factors have been studied with respect to myopia, including time outdoors, light exposure, near work, physical activity, education, urbanization and electronic device use, the three that most consistently emerge as contributing factors include time outdoors, education and near work.[5-8] Unfortunately, two of these—time outdoors and near work—are notoriously difficult to quantify. While new technology takes advantage of wearable sensors to continuously and objectively measure ambient illumination and viewing distance, there are numerous limitations that prevent the widespread use of these instruments in the context of myopia, including high cost, limited availability and complex user interfaces. Therefore, subjective estimates of environmental and behavioral factors remain relevant and informative for collecting data both from clinical patients and from large populations as part of epidemiological studies.

The issue with traditional myopia risk factor surveys is that they are often long, use surrogate measures to quantify near work—such as number of books read or grades in school—include ambiguous questions, do not consider recent advances in digital media or have

About the author

Dr. Ostrin is an associate professor at University of Houston College of Optometry. After conducting post-doctoral research in low vision and retinal prosthetics at John Hopkins University, she served as a clinician researcher at the University of California Berkeley with a focus on myopia. She ultimately returned to UH to continue her work in myopia, conducting studies in both human participants and animal models and teaching on gross and ocular anatomy. Dr. Ostrin is a fellow of the American Academy of Optometry, a Gold Fellow of ARVO and a recipient of the American Optometric Foundation Ezell Fellowship and the University of Houston College of Optometry Cora and J Davis Armistead Teaching Award. Dr. Ostrin has no financial interests to disclose.

not been validated or widely used.[5,9,10] Additionally, there is no single questionnaire that is standard across clinics or studies. To help address some of these limitations, the UH NEAR survey was developed to comprehensively addresses demographic, environmental and behavioral factors that can be widely used in research and clinical settings to assess risk factors for myopia.

Photo: Getty Images

Given that screen time is an established risk factor for myopia, UH NEAR asks parents to estimate how long their children spend on electronic device on weekdays and weekends each during the school year and summer break.

How the Survey was Developed

The UH NEAR survey was developed in several phases, as follows:

- Phase 1: The most sensitive and specific method of parental reporting for the presence of children's myopia was determined.
- Phase 2: Questions regarding demographic factors and visual behavior were compiled, assessed and refined by the research team based on a thorough review of the literature.
- Phase 3: The developed survey was administered to focus groups to collect feedback for further refinement.
- Phase 4: A scoring system was developed.

The study was approved by the institutional review board at the University of Houston. Procedures followed the tenets of the Declaration of Helsinki, and informed consent was obtained from participants after explaining the nature of the study.

From phase 1, it was determined that the most sensitive method for parents to correctly classify their child as myopic was the indirect method, as derived and adapted from the Orinda Longitudinal Study of Myopia.[11] The indirect method uses a series of three questions, including, "Does your child wear glasses?" and if so, "What age did they receive glasses?" and, thirdly, "What is the purpose for wear (distance vision, near vision or both)?" This method has a sensitivity of 0.84 and specificity of 0.53 in correctly classifying the child as myopic or non-myopic. Therefore, with only parent input, some children will be incorrectly classified as myopic or non-myopic. This limitation is eliminated if the child is seen by a clinician or a member of a research team.

The final survey includes the following demographic information: age, sex, race and ethnicity, place and type of residence, type of school setting and average grades. The ocular history section asks about the refractive status of the biological mother and father, as well as the child, using the indirect method. Parents are asked to note the child's prescription, if it is known. The parent should indicate if the child has had any of the following: myopia control contact lenses (orthokeratology or multifocal), myopia control spectacle lenses (*i.e.*, MiyoSmart, DIMS, Stellest, SightGlass), eye drops to treat myopia, cataract removal, LASIK or other laser refractive correction. Parents also have the opportunity to answer an open-ended question to indicate any further information about their child's eyes that they feel might be relevant.

Once parents complete the demographic and ocular history sections, they answer a series of visual activity questions. Here, parents are asked to estimate the time their children spend on various tasks on a weekday and a weekend day during school time as well as during summer break. The same 11 questions are asked for these four different times of the year, as the literature shows that children's visual activity is significantly different for weekdays and weekend days, and for school sessions and summer break.[12,13]

These 11 items were carefully curated to include the minimum number of questions that fully encompass myopia risk factors relating to time outdoors (any time the child is exposed to sunlight, including physical or leisure activity and riding in a car), near work (whether printed or electronic) and electronic device use, including handheld devices and computers. Additionally, parents are asked to estimate their child's sleep duration per night for the time periods mentioned previously. For each question, the parent marks the hours on a continuous rating scale from zero to 12 hours, with 15-minute increments indicated on the scale.

Scoring the Survey

A scoresheet is provided to aid clinicians and researchers in calculating relevant metrics. The demographics and ocular history do not require any calculations and allow clinicians and researchers to easily compile important myopia-related factors, including age, parental myopia, refractive error group (myopic or non-myopic) and refraction (when available).

For visual activity, given that parents estimate children's time spent in various activities separately for weekdays and weekend days, the overall time spent in each activity across an entire week is calculated using a weighted equation:

$$\frac{\left(\left(5 \times \text{mean of weekday hours}\right)+\left(2 \times \text{mean of weekend day hours}\right)\right)}{7}$$

This calculation is performed for each of the 11 questions for school time and then for summer break. From these values, further calculations will sum time outdoors, physical activity, near work and electronic device use.

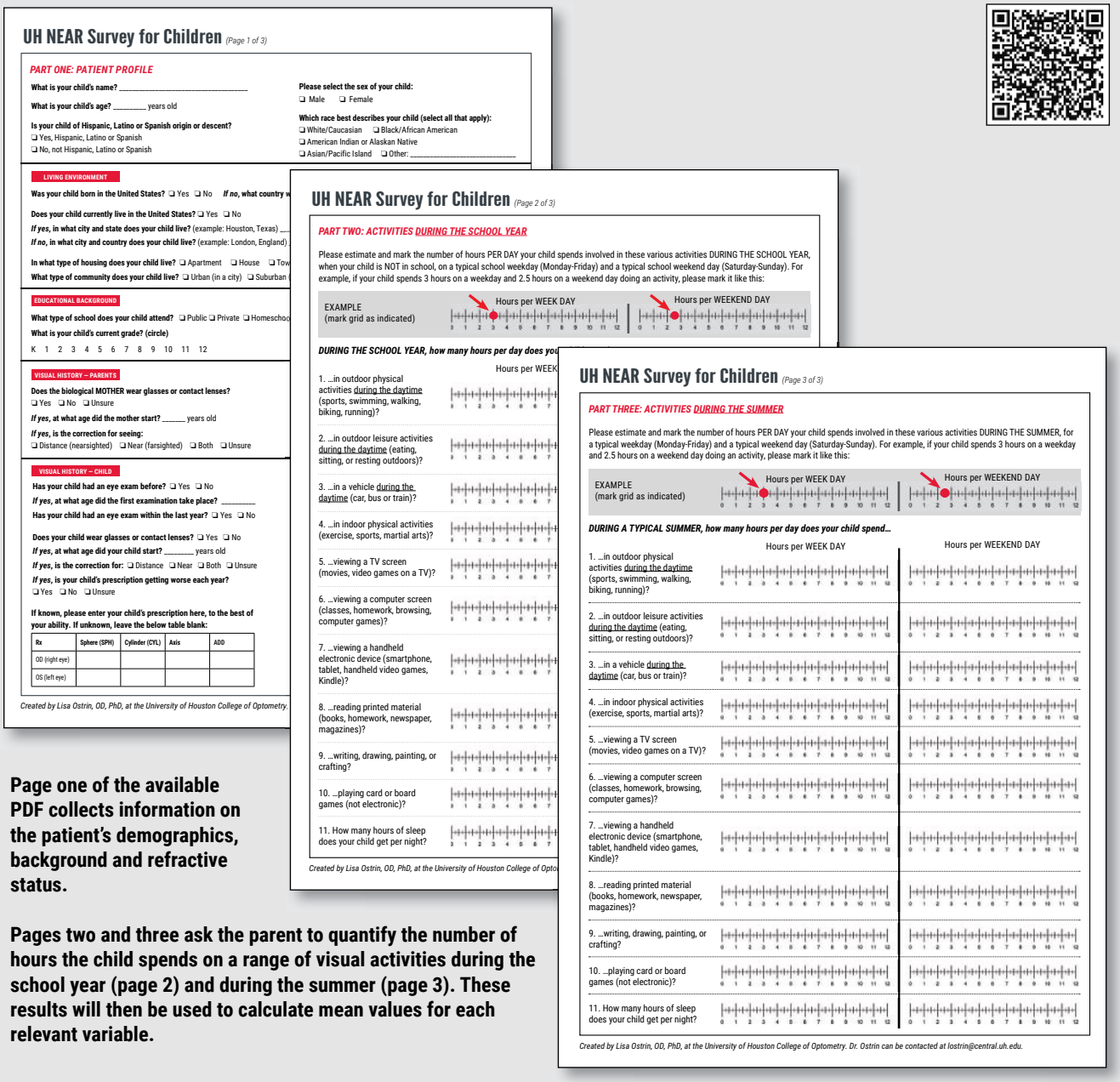
In this survey, time outdoors represents all of the time during the day that the child is exposed to sunlight, traditionally considered >1000 lux, and is calculated by adding the amount of time the child spends engaged in physical activity outdoors, leisure activity outdoors and riding in a vehicle (during the daytime).[14] Physical activity encompasses any sports or vigorous activity that the child may engage in and is calculated by adding the amount of time spent on both outdoor and indoor physical activity.

In order to quantify near viewing, activities known to be performed at 10cm to 50cm are considered "near" and include reading and writing on printed material and handheld device use.[15,16] Time spent using all screens is calculated by adding the amount of time the child spends using handheld devices, computers and gaming consoles and watching television.

An additional calculation provided on the score sheet is diopter hours: a weighted variable that takes into account the accommodative demand of each activity. Here, activities performed at certain distances were grouped together and multiplied by the dioptric demand.

How to Obtain the UH Near Survey Document for Use in Your Practice

A three-page version of the survey questionnaire, plus a separate one-page scoring sheet, is available for download in the online version of this article at www.reviewofoptometry.com, November 2023 issue. Scanning the QR code below will take you directly to the article:



UH NEAR Survey for Children (Page 1 of 3)

PART ONE: PATIENT PROFILE

What is your child's name? _____

What is your child's age? _____ years old

Is your child of Hispanic, Latino or Spanish origin or descent?
❑ Yes, Hispanic, Latino or Spanish
❑ No, not Hispanic, Latino or Spanish

Please select the sex of your child:
❑ Male ❑ Female

Which race best describes your child (select all that apply):
❑ White/Caucasian ❑ Black/African American
❑ American Indian or Alaskan Native
❑ Asian/Pacific Island ❑ Other: _____

LIVING ENVIRONMENT

Was your child born in the United States? ❑ Yes ❑ No *If no, what country w*

Does your child currently live in the United States? ❑ Yes ❑ No

If yes, in what city and state does your child live? (example: Houston, Texas) ___

If no, in what city and country does your child live? (example: London, England)

In what type of housing does your child live? ❑ Apartment ❑ House ❑ Tow

What type of community does your child live? ❑ Urban (in a city) ❑ Suburban

EDUCATIONAL BACKGROUND

What type of school does your child attend? ❑ Public ❑ Private ❑ Homeschoo

What is your child's current grade? (circle)

K 1 2 3 4 5 6 7 8 9 10 11 12

VISUAL HISTORY – PARENTS

Does the biological MOTHER wear glasses or contact lenses?
❑ Yes ❑ No ❑ Unsure

If yes, at what age did the mother start? _____ years old

If yes, is the correction for seeing:
❑ Distance (nearsighted) ❑ Near (farsighted) ❑ Both ❑ Unsure

VISUAL HISTORY – CHILD

Has your child had an eye exam before? ❑ Yes ❑ No

If yes, at what age did the first examination take place? _____

Has your child had an eye exam within the last year? ❑ Yes ❑ No

Does your child wear glasses or contact lenses? ❑ Yes ❑ No

If yes, at what age did your child start? _____ years old

If yes, is the correction for: ❑ Distance ❑ Near ❑ Both ❑ Unsure

If yes, is your child's prescription getting worse each year?
❑ Yes ❑ No ❑ Unsure

If known, please enter your child's prescription here, to the best of your ability. If unknown, leave the below table blank:

Rx	Sphere (SPH)	Cylinder (CYL)	Axis	ADD
OD (right eye)				
OS (left eye)				

Created by Lisa Ostrin, OD, PhD, at the University of Houston College of Optometry.

UH NEAR Survey for Children (Page 2 of 3)

PART TWO: ACTIVITIES DURING THE SCHOOL YEAR

Please estimate and mark the number of hours PER DAY your child spends involved in these various activities DURING THE SCHOOL YEAR, when your child is NOT in school, on a typical school weekday (Monday-Friday) and a typical school weekend day (Saturday-Sunday). For example, if your child spends 3 hours on a weekday and 2.5 hours on a weekend day doing an activity, please mark it like this:

EXAMPLE (mark grid as indicated) — Hours per WEEK DAY — Hours per WEEKEND DAY

DURING THE SCHOOL YEAR, how many hours per day does you

Hours per WEEK

1. ...in outdoor physical activities during the daytime (sports, swimming, walking, biking, running)?
2. ...in outdoor leisure activities during the daytime (eating, sitting, or resting outdoors)?
3. ...in a vehicle during the daytime (car, bus or train)?
4. ...in indoor physical activities (exercise, sports, martial arts)?
5. ...viewing a TV screen (movies, video games on a TV)?
6. ...viewing a computer screen (classes, homework, browsing, computer games)?
7. ...viewing a handheld electronic device (smartphone, tablet, handheld video games, Kindle)?
8. ...reading printed material (books, homework, newspaper, magazines)?
9. ...writing, drawing, painting, or crafting?
10. ...playing card or board games (not electronic)?
11. How many hours of sleep does your child get per night?

Created by Lisa Ostrin, OD, PhD, at the University of Houston College of Opto

UH NEAR Survey for Children (Page 3 of 3)

PART THREE: ACTIVITIES DURING THE SUMMER

Please estimate and mark the number of hours PER DAY your child spends involved in these various activities DURING THE SUMMER, for a typical weekday (Monday-Friday) and a typical weekend day (Saturday-Sunday). For example, if your child spends 3 hours on a weekday and 2.5 hours on a weekend day doing an activity, please mark it like this:

EXAMPLE (mark grid as indicated) — Hours per WEEK DAY — Hours per WEEKEND DAY

DURING A TYPICAL SUMMER, how many hours per day does your child spend...

Hours per WEEK DAY | Hours per WEEKEND DAY

1. ...in outdoor physical activities during the daytime (sports, swimming, walking, biking, running)?
2. ...in outdoor leisure activities during the daytime (eating, sitting, or resting outdoors)?
3. ...in a vehicle during the daytime (car, bus or train)?
4. ...in indoor physical activities (exercise, sports, martial arts)?
5. ...viewing a TV screen (movies, video games on a TV)?
6. ...viewing a computer screen (classes, homework, browsing, computer games)?
7. ...viewing a handheld electronic device (smartphone, tablet, handheld video games, Kindle)?
8. ...reading printed material (books, homework, newspaper, magazines)?
9. ...writing, drawing, painting, or crafting?
10. ...playing card or board games (not electronic)?
11. How many hours of sleep does your child get per night?

Created by Lisa Ostrin, OD, PhD, at the University of Houston College of Optometry. Dr. Ostrin can be contacted at lostrin@central.uh.edu.

Page one of the available PDF collects information on the patient's demographics, background and refractive status.

Pages two and three ask the parent to quantify the number of hours the child spends on a range of visual activities during the school year (page 2) and during the summer (page 3). These results will then be used to calculate mean values for each relevant variable.

Survey Applications

Since the UH NEAR has distinctive uses in clinical vs. research settings, below are some of its potential applications for both types of professionals.

Clinicians: Eyecare providers may find this survey useful when considering management plans for myopia patients and to collect myopia risk factor data across their patient populations. The survey can be sent to parents or guardians prior to the eye exam, filled out in-clinic while in the waiting room or administered to the parent during the child's exam. Older children can help parents estimate time in various activities to improve accuracy, and clinicians should perform cycloplegic refractions when possible.

During focus group administration, the full 44-item survey took approximately 10 minutes for parents to answer. For a simple snapshot of the child's activity, or to further reduce the time for completion, clinicians may decide to shorten the survey.

Factors from the survey that may indicate faster myopia progression are as follows:

- Younger age
- More myopic refraction
- Two myopia parents
- Less than 90 to 120 minutes of outdoor time per day
- High educational demands
- Extensive use of digital devices

The presence (or absence) of some or all of these factors can help clinicians identify the level of myopia risk each child potentially faces, and thus, may help to create a management plan tailored to each case.

Researchers: Myopia researchers can administer the UH NEAR survey to collect epidemiological data in clinical trials, from large populations or in laboratory-based research studies. Consistent use across labs will allow data to be pooled for diverse populations and varied geographic locations. The survey can be easily converted to an online format to facilitate wider administration and data compilation.

The greatest strength of the UH NEAR survey will come from its use in longitudinal studies, where it can be paired with objective wearable sensors to precisely quantify light exposure, near work, physical activity and sleep, along with a comprehensive eye exam including cycloplegic refractive measurement.

Photo: Getty Images

Parents filling out the survey must estimate how much time children spends doing outdoor physical or leisure activities and riding in a car to determine their approximate sunlight exposure, a known myopia risk factor.

How to Access

Clinicians or researchers interested in using the UH NEAR survey can find a downloadable version of the full questionnaire and scoring sheet in the online version of this article at www.reviewofoptometry.com. It can also be obtained through direct contact with the author of this article and one of the survey developers, Lisa Ostrin, OD.

Because this survey was produced based on the current understanding of myopiagenesis, it is expected to evolve and improve as potential new, previously unidentified risk factors become relevant. For use in countries other than the United States, clinicians and researchers can tailor demographic questions to the specific education system to make it most relevant to the population in question.

Whether you are a clinician or researcher, the UH NEAR survey offers a comprehensive and practical method of myopia risk assessment to encourage data-driven management of this growing patient population. ■

1. Gajjar S, Ostrin LA. Development of the University of Houston near work, environment, activity, and refraction (UH NEAR) survey for myopia. Clin Exp Optom. 2023:1-14.

2. Haarman AEG, Enthoven CA, Tideman JWL, et al. The complications of myopia: a review and meta-analysis. Invest Ophthalmol Vis Sci. 2020;61(4):49.

3. Jones-Jordan LA, Sinnott LT, Manny RE, et al. Early childhood refractive error and parental history of myopia as predictors of myopia. Invest Ophthalmol Vis Sci. 2010;51(1):115-21.

4. Holden BA, Fricke TR, Wilson DA, et al. Global prevalence of myopia and high myopia and temporal trends from 2000 through 2050. Ophthalmology. 2016;123(5):1036-42.

5. Rose KA, Morgan IG, Ip J, et al. Outdoor activity reduces the prevalence of myopia in children. Ophthalmology. 2008;115(8):1279-85.

6. Li SM, Li SY, Kang MT, et al. Near work related parameters and myopia in chinese children: the anyang childhood eye study. PloS one. 2015;10(8):e0134514.

7. Guo Y, Liu LJ, Xu L, et al. Outdoor activity and myopia among primary students in rural and urban regions of Beijing. Ophthalmology. 2013;120(2):277-83.

8. Choi KY, Chan SS, Chan HH. The effect of spatially-related environmental risk factors in visual scenes on myopia. Clin Exp Optom. 2022;105(4):353-61.

9. Rosner M, Belkin M. Intelligence, education, and myopia in males. Arch Ophthalmol. 1987;105(11):1508-11.

10. Simensen B, Thorud LO. Adult-onset myopia and occupation. Acta Ophthalmol (Copenh). 1994;72(4):469-71.

11. Zadnik K, Satariano WA, Mutti DO, Sholtz RI, Adams AJ. The effect of parental history of myopia on children's eye size. JAMA Ophthalmol. 1994;271(17):1323-7.

12. Ostrin LA, Sajjadi A, Benoit JS. Objectively measured light exposure during school and summer in children. Optom Vis Sci. 2018;95(4):332-42.

13. Gwiazda J, Deng L, Manny R, Norton TT, Group CS. Seasonal variations in the progression of myopia in children enrolled in the correction of myopia evaluation trial. Invest Ophthalmol Vis Sci. 2014;55(2):752-8.

14. Read SA, Collins MJ, Vincent SJ. Light exposure and physical activity in myopic and emmetropic children. Optom Vis Sci. 2014;91(3):330-41.

15. Williams R, Bakshi S, Ostrin EJ, Ostrin LA. Continuous objective assessment of near work. Sci Rep. 2019;9(1):6901.

16. Bhandari KR, Shukla D, Mirhajianmoghadam H, Ostrin LA. Objective measures of near viewing and light exposure in schoolchildren during COVID-19. Optom Vis Sci. 2022;99(3):241-52.

LensChek® & **OptoChek®** Pre-Test

RELIABLE **REFRACTION**.
TRUSTED **TONOMETRY**.

We share your passion for personalizing and improving vision testing and glaucoma care. For nearly two centuries, we've delivered innovative, precise, and efficient diagnostic devices to help you provide better patient care.

LEARN MORE

WATCH MORE AT **REICHERT.COM**

Ocular Response Analyzer® G3 with Corneal Hysteresis + IOPcc

Phoroptor® – Digital or Traditional featuring **Phoroptor® VRx** with **ClearChart®**

Tono-Pen AVIA® Tonometer

Reichert®
AMETEK®

passionate about eye care

Designed & assembled in USA

UNDERSTANDING CORNEAL ULCERS AND INFILTRATES

How to distinguish one from another and avoid misdiagnosis when the history and symptoms don't match the presentation.

CHRISTINA CHERNY, OD
NEW YORK CITY

For many ocular conditions, history and clinical presentation provide sufficient clues to arrive at an accurate diagnosis and treatment plan with a great degree of certainty. This is not always the case for corneal infiltrative disease, as symptoms and signs can present in similar ways yet beget differing treatment plans.

In order to ensure appropriate outcomes for patients, we have to evaluate all of the clinical clues presented to us, take into account the relevant context, history and symptoms and make an educated decision regarding diagnosis and treatment regimen. A basic understanding of corneal immunity, as well as sterile corneal infiltrative and microbial disease process, is essential for us to make an appropriate diagnosis in a timely fashion and achieve best visual and ocular outcomes for our patients.

Corneal Immune System

The cornea, the eye's barrier to the outside world, is constantly in contact with microorganisms that may be pathogenic, yet it is able to maintain an excellent degree of resistance to microbial invasion. This resistance consists of both innate and adaptive immunity.

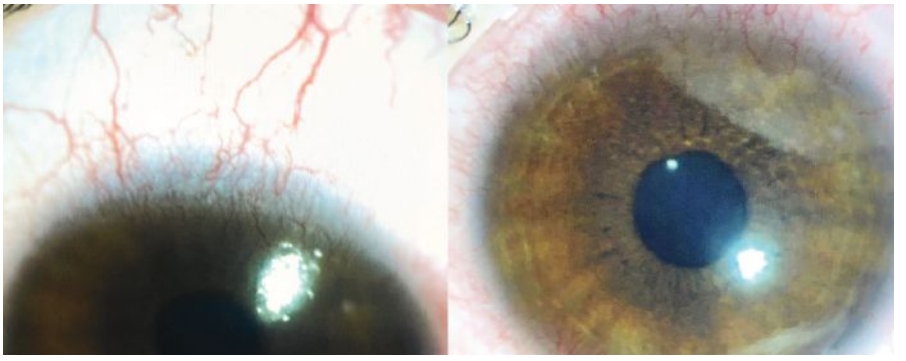


Fig. 1. Contact lens peripheral ulcer (CLPU) in the setting of contact lens over wear.

Innate immunity, which begins at the corneal epithelium as the first line of defense, conveys protection within minutes of encounter with an infectious element by releasing cytokines and chemokines. Previously, innate defenses were considered to consist of nonspecific engulfment of pathogens by macrophages, but we now know that innate toll-like receptors confer specificity and enhance discrimination between pathogen and host during the immediate immune response, and keratocytes work with interferons, neutrophils, natural killer cells and macrophages to identify and eliminate the pathogen.[1]

Adaptive immunity, which may take several days, responds to specific pathogens and antigens by mediating B and T lymphocytes that proliferate and are able to generate memory cells.[2] This cellular immune response leads to the migration of white blood cells—including polymorphonuclear leukocytes and mononuclear cells—arising from the limbal arcades and the precorneal tear film into within the cornea, resulting in an infiltrate.[3,4]

About the author

Dr. Cherny is an instructor in ophthalmology at the New York Eye and Ear Infirmary of Mount Sinai. She specializes in complex contact lens fittings, anterior segment and corneal surgery comanagement, as well as primary and emergent eye care. Dr. Cherny is a fellow of the American Academy of Optometry. She has no financial disclosures.

Corneal Infiltrates

These are often seen with contact lens wear and considered either sterile or infectious, and several distinguishing characteristics need to be evaluated in order to best decide on the etiology (*Table 1*).[1,3] Historically, corneal infiltrative events in the setting of contact lens wear were considered to be sterile in all cases, but we now know that some presumed sterile infiltrates may indeed be culture positive.[6]

Sterile infiltrates tend to be smaller in size (often less than 1mm to 1.5mm), may be multiple or arcuate, and present with minimal to no pain, epithelial cell staining, conjunctival inflammation, discharge and anterior chamber reaction. These often involve the host or immune response to a microbial antigen in the absence of a live microorganism.[6,7] This is in contrast with infected ulcers, which present with increased pain, moderate-to-severe discomfort, discharge, epithelial cell staining, increased size (often greater than 2mm) and moderate or severe anterior chamber reaction.[3,5] These are considered to be microbial keratitis, which involves the presence of live proliferating pathogens and the involvement of a secondary immune response.[6]

Infiltrate size has been found to be less predictive of etiology, as a sizable percentage of culture-positive infiltrates were found to be small in size. Of greater predictive value is the presence of an overlying epithelial defect size, which was found to be present in all cases of culture-positive infiltrates and only about a third of culture-negative cases.[5] Noninfectious infiltrates often presented either with no overlying epithelial defect or simply with overlying superficial punctate keratitis.[5,8]

Most often, sterile infiltrates have been found to be located in the peripheral cornea, often within 4mm of the limbus; they are often subepithelial or anterior stromal in depth.[7,8] Sterile infiltrates tend to be nonprogressive and/or self-limiting, responsive to therapy and often do not result in serious sequelae such as an impact on visual acuity, as may be the case with microbial keratitis.[3,6-9] In more serious cases, they can result in scarring which can negatively impact visual acuity.[3]

TABLE 1. STERILE VS. INFECTIOUS INFILTRATES[5]

	Sterile	Infectious
Location	Periphery	Central
Size	Small <1mm to 1.5mm	Larger >1mm to 2mm
Inflammation	Minimal or absent anterior chamber reaction	Moderate to severe anterior chamber reaction, with or without hypopyon
Epithelial Involvement	Minimal or absent epithelial defect	Epithelial defect completely overlying stromal infiltrate
Symptoms	Absent or mild pain/photophobia/foreign body sensation	Significant mucopurulent discharge, pain, redness, photophobia, lid edema

Noninfectious infiltrates often presented either with no overlying epithelial defect or simply with overlying superficial punctate keratitis.

Sterile corneal infiltrates may be considered marginal, which are self-limiting hypersensitivity reactions due to *Staphylococcal* antigens in the setting of bacterial eyelid disease; in these cases, the infiltrates are small, circumlimbal, with a 1mm clear interval, often abutting the eyelid margin with mild focal hyperemia.[10,11] Marginal infiltrates may be seen in the setting of blepharokeratoconjunctivitis and can result in ulceration of the overlying epithelium.[12] Such infiltrates typically respond well to a topical antibiotic-steroid combination drop.

Contact Lens Wear

The infiltrative process may arise from contact lens wear, preservative toxicity, corneal hypoxia, *Staphylococcal* immune complex formation, poor hygiene and infectious etiologies.[8] Risk factors for corneal infiltrative events in the setting of contact lens wear include age under 25 years (with a peak between ages 15 and 25), ametropia, bacterial burden on eyelids, smoking, silicone hydrogel contact lens materials, male gender, refractive error greater than ±5D, limbal redness, previous corneal infiltrative events, overnight and extended soft contact lens wear, use of multi-purpose contact lens solutions and being new to soft contact lens wear.[3,6,7,9]

In cases of extended contact lens wear, corneal infiltrates often occur in the superior corneal quadrant.[7,13] The use of daily disposable contact lenses has been shown to decrease the risk of corneal infiltrative events by over twelvefold in comparison with planned replacement contact lenses.[6]

Corneal infiltrative events in the setting of contact lens wear can be classified based on their presenting signs and symptoms. According to one study, the most serious and symptomatic category of corneal infiltrative events presents in the form of microbial keratitis.[14] This is an infectious corneal event in which there is excavation, diffuse infiltration and necrosis of the epithelium, Bowman's layer and stroma. Infiltrates are often focal, large and irregular, and may be accompanied by satellite lesions, severe limbal and bulbar redness anterior chamber reaction and mucopurulent discharge. Patients may be rapidly symptomatic for moderate to severe pain, decreased vision, tearing, photophobia and eyelid edema.

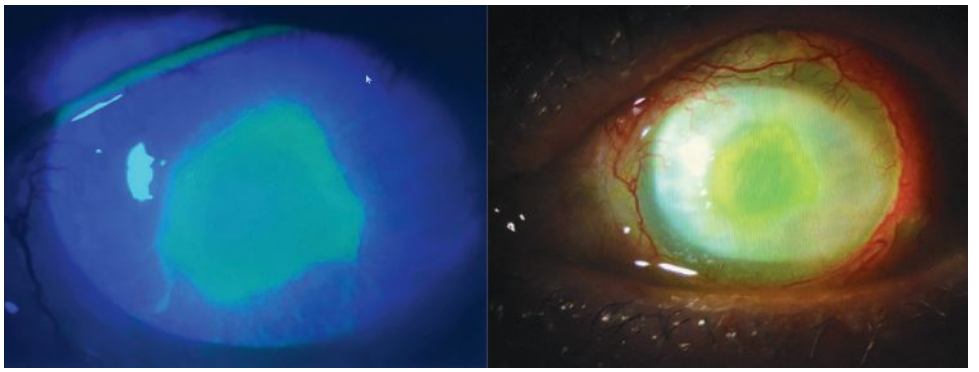


Fig. 2. *Pseudomonas aeruginosa* corneal ulcer. Epithelial defect overlies and mirrors the size of round, central stromal infiltrate.

Less serious but also clinically significant and symptomatic corneal infiltrative events are the entities known as contact lens–induced red eye (CLARE), contact lens peripheral ulcer (CLPU) and infiltrative keratitis.

• ***CLARE.*** Patients are symptomatic for moderate pain, tearing and photophobia on waking. Clinical signs include circumferential hyperemia and multiple focal small infiltrates peripherally without an overlying epithelial defect.

• ***CLPU.*** These patients can be asymptomatic, or they can experience moderate pain and/or foreign body sensation. Clinical signs include limbal and bulbar hyperemia, small single focal circular infiltrates less than 2mm in size and in close proximity of the limbus, focal epithelial excavation, infiltration and necrosis of anterior stroma (*Figure 1*).

• ***Infiltrative keratitis.*** Patients are symptomatic for mild to moderate irritation, discharge and redness. Clinical signs include one or multiple small infiltrates within the peripheral anterior stroma, with possible epithelial involvement.

In certain cases, corneal infiltrative events may be asymptomatic and bear little clinical significance. These are usually focal and small, 0.2mm or less, and present with no epithelial staining. Also clinically non-significant and asymptomatic are asymptomatic cases of interstitial keratitis, in which case small focal infiltrates are often seen with epithelial punctate staining and limbal/bulbar redness.[6,14]

Infectious Keratitis

When a stromal infiltrate presents with significant overlying epithelial disruption anterior chamber reaction, along with acute symptoms including pain, redness, discharge, decreased vision and photophobia, particularly in the context of a prior corneal wound disrupting the epithelium, the etiology is more likely to be infectious.[15-18] It is important to identify and appropriately treat microbial keratitis, as severe cases may progress to thinning or ulceration of the stroma, corneal perforation, corneal scarring, endopthalmitis and vision loss.[16,18,19-21] Infectious keratitis may be due to bacterial, viral, fungal and protozoan etiology.

• ***Bacterial keratitis.*** This is often associated with gram-positive organisms including *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Streptococcus pneumoniae* and gram-negative organisms including *Pseudomonas aeruginosa* (*Figure 2*). The latter is often associated with prolonged daily and extended contact lens wear and can present with a large central epithelial defect overlying a large infiltrate in the setting of severe pain, redness, photophobia, discharge, decreased vision, anterior chamber reaction and hypopyon.[5,19,22,23] In cases of bacterial keratitis, an infiltrate is often located centrally or paracentrally and is greater than 1mm with a large and deep epithelial defect extending into the stroma, and may be seen with surrounding corneal edema and multiple satellite lesions.[14,24]

Factors associated with bacterial keratitis in the setting of contact lens wear include poor contact lens hygiene (including the use of tap water), soft contact lens wear (as there is less tear exchange than with rigid gas permeable contact lens wear and bacterial antigens are allowed to build up), extended contact lens wear and hypoxia secondary to overnight wear.[14,24]

• ***Protozoa/parasitic keratitis.*** In the setting of keratitis, particularly with contact lens wear—while rare—the usual parasitic culprit is *Acanthamoeba*. This is most often seen in patients who sleep or swim in contact lenses (in pools, hot tubs or freshwater), as well as those that store contact lenses in homemade saline prepared with water.[5] *Acanthamoeba* may have reduced corneal sensation early on, or can first present with severe ocular pain and photophobia; signs may at

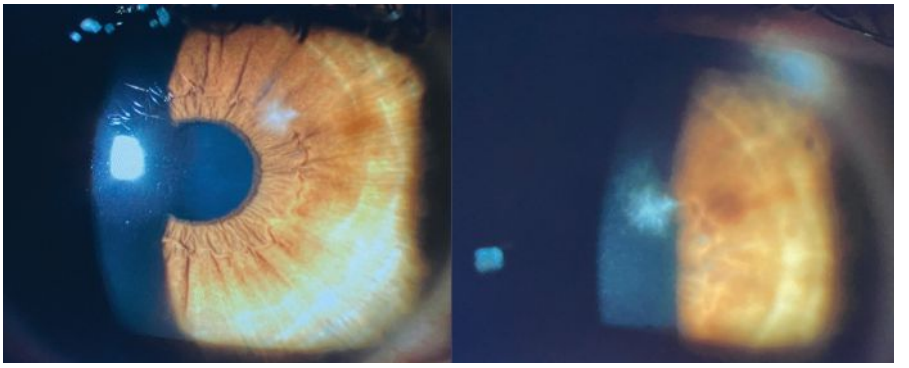


Fig. 3. Small, discrete, focal stromal infiltrate masquerading as sterile infiltrate given minimal concomitant signs and symptoms; however, culture positive for yeast. Central location and feathery margins are often seen in fungal ulcers.

BRIGHTER LOOKING EYES WITH ONE DROP

The Conversation Eye Care Providers Should Be Having with Patients

Melissa Toyos, MD
Practices at Toyos Clinic located in Tennessee, Mississippi, and New York

Aesthetics are an important patient concern that can affect how they feel about themselves and around other people. Patients commonly use products and services that promise aesthetic enhancement, including lash extensions, eyelash growth treatments, colored contact lenses, eye makeup, eye creams, and serums. Increasingly, patients also seek out redness-relieving eye drops to improve the appearance of their eyes.

Ocular Redness: A Key Patient Concern

Demand is substantial: 4 in 10 sales in the over-the-counter (OTC) eye drop category are for redness relievers.[1] Because ocular redness is often caused by "minor" eye irritations, patients may not recognize it as a valid concern that they can discuss with their eye care provider (ECP) and are, therefore, not always professionally counseled on which redness reliever is best for them. Without their ECP's input, patients can sometimes lean on potentially unreliable sources, such as the store shelf, their peers, commercials, or the internet. Herein lies an opportunity to educate patients and guide them through the enormous ocular redness market while also addressing the root cause of their symptoms.

LUMIFY®: A Clinically Proven Approach to Treating Ocular Redness

LUMIFY® (brimonidine tartrate ophthalmic solution) 0.025% drops are indicated for relieving redness of the eye due to minor eye irritations.[2] Most redness relievers are α1- or α1/α2-adrenergic receptor agonists; α1-adrenergic receptor agonism constricts corneal arterioles, hindering oxygen delivery to the cornea, which causes rebound redness. Brimonidine tartrate, by contrast, is selective for the α2-adrenergic receptor, primarily constricting ocular surface venules, which do not affect ocular surface oxygen delivery and therefore is not associated with high levels of rebound redness.[3]

In 6 clinical studies with over 600 patients, low-dose brimonidine tartrate demonstrated a 1 minute onset of action, which persisted for up to 8 hours.[4] It had a favorable safety profile and, consistent with its mechanism of action, a low incidence of rebound redness (1.2%).[4,5,6] Adverse event rates did not significantly differ from control, and the most common adverse events in brimonidine-treated eyes were reduced visual acuity (4.0%) and conjunctival redness (2.6%).[5]

Opportunity for ECPs to Step In

Market research indicates that patients report using of redness relievers an average of 3 days per week.[7] Ocular redness is a key concern for many patients, but the OTC eye care market contains an often overwhelming array of products. Understanding and communicating the benefits and challenges of available products is key to helping patients narrow down which products—out of everything on the shelf—might work best for them.

> **LUMIFY® provides safe and effective redness relief for my patients dealing with minor eye irritations**

LUMIFY® is a redness reliever drop differentiated in its mechanism of action, rapid effects, and minimal rebound redness. LUMIFY® provides patients with excellent redness relief. In recommending a product as efficacious and reliable as LUMIFY®, ECPs can establish themselves as trusted professionals who can address patients' needs—both clinical and aesthetic. This can lead not only to improved patient outcomes and satisfaction but could also enhance trust in their relationship with their ECP.

Incorporating ocular aesthetics into the patient conversation

- Ask patients if they are happy with how their eyes look and feel
- Ask patients if they use OTC eye care products and if they are satisfied with them
- Consider that the aesthetic aspect of eye care may be just as important to a patient as the clinical aspect
- Be ready and willing to provide OTC recommendations

1. IQVIA Sales Data, Latest 52 weeks ending 6/18/2023
2. LUMIFY® [Drug facts]. Bausch & Lomb Incorporated, Bridgewater, NJ.
3. Corboz MR, Rivelli MA, Varty L, et al. Pharmacological characterization of postjunctional α-adrenoceptors in human nasal mucosa. *Am J Rhinol.* 2005;19(5):495-502.
4. 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.
5. Ackerman SL, Torkildsen GL, McLaurin E, Vittitow JL. Low-dose brimonidine for relief of ocular redness: integrated analysis of four clinical trials. *Clin Exp Optom.* 2019;102(2):131-139.
6. Torkildsen GL, Sanfilippo CM, DeCory HH, Gomes PJ. Evaluation of efficacy and safety of brimonidine tartrate ophthalmic solution, 0.025% for treatment of ocular redness. *Curr Eye Res.* 2018;43(1):43-51.
7. Data on file. Bausch & Lomb. Rochester, NY

BAUSCH+LOMB

LUM.0100.USA.23

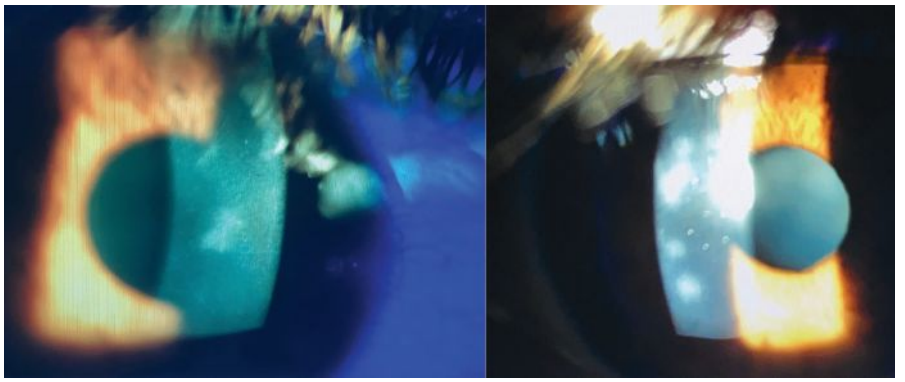


Fig. 4. Multiple recurrent SEIs following epidemic keratoconjunctivitis.

first be nonspecific, including punctate epithelial erosions, mild inflammation dendritic lesions or a central superficial infiltrate and may progress into a ring infiltrate.[25] *Acanthamoeba* diagnosis can be made with stained smear or culture, as well as by confocal microscopy, PCR or metagenomic sequencing.[8,25]

• ***Fungal keratitis.*** While rare, fungal keratitis needs to be considered when there is an ulcer in the setting of corneal trauma, particularly with vegetative matter, as well as with contact lens wear or topical corticosteriod use. Fungal ulcers present with deep stromal infiltrates and are often described as having feathery margins and satellite lesions. These ulcers may be accompanied by a hypopyon and need to be considered if there is a prior history of topical steroid use as they can exacerbate the fungal infection.[25]

• ***Epidemic keratoconjunctivitis.*** In the setting of adenoviral epidemic keratoconjunctivitis, multiple small, grayish, nummular, lymphocytic subepithelial infiltrates (SEIs) may develop within the superficial stromal due to an immune reaction (*Figure 4*). These SEIs generally present bilaterally and in the context of significant hyperemia, eyelid edema, epiphora, chemosis, foreign body sensation, photophobia, membranes, follicular reaction, symblepharon formation and blurry vision.[26,27] Systemic signs also include preauricular lymphadenopathy, fever, headache and fatigue.[27] Given the effect of SEIs on visual acuity, as well as the potential for vision-threatening scarring, treatment with topical corticosteroids is imperative and is also of significant benefit in the presence of membranes and pseudomembranes. SEI recurrence is possible when steroids are discontinued, so in cases of mild SEI recurrences, topical cyclosporine can be utilized as a steroid-sparing agent.[26]

• ***Herpetic.*** Herpes simplex virus (HSV) and herpes zoster ophthalmicus (HZO) are two viral corneal infections that should be on the list of differentials, particularly if there is a history of herpes zoster or varicella zoster infection, significant recent stress, sun exposure and decreased corneal sensation. HSV keratitis may present with epithelial involvement which can range from nonspecific punctate keratopathy to dendritic ulcers with true terminal end bulbs.[28] In cases where HSV involves the stroma, dense stromal edema may be seen with endothelial folds, anterior uveitis and elevated intraocular pressure.[28,29] In HZO, epithelial involvement presents with pseudodendrites without true terminal end bulbs.[28,29]

Diagnosis and Treatment

When a patient presents with clinical signs and symptoms of a corneal infiltrate, it is essential to arrive at an accurate diagnosis and initiate appropriate treatment. If the patient wears contact lenses, clinical signs and symptoms on presentation can provide important clues as to the origin of the infiltrate. If the symptoms are mild or absent, the infiltrate is more likely to be sterile. If significant pain, discharge, and/or anterior chamber reaction are present, particularly if there is an overlying epithelial defect, it is reasonable to presume an infectious etiology until proven otherwise and to subsequently obtain scrapings for cultures and smears.[5] When infectious etiology is suspected, it is vital to immediately discontinue contact lens wear and to initiate treatment with topical antibiotics with close monitoring and clear return precautions, even if a clear diagnosis has yet to be established, so that treatment is not delayed.[5]

In the settling of contact lens wear, if the infiltrate is focal and peripheral, less than 1.5mm and without epithelial disturbance, cultures are not required and the infiltrate can be treated with antibiotics or topical antibiotic-steroid combination drops in addition to discontinuation of contact lens wear.[7,13] In very mild cases, observation alone may be appropriate. However, if a large overlying epithelial defect is present in the setting of an inflamed eye, a culture is prudent prior to initiating topical antibiotic therapy, followed by steroid treatment 24 to 48 hours after epithelialization has occurred.[7]

If the patient is developing peripheral corneal infiltrates with extended-wear soft contact lenses, it is essential to refit the patient into daily wear soft or rigid contact lenses.[7,8] Rigid gas permeable contact lenses provide superior tear exchange and deposit resistance relative to soft lenses, which is protective against corneal infiltrative events.[23,24]

When a patient presents with a corneal ulcer, a systematic algorithm for assessment and treatment—called the 1-2-3-ACT (Assess, Culture, Treat) Rule, originally adapted by the Massachusetts Eye and Ear Infirmary—can be used to identify sight-threatening ulcers and manage them accordingly (*Table 2*).

A corneal ulcer that meets criteria for the 1-2-3 rule will present with any one of the following criteria: 1+ or greater anterior chamber cell, 2mm or greater, two or more adjacent lesions, and/or 3mm or less distance from the corneal center. If the ulcer meets this

Review Tops the Charts Again!

REVIEW of OPTOMETRY

The OD's FIRST CHOICE

Practitioners rely on *Review of Optometry* more than any other eye care publication

Ranked #1
Eye Care Publication In FIVE Critical Readership Categories:

- Total Readers
- Most Read Publication/ Website Within the Last Six Months
- Average Page Exposures
- Websites Visited within the Last Six Months
- Quality Clinical Content I Use in My Practice

Source: *Kantar Media Eyecare 2023 Study*

***Review* also is number one in readership across the following categories:**

- Total Optometrists
- ODs in High-Volume Practices (76pts/wk)
- Solo Practitioners
- Annual Practice Revenue ($500k+)
- ODs who Purchase Examination Equipment
- Write Prescriptions (11+ per week)
- Perform Refractions (51+ per week)
- Contact Lens Prescribers
- Years in Practice (1-15 and 15+)
- Among Key Opinion Leaders

***To our readers:* Thank you for your loyalty, time and trust. We'll keep working hard to earn your support.**

TABLE 2. 1-2-3 ASSESS-CULTURE-TREAT RULE FOR SIGHT-THREATENING CORNEAL ULCERS[30]

Criteria:
- 1+ anterior chamber cell
- 2mm or greater in size
- Two or more adjacent lesions
- 3mm or less from corneal center

Meets Criteria	Does Not Meet Criteria
Obtain cultures: · Blood, chocolate, sabouraud agar · Glass slides with gram stain, calcofluor stain · Thioglycollate broth Initiate fortified antibiotics: · Fortified vancomycin 25mg/mL hourly · Fortified tobramycin 13.5mg/mL hourly · Cycloplegia: atropine twice daily Follow-up 24 to 36 hours	Cultures not necessary Initiate topical fluoroquinolone: · Moxifloxacin 0.5% hourly or gatifloxacin 0.5% hourly Follow-up 24 to 36 hours

criteria, it is recommended to obtain cultures (blood, chocolate and sabouraud agar, gram stain and calcofluor stains on glass slides, and thioglycollate broth), followed by initiation of fortified antibiotics (vancomycin 25mg/mL and tobramycin 13.5mg/mL) hourly in the affected eye in addition to twice daily topical cycloplegia with atropine.[30] Follow-up should be arranged within 24 to 36 hours with a provider trained in corneal pathology. Additional indications for corneal culturing include a recent history or ocular trauma, topical or systemic corticosteroid use or immunocompromised status.

For corneal ulcers that do not satisfy the criteria of the 1-2-3 rule, it is reasonable to presume the ulcer is not immediately sight-threatening, forgo culture and begin empirical treatment with a topical fluoroquinolone, such as moxifloxacin 0.5% or gatifloxacin 0.5%, one drop hourly. Follow-up should occur within 24 to 36 hours to monitor progress.[30]

Takeaways

When patients with presumed corneal infiltrative and infectious disease present for evaluation, a lengthy list of differential diagnoses can come to mind. In order to narrow down the correct differential and provide appropriate treatment, it is essential to carefully consider patient history, symptoms and clinical corneal signs in the context of other ocular findings. If the diagnosis is unclear but clinical signs and symptoms are significant, it may be prudent to first obtain confirmatory testing, such as cultures and smears, and then immediately initiate empirical treatment for an infectious etiology until a definitive answer arrives. Comanagement with corneal ophthalmology subspecialists may be essential, particularly if the signs are worsening or a visually threatening event is imminent. ■

1. Akpek EK, Gottsch JD. Immune defense at the ocular surface. Eye. 2003;17:949-56.

2. Kumar A, Yu FS. Toll-like receptors and corneal innate immunity. Curr Mol Med. 2006;6(3):327-37.

3. Jansen ME, Situ P, Begley CG, et al. Characterizing contact lens-related corneal infiltrates: a pilot study. Cornea. 2016;35(12):1578-83.

4. Bazan NG, Bazan HP. Ocular responses to inflammation and the triggering of wound healing: lipid mediators, proto-oncogenes, gene expression and neuromodulation. In: Bazan NG, ed. Lipid Mediators in Eye Inflammation. Braquet P, ed. New Trends in Lipid Mediators Research, 5th ed. Basel: Karger; 1990:168-80.

5. Stein RM, Clinch TE, Cohen EJ, et al. Infected vs. sterile corneal infiltrates in contact lens wearers. Am J Ophthalmol. 1988 ;105(6):632-6.

6. Steele KR, Szczotka-Flynn L. Epidemiology of contact lens-induced infiltrates: an updated review. Clin Exp Optom. 2017;100(5):473-81.

7. Donshik PC, Suchecki JK, Ehlers WH. Peripheral corneal infiltrates associated with contact lens wear. Trans Am Ophthalmol Soc. 1995;93:49-60; discussion 60-4.

8. Suchecki, JK, Ehlers WH, Donshik, PC. Peripheral corneal infiltrates associated with contact lens wear. CLAO Journal. 1996;22(1):41-6.

9. Chalmers RL, Wagner H, Mitchell GL, et al. Age and other risk factors for corneal infiltrative and inflammatory events in young soft contact lens wearers from the Contact Lens Assessment in Youth (CLAY) study. Invest Ophthalmol Vis Sci. 2011;52(9):6690-6.

10. Mondino BJ. Inflammatory disease of the peripheral cornea. Ophthalmology. 1988;95(4):463-72.

11.The American Academy of Ophthalmology. Immune-related disorders of the external eye. In: External Disease and Cornea (Basic and Clinical Science Course). American Academy of Ophthalmology; 2016-2017:195.

12. Mack HG, Fazal A, Watson S. Corneal ulcers in general practice. Aust J Gen Pract. 2022;51(11):855-60.

13. Baum J, Dabezies OH. Pathogenesis and treatment of "sterile" midperipheral corneal infiltrates associated with soft contact lens use. Cornea. 2000;19(6):777-81.

14. Sweeney DF, Jalbert I, Covey M, et al. Clinical characterization of corneal infiltrative events observed with soft contact lens wear. Cornea. 2003;22(5):435-42.

15. Ni N, Srinivasan M, McLeod SD, et al. Use of adjunctive topical corticosteroids in bacterial keratitis. Curr Opin Ophthalmol. 2016;27(4):353-7.

16. Palioura S, Henry CR, Amescua G, Alfonso EC. Role of steroids in the treatment of bacterial keratitis. Clin Ophthalmol. 2016;10:179-86.

17. Moshirfar M, Hopping GC, Vaidyanathan U, et al. Biological staining and culturing in infectious keratitis: controversy in clinical utility. Med Hypothesis Discov Innov Ophthalmol. 2019;8(3):145-51.

18. Lin A, Rhee MK, Akpek EK, et al. Bacterial keratitis preferred practice pattern. Ophthalmology. 2019;126(1):P1-55.

19. Fortingo N, Melnyk S, Sutton SH, et al. Innate immune system activation, inflammation and corneal wound healing. Int J Mol Sci. 2022;23(23):14933.

20. McDonald EM, Ram FS, Patel DV, McGhee CN. Topical antibiotics for the management of bacterial keratitis: an evidence-based review of high quality randomized controlled trials. Br J Ophthalmol. 2014;98(11):1470-7.

21. Austin A, Lietman T, Rose-Nussbaumer J. Update on the management of infectious keratitis. Ophthalmology. 2017;124(11):1678-89.

22. Cohen EJ. Management of small corneal infiltrates in contact lens wearers. Arch Opthalmol. 2000;118(2):276-7.

23. Bourcier T, Thomas F, Borderie V, et al. Bacterial keratitis: predisposing factors, clinical and microbiological review of 300 cases. Brit J Ophthalmol. 2003;87(7):834-8.

24. Carnt N, Samarawickrama C, White A, Stapleton F. The diagnosis and management of contact lens-related microbial keratitis. Clin Exp Optom. 2017;100(5):482-93.

25. The American Academy of Ophthalmology. Infectious diseases of the external eye: microbial and parasitic infections. In: External Disease and Cornea (Basic and Clinical Science Course). American Academy of Ophthalmology; 2016-2017:152-7.

26. Arici C, Sultan P, Mergen B. Evaluation of the impact of subepithelial corneal infiltrates on corneal biomechanics after epidemic keratoconjunctivitis. Arq Bras Oftalmol. 2022;85(5):478-84.

27. Bawazeer, Ahmed. Epidemic keratoconjunctivitis. Medscape. http://emedicine.medscape.com/article/1192751-overview#a0101. March 20, 2013. Accessed September 28, 2023.

28. Krachmer JH, Mannis MJ, Holland EJ. Cornea. St, Louis, MO: Mosby/Elsevier; 2011.

29. Rapuano C. Corneal infections, inflammations and surface disorders. In: Color Atlas and Synopsis of Clinical Ophthalmology. Wills Eye Institute. Philadelphia: Wolters Kluwer; 2012:188.

30. Ung L, Wang Y, Vangel M, et al. Validation of a comprehensive clinical algorithm for the assessment and treatment of microbial keratitis. Am J Ophthalmol. 2020;214:97-109.

Restore Balance for MGD Patients

with Retaine® MGD® Ophthalmic Emulsion

Retaine® MGD® targets all three layers of the tear film for long-lasting comfort.

- ✓ **Preservative-Free**
- ✓ **Developed for MGD Patients**
- ✓ **Lipid Active Ingredients**
- ✓ **Positively Charged Nano-droplets**

Part of a complete line of Retaine® Brand Products

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

OCuSOFT®

REAL-WORLD USES OF AUTOLOGOUS SERUM EYE DROPS

Here's guidance on when and how to employ this "big gun" in the fight against dry eye disease.

LUIS ROJAS, OD
SAN ANTONIO, TX

We have witnessed an impressive surge of therapeutic advancements for the treatment of ocular surface disease (OSD) in the last two decades. Increased awareness of dry eye disease (DED), availability of new therapies targeting specific etiologies and greater understanding of the multifactorial nature of OSD by fellow clinicians have made these treatments a viable in everyday practice.

Autologous serum eye drops (ASEDs) remain one of the most advanced therapeutics for acute and chronic ocular complications. The primary goal of this article is to guide you in overcoming some of the common obstacles and limitations we may face when prescribing these treatments; specifically, which patients are likely candidates, when and how to add this modality to your practice, as well as how to assess a patient's progress.

Autologous Serum

The therapeutic benefit of ASEDs has been observed in studies dating back to 1975 in patients with multiple systemic disease with ocular involvement and post-surgical ocular surface pathology.[1] Since then, its clinical use has been broadened to cover a wide range of OSD cases such as severe DED, exposure keratopathy, neurotrophic keratitis, Sjögren's syndrome, Steven Johnson syndrome, toxic epidermal necrolysis, graft versus host disease (GVHD), chemical burns, trauma and post-surgical complications. They are also used for other etiologies such as herpetic keratitis, trauma-based recurrent corneal erosions and many other conditions.[2-5]

Some of the unique biochemical characteristics that make ASEDs the "Holy Grail" of topical treatments include pH, osmolarity, micronutrients such as vitamins A and E, proteins such as albumin and fibronectin, and platelet-derived epitheliotrophic factors that are similar to that of human tears.[2,3] ASEDs therefore play an important role in the epithelial healing process of the ocular surface by having anti-inflammatory, antioxidant and antiangiogenic properties.

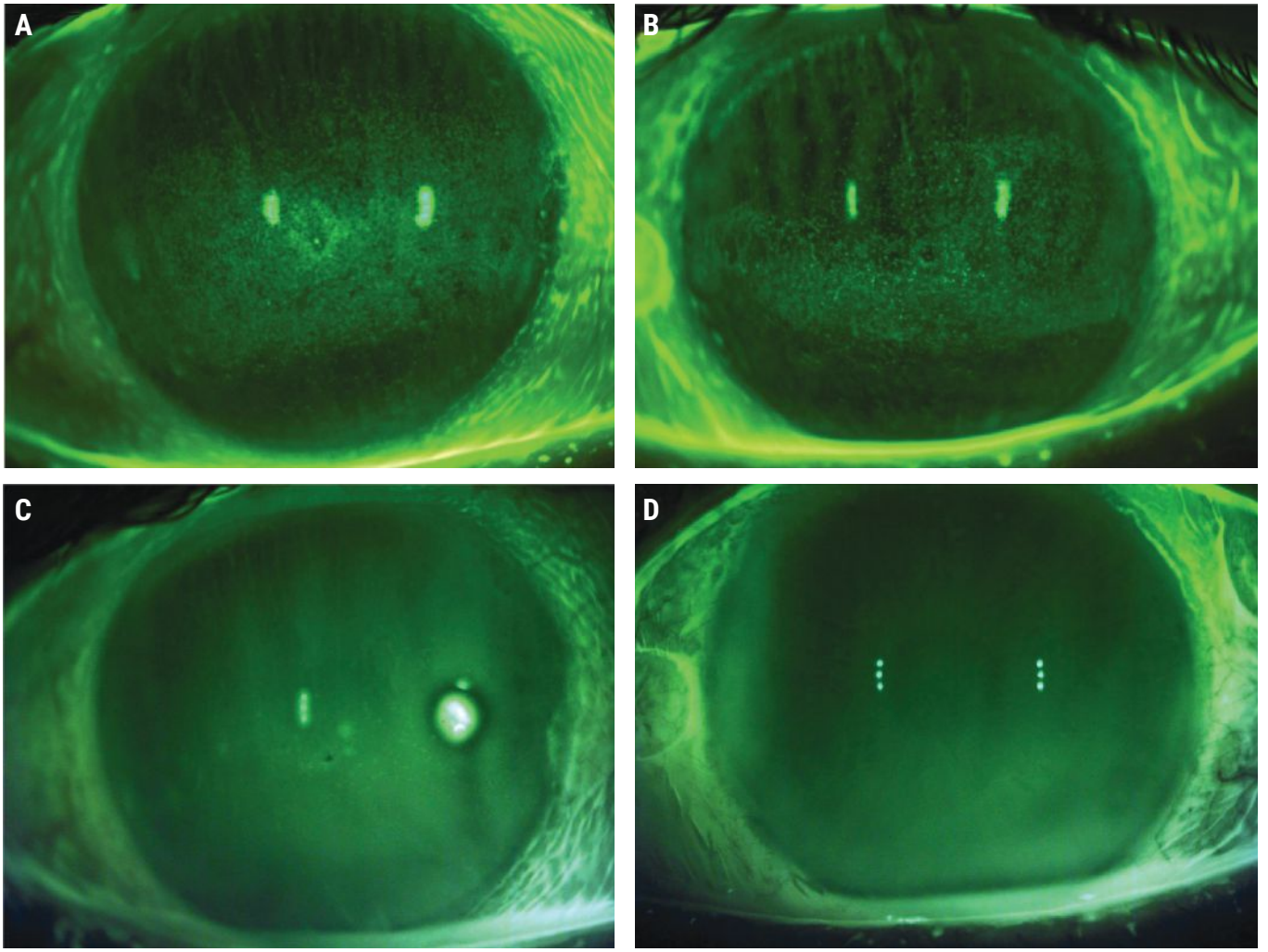
The Best Candidates

Whether it's your first time considering ASEDs or you've had a successful track record of using them, it is helpful to review common clinical applications and scenarios where these drops can be applied in practice. One of the more classic examples include recalcitrant cases of severe aqueous deficient dry eye after maximum topical treatment and anti-inflammatory agents. The second involves post-surgical cases with advanced OSD where there is recurrent epithelial compromise or delayed epithelial regeneration. Next is persistent epithelial defects in chronic OSD such as GVHD, cicatricial pemphigoid, exposure keratopathy, neurotrophic keratitis, chemical burns and radiation keratopathy. Lastly, consider ASEDs when dealing with ocular neuropathic pain, also known as "pain without stain" or corneal neuralgia.[6]

However, if we strictly look at patient candidacy based on disease severity in advanced DED, those who would benefit from ASEDs can be classified as patients who have not shown significant improvement using the conventional steps one and two staged management and treatment recommendations as per the TFOS DEWS II report.[3] This classic scenario can be seen in patients that are insufficiently or unsuccessfully managed who suffer from a systemic autoimmune-based etiology such as Sjögren's syndrome or GVHD. Other

About the author

Dr. Rojas is the founder of Innovista Eye in Boerne, TX, and co-founder of DeNovo Eye in McKinney, TX. He specializes in ocular disease, specialty contact lenses and myopia management. He is a consultant for Eye Concierge and Johnson & Johnson Vision.



Baseline sodium fluorescein photos prior to ASEDs (A, B) and post-40% ASED use (C, D).

common cases include medication and/or preservative-associated persistent epithelial defects found in over-the-counter decongestants and lubricants, and toxic keratoconjunctivitis from chronic use of topical glaucoma medications.[6] Of course, this is not an exhaustive list, so keep in mind the complex and multifactorial nature of the disease when treating patients, including any impairment to the lacrimal functional unit from environmental, anatomical, endocrinologic and cortical causes.[3,5]

Implementing ASEDs

There are many instances where one might want to either switch to ASEDs or incorporate them as an adjunct therapy. Many clinicians consider ASEDs as a late-stage treatment option, and TFOS DEWS II also places it as step three in their treatment paradigm. However, I believe the direction and decision to incorporate such treatment should be based on multiple factors aside from direct clinical signs. For example, one should pay close attention to visual acuity changes throughout the patient's therapeutic journey. We know that chronic OSD can wax and wane over time and can have an effect on visual acuity in some patients, so watching out for any reduction in acuity or increasing subjective visual complaints should prompt the clinician to reanalyze the current treatment and explore advanced treatment options such as ASEDs.

Another scenario is when a patient has a non-healing case of persistent superficial punctate keratitis and has shown little to no improvement despite topical immunomodulators, aggressive topical lubrication, amniotic membranes grafts and/or steroids. In this instance, you could use ASEDs to potentially replace a medication in their regimen that has failed to provide adequate benefit or one that is more difficult to continue using based on side effects, cost or long-term accessibility.

If replacing a medication could cause some potential regression, you could then add ASEDs and monitor the patient's progress closely to determine when or if their regimen can be simplified. Most patients at this level of treatment suffer from chronic conditions, therefore regimen longevity and medication compliance are of utmost importance.

Overcoming Barriers

Aside from logistics and accessibility, one of the largest barriers to ASEDs is

the economic cost and financial sustainability of the treatment. While there may be some exceptions to specific plans, ASEDs are usually not covered by insurance carriers as it is currently not an FDA-approved therapy for ocular surface disorders.[2] Financial cost can range greatly depending on location, dosage and concentration used, lab fees for blood draws and compounding pharmacy preparation fees. These fees range from $200 to $450 for a 90-day supply and up depending on which company is used. Some pharmacies may charge a bundled price, including the blood draw, if they have an in-house phlebotomist or contract a third-party phlebotomy company that assists with mobile at-home services and logistics. Unfortunately, or fortunately, the price paradox is that for some uninsured patients or those with either high deductibles or no coverage, the out-of-pocket cost for ASEDs is sometimes less than what other novel FDA-approved therapies, artificial tears and other over-the-counter products may cost.

Access to nearby accredited sterile compounding pharmacy can be challenging, especially in rural areas, so one must consider the ability for a patient to coordinate this appropriately or obtain assistance from a family member or caregiver as needed. Some companies, such as Vital Tears, facilitate the process for both the provider and the patient by having a service specialist contact the patient, schedule the blood draw at a local partnering lab or mobile phlebotomist, collect payment, process the serum tears and ship within 48 hours, and review the proper usage and storage for ASEDs. This can greatly reduce the burden for both patient and provider, as well as increase compliance.

Most studies have not shown significant adverse events with ASEDs; however, the risk of microbial growth does exist when using preservative-free therapies. Therefore, patients should be advised on proper handling and storage to minimize risk of microbial contamination especially in patients with a compromised ocular surface.[4,6] Irritation, redness, changes to vision and swelling should not occur with ASEDs. If a patient experiences any of these symptoms, instruct them to discontinue use immediately and return for a follow-up consult to rule out other etiologies or possible contamination of the batch. If a patient does not meet serum donor criteria and screening (good venous access, adequate Hb levels, void of blood-borne diseases), is unable to store them under refrigeration, has limited mobility or does not tolerate repeated blood draws, then one can consider allogeneic serum drops, as studies have shown to be as effective as ASEDs and have similar tolerability.[2]

Adding ASEDs to Your Practice

Aside from companies such as Vital Tears that specialize in processing and dispensing of ASEDs, you could also partner with local independent labs, private sterile compounding pharmacies or work with hospital-associated labs to build a referral network that could cut down on cost and improve patient accessibility. Most companies should be on board partnering with your office to expand care and likely offer other sterile compounded preservative-free topical treatments to replace existing branded or preserved products. Depending on your practice modality, specialty, state regulations and patient volume, you can even consider bringing this specialized service directly into your practice to increase patient access and expand your referral network.

For most of us in private practice, working to establish relationships with local businesses and minimize the patient's overall cost and burden is a win-win scenario. Meet with local lab representatives or compounding pharmacists to compare pricing and learn about their protocols.

Another approach when incorporating ASEDs is to consider using this option earlier in the disease process, if applicable, instead of waiting to reach a specific severity target. In my experience, for example, a moderate-to-severe dry eye patient who historically cannot tolerate commercially available immunomodulators or anti-inflammatories tends to have a better prognosis, quality of life and a greater chance of preventing further corneal compromise if ASEDs are introduced earlier or pulsed during certain times of the year when flare-ups are expected. Of course, those who have OSD secondary to systemic autoimmune disorders require adequate systemic management and also lifelong ophthalmic control, so tapering or temporary discontinuation may not be feasible.

Pharmacy's Policies and Protocols

The following steps are simply guidelines and may vary based on individual compounding pharmacy's policies and protocols to process and dispense ASEDs. Be sure to contact the specific pharmacy in your area to learn more about their exact protocols and preferences.

Step one: submitting prescriptions. These can be submitted to a compounded pharmacy just like any other prescription

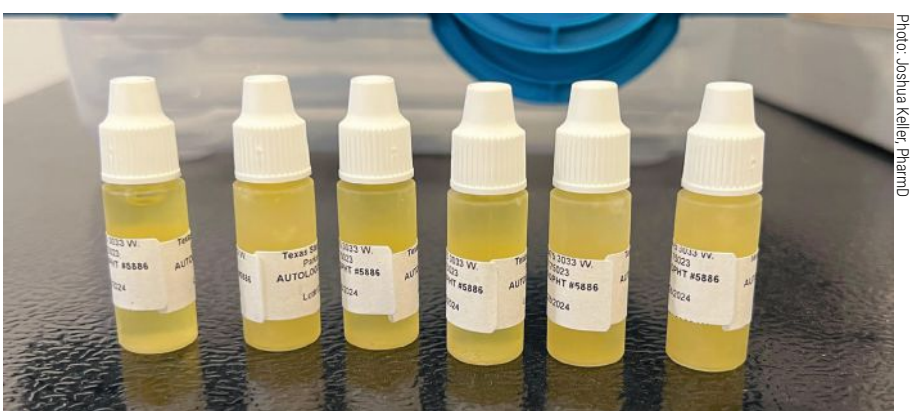


Photo: Joshua Keller, PharmD

A batch of six 3mL droptainers of 20% ASEDs.

Serum Tears Made Simple.

Give your patients **fast, hassle-free access** to serum tears.

Eye care providers have offered serum tears to patients with ocular surface conditions for over 30 years, but access to these drops has been limited.

With **Vital Tears**, you and your patients now have access to:

- **Rapid serum drop delivery**
- **Convenient blood draw options**
- **Affordable payment options**
- **Superior customer service**

DOWNLOAD OUR
PHYSICIAN PACKET

Vital Tears™
THE LEADER IN SERUM TEARS

www.vitaltears.org

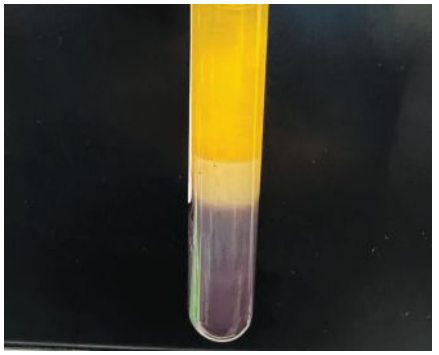


Photo: Joshua Keller, PharmD

Separation of blood components. Note the serum is bright yellow, clear and free from visible particles and red blood cells. Serum (top), red blood cells (bottom), serum separator (middle).

medication; verbally, faxed, as a walk-in prescription or via electronic prescriptions. It will include the autologous serum concentration needed, dosage, length of therapy and number of refills.

A prescription example may read: 'Autologous serum eye drops (40%), Sig: Instill one drop in both eyes six times per day x 60 days, Refills: 1'.

Once the prescription is processed by the pharmacy, a phlebotomist receives the order, schedules the patient for the blood draw and collects between six and 12 serum separator tubes of whole venous blood depending on the dose, quantity and the patient's ability to donate the necessary volume. The serum separator tubes are also known as "tiger tubes" due to their gray/red speckled colored tops and do not contain anticoagulants, but rather a clot activator and serum separator gel. The tubes are refrigerated during transportation if collected off-site and most pharmacies will not compound ASEDs with aged blood over five days since the initial draw. Also, not all pharmacies have a phlebotomist on-site, so depending on the pharmacy, you may need to submit a lab order and prescription separately.

Step two: centrifuged, combined. The tubes are then centrifuged to separate the serum from the rest of the blood. The pharmacist will first inspect the tiger tubes to ensure they are suitable for use and contain about 3mL of clear/yellow serum that is easily retrievable from the top of the tube. The serum cannot be cloudy or red, as this indicates that the serum may contain red blood cells and is not suitable for therapy.

Next, the tubes are combined with appropriate amount of 0.9% sodium chloride solution in a sterile lab, filtered for sterility and dispensed into 3mL eye drop bottles known as droptainers. The total volume dispensed is usually between 36mL and 72mL, so most patients can expect to get between 12 and 24 bottles, respectively. Assuming a conservative conversion of 15 drops per mL of serum, due to the natural variation in viscosity and storage temperature, this can yield anywhere from 540 drops to 1,080 total drops. The duration of the supply depends on the concentration and dosage used.

Assuming six tubes of blood yield 18mL of serum and the patient is prescribed a common dose of six times per day, a 20% concentration can last up to 112 days (although the pharmacy will only dispense a 90-day supply), 40% up to 56 days and 80% up to 28 days. The phlebotomist will generally collect more tubes of blood when a higher concentration is prescribed, as the serum is less diluted.

Step three: properly storing drops. Although most pharmacists will perform a medication review on how to use and store the drops with the patient, the eyecare provider should reiterate the importance of storing the supply of ASEDs in the freezer. Patients are asked to then thaw one bottle at a time stored in the refrigerator between administrations. The in-use bottle should be discarded after seven days.

Due to the preservative-free nature of ASEDs, patients wash hands and practice good hygiene when handling the dropper. They are encouraged to inspect for particulate matter in the dropper prior to use, and when in doubt, use a new bottle.

Likely Outcomes

A recent systematic review and meta-analysis including seven randomized controlled trials with 267 subjects on the outcomes of ASEDs for DED indicated that ASEDs outperformed artificial tears in both subjective symptoms, as per the ocular surface disease index (OSDI) scores, as well as objective data such as vital dye staining scores (rose bengal) and tear film break-up time (TBUT).[6,7] ASEDs can play an important role in corneal neuro-regenerative therapy for patients with corneal neuropathy and photoallodynia at the subbasal nerve plexus by improving nerve density and morphology.[8,9] The benefit of this treatment is that ASEDs have been shown to have a quick symptomatic improvement in as little as 10 days. It is helpful for both the patient and practitioner to determine its efficacy and candidacy to decide if the treatment is appropriate.[3,10] With that being said, I also tend to prescribe ASEDs in patients who may have ocular neuropathic pain or photoallodynia due to its corneal regeneration properties, as these patients—despite clinical signs on examination in some—have impaired social functioning and tend to experience difficulty with different light sources and brightness, which may lead

Photo: Joshua Keller, PharmD

Typical batch of tiger tubes showcasing natural variation in color. Tubes are examined under a bright light to ensure quality of serum. Some tubes may not be used due to the visible presence of red blood cells in the serum layer (second tube from the right).

LOOKING FOR A BETTER FIT FROM YOUR SCLERAL LENS?

Built-in oval optic zones
better centration

SmartSight®
superior visual acuity

Smart360®
free form digital lens design

SplineCurve®
parameter independence in a quad specific manner

SmartChannel®
vault anatomical obstacles and reduce suction

16-19mm Diameters

Extra Customization
- with Smart Features

Less than 2 cuts
- on average per eye

3 out of 4
- fits achieved with the standard lens in the FitKit®

BostonSight® SCLERAL

www.BostonSightSCLERAL.org/lens

Your partner in saving sight®

Preferred Material
OPTIMUM by Contamac

to anxiety, depression and lower quality of life.

I also educate my patients to maximize their outcome not only during therapy but also leading up to their blood draw. I encourage them to prioritize restful sleep leading up to their draw, stay hydrated to increase blood volume, eat a balanced diet and avoid foods high in saturated fats, manage stress with breathing exercises or yoga and avoid diuretics such as caffeine or alcohol.

Gauge Success at Follow-ups

Setting realistic expectations with your patients and being open-minded to treatment plan modifications along their journey is imperative when dealing with chronic disease. Just as important is customizing their treatment plan to their specific needs, as well as being empathetic, as some patients usually have a lifelong battle with these conditions with expected flare-ups along the way. Although I've seen improvements in as little as two weeks after starting ASEDs, I inform them that it may take up to four to six weeks before we see significant clinical change, so I tend not to alter the dosage or concentration until they are seen at their progress visit.[11,12] However, in my practice, I generally taper the dosage frequency and/or concentration over weeks to months if the patient's condition shows significant improvement in signs and symptoms.

Although there appears to be no consensus for selecting an optimal concentration, most studies use 20% as it mimics the biological factors that are found in our tears.[11] However, higher concentrations (up to 100%) have been used in other clinical studies.[11] I typically start with a concentration of 40% but have prescribed above 50% in select patients, as most of my cases have responded well with 40%. I have personally found 40% to be a sweet spot as it allows for the patient's supply to last about two months with a dosage of six times per day, reducing the number of trips for blood draws, while keeping a meaningful therapeutic concentration for most conditions. Also, dosing frequencies can vary considerably from three times a day to hourly, while six to eight times per day appears to be the most common.[11,12]

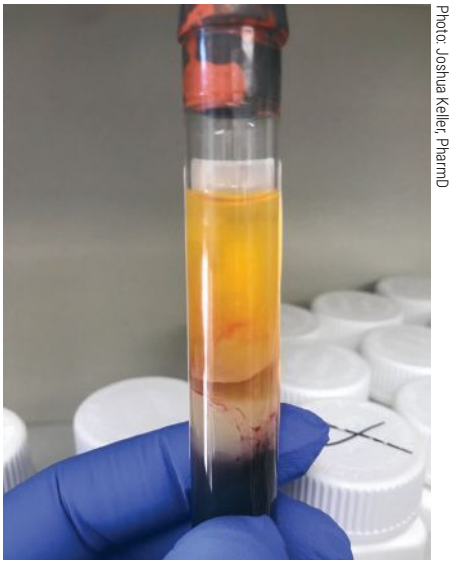


Photo: Joshua Keller, PharmD

Close up of a discarded tube seen in the previous image (second from the right) with obvious red blood cells present in the serum layer, creating a non-uniform pink-red color.

Obtaining both objective and subjective data at every visit is imperative for gauging treatment success versus failure. There are many symptom-based questionnaires that are efficient and cost-effective and help understand and track your patient's subjective progress that is sometimes overlooked when we are clinically focused on objective improvements. I recommend using as many data points as possible, whether you're using anterior segment photography to help the patient visualize their own progress or direct observation with vital dye staining (sodium fluorescein and/or lissamine green) to assess objective changes.

Other useful markers include conjunctival hyperemia scoring, ocular surface staining scores, osmolarity, TBUT and qualitative measures (MMP-9), or quantitative markers (phenol red threat test, Schirmer's test) and visual acuity to track progress. Remember to always compare data points to a patient's baseline (similar to visual field analyses in glaucoma management) and establish new baselines any time a new therapy is added to help guide your treatment. Serial photography helps visualize progress trends over time and has been beneficial in my clinic to pinpoint—and predict—the time of year that a patient usually experiences flare ups.

It is sometimes helpful to review and remove/replace an item from a patient's existing complex regimen that does not provide a significant improvement to the disease process and/or the patient's quality of life. However, some eyecare providers will prescribe topical steroids or other immunomodulators along with ASEDs for a synergistic effect, so discontinuation of their current regimen is not required.

Other Alternatives

One that should be considered if a patient experiences significant logistical or financial barriers, lack of therapeutic benefit or is unable to tolerate the treatment, including cryogenically preserved and dehydrated amniotic membrane grafts, scleral lenses, and other hemoderivatives such as allogenic serum drops, albumin drops and platelet-rich plasma (PRP) to name a few.

A recent study compared the effect of 100% autologous serum to 100% PRP for the treatment of severe dry eye in primary Sjögren's syndrome and found a similar statistically significant improvement in signs and symptoms; however, a greater reduction OSDI scores were observed in the PRP group.[13] They found a reduction in OSDI scores in 100% of patients in the PRP group vs 77.3% in the autologous serum group compared to baseline. The authors believe that PRP, due to its concentration of platelets, has greater immunomodulatory and anti-inflammatory components necessary in cell proliferation, wound healing and angiogenesis due to a larger amount of nerve growth factor, platelet-derived growth factor and fibronectin found in PRP than autologous serum.[1] Despite this, there is limited data proving superiority of PRP to autologous serum, and comparative studies are challenging due to differences in blood preparation protocols, patient's age, race, diet, dosage, instrumentation, patient selection, diagnosis, study size and duration to name a few.[13]

Takeaways

ASEDs play a critical role in OSD treatment and management and offer a

significant improvement in a patient's disease trajectory. With over 300 million people worldwide suffering from some degree of dry eye, incorporating this in your clinic can be the key factor in making a positive change in a patient's quality of life.[14] Although ASEDs are typically not a first-line therapy in many cases, I hope I demystified the common barriers and questions that exist surrounding the use of this so-called "big gun" that can lead to making this treatment a more accessible solution. ■

Special thanks to Joshua Keller, PharmD (Pharmacy Experience Manager) at Texas Star Pharmacy for assisting in this article.

1. Ralph RA, Doane MG, Dohlman CH. Clinical experience with a mobile ocular perfusion pump. Arch Ophthalmol. 1975;93(10):1039-43.

2. Davis A, Franco E, Nischal K, Halfpenny C. Autologous and allogenic serum tears. EyeWiki. Published December 8, 2022. Accessed September 10, 2023. eyewiki.aao.org/autologous_and_allogenic_serum_tears.

3. Jones L, Downie LE, Korb D, et al. TFOS DEWS II Management and Therapy Report. Ocul Surf. 2017;15(3):575-628.

4. Shtein RM, Shen JF, Kuo AN, et al. Autologous serum-based eye drops for treatment of ocular surface disease. Ophthalmology. 2020;127(1):128-33.

5. Feroze KB, Patel BC. Neurotrophic keratitis. PubMed. Published 2022. Accessed July 1, 2022. ncbi.nlm.nih.gov/books/NBK431106/.

6. Vazirani J, Sridhar U, Gokhale N, et al. Autologous serum eye drops in dry eye disease: preferred practice pattern guidelines. Ind J Ophthalmol. 2023;71(4):1357-63.

7. Wang L, Cao K, Wei Z, et al. Autologous serum eye drops versus artificial tear drops for dry eye disease: a systematic review and meta-analysis of randomized controlled trials. Ophthalmic Res. 2020;63(5):443-51.

8. von Hofsten J, Egardt M, Zetterberg M. The use of autologous serum for the treatment of ocular surface disease at a Swedish tertiary referral center. Int Med Case Rep J. 2016;9:47-54.

9. Aggarwal S, Kheirkhah A, Cavalcanti BM, et al. Autologous serum tears for treatment of photoallodynia in patients with corneal neuropathy: efficacy and evaluation with in vivo confocal microscopy. Ocul Surf. 2015;13(3):250-62.

10. Mondy P, Brama T, Fisher J, et al. Sustained benefits of autologous serum eye drops on self-reported ocular symptoms and vision-related quality of life in Australian patients with dry eye and corneal epithelial defects. Transfus Apher Sci. 2015;53(3):404-11.

11. Pan Q, Angelina A, Marrone M, et al. Autologous serum eye drops for dry eye. Cochrane Database Syst Rev. 2017;2(2):CD009327.

12. Geerling G. Autologous serum eye drops for ocular surface disorders. Brit J Ophthalmol. 2004;88(11):1467-74.

13. Wróbel-Dudzińska D, Przekora A, Kazimierczak P, et al. The comparison between the composition of 100% autologous serum and 100% platelet-rich plasma eye drops and their impact on the treatment effectiveness of dry eye disease in primary Sjögren's syndrome. J Clin Med. 2023;12(9):3126.

14. Market Scope. 2016 Dry Eye Products Report: A Global Market Analysis for 2015 to 2021. St Louis: Market Scope; 2016.

OCULAR SURFACE SIDE EFFECTS OF GLAUCOMA MEDS

These drugs may be essential for IOP control, but that's no reason to let them compromise the cornea. Here's a look at the many possible iatrogenic complications—and what do to about them.

BY KOREY PATRIZI, OD
ELKINS PARK, PA

Eye drops intended to lower intraocular pressure (IOP) are often chosen as first-line therapy for primary open-angle glaucoma (POAG), as the medication is generally effective and well-tolerated with good safety profiles. Of the various side effects associated with these topical therapies, symptoms and clinical signs involving the ocular surface are among the most common reported by patients and clinicians.

Mitigating these side effects is an important responsibility of the clinician, as they can be troublesome in patients' everyday activities. Not only does this increase patient satisfaction and quality of life, but it likely increases compliance. Before discussing mitigation tactics, we first need to understand the mechanisms of ocular surface disease on a pathophysiological level. Each class of pressure-lowering eye drops has its own set of ocular surface-associated side effects and different mechanisms of action.

Prostaglandin Analogs

Of all the topical IOP-lowering medications, prostaglandin analogs are the class most commonly prescribed as a first-line therapy for POAG. They are typically the most efficacious option—on average, prostaglandin analogs lower IOP by 30%.[1] This class of drugs includes latanoprost, latanoprostene bunod, travoprost, bimatoprost, tafluprost and the combination drop Rocklatan (netarsudil + latanoprost ophthalmic, Aerie Pharmaceuticals). The use of prostaglandin analogs can cause ocular surface side effects, including conjunctival hyperemia and dry eye disease.[2,3]

The active agents in prostaglandin analogs are thought to cause dilation of conjunctival blood vessels, leading to conjunctival redness, which is a relatively simple explanation.[4] Conversely, there are many more theorized mechanisms by which prostaglandin analogs may cause dry eye symptoms. First, prostaglandin analogs can induce tear film instability through a few differing processes. These drugs cause a local inflammatory response within the trabecular meshwork, contributing to their intended effect of lowering IOP. However, this local inflammatory response also occurs on the ocular surface.[5] Consequently, these changes in concentration of inflammatory mediators can be enough to destabilize the tear film.

Additionally, this class of drugs has the potential to affect the production of every layer of the tear film. Mucin-producing cells within the conjunctiva are particularly sensitive to inflammation, so chronic exposure to prostaglandin analogs may also cause a decrease in mucin quality and quantity over time, thereby further impacting tear film stability.[2,3,5] Local inflammation can occur at the lid margin, leading to thickening and blockage of the meibomian gland ducts; this obstructive meibomian gland dysfunction could then lead to evaporative dry eye.[2,4]

Topical prostaglandin analogs may also affect aqueous tear volume. Increased uveoscleral outflow of aqueous, a mechanism by which these medications lower IOP, also affects the osmotic dynamics of the eye and may potentially lead to decreased tear volume. Prostaglandin analogs can alter the flow of blood to the lacrimal

About the author

Dr. Patrizi completed her Doctor of Optometry at the University of the Incarnate Word Rosenberg School of Optometry in San Antonio, Texas. She also completed a residency in ocular disease and primary care at Salus University Pennsylvania College of Optometry, where she is currently an assistant professor.

glands as well as cause inflammation to them—both processes having the potential to reduce lacrimal gland function, consequently reducing aqueous tear production.[6,7]

Beta Blockers

The most commonly used IOP-lowering beta blockers include timolol and two combination drops—Combigan (brimonidine tartrate + timolol maleate ophthalmic, Allergan) and Cosopt (dorzolamide hydrochloride + timolol maleate ophthalmic, Thea). The active beta blocker component in this class of medications can sometimes cause local allergic reactions, corneal hypoesthesia and its sequelae and dry eye symptoms.[8,9]

Beta blockers have a multifactorial effect on the autonomic nervous system's control of tear secretion. They cause a reduction in the sympathetic production and secretion of the aqueous component of tears by blocking beta-2 adrenergic receptors on the lacrimal gland.[10] This imbalance of the sympathetic and parasympathetic activity in the lacrimal glands leads to decreased sensitivity to acetylcholine, the parasympathetic neurotransmitter that stimulates the lacrimal glands to produce tears.

Alpha Agonists

Topical alpha-2 adrenergic agonists used to treat glaucoma include brimonidine, apraclonidine, and two combination drops—the already mentioned Combigan and Simbrinza (brinzolamide + brimonidine tartrate ophthalmic, Alcon). Documented ocular surface side effects of this class are often allergic in nature, causing conjunctival hyperemia, itching and foreign body sensation.[8,10,11]

Another documented side effect is punctate keratopathy, which may manifest as punctate epithelial erosions or epithelial microcysts.[8,9] Punctate keratopathy in this case may be caused by an inflammatory response to the active agent as well as tear film instability. Regarding the latter, although the mechanisms are not perfectly understood, there are likely a few factors at play. For one, alpha agonists can decrease the amount of acetylcholine release in the lacrimal glands, thus decreasing tear volume. They can also decrease corneal nerve sensitivity, which will decrease the cornea's ability to recognize dryness or irritation and adequately signal this information to the lacrimal gland for needed tear production.[10,12,13]

The mechanism of corneal epithelial microcyst formation is also not fully understood, but it is believed that the direct binding of alpha agonists to corneal epithelial cells results in changes in cell-to-cell adhesions, allowing fluid to flow more readily into intracellular spaces in the epithelium. This direct binding may also affect epithelial cell migration and turnover, leading to irregular cell orientation and spacing, therefore also leading to fluid-filled intracellular spaces. Alpha agonists additionally may alter the osmotic gradient between the tear film and corneal epithelial cells, causing a flow of fluid into cells which then may lead to microcysts.[8,9,12]

Carbonic Anhydrase Inhibitors

Topical CAIs used to manage glaucoma include dorzolamide, brinzolamide and the two combination drops of Cosopt, also a beta blocker, and Simbrinza, also an alpha agonist. Documented corneal side effects of CAIs include local allergic reactions and mild punctate keratopathy.[10,14] The mechanism responsible for the development of punctate keratopathy is not fully understood but is likely multifactorial.

Drugs in this class alter the pH of the tear film.[8,10] When the carbonic anhydrase enzyme is inhibited, formation of bicarbonate ions decreases. The tear pH becomes dysregulated, which can cause corneal epithelial disruption. This disruption may then impair the barrier function of the corneal epithelium, disrupt ion transport across the corneal epithelium, change cellular adhesion within the epithelium and may impact the osmotic effects between the cornea and the tear film. It is also hypothesized that all of these insults to the corneal epithelium's integrity and cornea's hydration can have a negative influence on corneal nerve sensitivity. As discussed in the section on alpha agonists, decreasing corneal nerve sensitivity leads to a less ability of the cornea to recognize dryness or irritation. As a result, the signaling of information to the lacrimal glands for tear production is negatively impacted.[8,14,15]

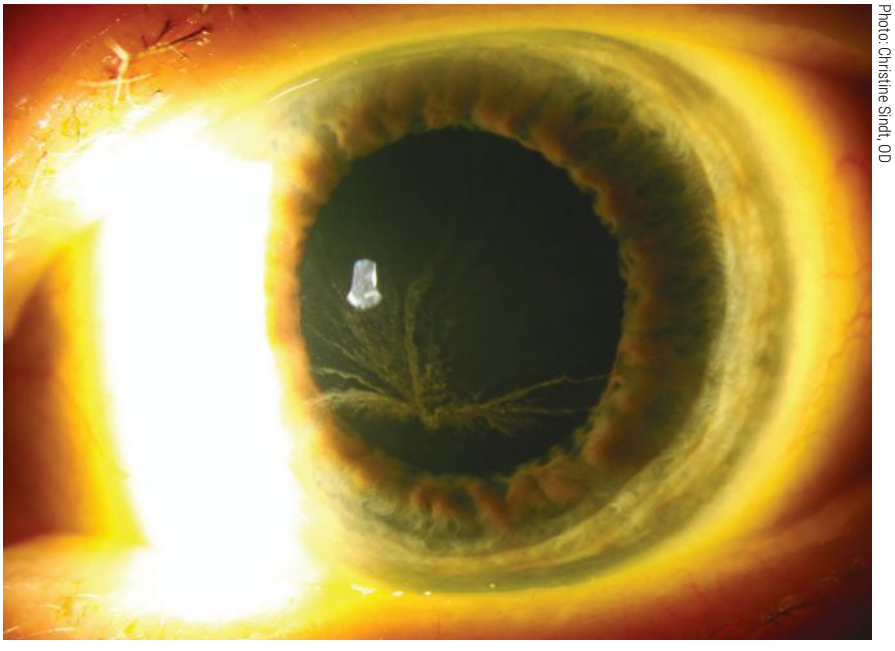


Photo: Christine Sindt, OD

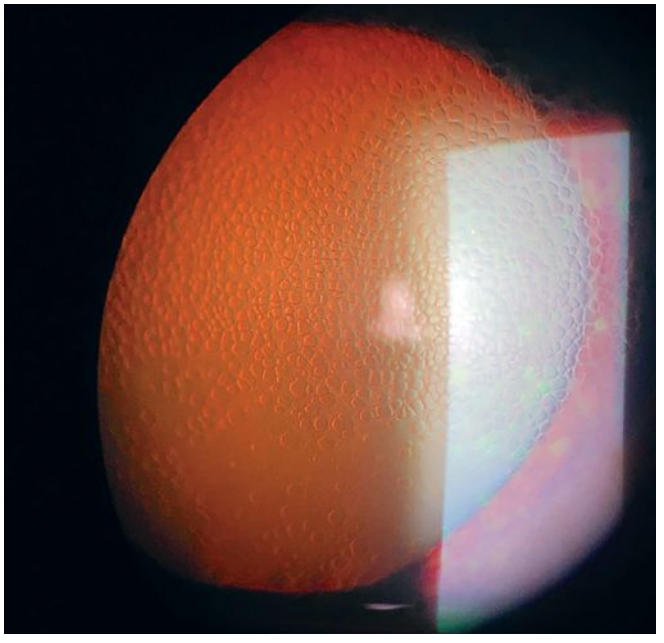
An example of drug-induced corneal verticillata (in a patient on amiodarone therapy).

Rho Kinase Inhibitors

This relatively new class of medications used topically to treat glaucoma include netarsudil and the combination drop Rocklatan. The active component in these can cause local allergic reactions, mild punctate keratopathy and whorl keratopathy.[16-18]

As with many of these topical glaucoma-mitigating drugs, the mechanism by which topical rho kinase inhibitors may cause the exacerbation or new onset of ocular surface dryness is caused for many reasons. One of which is that they may act on the lacrimal glands in various ways to decrease aqueous tear production.[10,17,19] Rho kinase enzymes play a role in smooth muscle contraction. Within the lacrimal glands, there are myoepithelial cells that must contract in order to expel tears from the gland and into the tear duct system. When rho kinase enzymes are inhibited within the lacrimal glands, this contraction is suppressed. This causes an overall decrease in aqueous tear production and thus, an unstable tear film.[10,17]

Similar to some of the drug classes already discussed, these medications may also cause alterations in corneal epithelial cell behavior.[9,10] A crucial function of the rho kinase enzyme within the cornea is regulation of the actin cytoskeleton. This structural framework is comprised of actin filaments and it is present not only within the corneal epithelium, but also in the stroma and the endothelium. The actin cytoskeleton is organized in specific configurations to provide structural stability that can withstand mechanical stress while simultaneously promoting corneal transparency. These actin filaments are also responsible for cell-to-cell adhesion, allowing epithelial cells to adhere to adjacent epithelial cells as well as the underlying basement membrane. This adhesion is an important component of the barrier between the cornea and the external environment.



Honeycomb corneal edema as a result of topical netarsudil use.

What's more, this actin framework is dynamic and promotes cell migration during corneal wound healing, as well as being responsible for the formation and maintenance of corneal epithelial tight junctions which regulate corneal permeability to ions and water. At the level of the endothelium, a lack of actin would compromise the structures responsible for regulating corneal transparency and hydration. Lastly, the corneal actin filaments are influenced by different signaling pathways to regulate cell shape and function in response to different external stimuli. These many functions of actin are all impacted when rho kinase is inhibited, and a collapse in this structural framework would have a significant impact on the health of the ocular surface at every layer of the cornea and tear film.[20]

Similar to the effects of prostaglandin analogs, rho kinase inhibitors may also affect corneal nerve function and sensitivity. They may cause localized inflammation of the ocular surface with chronic use that can negatively impact corneal structure and function, and they can cause changes in blood flow throughout the anterior segment of the eye.[5,16,17] Compromised anterior segment blood flow may negatively impact the delivery of oxygen and vital nutrients to the cornea.

Whorl keratopathy, also known as vortex keratopathy or corneal verticillata, is characterized by fine deposits appearing in a "whorl"-like configuration within the corneal epithelium. These deposits can be whiteish-gray, yellow or brown in color and are typically located in the inferior-central cornea. This finding can be a sign of various underlying systemic conditions and is also a known side effect of certain medications, including rho kinase inhibitors.[21,22]

The exact mechanism of drug-induced whorl keratopathy is not fully known. However, some theories suggest that it is an accumulation of metabolic waste due to epithelial cell dysfunction. Fortunately, whorl keratopathy is widely considered a benign finding that does not typically cause any visual or ocular symptoms; most cases can be monitored without intervention. It is reversible with cessation of the responsible agent in visually significant cases.[22]

Some patients may exhibit honeycomb corneal edema or reticular corneal edema—side effects unique to rho kinase inhibitors. An adverse reaction like this is more likely to occur in patients with pre-existing corneal edema or corneal endothelial decompensation.[23,24]

Benzalkonium Chloride (BAK)

The active components in each class of glaucoma drop mentioned above have their own unique effects on ocular surface health. As discussed, many of these are poorly understood and require more research to determine their clinical significance. This is not the case for BAK, a preservative whose ocular surface side effects are well-documented. BAK is found in many topical ophthalmic medications, including many of the drug classes of drops mentioned above. The adverse effects of this preservative on the ocular surface include corneal and conjunctival cell cytotoxicity and dry eye disease.[8-10,25,26]

BAK has detergent properties, which allow it to disrupt the lipid layer of the tear film and the lipid bilayer of corneal epithelial cells, both of which processes increase penetration of the BAK-containing medications. This lipid layer disruption is a direct mechanism of corneal and conjunctival cell damage that contributes to ocular surface discomfort. Additionally, breakdown of lipids within the tear film leads to tear instability and, consequently, exacerbation of evaporative dry eye disease.[8-10,25,26]

Mitigating Adverse Reactions

Not all patients experience adverse effects to these drops or to the preservative of BAK. While clinicians cannot always predict who will be affected, there are factors that may increase a patient's susceptibility to drug- or preservative-induced corneal toxicity. Patients with pre-existing ocular surface disease, such as dry eye disease, meibomian gland dysfunction and history of chronic conjunctival irritation like allergic conjunctivitis, may already have compromised corneal and conjunctival cell integrity as well as tear film insufficiency and instability. Adding these drops' agents into this compromised environment has the potential to exacerbate these already suboptimal ocular surface conditions.

With BAK specifically, contact lens wearers sometimes experience greater sensitivity to the preservative for a few reasons. One is that there is potential for an interaction between the preservative and certain contact lens materials. Another reason is the inherent mechanical disruption of the tear film during contact lens use, which may be exacerbated when adding BAK to the patient's ocular surface. Additionally, BAK sensitivity seems to be dose-dependent and cumulative, meaning that patients who take more frequent doses of BAK-containing medications, who have been using these medications over a longer duration of time and those who take medications that have higher BAK concentrations are all more likely to experience these adverse side effects.

Clinicians may decide to forgo prescribing BAK-preserved medications altogether for patients apart of these susceptible populations. In these cases, one can consider preservative-free formulations or those containing milder preservatives. Such examples include the preservative-free drugs Zioptan (tafluprost ophthalmic, Thea) Cosopt PF (Thea), Timoptic in Ocudose (timolol maleate ophthalmic, Thea) and Iyuzeh (latanoprost 0.005%, Thea), or the mildly preserved options of Travatan Z (travoprost ophthalmic, preserved with Sofzia, Alcon), Alphagan P (brimonidine tartrate ophthalmic, preserved with Purite, Allergan) and Xelpros (latanoprost ophthalmic, preserved with potassium sorbate, Sun Pharmaceutical).[9,26,27]

Clinicians may also consider limiting overall exposure by only prescribing agents with lower BAK concentrations. Choosing ones that require less frequent dosing is another good option if this can sufficiently control IOP.

If a patient experiences ocular surface side effects with a particular medication, the clinician can consider prescribing

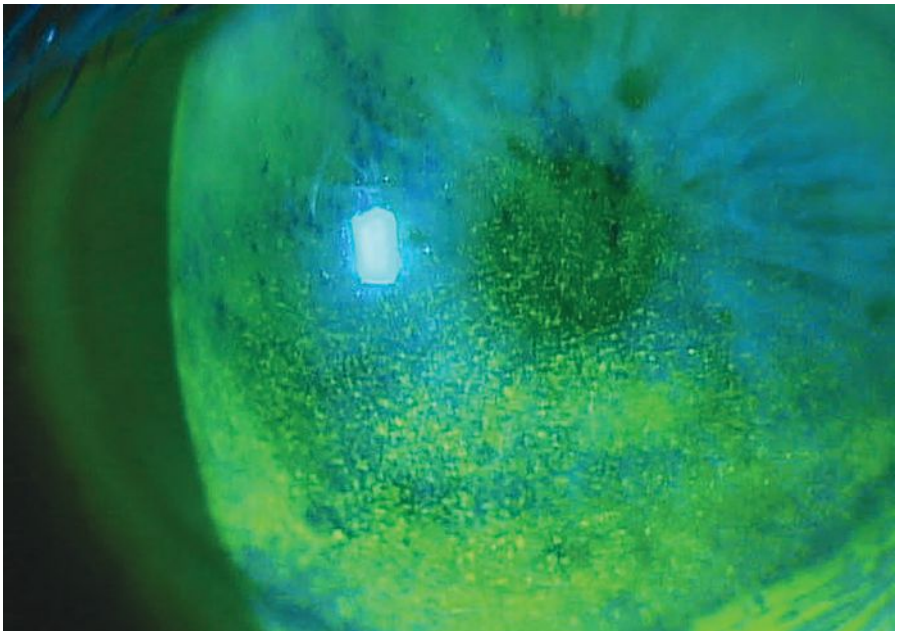


Photo: Paul M. Karpecki, OD

Superficial punctate keratitis in a patient on multiple topical glaucoma medications.

a different class of drug with a different mechanism of action. Selective laser trabeculoplasty, sustained-release drug delivery implants or minimally invasive glaucoma surgery may also be considered. These three options typically have a much lower risk of adverse effects involving the ocular surface, as they often minimize the frequency of eye drops, thereby decreasing exposure risk.[9] If choosing to keep susceptible patients on these medications, it is important to monitor ocular surface health regularly in order to detect any early signs of toxicity.

Treatment of ocular surface disease in these cases can vary and may involve supplementation with preservative-free artificial tears, opting for lubricating gel or ointment at nighttime, prescribing cyclosporine or lifitegrast eye drops to control ocular surface inflammation, instilling Lumify (brimonidine tartrate ophthalmic, Bausch + Lomb) for redness, stressing the practice of warm compresses and lid hygiene and use of omega-3 or flaxseed supplements.[28]

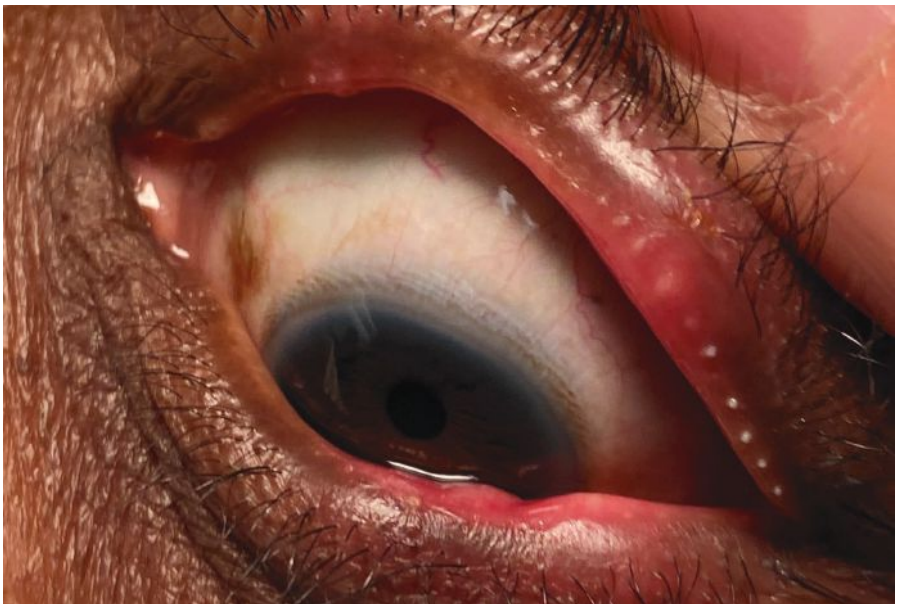
The use of punctal plugs is controversial, as many of these drops increase the concentration of inflammatory mediators in the tear film, with increased exposure time potentially making symptoms worse.[29] The decision is dependent on which type of drug is causing the symptoms and whether the issue stems from aqueous deficiency, evaporative dry eye or a combination.

Takeaways

Ocular surface irritation is a very common but remediable side effect that has been documented for each class of topical glaucoma medication, with some classes demonstrating more significant or more common side effect profiles than others. Mitigating these side effects while also prioritizing efficacy of the chosen treatment is important in maintaining ocular surface health and, therefore, better chance of patient compliance. We as eyecare clinicians are fortunate to have a plethora of options for glaucoma management: many different ophthalmic drops, BAK-free alternatives and surgeries varying by invasiveness. Looking at the complete clinical picture, each patient will have a different best-fit treatment plan.

We are also armed with many treatments for ocular surface disease that do not exhibit poor interactions with the glaucoma treatments mentioned in this article. The decision to prophylactically treat dry eye disease when prescribing anti-glaucoma medication should be determined on a case-by-case basis. A balance must be struck between maintaining ocular surface comfort and keeping treatment regimens as streamlined as possible to facilitate good compliance. Patients who are identified as being particularly susceptible to adverse ocular surface reactions, as discussed above, can be considered. At the very least, patients should have any pre-existing ocular surface disease under good control, as they are the most susceptible.

Mitigating ocular surface discomfort is significant for a patient's daily experi-



Severe obstructive MGD with gland inspissation and lid margin scalloping.

ence and should be a high priority. Ultimately, we owe it to our patients to protect their vision with the best treatment option to provide a satisfactory quality of life. ■

1. Lee AJ, McCluskey P. Clinical utility and differential effects of prostaglandin analogs in the management of raised intraocular pressure and ocular hypertension. Clin Ophthalmol. 2010;4:741-64.

2. Mocan MC, Uzunosmanoglu E, Kocabeyoglu S, Karakaya J, Irkec M. The association of chronic topical prostaglandin analog use with meibomian gland dysfunction. J Glaucoma. 2016;25(9):770-4.

3. Horsley MB, Kahook MY. Effects of prostaglandin analog therapy on the ocular surface of glaucoma patients. Clin Ophthalmol. 2009;3:291-5.

4. Shen W, Huang B, Yang J. Ocular surface changes in prostaglandin analogue-treated patients. J Ophthalmol. 2019;2019:9798272.

5. Cracknell KPB, Grierson I. Prostaglandin analogues in the anterior eye: their pressure lowering action and side effects. Exp Eye Res. 2009;88(4):786-91.

6. Arita R, Itoh K, Maeda S, et al. Effects of long-term topical anti-glaucoma medications on meibomian glands. Graefes Arch Clin Exp Ophthalmol. 2012;250(8):1181-5.

7. Park HYL, Kim JH, Lee KM, Park CK. Effect of prostaglandin analogues on tear proteomics and expression of cytokines and matrix metalloproteinases in the conjunctiva and cornea. Exp Eye Res. 2012;94(1):13-21.

8. Asiedu K, Abu SL. The impact of topical intraocular pressure lowering medications on the ocular surface of glaucoma patients: a review. J Curr Ophthalmol. 2018;31(1):8-15.

9. Zhang X, Vadoothker S, Munir WM, Saeedi O. Ocular surface disease and glaucoma medications: a clinical approach. Eye Contact Lens. 2019;45(1):11-8.

10. Zhou X, Zhang X, Zhou D, Zhao Y, Duan X. A narrative review of ocular surface disease related to anti-glaucomatous medications. Ophthalmol Ther. 2022;11(5):1681-704.

11. Parkkari M, Purola P, Uusitalo H. Ocular surface disease signs and symptoms of glaucoma patients and their relation to glaucoma medication in Finland. Eur J Ophthalmol. 2022;33(2):11206721221144339.

12. Lusthaus JA, Goldberg I. Brimonidine and brinzolamide for treating glaucoma and ocular hypertension; a safety evaluation. Expert Opin Drug Saf. 2017;16(9):1071-8.

13. Oh DJ, Chen JL, Vajaranant TS, Dikopf MS. Brimonidine tartrate for the treatment of glaucoma. Expert Opin Pharmacother. 2019;20(1):115-22.

14. Scozzafava A, Supuran CT. Glaucoma and the applications of carbonic anhydrase inhibitors. Subcell Biochem. 2014;75:349-59.

15. Supuran CT, Altamimi ASA, Carta F. Carbonic anhydrase inhibition and the management of glaucoma: a literature and patent review 2013-2019. Expert Opin Ther Pat. 2019;29(10):781-92.

16. Al-Humimat G, Marashdeh I, Daradkeh D, Kooner K. Investigational rho kinase inhibitors for the treatment of glaucoma. J Exp Pharmacol. 2021;13:197-212.

17. Saha BC, Kumari R, Kushumesh R, Ambasta A, Sinha BP. Status of rho kinase inhibitors in glaucoma therapeutics—an overview. Int Ophthalmol. 2022;42(1):281-94.

18. Wang J, Wang H, Dang Y. Rho-kinase inhibitors as emerging targets for glaucoma therapy. Ophthalmol Ther. October 14, 2023. [Epub ahead of print].

19. Moshirfar M, Parker L, Birdsong OC, et al. Use of rho kinase inhibitors in ophthalmology: a review of the literature. Med Hypothesis Discov Innov Ophthalmol. 2018;7(3):101-11.

20. Amano M, Chihara K, Kimura K, et al. Formation of actin stress fibers and focal adhesions enhanced by rho-kinase. Science. 1997;275(5304):1308-11.

21. Raizman MB, Hamrah P, Holland EJ, et al. Drug-induced corneal epithelial changes. Surv Ophthalmol. 2017;62(3):286-301.

22. MacIver S, Stout N, Ricci O. New considerations for the clinical efficacy of old and new topical glaucoma medications. Clin Exp Optom. 2021;104(3):350-66.

23. Bhargava M, Sen S, Bhambhani V, Paul RS, Dutta C. Reticular epithelial corneal edema as a novel side-effect of rho kinase inhibitors: an Indian scenario. Indian J Ophthalmol. 2022;70(4):1163-70.

24. Lyons LJ, Wu KY, Baratz KH, Sit AJ. Honeycomb epithelial edema associated with rho kinase inhibition: a case series and review of the literature. Cornea. 2022;41(2):243-8.

25. Pflugfelder SC, Baudouin C. Challenges in the clinical measurement of ocular surface disease in glaucoma patients. Clin Ophthalmol. 2011;5:1575-83.

26. Kumar S, Singh T, Ichhpujani P, Vohra S. Ocular surface disease with BAK preserved travoprost and polyquaternium 1(Polyquad) preserved travoprost. Rom J Ophthalmol. 2019;63(3):249-56.

27. Skov AG, Rives AS, Freiberg J, et al. Comparative efficacy and safety of preserved versus preservative-free beta-blockers in patients with glaucoma or ocular hypertension: a systematic review. Acta Ophthalmol. 2022;100(3):253-61.

28. Saini M, Dhiman R, Dada T, Tandon R, Vanathi M. Topical cyclosporine to control ocular surface disease in patients with chronic glaucoma after long-term usage of topical ocular hypotensive medications. Eye (Lond). 2015;29(6):808-14.

29. Sherwin JC, Ratnarajan G, Elahi B, Bilkiewicz-Pawelec A, Salmon JF. Effect of a punctal plug on ocular surface disease in patients using topical prostaglandin analogues: a randomized controlled trial. Clin Exp Ophthalmol. 2018;46(8):888-94.

Earn 2 CE Credits
(COPE APPROVED)

ADDRESSING PTERYGIUM IN OPTOMETRIC PRACTICE

Successful management of this condition requires a comprehensive understanding of its pathophysiology, clinical features and diagnostic criteria.

BY ELIZABETH CHETTY, DPHIL, AND ANNELIZE VAN ZYL, MPHIL
JOHANNESBURG, SOUTH AFRICA

Pterygium, or surfer's eye, is a common fibrovascular degenerative conjunctival condition associated with chronic exposure to ultraviolet (UV) radiation. The term pterygium is derived from the Greek word "pterygion," meaning "wing," which reflects the condition's characteristic appearance: a wing-like or triangular raised centripetal lesion that grows from the conjunctiva onto the cornea (*Figure 1*). It is usually bilateral and found on the nasal aspect of the eye but can also be present on the temporal side as well.

The prevalence of pterygium globally averages 12%; however, the numbers vary vastly from 1.3% to 53%.[1-3] Various risk factors such as demography and environment play a role in the discrepancy in reported prevalence, with higher numbers reported for older individuals living in sunny, dusty, equatorial regions or those with outdoor occupations.[1]

To fully understand our role as eyecare practitioners in managing this condition, it is necessary to understand its multifactorial pathophysiology, clinical features, diagnostic criteria and current management strategies.

Understanding Pathophysiology

While the pathophysiology is complex and poorly understood, there has been a long-standing association between prolonged UV radiation (sunlight) exposure and pterygium formation.[4] Ultraviolet radiation is pivotal in initiating and promoting pterygium formation through several mechanisms, including inflammation, fibroblast activation, extracellular matrix remodeling, angiogenesis and tissue invasion. Genetic factors and viral infection have also been associated with the pathophysiology.[5,6]

Inflammation is a central component of pterygium pathophysiology. Chronic UV exposure causes oxidative stress on the DNA of conjunctival cells, which triggers an inflammatory cascade in the conjunctiva, characterized by releasing pro-inflammatory cytokines and chemokines.[7,8] Inflammatory mediators stimulate the release of growth factors, such as vascular endothelial growth factor (VEGF) and fibroblast growth factor (FGF), in pterygium tissue.[9] Angiogenesis, or the formation of new blood vessels, is promoted by VEGF, and these new blood vessels supply oxygen and nutrients to the developing pterygium and give the characteristic red eye appearance often associated with pterygia (*Figure 2*).[10]

Expression of FGF within the conjunctival tissues stimulates the activation of fibroblasts. These normally

About the authors

Dr. Chetty is an academic optometrist with a profound passion for specialised contact lenses and keratoconus. She holds a doctoral degree on keratoconus, has presented her research at various international and national conferences and published many peer reviewed articles over the years. She is a fellow of the International Association of Contact Lens Educators (IACLE) and of the British Contact Lens Association. She is also the IACLE Ambassador for Africa. She is a key opinion leader for Alcon. **Ms. van Zyl** is the owner and optometrist at the Low Vision Pretoria practice in the Pretoria Eye Institute. She has been on the committee of the Contact Lens Society of South Africa since 2014 and has organised three international Contact Connect conferences. In 2021, she joined Saks, Taylor and Brauer Optometrists, one of the oldest practices in South Africa, where she spends most of her week. She has no financial disclosures.

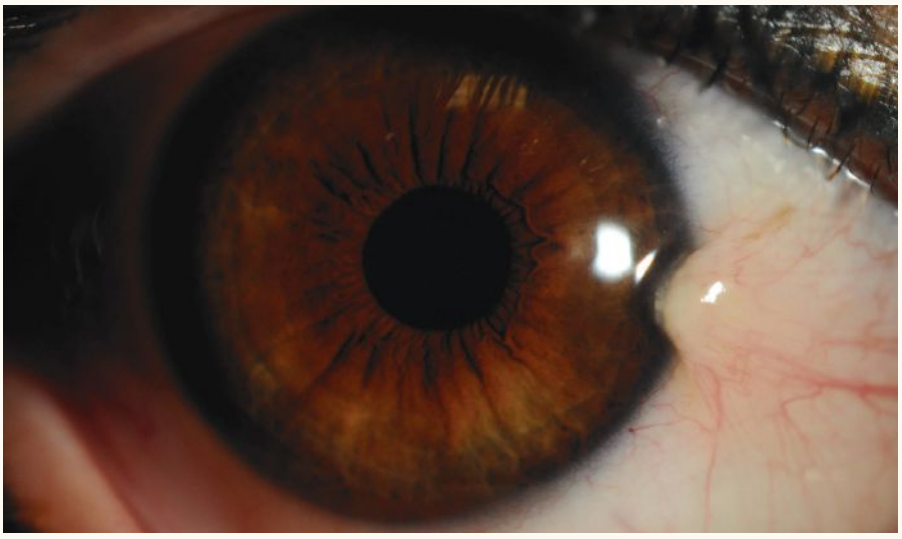


Fig. 1. Pterygium is a wing-like or triangular raised centripetal lesion that grows from the conjunctiva onto the cornea.

quiescent cells transform into myofibroblasts, which are highly contractile and capable of synthesizing and depositing extracellular matrix components like collagen and fibronectin.[9] Myofibroblasts contribute to the fibrotic nature of pterygium tissue.[9]

Another consequence of chronic inflammation is the over-expression of matrix metalloproteinases (MMPs), which leads to remodeling the conjunctiva's extracellular matrix (ECM).[11] The cleaving of ECM structural proteins (collagen, fibronectin and proteoglycans) by MMPs achieves the degradation and remodeling of the conjunctival tissue. The presence of MMPs in pterygium tissue contributes to tissue invasion. As MMPs degrade the corneal basement membrane and collagen fibers, they create pathways for pterygium tissue to infiltrate and invade the cornea.[8] This is a critical step in the progression of pterygium, as it allows the lesion to encroach further onto the cornea, thereby affecting vision.

While UV radiation remains a prominent risk factor, genetic and molecular factors also contribute to pterygium development. Research has identified specific genetic polymorphisms and molecular alterations associated with an increased susceptibility to pterygium.[12] These factors may modulate the individual response to UV radiation and inflammation, further highlighting the relationship between genetics and environmental factors in the condition's pathophysiology.

Recently, viral infections such as herpes simplex (HSV) and human papilloma (HPV) have been found in pterygium tissue samples.[13,14] The role of viruses in the pathophysiology of pterygium progression is controversial, but further research may lead to antiviral medication options for pterygium treatments.

Diagnostic Assessment

Although pterygium has potentially significant visual and ocular discomfort implications, the accurate diagnosis of the condition is sometimes overlooked. Due to its variable presentation, diagnosis can be difficult, but it is

Addressing Pterygium in Optometric Practice

Jointly provided by Postgraduate Institute for Medicine (PIM) and Review Education Group

Release Date: November 15, 2023

Expiration Date: Novemer 15, 2026

Estimated Time to Complete Activity: two hours

Target Audience: This activity is intended for optometrists who seek successful management of this condition.

JOINTLY ACCREDITED PROVIDER™ INTERPROFESSIONAL CONTINUING EDUCATION

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

- Recognize the multifactorial pathophysiology of pterygium.
- Identify the clinical factors associated with this condition.
- Recognize the risk factors of pterygium and educate patients accordingly.
- Effectively manage pterygium patients alongside a multidisciplinary team.

Faculty: Elizabeth Chetty, DPhilOptom, and Annelize van Zyl, BOptom, MPhilOptom

Disclosure of Conflicts of Interest: PIM requires faculty, planners and others in control of educational content to disclose all their financial relationships with ineligible companies. All identified conflicts of interest are thoroughly vetted and mitigated according to PIM policy. PIM is committed to providing its learners with high-quality, accredited CE activities and related materials that promote improvements or quality in health care and not a specific proprietary business interest of an ineligible company.

Those involved reported the following relevant financial relationships with ineligible entities related to the educational content of this CE activity: *Faculty* – Dr. Chetty and Ms. van Zyl have nothing to disclose. *Planners and Editorial Staff* – PIM has nothing to disclose. The Review Education Group has nothing to disclose.

Accreditation Statement: In support of improving patient care, this activity has been planned and implemented by PIM and the Review Education Group. PIM 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 CE for the healthcare team. PIM is accredited by COPE to provide CE to optometrists.

Credit Statement: This course is COPE-approved for two hours of CE credit. Activity #127176 and course ID 88074-TD. Check with your local state licensing board to see if this counts toward your CE requirement for relicensure.

Disclosure of Unlabeled Use: This educational activity may contain discussion of published and/or investigational uses of agents that are not indicated by the FDA. The planners of this activity do not recommend the use of any agent outside of the labeled indications. The opinions expressed in the educational activity are those of the faculty and do not necessarily represent the views of the planners. Refer to the official prescribing information for each product for discussion of approved indications, contraindications and warnings.

Disclaimer: Participants have an implied responsibility to use the newly acquired information to enhance patient outcomes and their own professional development. The information presented in this activity is not meant to serve as a guideline for patient management. Any procedures, medications or other courses of diagnosis or treatment discussed or suggested in this activity should not be used by clinicians without evaluation of their patient's condition(s) and possible contraindications and/or dangers in use, review of any applicable manufacturer's product information and comparison with recommendations of other authorities.

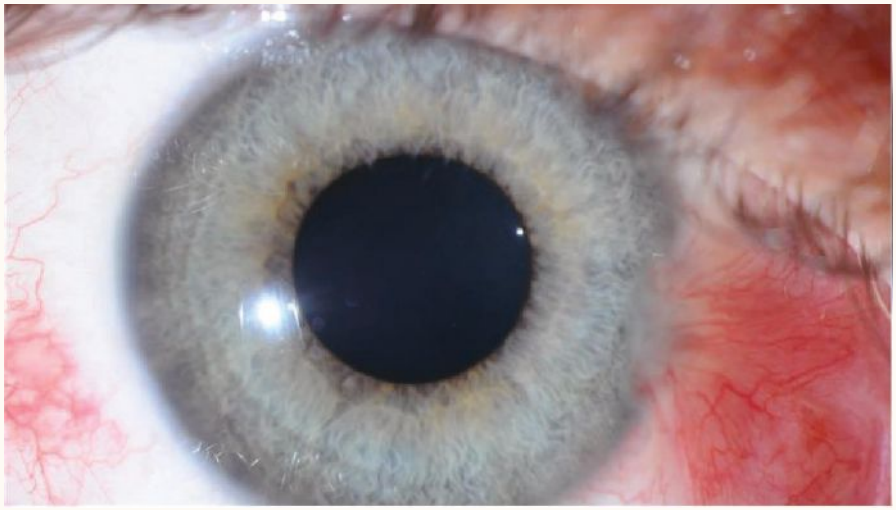


Fig. 2. Red appearance of eye due to angiogenesis in pterygium tissue.

necessary for clinical decision-making. It is helpful for eyecare practitioners to integrate the diagnostic assessment for pterygium into their usual clinical evaluation, especially for those who work in communities with high-risk factors. Living close to the equator, in a hot and dusty environment, older age, males, and many hours of sunlight exposure have all been identified as risk factors for the formation of pterygium.[1]

A thorough patient history will elucidate exposure to risk factors and determine if the patient has any symptoms associated with pterygium, such as eye irritation, redness, restricted ocular movements or induced astigmatism leading to blurry vision (only in advanced cases where the growth has invaded the cornea significantly).[15] Slit-lamp examination remains the cornerstone of pterygium diagnosis as it is an instrument that all eyecare practitioners have access to. It allows for a detailed pterygium size, location and vascularity evaluation.[16] Stoker's line is an iron deposition in the superficial cornea at the head of the pterygium and can also be viewed with a slit lamp.[17]

Anterior segment optical coherence tomography (AS-OCT) is becoming more popular in assessing and tracking the progression of pterygium as it provides more detail than a slit-lamp evaluation.[18] Automated methods using anterior segment images and computer programs are also being developed for screening purposes in rural areas to enhance diagnostic capacity in underserved areas.[19] Pterygium can induce astigmatism and an irregular corneal surface, affecting visual acuity (VA).

Measurement of VA, refraction, and topography is necessary to monitor the effect of the pterygium if it has invaded the cornea.

Pterygia can be described as having a head (the part that grows towards the cornea), body (the area that joins the head and base) and a base (the largest part of the pterygium, which lies over the bulbar conjunctiva). The pterygium can be graded once a diagnosis has been established based on the above assessment. Grading of pterygium is commonly based on its clinical characteristics, including size, vascularity and involvement of the cornea. A few grading systems have been proposed in the literature for primary and recurrent pterygia.[20-23] Different grading scales are necessary as some recurrent pterygia lack episcleral vessels, which is a feature of some grading systems for primary pterygia.

The Tan classification is a widely used grading system based on morphology (*Table 1*).[20] *Table 2* shows the grading system based on size.[24] *Figure 3* shows the different grades of pterygium based on the scale suggested by one study. [24]

Several conditions may mimic pterygium, making differential diagnosis crucial.

TABLE 1. GRADING OF PTERYGIUM BASED ON MORPHOLOGY[20]

Grade	Clinical Characteristics
1	Clearly visible episcleral vessels under an atrophic pterygium.
2	Any pterygium that exhibits characteristics between grades 1 and 3.
3	Episcleral vessels cannot be seen clearly because the pterygium is fleshy.

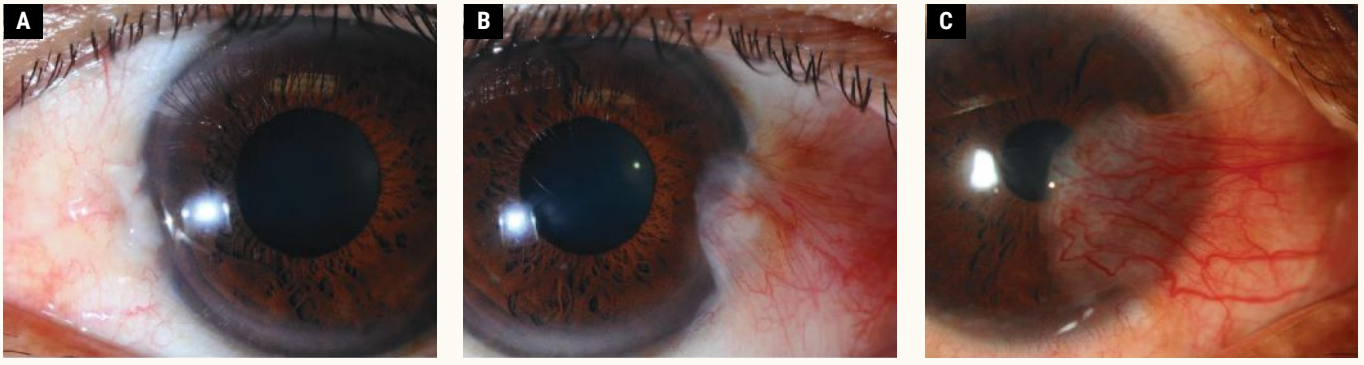


Fig. 3. Grading based on the size of the lesion: (A) Grade 1, (B) Grade 2, (C) Grade 3.

TABLE 2. GRADING OF PTERYGIUM BASED ON SIZE[24]

Grade	Extent (mm) on the cornea
1	0mm to 2mm from the limbus
2	2mm to 4mm from the limbus
3	More than 4mm from the limbus

The differential diagnosis includes nevi, conjunctival lymphoma, limbal dermoid, ocular surface squamous neoplasia (OSSN), pseudo-pterygium and ocular cicatricial pemphigoid.[6] Distinguishing between a benign pterygium and a malignant lesion, such as OSSN, requires a comprehensive clinical evaluation and, in some cases, additional diagnostic procedures. There have been cases where OSSN was detected in pterygium samples.[25]

If there is diagnostic uncertainty or clinical suspicion of malignancy, a biopsy to obtain tissue samples for histopathological examination is necessary. Histopathological examination of tissue samples can provide definitive evidence of malignancy. Dysplastic or malignant epithelial cell features, such as nuclear atypia, increased mitotic activity and abnormal cell architecture, would confirm malignancy.

Management Options

Addressing pterygium involves a range of treatment options depending on the severity of the condition and the presence of associated symptoms. In mild cases where the pterygium is small and asymptomatic, observation with regular follow-up may be appropriate. Patients can use lubricating eye drops to alleviate dryness and discomfort. A steroid eye drop can be prescribed to manage mild ocular irritation and redness symptoms.

Surgical removal of the pterygium is the primary treatment for cases with significant symptoms, visual obstruction or cosmetic concerns. *Figures 4* and *5* show the difference in appearance of the eye before and after surgery. *Figure 4* shows a follow-up period of three months where the sclera is still red and recovering from the procedure. *Figure 5* shows a fully healed sclera one-year post-surgery.

The chief complication of surgery is the high recurrence rate. Risk factors for pterygium recurrence following surgery are younger age, more advanced stage of disease and untreated postoperative inflammation.[26] The recurrence rate has been found to be as high as 97% within the first year postoperative.[27]

The bare sclera technique is one of the quickest, most straightforward surgical interventions; however, it has a high recurrence rate. An incision is made near the head of the pterygium, and the tissue is removed from the underlying cornea or conjunctiva. Unlike other techniques involving grafting tissue to cover the excision site, the bare sclera technique leaves the sclera exposed after removing the pterygium. The rationale is to minimize the risk of graft-related complications and reduce surgical time.

Depending on the surgeon's preference and the patient's condition, adjunctive therapies may be applied to the bare sclera, such as the intraoperative use of mitomycin C (an antineoplastic antibiotic), which aids in reducing the recurrence of pterygium.[24] Surgeons have been advised to refrain from using this technique in isolation as it has been shown that pterygia is up to 25-times more likely to recur with this technique.[28]

Additional procedures were explored to reduce the recurrence rate after surgical removal. Conjunctival autograft is a more favorable technique as it has a lower rate of recurrence in comparison to the bare sclera technique. Upon pterygium removal, a conjunctival graft is placed over the exposed area and is either sutured or glued on. The conjunctival tissue is grafted from the same eye from the bulbar conjunctiva under the upper lid as it is not exposed to UV radiation and is generally healthy tissue. The site from which the grafted tissue is taken is left exposed as it will re-epithelize.[29]

A variation of this technique is limbal conjunctival autograft, where limbal stem cells are included in the grafted tissue.[30] Amniotic membrane graft is another fairly recent technique in which the graft that covers the excision site is derived from a donor amniotic membrane. Amniotic membrane has proven useful in ophthalmic surgeries as the tissue is similar to corneal tissue in that it has an epithelium, basement membrane and stroma and is capable of re-epithelization and adhesion to the host tissue. In pterygium excision surgery, the membrane is placed with the stromal side on the exposed sclera and attached with fibrin glue or sutures.[31] Conjunctival autograft, limbal conjunctival autograft and amniotic membrane graft have all been shown to have lower recurrence rates than the bare sclera technique.[32]

Adjuvant therapy used pre-, post- and/or intraoperatively has been shown to reduce recurrence rates when paired with one of the procedures discussed above. Common adjuvant therapies include mitomycin-C, beta-irradiation, cyclosporine and 5- fluorouracil.[33] These adjuvant therapies do, however, have adverse effects, but the latest research suggests that the best outcomes thus far have been achieved with conjunctival autograft and topical cyclosporine.[34]

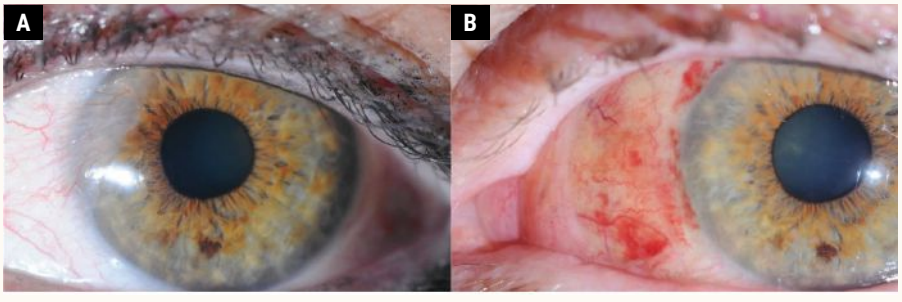


Fig. 4. (A) Before pterygium removal surgery. (B) Three months after surgery.

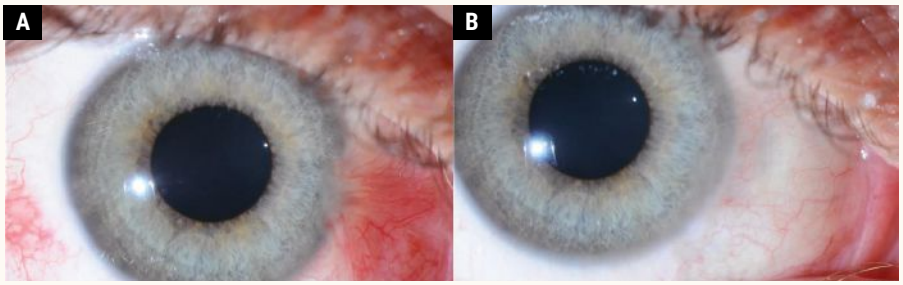


Fig. 5. (A) Before pterygium removal surgery. (B) A fully healed sclera one year after surgery.

Takeaways

Knowledge of this common ocular surface disorder's pathophysiological mechanisms, diagnostic assessments and the range of management options available remains crucial. Pterygium, primarily driven by chronic UV radiation exposure, inflammation and genetic factors, presents a complex interaction of pathological processes involving epithelial cells, fibroblasts, extracellular matrix remodeling and angiogenesis.

Its diagnostic assessment involves a multifaceted approach, where clinical exam, imaging techniques and histopathological evaluation play vital roles in accurate diagnosis and differentiation from malignant lesions, such as OSSN. Understanding the risk factors, clinical characteristics and histological features is essential for ODs and ophthalmologists to make informed patient care and management decisions.

Regarding management, a spectrum of options is available, ranging from conservative measures for mild cases to surgical interventions for moderate to severe pterygium. Surgical excision remains the primary choice for symptomatic and visually significant pterygium, with techniques like conjunctival autografting and amniotic membrane transplantation to minimize recurrence. Adjunctive therapies, postoperative care and vigilant follow-up are integral to a successful management strategy. For patients and clinicians, the decision on the appropriate approach depends on carefully evaluating clinical factors and patient preferences.

It is also important to emphasize prevention and early intervention in pterygium management. Education on UV protection and eye health is essential to reduce the risk of pterygium development. A multidisciplinary approach involving optometrists, ophthalmologists, pathologists and other eye care specialists is crucial in pursuing optimal patient outcomes. With a deeper understanding of the pathophysiology, accurate diagnostic assessment and a tailored approach to management, we can provide our patients with the best possible care for this challenging ocular condition. ■

We would like to thank Amy Humphreys from Northern Vision Clinic, Johannesburg for all the images used in this article.

1. Rezvan F, Khabazkhoob M, Hooshmand E, et al. Prevalence and risk factors of pterygium: a systematic review and meta-analysis. Surv Ophthalmol. 2018;63(5):719-35.

2. Fotouhi A, Hashemi H, Khabazkhoob M, et al. Prevalence and risk factors of pterygium and pinguecula: the Tehran Eye Study. Eye. 2009;23(5):1125-9.

3. Lin SF, Tsai RK, Tung IC, et al. An epidemiologic study of pterygium in middle-aged and elderly aboriginal populations of the Tao Tribe of Orchid Island in Taiwan. Tzu Chi Med J. 2006;18(4):283-6.

4. Moran DJ, Hollows FC. Pterygium and ultraviolet radiation: a positive correlation. Br J Ophthalmol. 1984;68(5):343-6.

5. Chui J, Di Girolamo N, Wakefield D, et al. The pathogenesis of pterygium: current concepts and their therapeutic implications. Ocul Surf. 2008;6(1):24-43.

6. Shahraki T, Arabi A, Feizi S. Pterygium: an update on pathophysiology, clinical features, and management. Ther Adv Ophthalmol. 2021;13: 25158414211020152.

7. Kau HC, Tsai CC, Lee CF, et al. Increased oxidative DNA damage, 8-hydroxydeoxy-guanosine, in human pterygium. Eye. 2006;20(7):826-31.

8. Di Girolamo N, Chui J, Coroneo MT, et al. Pathogenesis of pterygia: role of cytokines, growth factors, and matrix metalloproteinases. Prog in Retin Eye Res. 2004;23(2):195-228.

9. Kria L, Ohira A, Amemiya T. Immunohistochemical localization of basic fibroblast growth factor, platelet derived growth factor, transforming growth factor-β and tumor necrosis factor-α in the pterygium. Acta Histochemica. 1996;98(2):195-201.

10. Livezeanu C, Craitoiu MM, Manescu R, et al. Angiogenesis in the pathogenesis of pterygium. Rom J Morphol Embryol. 2011;52(3):837-44.

11. Dushku N, John MK, Schultz GS, et al. Pterygia pathogenesis: corneal invasion by matrix metalloproteinase expressing altered limbal epithelial basal cells. Arch Ophthalmol. 2001;119(5):695-706.

12. Ang LP, Chua JL, Tan DT. Current concepts and techniques in pterygium treatment. Curr Opin Ophthalmol. 2007;18(4):308-13.

13. Chalkia AK, Spandidos DA, Detorakis ET. Viral involvement in the pathogenesis and clinical features of ophthalmic pterygium. Int J Mol Med. 2013;32(3):539-43.

14. Rodrigues FW, Arruda JT, Silva RE, et al. TP53 gene expression, codon 72 polymorphism and human papillomavirus DNA associated with pterygium. Genet Mol Res. 2008;7(4):1251-8.

15. Wanzeler AC, Barbosa IA, Duarte B, et al. Mechanisms and biomarker candidates in pterygium development. Arq Bras Oftalmol. 2019;82:528-36.

16. Mohammad-Salih PA, Sharif AF. Analysis of pterygium size and induced corneal astigmatism. Cornea. 2008;27(4):434-8.

17. Arai Y, Makino S, Obata H. Stocker's line in pterygium. J Gen Fam Med. 2017;18(2):92-3.

18. Batur M, Seven E, Tekin S, et al. The role of anterior segment optical coherence tomography in the evaluation of the pterygium. Photodiagnosis Photodyn Ther. 2023;43:103704.

19. Zaki WM, Daud MM, Abdani SR, et al. Automated pterygium detection method of anterior segment photographed images. Comput Methods Programs Biomed. 2018;154:71-8.

20. Tan DT, Chee SP, Dear KB, et al. Effect of pterygium morphology on pterygium recurrence in a controlled trial comparing conjunctival autografting with bare sclera excision. Arch Ophthalmol. 1997;115(10):1235-40.

21. Maheshwari S. Pterygium-induced corneal refractive changes. Indian J Ophthalmol. 2007;55(5):383.

22. Prabhasawat P, Barton K, Burkett G, et al. Comparison of conjunctival autografts, amniotic membrane grafts, and primary closure for pterygium excision. Ophthalmology. 1997;104(6):974-85.

23. Liu J, Fu Y, Xu Y, et al. New grading system to improve the surgical outcome of multirecurrent pterygia. Arch Ophthalmol. 2012;130(1):39-49.

24. Verma NI, Garap JA, Maris RO, et al. Intraoperative use of mitomycin C in the treatment of recurrent pterygium. P N G Med J. 1998;41(1):37-42.

25. Van Acker SI, Van den Bogerd B, Haagdorens M, et al. Pterygium—the good, the bad, and the ugly. Cells. 2021;10(7):1567.

26. Janson BJ, Sikder S. Surgical management of pterygium. Ocul Surf. 2014;12(2):112-9.

27. Hirst LW, Sebban A, Chant D. Pterygium recurrence time. Ophthalmology. 1994;101(4):755-8.

28. Sánchez-Thorin JC, Rocha G, Yelin JB. Meta-analysis on the recurrence rates after bare sclera resection with and without mitomycin C use and conjunctival autograft placement in surgery for primary pterygium. Br J Ophthalmol. 1998;82(6):661-5.

29. Cioba C, Marafon SB, Fortes BG, et al. Autologous fibrin glue versus sutures for conjunctival autograft in primary pterygium: a randomized clinical trial. Int Ophthalmol. 2023;43(7):2371-81.

30. Mery G, Maalouf T, George JL, et al. Limbal-conjunctival autograft in pterygium surgery. J Fr Ophtalmol. 2010;33(2):92-8.

31. Jirsova K, Jones GL. Amniotic membrane in ophthalmology: properties, preparation, storage and indications for grafting—a review. Cell Tissue Bank. 2017;18:193-204.

32. Paganelli B, Sahyoun M, Gabison E. Conjunctival and limbal conjunctival autograft vs. amniotic membrane graft in primary pterygium surgery: a 30-year comprehensive review. Ophthalmol Ther. 2023;12(3):1501-17.

33. Fonseca EC, Rocha EM, Arruda GV. Comparison among adjuvant treatments for primary pterygium: a network meta-analysis. Br J Ophthalmol. 2018;102(6):748-56.

34. Chu WK, Choi HL, Bhat AK, et al. Pterygium: new insights. Eye. 2020;34(6):1047-50.

OPTOMETRIC STUDY CENTER QUIZ

To obtain CE credit through the Optometric Study Center, complete the test form on the following page and return it with the $35 fee to: Jobson Healthcare Information, Attn.: CE Processing, Jobson Healthcare Information, LLC/WebMD, 283-299 Market Street, 2 Gateway Center, 4th Floor, Newark, NJ 07102. To be eligible, please return the card within three years of publication. You can also access the test form and submit your answers and payment via credit card online at revieweducationgroup.com. You must achieve a score of 70 or higher to receive credit. Allow four weeks for processing. For each Optometric Study Center course you pass, you earn two hours of credit. Please check with your state licensing board to see if this approval counts toward your CE requirement for relicensure.

1. Which of the following is the main cause of pterygia?
a. Allergies.
b. Dry eye syndrome.
c. Ultraviolet radiation.
d. None of the above.

2. Angiogenesis is promoted by the release of which of the following?
a. VEGF.
b. FGF.
c. MMPs.
d. All of the above.

3. All of the following are considered to be a differential diagnosis for pterygia EXCEPT:
a. Pinguecula.
b. Lattice degeneration.
c. Limbal dermoid.
d. OSSN.

4. Which of the following surgeries has the highest recurrence rate?
a. Conjunctival autograft.
b. Amniotic membrane graft.
c. Limbal conjunctival autograft.
d. Bare sclera technique.

5. Which viral infection has been linked to pterygium pathophysiology?
a. COVID 19.
b. HPV.
c. HIV.
d. All the above.

6. Which of the following is NOT identified as a risk factor for the formation of pterygium?
a. Viral infection.
b. Living close to the equator.
c. Humid environments.
d. Older age.

7. Pterygia are described having which of the following?
a. A head, body and feet.
b. A head, neck and roots.
c. A head, body and base.
d. A crown, body and wing.

8. Grading scales are commonly based on which of the following clinical characteristics?
a. Size.
b. Vascularity.
c. Involvement of the cornea.
d. All the above.

9. Anterior segment OCT is becoming more popular in assessing and tracing the progression of pterygium because _____.
a. It provides more detail than the slit-lamp.
b. OCTs are more cost effective.
c. OCTs are widely available in all practices.
d. None of the above

10. Which surgical removal technique have surgeons been advised to refrain from using in isolation to remove pterygia?
a. Bare sclera.
b. Conjunctival Autografting.
c. Amniotic membrane transplantation.
d. Limbal conjunctival autograft.

11. Which of the following conditions may look like pterygium?
a. Pinguecula.
b. Limbal dermoid.
c. Conjunctival lymphoma.
d. All the above.

12. When malignancy is suspected or there is diagnostic uncertainty which of the following should occur?
a. Follow-up in six months to monitor change in size or height.
b. Biopsy is necessary to send tissue samples for histopathological examination.
c. Treat with lubricating drops.
d. Treat with steroid and lubricating drops.

13. The chief complication of surgical removal of the pterygium is _____.
a. Unsightly scarring after removal.
b. Chronic pain.
c. High recurrence rate.
d. The necessity of sunglasses whenever the patient is outdoors.

14. Pterygium formation occurs through all of the following mechanisms EXCEPT:
a. Inflammation.
b. Apoptosis.
c. Fibroblast activation.
d. Angiogenesis.

15. Which of the following eye drops are mostly prescribed to alleviate symptoms in mild cases?
a. Antibiotics and lubricating eye drops.
b. Steroid and lubricating eye drops.
c. Miotics and antibiotic eye drops.
d. None of the above.

16. Risk factors for pterygium recurrence after surgery include which of the following?
a. Younger age.
b. Untreated postoperative inflammation.
c. More advanced stage of disease.
d. All the above.

17. Treatment options for pterygiums depends on which of the following?
a. Age of the patient.
b. Size of the eye.
c. Severity of the condition and presence of associated symptoms.
d. Whether the patient is a smoker or not.

18. With the conjunctival autograft technique, the conjunctival tissue is grafted from which of the following?
a. The other eye from the bulbar conjunctiva under the upper lid.
b. The same eye from the bulbar conjunctiva under the lower lid.
c. The same eye from the bulbar conjunctiva under the upper lid.
d. The same eye from the bulbar conjunctiva from the temporal side.

19. Which of the following characteristics would confirm malignancy in conjunctival tissue?
a. Dysplastic epithelial cell features.
b. Increased mitotic activity.
c. Abnormal cell architecture.
d. All of the above.

20. Which of the following procedures have been shown to have lower recurrence rates than the bare sclera technique?
a. Conjunctival autograft.
b. Limbal conjunctival autograft.
c. Amniotic membrane graft.
d. All of the above.

Examination Answer Sheet

Addressing Pterygium in Optometric Practice

Valid for credit through November 15, 2026

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

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

Mail to: Jobson Healthcare Information, LLC/WebMD, 283-299 Market Street, 2 Gateway Center, 4th Floor, Newark, NJ 07102.

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

Credit: This course is COPE-approved for two hours of CE credit. Course ID 88074-TD.

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

Jointly provided by PIM and the Review Education Group.

Answers to CE exam:

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

Post-activity evaluation questions:

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

21. Recognize the multifactorial pathophysiology of pterygium. ① ② ③ ④ ⑤
22. Identify the clinical factors associated with this condition. ① ② ③ ④ ⑤
23. Recognize the risk factors of pterygium and educate patients accordingly. ① ② ③ ④ ⑤
24. Effectively manage pterygium patients alongside a multidisciplinary team. 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 diagnostic methods
Ⓒ Choice of management approach
Ⓓ Change in current practice for referral
Ⓔ Change in vision correction offerings
Ⓕ Change in differential diagnosis
Ⓖ More active monitoring and counseling
Ⓗ Other, please specify: _____

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

Ⓐ Very confident Ⓑ Somewhat confident Ⓒ Unsure Ⓓ Not confident

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

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

30. Additional comments on this course: _____

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

First Name
Last Name
E-Mail
The following is your: ☐ Home Address ☐ Business Address
Business Name
Address
City State
ZIP
Telephone # - -
Fax # - -
OE Tracker Number

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

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 124417 RO-OSC-1123

eyes on EYECARE

Find qualified opticians fast

Finding a qualified optician for your practice can be difficult. That's why private practices and large employers alike trust Eyes On Eyecare® for specialized job posting and recruiting services.

SOURCE TALENT MORE EFFICIENTLY WITH OUR:

- **Large talent pool of active and passive job seekers**
- **Syndication to major job platforms and cross-promotion to our affiliate network**
- **Dedicated recruiting team with years of eyecare experience sourcing talent for specialized positions**

"I had such a wonderful experience using Eyes On Eyecare. It was so easy to post a job and they walk you through the entire process. I recommend them to everyone I know."

- Ashley Wojcik

Learn more at eyesoneyecare.com/hire-now

PROUD PARTNER OF JOBSON OPTICAL GROUP

eyes on EYECARE

REVIEW of OPTOMETRY

BY PAUL M. KARPECKI, OD
CHIEF CLINICAL EDITOR

Not So Benign OSD

If your patient isn't responding to treatment, look beyond the typical forms of ocular surface disease.

Although most clinicians consider dry eye and blepharitis as milder forms of ocular surface disease (OSD), they aren't to most patients, and masquerading conditions can be disfiguring or even life-threatening. The following rare but significant conditions are ones you don't want to miss.

Sebaceous Carcinomas

Various terminology exists for this carcinoma, including sebaceous gland carcinoma, sebaceous cell carcinoma and meibomian gland carcinoma. Sebaceous carcinoma is a very aggressive and malignant tumor that originates from anywhere sebaceous glands are found, but is most commonly found on the eyelid from meibomian glands, which have a sebaceous gland origin. The lesion appears as a slow-growing, yellowish mass that is firm but painless to the touch, most commonly on the upper eyelid (*Figure 1*).[1] Often masquerading as a chalazion, this cancerous lesion is quite rare, accounting for about 3% of all malignant tumors and only 0.8% of eyelid tumors.[2] Since it is found in meibomian glands, it can also appear as a non-responsive meibomianitis. Signs include madarosis and irregular eyelid margins, and risk factors include radiation exposure, immunosuppression and Muir-Torre syndrome.[3] This condition is an autosomal dominant form of hereditary colorectal cancer caused by mutations in the DNA mismatch repair genes.

Individuals with sebaceous carcinoma have a five-year overall survival rate of 78% for localized disease and 50% for metastatic disease.[4] If both the upper and lower eyelid are involved or if the lesion is more than 10mm in size, the prognosis is far worse. Once diagnosed, sebaceous cell carcinoma is typically treated via surgical excision and radiotherapy. The lesion, however, tends to be quite infiltrative, therefore it's not uncommon for a patient with a delayed sebaceous carcinoma diagnosis to have more than 50% of the eyelid removed.[5] If not diagnosed, these can metastasize via the lymph nodes to remote sites.

Basal Cell Carcinomas

A far more common skin cancer often found around the eyelid margins is a basal cell carcinoma (BCC). Studies show BCCs are on the rise.[6] The most common sites for BCC include the eyelid margins, the area where nose pads on glasses rest (although nose pads have nothing to do with the formation of a BCC) and behind the ears. Basal cells are responsible for producing new skin cells as old ones die off. Abnormal replication, secondary to risk factors such as UV exposure, can lead to BCC.[7] The classic appearance is that of a pearly, translucent margined lesion with an umbilicated

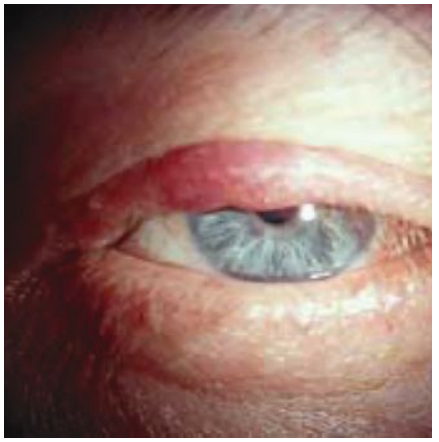


Fig. 1. Sebaceous carcinoma in a patient presenting with a recurrent chalazion.

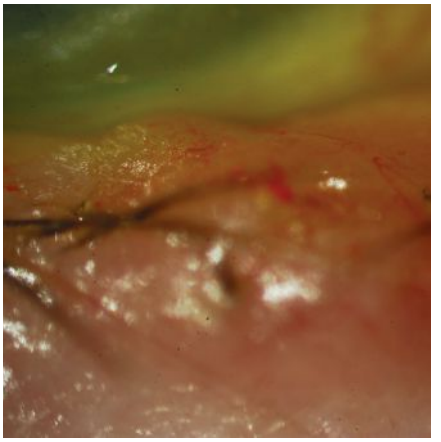


Fig. 2. Basal cell carcinoma with pearly margins and madarosis.

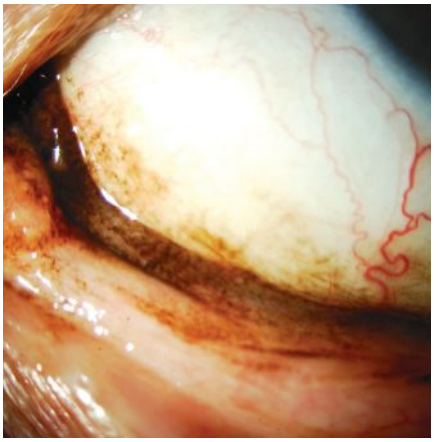


Fig. 3. Malignant melanoma of the conjunctiva.

About Dr. Karpecki

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

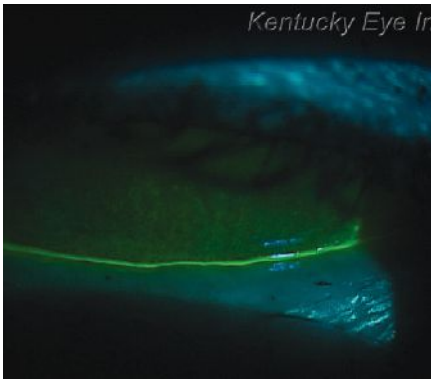


Fig. 4. Thin tear meniscus height and significant corneal staining in a patient with Sjögren's syndrome k. sicca.

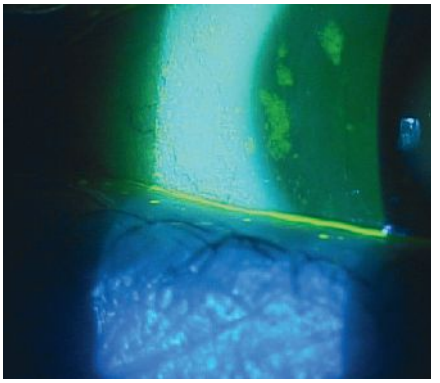


Fig. 5. Patchy staining and minimal tear meniscus height in a patient with Sjögren's syndrome keratoconjunctivitis sicca.

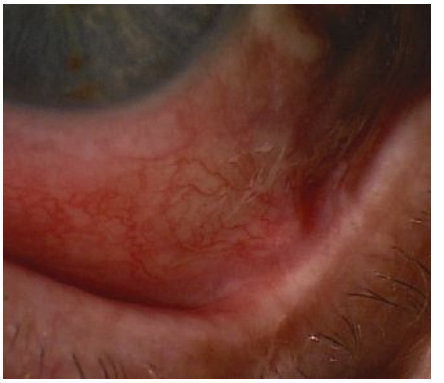


Fig. 6. This patient presented for a dry eye evaluation. The very shortened fornix suggests ocular cicatricial pemphigoid.

center (*Figure 2*). Hallmark symptoms include repeated crusting and bleeding of the lesion.[8] Pain typically occurs as the lesions bleed or especially if they grow to include surrounding tissue like bone and cartilage.

One unique aspect of BCC is that it rarely results in metastasis.[9] However, it is extremely invasive in that it grows deep within the tissue. It can result in disfigurement and even be fatal. For this reason, early diagnosis and removal via surgical excision, involving Mohs surgery or other less invasive surgery, is recommended. If caught early and superficial, Imiquimod cream can be applied directly to the lesion for about six weeks. While they can cause significant tissue loss due to depth, they don't spread like that of a sebaceous carcinoma and are rarely metastatic.[6]

Malignant Melanoma

One of the more serious skin cancers that can be found around the eyes is a malignant melanoma, which is cancer from the malignant transformation of melanocytes in the skin and can occur anywhere on the body, including the conjunctiva, eyelids, as well as on the iris or choroid (*Figure 3*).[10,11] The stage when diagnosed dictates the prognosis. For example, stage I melanoma has a five-year survival rate of about 97%, whereas stage IV has a 10% survival rate.[10]

The five key signs are known by the mnemonic of ABCDE:

- ***A—Asymmetry.*** If you could fold the lesion in half, it wouldn't line up.
- ***B—Irregular borders.***
- ***C—Color.*** Portions of the lesion are brown and others are black.
- ***D—Diameter.*** If it's over 6mm in size, it is highly suspicious for a malignant melanoma.
- ***E—Evolving.*** Lesion is growing, spreading or changing in some fashion.

Although melanomas are the most common intraocular tumor, they are rare on the ocular surface. Metastasis of ocular melanomas are typically through the lymph nodes and the most common site is the liver.[12]

Non-Hodgkin Lymphoma

Non-Hodgkin lymphoma is the most common hematological malignancy in the world, accounting for nearly 3% of cancer diagnoses and deaths.[13] Sjögren's syndrome is most often diagnosed in patients with dry eye symptoms and keratoconjunctivitis sicca (*Figures 4 and 5*).[14] Patients tend to show patchy corneal staining with a thin tear meniscus height. They often complain of concurrent xerostomia or dry mouth and may carry a water bottle with them to the eye exam. This condition is commonly diagnosed by primary eyecare providers as dry eye patients typically see them first.[14]

Once the diagnosis is made, either by serology or sometimes a lip biopsy, patients receive aggressive dry eye therapy. Sjögren's syndrome patients should also be educated about the 16 times greater risk of developing non-Hodgkin lymphoma, but also have higher risks of other forms of cancer.[15] Patients with primary Sjögren's syndrome have a 53% higher likelihood of developing malignancies.[16] It is important to educate them about the symptoms of non-Hodgkin lymphoma including night sweats, unexplained weight loss, chronic fatigue and swollen lymph nodes in the neck, axillary region or groin. Medications that can be considered include monoclonal antibodies such as rituximab that affects B-cells and targets both Sjögren's syndrome and non-Hodgkin lymphoma.[17]

Ocular Cicatricial Pemphigoid

Another severe autoimmune disease resulting in potential vision loss is ocular cicatricial pemphigoid, which is a form of mucous membrane pemphigoid. As the name implies, scarring (cicatrization) is a sign that leads to symblepharon, trichiasis and ectropion.[18] This eventually results in further damage and scarring on the conjunctiva and cornea. A chronic, insidious disease, patients typically present to their PECP with dry eyes and early diagnosis is difficult (*Figure 5*).[19]

As the disease progresses, photophobia, foreign body sensation and pain become more common. By examining the lower fornix to see if it is shortened, one can make a positive initial diagnosis of ocular cicatricial pemphigoid (*Figures 6 and 7*). Patients are initially treated with topical steroids

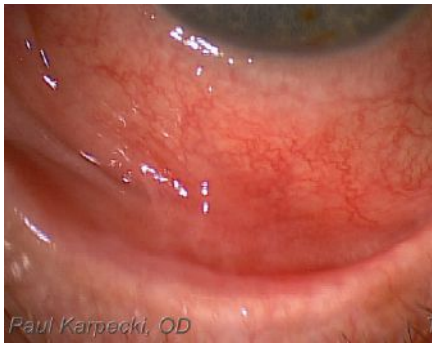


Fig. 7. A shortened inferior fornix, indicative of ocular cicatricial pemphigoid.

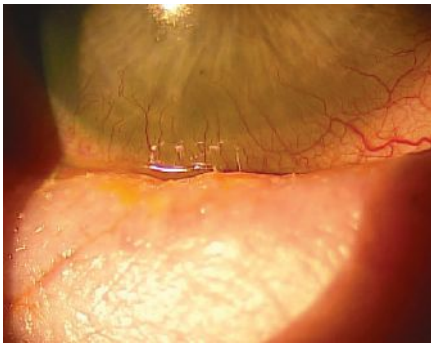


Fig. 8. A patient with GVHD experiencing trichiasis and severe inflammation.

but a systemic diagnosis needs to be made. This is accomplished via a biopsy identifying the presence of IgG, IgA and/or complement components C3 or C4. Patients with ocular cicatricial pemphigoid may be treated systemically with oral dapsone or systemic immunomodulatory therapy like methotrexate, and oral steroids typically prescribed by a rheumatologist.[20] These medications often begin with a lower dose and increase over time based on tolerability. Ocular management involves routinely epilating lashes, using topical corticosteroids and immunomodulators. Another successful option are adrenocorticotropic hormone analogue injections (Acthar) bi-weekly, which are often prescribed by eyecare providers.[21]

Ocular Graft-vs Host Disease

This is a common complication following a hematopoietic stem cell (bone marrow) transplant.[22] Although ocular GVHD is not one of the three most common presentations (skin, mouth and GI tract), some form of GVHD occurs in approximately 40% to 60% of patients.[23] Ocular GVHD presents as keratoconjunctivitis sicca manifesting moderate to severe ocular surface staining, then eventual scarring of the lid margins and conjunctiva (*Figure 8*). Most patients are treated with autologous serum drops, topical immunomodulators, placenta-based drops (RegenerEyes), amniotic membranes (*e.g.* Prokera or Atlas Apollo), corticosteroids and/or scleral lenses. Scleral lenses have been shown to be effective in mitigating complications and improving the ocular surface of ocular GVHD patients.[24]

The condition can vary from mild to life-threatening. The hope is that the GVHD will dissipate as the body begins to make its own lymphocytes from the donor cells. Chronic GVHD is the most common cause of death in patients receiving a bone-marrow transplant. Even with newer medications, the 10-year survival rate—post diagnosis—is about 42%.[25] Risks increase if there is a slight mismatch, such as a donor that is not a family member. New therapies such as autologous mesenchymal stromal stem cells may improve survival rates and morbidity.[26] It is important to include a history of a bone marrow or hematopoietic stem cell transplant in your OSD work-up.

OSDs are not all benign and need to be considered during an examination, especially in cases not responding to treatment. Examine the eyelids and adnexa thoroughly, including the areas around the nose, understand links between severe forms of dry eye and cancers and identify rare but significant presentations of keratoconjunctivitis sicca. These steps are imperative to sound clinical practice and saving patients well-being, and sometimes their lives. ■

1. Shields JA, Demirci H, Marr BP, et al. Sebaceous carcinoma of the eyelids: personal experience with 60 cases. Ophthalmology. 2004;111(12):2151-7.

2. Owen JL, Kibbi N, Worley B, et al. Sebaceous carcinoma: evidence-based clinical practice guidelines. Lancet Oncol. 2019;20(12):e699-714.

3. Sargen MR, Cahoon EK, Lynch FC, et al. Sebaceous carcinoma incidence and survival among solid organ transplant recipients in the United States, 1987-2017 JAMA Dermatol. 2020;156(12):1307-14.

4. Sargen MR, Starrett GJ, Engels EA, et al. Sebaceous carcinoma epidemiology and genetics: emerging concepts and clinical implications for screening, prevention and treatment. Clin Cancer Res. 2021;27(2):389-93.

5. Vissers G, Corthouts J, Van Haverbeke C, et al. Misdiagnosis of sebaceous carcinoma. Acta Chir Belg. 2022;122(2):127-32.

6. Kim DP, Kus KJB, Ruiz E. Basal cell carcinoma review. Hematol Oncol Clin North Am. 2019;33(1):13-24.

7. Teng Y, Yu Y, Li S et al. Ultraviolet radiation and basal cell carcinoma: an environmental perspective. Front Public Health. 2021:9:666528.

8. Kuflik AS, Janniger CK. Basal cell carcinoma. Am Fam Physician.1993;48(7):1273-6.

9. Petreanu CA, Şerban ED, Constantin MM, et al. Basal cell carcinoma—not always the 'good guy': case report of a life-threatening basosquamous carcinoma and review of the literature. Exp Ther Med. 2021;22(4):1158.

10. Heistein JB, Acharya U, Kumar S. Malignant melanoma. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. January 2023. Updated May 2023.

11. Oglesby CD. Malignant melanoma. Am J Ophthalmol. 1964:58:136-7.

12. Balasubramanya R, Selvarajan SK, Cox M, et al. Imaging of ocular melanoma metastasis. Br J Radiol. 2016;89(1065):20160092.

13. Thandra KC, Barsouk A, Saginala K, et al. Epidemiology of non-Hodgkin's lymphoma. Med Sci (Basel). 2021;9(1):5.

14. Bjordal O, Norheim KB, Rødahl E, et al. Primary Sjögren's syndrome and the eye. Surv Ophthalmol. 2020;65(2):119-32.

15. Solans-Laqué R, López-Hernandez A, Bosch-Gil JA, et al. Risk, predictors and clinical characteristics of lymphoma development in primary Sjögren's syndrome. Semin Arthritis Rheum. 2011;41(3):415-23.

16. Zhong H, Liu S, Wang Y, et al. Primary Sjögren's syndrome is associated with increased risk of malignancies besides lymphoma: a systematic review and meta-analysis. 2022;21(5):103084.

17. Tarella C, Gueli A, Ruella M, et al. Lymphocyte transformation and autoimmune disorders. Autoimmun Rev. 2013;12(8)802-13.

18. Schonberg S, Stokkermans TJ. Ocular Pemphigoid. In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. July 31, 2023.

19. Besagar S, London AO, Jairam MP, et al. Chronic early-stage ocular cicatricial pemphigoid. Ophthalmic Plast Reconstr Surg. 2021;37(6):e209-13.

20. Chang JH, McCluskey PJ. Ocular cicatricial pemphigoid: manifestations and management. Curr Allergy Asthma Rep. 2005;5(4):333-8.

21. Sharon Y, Chu DS. Adrenocorticotropic hormone analogue as novel treatment regimen in ocular cicatricial pemphigoid. Am J Ophthalmol Case Rep. 2018:10:264-7.

22. Ramachandran V, Kolli SS, Strowd LC. Review of graft-versus-host disease. Dermatol Clin. 2019;37(4):569-82.

23. Choi SW, Reddy P. Current and emerging strategies for the prevention of graft-versus-host disease. Nat Rev Clin Oncol. 2014;11(9):536-47.

24. Magro L, Gauthier L, Richet M, et al. Scleral lenses for severe chronic GvHD-related keratoconjunctivitis sicca: a retrospective study by the SFGM-TC bone marrow transplant. 2017;52(6):878-82.

25. Tan Y, Shan L, Zhao L, et al. Long-term follow-up of donor-derived CD7 CAR T-cell therapy in patients with T-cell acute lymphoblastic leukemia. J Hematol Oncol. 2023;16(1):34.

26. Stenger E, Giver CR, Langston A, et al. Safety of autologous freshly expanded mesenchymal stromal cells for the treatment of graft-versus-host disease. Front Immunol. 2022:13:959658.

Meivertor™

US Patent 11,446,017

The ONLY SINGLE-HANDED UPPER and lower eyelid EVERSION TOOL

- Optimize the functionality of your meibographer
- Empower your technician to take the images you need – flipping a lid has never been easier
- Whenever you evert an upper eyelid – AND need a free hand – use your Meivertor

"Amazingly well designed, incredible balance to the instrument, and ease of use. I would recommend every technician who does meibography have one."

-Dr. Paul Karpecki, OD, FAAO

"Love the Meivertor. First true game changer in the meibography game in my opinion."

-Dr. Bradley Barnett, MD

"The Meivertor is a terrific product that has become one of my staff's favourite in a very short time!"

-Dr. Kimberly K. Friedman, OD, FAAO

"Anyone struggle with lid eversion for meibomian gland imaging? Try using the Meivertor. Teaching techs has been a breeze and we can image both the upper and lower lids with ease!"

-Dr. Preeya Gupta, MD

For more information and to purchase go to **meivertor.com**

BY ALISON BOZUNG, OD

URGENT CARE

A Cold You Can See

This condition resolves on its own, but is still troubling to patients.

A 52-year-old Nicaraguan male presented to the emergency department with a subjective blind spot in the temporal field of his left eye starting the day prior. He also observed floaters, photopsias and central blurred vision in the same eye. He denied any ocular trauma, pain or recent surgery. His medical history included hypertension and hypercholesteremia, both controlled with medications.

On examination, the patient's visual acuity with pinhole was 20/25 in both eyes. His intraocular pressures, color vision and confrontation visual fields were normal. He did not have an afferent pupillary defect. The anterior segment exam was unremarkable in both eyes, but there were rare white blood cells in the vitreous cavity of the left eye. The fundus exam revealed moderate cup-to-disc ratios in both eyes with fine pigmentary changes in the left eye (*Figure 1*). Fundus photography, OCT and fundus autofluorescence (FAF) were obtained and revealed interesting findings (*Figures 2 and 3*). All imaging of the right eye was unremarkable.

Fundus findings prompted a more detailed case history, and the patient denied any recent viral infection symptoms, skin rashes, mucocutaneous ulcers, recent travel, non-productive cough or shortness of breath. He also denied any known history of bacterial infections, such as syphilis or tuberculosis.

Diagnosis

Based on the clinical vignette and imaging, a diagnosis of multiple evanescent white dot syndrome (MEWDS) was made. No medications were initiated, and the patient was instructed to return for short-interval follow-up. Laboratory testing was ordered at a follow-up visit to rule out syphilis and tuberculosis, which the patient ultimately chose not to receive. Three weeks after his initial presentation, the retinal lesions had begun resolving and his vision improved to 20/20. Presumably due to resolution of his symptoms, the patient did not return for his follow-up appointment.

Fig. 1. Right and left fundus photos. The left fundus (right image) has subtle whitish granular lesions in the posterior pole.

Presentation

MEWDS is often listed amongst the "white dot syndromes." The inflammatory condition is unilateral in the majority of cases and is most common in the third to fourth decades of life. As with many posterior uveitis syndromes, it has a predilection for myopic women. About one-third to one-half of individuals with MEWDS experience a flu-like viral prodrome. Others have been diagnosed after receiving various vaccinations.[1] Although the exact mechanism of disease is still unknown, an autoimmune, post-viral pathogenesis has been suggested.[2] There may also be a genetic component, as the HLA-B51 haplotype has been implicated.[3] The exact location of the pathologic process is contested, with some stating the choriocapillaris is the primary location of insult and others claiming the outer retina and photoreceptors are predominantly impacted.[1,4,5]

Clinical findings in MEWDS include macular granularity and 100µm to 200µm transitory granular grayish spots through the posterior pole. Patients may also present with optic nerve edema and mild vitreous cell. Imaging modalities that can support a diagnosis include FAF, OCT and fluorescein angiography (FA). FAF classically demonstrates abnormal hyperautofluorescence with scattered lesions around the optic nerve and macula extending outwards. OCT imaging generally reveals outer retinal changes such as disruption of the retinal pigmented epithelium and ellipsoid zone that generally agree with the hyperautofluorescent areas on FAF.

About Dr. Bozung

Dr. Bozung currently practices at Bascom Palmer where she primarily sees patients in the hospital's 24/7 ophthalmic emergency department. She also serves as the optometry residency program coordinator. Dr. Bozung is a fellow of the American Academy of Optometry and a member of the Florida and American Optometric Associations. She is a founding board member of Young OD Connect and serves on the editorial board for *Review of Optometry*. She has no financial interests to disclose.

Reveal the Beauty Within Your Eyes

Discover the inherent beauty and health of your eyes by experiencing the revitalizing power of Myboclean's Eyelid Cleansing Brush and Hydrating Lids and Lash Cleansing Gel

"Until MyboClean, there were no successful treatment options for demodex blepharitis other than expensive in-office procedures like photobiomodulation or agents that caused excessive burning and stinging, like high concentration tea tree oil. Internationally, manuka extract is well known as a very effective and comfortable treatment for demodex blepharitis--- and it's the key ingredient in MyboClean. The other ingredients, including coconut oil and aloe, contribute to the comfort and impressive treatment results of this one-of-a-kind, lid-hygiene product. It has changed our practice success, our patient response, and we're finally seeing successful resolution of this most recalcitrant form of blepharitis."

-Paul Karpecki, OD

Learn how you can make Myboclean part of your dry eye management plan and join the CARE Program.

Now comes repackaged with 1 sensitive skin brush, 1 cleansing lash gel, and 1 travel bag. Easy, affordable, and convenient for your patients.

MYBO CLEAN ™

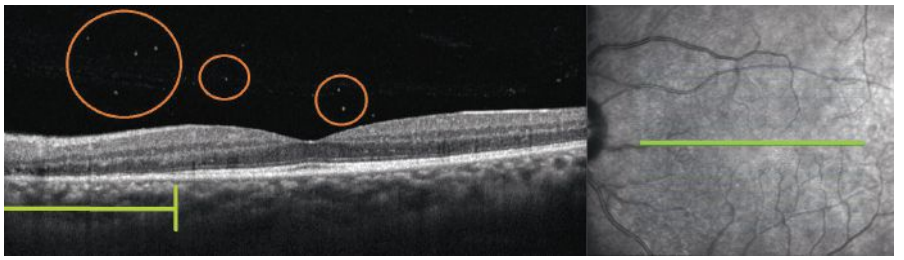


Fig. 2. OCT of the left eye, revealing outer retinal loss of the ellipsoid zone (denoted by underlying green bracket) and subtle vitreous cell (circled in orange). These findings were unilateral.

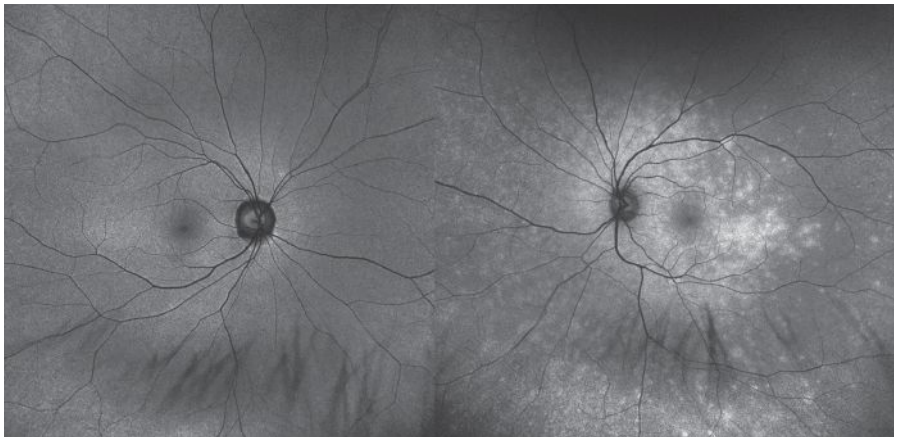


Fig. 3. Montage FAF of the right and left eyes. Spotty hyperautofluorescence is seen throughout the posterior pole, coalescing in the macula of the left eye (right image).

FA and indocyanine green angiography (ICG) may also used to evaluate MEWDS, and they reveal lesions that are hyperfluorescent on FA but hypocyanescent on ICG. The lesions on FAF and FA/ICG are often more apparent than those seen funduscopically.

Differentials

Other white dot syndromes are included in the differential diagnosis of MEWDS, and the presentation may have overlapping features with conditions such as multifocal choroiditis and panuveitis, acute zonular occult outer retinopathy, serpiginous choroidopathy, acute posterior multifocal placoid pigment epitheliopathy, birdshot chorioretinopathy and punctate inner choroidopathy. Additionally, autoimmune or infectious etiologies such as sarcoidosis, syphilis and tuberculosis should be considered. Interestingly, intraocular lymphoma has even been a documented masquerader.[6] In the case of MEWDS, the diagnosis may be slightly more straightforward given that only a few of the aforementioned conditions also present unilaterally. The fundus lesions in MEWDS are also often finer and more fleeting than those seen in other differentials. The differentiation can often be made with a careful clinical examination, multimodal imaging and supporting laboratory studies.

Given the fact that the vast majority of patients have a full spontaneous recovery, MEWDS has been termed the "common cold" of the retina by one study.[7] For this reason, intervention is typically not pursued. However, there are also reported cases in which the visual acuity did not recover completely. It has been suggested that the entering visual acuity is the strongest predictor of visual recovery, with a worse entering visual acuity portending a worse visual outcome.[8,9]

After ruling out other (particularly infectious) etiologies via bloodwork, some authors have used corticosteroids to hasten recovery. One such case describes the use of systemic corticosteroids for a young sumo wrestler who was anxious to improve his vision before an upcoming match.[10] Though rare, patients can develop neovascular complications in MEWDS. Anti-VEGF agents have been used with success in many of these cases.[11,12]

Takeaway

Consider white dot syndromes in a patient who presents with blind spots, blurred vision and photopsias. In the case of a unilateral presentation and the previously described classic fundus findings, MEWDS should be at the top of our list. Remember other differential diagnoses, and pursue laboratory workup to rule out other etiologies. Although most patients experience a complete resolution of symptoms, careful monitoring can rule out progressive masquerading disease or an atypical course. ■

1. Papasavvas I, Mantovani A, Tugal-Tutkun I, Herbort CP. Multiple evanescent white dot syndrome (MEWDS): update on practical appraisal, diagnosis and clinicopathology; a review and an alternative comprehensive perspective. J Ophthalmic Inflamm Infect. 2021;11(1):45.

2. Standardization of Uveitis Nomenclature (SUN) Working Group. Classification criteria for multiple evanescent white dot syndrome. Am J Ophthalmol. 2021;228:198-204.

3. Desarnaulds AB, Borruat FX, Herbort CP, Spertini F. Multiple evanescent white dot syndrome: a genetic predisposition? Klin Monbl Augenheilkd. 1996;208(5):301-2.

4. Yannuzzi NA, Swaminathan SS, Zheng F, et al. Swept-source oct angiography shows sparing of the choriocapillaris in multiple evanescent white dot syndrome. Ophthalmic Surg Lasers Imaging Retina. 2017;48(1):69-74.

5. Kang HG, Kim TY, Kim M, et al. Expanding the clinical spectrum of multiple evanescent white dot syndrome with overlapping multifocal choroiditis. Ocul Immunol Inflamm. 2022;30(1):81-9.

6. Russell JF, Pichi F, Scott NL, et al. Masqueraders of multiple evanescent white dot syndrome (MEWDS). Int Ophthalmol. 2020;40(3):627-38.

7. Tavallali A, Yannuzzi LA. MEWDS, common cold of the retina. J Ophthalmic Vis Res. 2017;12(2):132-4.

8. Barile GR, Harmon SA. Multiple evanescent white dot syndrome with central visual loss. Retin Cases Brief Rep. 2017;11 Suppl 1:S219-25.

9. Takahashi Y, Ataka S, Wada S, Kohno T, Nomura Y, Shiraki K. A case of multiple evanescent white dot syndrome treated by steroid pulse therapy. Osaka City Med J. 2006;52(2):83-6.

10. Bosello F, Westcott M, Casalino G, et al. Multiple evanescent white dot syndrome: clinical course and factors influencing visual acuity recovery. Br J Ophthalmol. 2022;106(1):121-7.

11. Wyhinny GJ, Jackson JL, Jampol LM, Caro NC. Subretinal neovascularization following multiple evanescent white-dot syndrome. Arch Ophthalmol. 1990;108(10):1384-5.

12. Battaglia Parodi M, Iacono P, Zucchiatti I, Bandello F. Choroidal neovascularization associated with multiple evanescent white dot syndrome treated with intravitreal ranibizumab. Ocul Immunol Inflamm. 2018;26(4):608-11.

Dry eye relief that **goes the distance**

VeraPlug™
FlexFit™
Long-term occlusion with enhanced fit, comfort and retention

Vera180™
Synthetic absorbable plugs for approximately **6 months of treatment**

VeraC7™
7 day absorbable plugs for diagnostic use

For every leg of the race, we'll help you keep the pace. From **temporary diagnostic** occlusion to **long-term silicone plugs**, Lacrivera offers a complete line of innovative products for the treatment of dry eye.

A FRESH PERSPECTIVE™

LACRIVERA®

lacrivera.com (855) 857-0518

2500 Sandersville Rd • Lexington KY 40511 USA

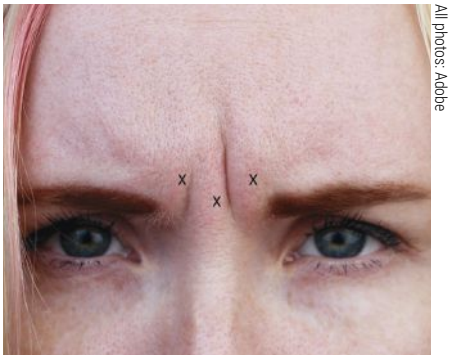
Ace this Aesthetic Injection

Neurotoxins, if administered correctly, can provide precise and safe results for your patients.

BY SELINA R. MCGEE, OD
EDMOND, OK

The pursuit of a more youthful appearance has led to innovative treatments that extend beyond skincare products that rarely deliver the results people seek. Surgical procedures have a role but there is downtime and risk involved. Neurotoxin injections have emerged over the last twenty years and are a powerful tool for enhancing the aesthetics of the eyes. This minimally invasive method offers a highly effective solution. If you have given a patient a new prescription for spectacles or contact lenses, you have witnessed the transformation that people experience when they enhance the way the look with a fabulous frame or when they gain spectacle freedom.

Why should we stop there? Let's explore the transformative potential neurotoxin injections have in eye care and shed light on the mechanism, the safety and the impact on the overall appearance of the eyes.



All photos: Adobe

Injection sites for glabella into procerus and corrugators.

Background

Neurotoxin is the number one minimally invasive procedure performed in the US according to the American Society of Plastic Surgeons. These treatments involve the use of purified botulinum toxin, which is a potent neurotoxin produced by the bacterium Clostridium botulinum. These injections have gained immense popularity for their ability to reduce the appearance of wrinkles and fine lines. The intramuscular injection of botulinum toxin inhibits the release of acetylcholine from the presynaptic motor neurons which cause muscle paralysis temporarily.[1]

When properly reconstituted and effectively administered in a trained provider's hands, the relaxation of the muscle and the diminishment of wrinkles and fine lines can give very pleasing aesthetic results.[2] In our context, there are a lot of muscles that can be intentionally manipulated around the eyes. Remember, neurotoxin works well on dynamic wrinkles because it prevents the muscle from working during movement. Frowning, squinting, smiling, raising eyebrows, all common facial expressions, result from muscle movement. These in turn can cause frown lines or "11s", crow's feet aka lateral canthal rhytids and forehead lines. These repeated muscle movements result in wrinkles. Selectively targeting the muscles involved in each of these movements, injecting the appropriate dose and location, allows for the skin to smooth out and offer a rejuvenated look.[3]

One of the advantages of neurotoxin injections is their precise, targeted placement, which can create beautiful

TABLE 1. THE GLABELLA REGION

	Onabotulinumtoxin-A, Incobotulinumtoxin-A Prabotulinumtoxin-A Women/Men # of Units	**Abobotulinumtoxin-A** Women/Men # of Units	**Daxibotulinumtoxin-A** Women/Men # of Units
Glabellar Lines	Four to six/six to eight (each site)	10 to 13/10 to 15 (each site)	Eight to 12/12 to 16 (each site)
# of Injections	Three to seven sites/three to five sites	Three to seven sites/three to five sites	Three to five sites/three to five sites
Type of injection	Intramuscular	Intramuscular	Intramuscular
Total # of Units	12 to 40	50 to 105	40 to 80

About Dr. Lighthizer

Dr. Lighthizer is the associate dean, director of continuing education and chief of specialty care clinics at the NSU Oklahoma College of Optometry. He is a founding member and immediate past president of the Intrepid Eye Society. Dr. Lighthizer's full disclosure list can be found in the online version of this article at www.reviewofoptometry.com.

results. However, one challenge is that you don't see the full effects of placement for two full weeks. This means that patience, attention to detail and practice will be paramount in successful injections.

One Size Does Not Fit All

The biggest mistake I see is new injectors taking a cookie cutter approach to each patient, treating them all the same. Ultimately, a tailored approach will result in meeting patients' needs and exceeding their expectations, and this precise delivery ensures natural looking results. I want my patients to look well rested and more youthful, not overdone and obvious. Patients should still have some movement and be able to show emotion. I do not want to rob people of their unique facial characteristics or the ability to emote.

This balance between preserving facial expressions and wrinkle reduction is the hallmark of a great injector. It's also why this procedure is such a popular choice for those seeking subtle, yet highly impactful, improvements in their appearance-and it starts with their eyes. Notably, when patients have dry eye disease, then there are no injections in the orbicularis oculi as this can dampen the blink and exacerbate their disease. Another reason why eyecare providers are primed to perform this procedure!

TABLE 2. THE TRAVERSE RHYTIDS OF THE FOREHEAD

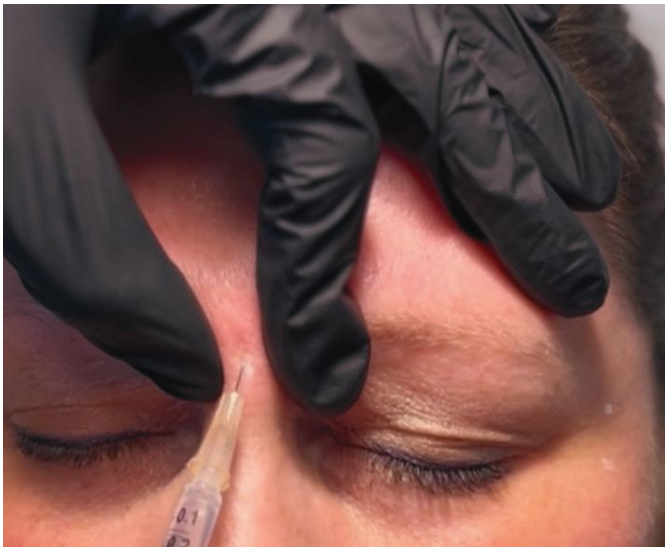
	Onabotulinumtoxin A **Incobotulinumtoxin A** **Prabotulinumtoxin-A** Women/Men # of Units	**Abobotulinumtoxin A** Women/Men # of Units
Traverse Rhytids	Two to four (each site)	Five to 10 (each site)
# of Injections	Varies	Varies
Type of Injection	Intradermal	Intradermal
Total # of Units	10 to 40	25 to 100

To enhance the periorbital region, first understand the muscles and their actions (*Figure 5*). Remember the skin around the eyes is thinnest on the body and therefore shows aging more quickly. If we want to paralyze a muscle temporarily with neurotoxin, we must understand its opposing result. If we paralyze a depressor, we create elevation. If we paralyze an elevator, we create depression.

The Procedure Process

Neurotoxin injections are renowned for their safety profile and minimal downtime. The procedure done in the right patient is generally well-tolerated and has few side effects. The most common are headache and redness. Swelling and bruising can also be common at the injection site. Patients usually return to their normal activities after treatment as long as there is no hat or pressure placed on the injection sites for the first few hours after treatment that would diffuse the medication causing it to migrate to a muscle that you don't want to paralyze. Our understanding of the periorbital muscles makes eyecare providers the perfect injectors, if that is something you desire.

To reconstitute the drug, use the manufacturer's and FDA's recommended dilution rates. For onabotulinumtoxin-A, incobotulinumtoxin-A and prabotulinumtoxin-A, the dilution rates are 2.5mL into a 100-unit vial with 0.9% sodium chloride which results in 4.0 units per 0.1mL dose. For daxibotulinumtoxin-A, the dilution rates for a 100-unit vial are double that of onabotulinumtoxin-A, so 8.0 units per 0.1mL dose. These dilution rates give you 4.0 or 8.0 (for daxibotulinumtoxin-A) units respectively per 0.1mL

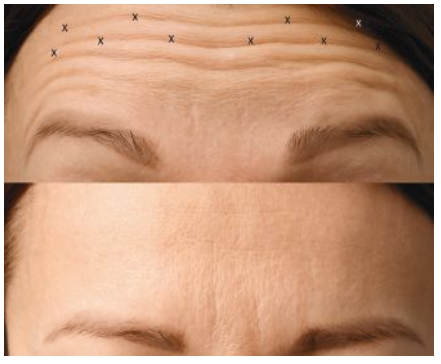


Injecting 4.0 units of neurotoxin into the procerus muscle.

Injecting 4.0 units of neurotoxin into the corrugator muscle.

TABLE 3. THE LATERAL CANTHAL RHYTID, OR "CROW'S FEET" AREA

	OnabotulinumtoxinA, Incobotulinumtoxin A Prabotulinumtoxin A Women/Men # of Units	**Abobotulinumtoxin A** Women/Men # of Units
Crow's Feet	two to four (each site)	Five to 10 (each site)
# of Injections	Two to five on each side	Two to five on each side
Type of Injection	Intradermal	Intradermal
Total # of Units	Eight to 30 units	20 to 100 units



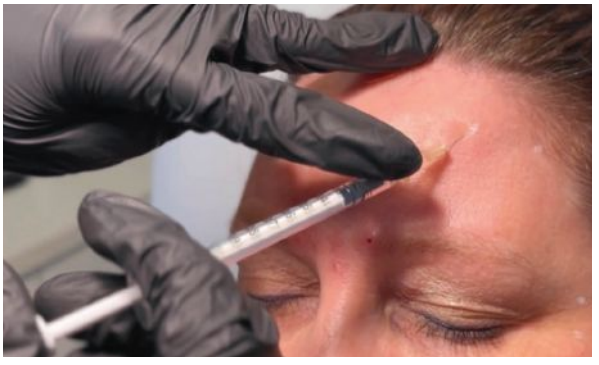
Injection sites (top) and post-injection and lack of movement (bottom). The Xs depict where I would inject this patient.

dose, which has migration at about the size of a nickel. Having 2.0 or 4.0 (for daxibotulinumtoxin-A) units will have migration of approximately the size of a dime. Abobotulinumtoxin-A is diluted according to the manufacturer's guidelines for a 100-unit bottle at 3.0mL of 0.9% sodium chloride diluent added results in 10.0 units per 0.1mL dose.

See *Tables 1*, *2* and *3* for the typical number of injection sites, units, and type of injection for each facial area.

Store reconstituted medication in refrigerator between 2º to 8º C. Best practices are to use it within seven hours of dilution, but there was a consensus paper that showed it can be stored for up to four weeks, with 87% potency using preserved or bacteriostatic saline preferably.[4] The stored medication should be clear, colorless and free of particulate matter before being administered.

Neurotoxin injections for aesthetics provide results that can last anywhere from three to six months. Individual experiences with how long it lasts depend on that person, their metabolism rates and how much they use the muscle. I have patients return to my clinic in two weeks to fully assess their result and see if they need a touch up if I'm injecting them for the first time. This allows me to learn their specific anatomy and correct any muscle that may need an adjustment. After that, patients are scheduled every 90 days to receive their injections. I do often combine neurotoxin alongside energy-based devices that address redness and pigment as well as also build collagen. I always wait at least two weeks before performing an energy-based treatment like intense pulsed light, radiofrequency or laser resurfacing.



Injecting 2.0 units of neurotoxin into the frontalis muscle.

Takeaways

The power of neurotoxin injections in eye care is in our ability to deliver precise, safe and impressive results to our patients. They value our relationship that is built on trust and the optometrist's proficiency in other procedures. I have many patients who have had prior injectors that have given me great confidence by saying, "This is the best I've ever looked, it's so natural and I'm thrilled with the results. I'm never having anyone else inject me."

These injections offer a minimally invasive solution to address periorbital concerns that come with aging. Helping patients with rejuvenation can be a transformative experience for both your patient and you. So, go out there and enhance beauty in whatever way you can.

Injecting 2.0 units of neurotoxin into the orbicularis oculi.

1. Carruthers J, Carruthers A. The use of botulinum toxin type A in the brow and periorbital rhytides. Semin Cutan Med Surg. 2007;26(2):66-70.

2. Kane MA, Lorenc ZP. Botulinum toxin and the brow: evolution of a technique. Plast Reconstr Surg. 2013;132(3S):7S-15S.

3. Lorenc ZP, Smith S. Chemical brow lift with botulinum toxin. Aesthetic Plast Surg. 2017;41(5):1060-6.

4. Carruthers J, Fagien S, Matarasso SL; Botox Consensus Group. Consensus recommendations on the use of botulinum toxin type a in facial aesthetics. Plast Reconstr Surg. 2004;114(6 Suppl):1S-22S

ABOUT THE AUTHOR

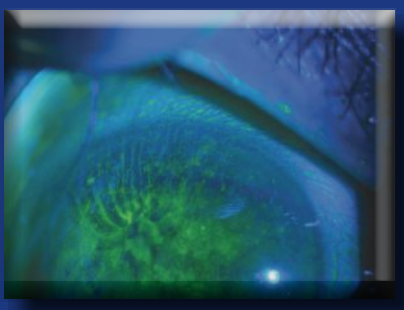
Dr. McGee is founder and owner of BeSpoke Vision, a boutique private practice that offers patients a wide range of optometric care. She is also an adjunct assistant professor at the Northeastern State University College of Optometry and on faculty at the Oklahoma Medical Research Foundation at its Sjögren's clinic. She is a fellow of the American Academy of Optometry, a diplomate of the American Board of Optometry and is past president of the Oklahoma Association of Optometric Physicians. Dr. McGee consults for Allergan, Kala Pharmaceuticals and Novartis Pharmaceuticals.

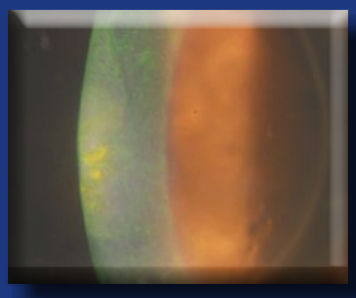
EyeRes™

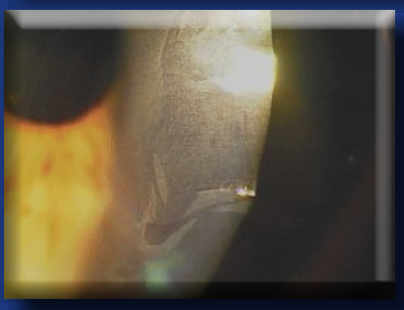
Digital Imaging Systems

by **TelScreen**

Slit Lamps • Digital Imaging Systems for Lasers and Slit Lamps • Functional Meibography



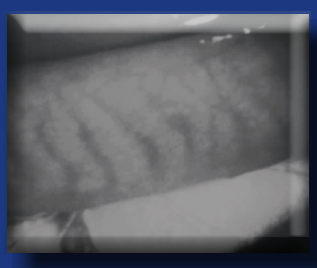


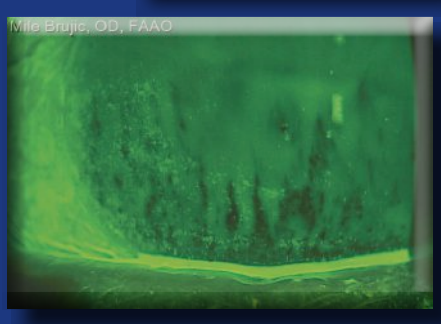


Diamond

Platinum

Gold





@telscreen

@telscreen

TelScreen

Effortless imaging for
Maximum Results!

info@TelScreen.com
502.515.1806

BY RAMI ABOUMOURAD, OD

RETINA QUIZ

Bigger Isn't Better

Thickening of the retina is a sign of this condition.

An 85-year-old Hispanic female presented for evaluation of longstanding poor vision OU. She denied any pain, redness, photophobia, photopsias or floaters. Her past medical history included hypertension, diabetes mellitus, hypothyroid and cardiac arrhythmias, all of which were controlled medically. Her past ocular history included macular hole repair OS 15 years prior with subsequent cataract extraction.

Best-corrected visual acuity was 20/50 OD and the 20/200 "E" at two feet OS. Intraocular pressure was 14mm Hg OU, confrontation fields were grossly full OU, extraocular motilities were full OU and pupils were equal in size and reactivity without a relative afferent pupillary defect. There was 2+ nuclear sclerotic cataract OD and a well-centered posterior chamber intraocular lens with open posterior capsule OS.

Take the Retina Quiz

1. Fundus imaging (Figures 1 and 2) depicts:
a. A type I posterior staphyloma OD.
b. Type III peripapillary staphyloma OS.
c. Central chorioretinal atrophy OU.
d. All of the above.

2. Which of the following is not true of the OCT of the right eye?
a. There is a retinoschisis affecting the outer plexiform layer.
b. There is an epiretinal membrane (ERM) inducing traction.
c. There is a posterior staphyloma.
d. There is peripapillary atrophy.

3. What is the most likely diagnosis for the patient's right eye?
a. Cystoid macular edema.
b. Lamellar macular hole.
c. Myopic foveoschisis.
d. X-linked juvenile retinoschisis.

4. What is the indicated management for this patient's right eye?
a. Observation.
b. Intravitreal anti-VEGF.
c. Macular buckle.
d. Pars plana vitrectomy with inner limiting membrane (PPV/ILM) peel and silicone oil tamponade.

5. Which of the following is not a risk factor for developing the condition in the right eye?
a. A large, wide and deep posterior staphyloma.
b. Axial length of 30mm.
c. Presence of dome-shaped macula.
d. All of the above.

For answers to the quiz, see page 98.

Diagnosis

Fundus examination revealed a type I posterior staphyloma OD and type III peripapillary staphyloma OS, optic nerve cupping with peripapillary atrophy OU, central chorioretinal atrophy OS>OD and a thickened and mottled appearance to the macula OD (*Figures 1 and 2*). OCT revealed staphylomatous contour of the macula OD and optic nerve OS,

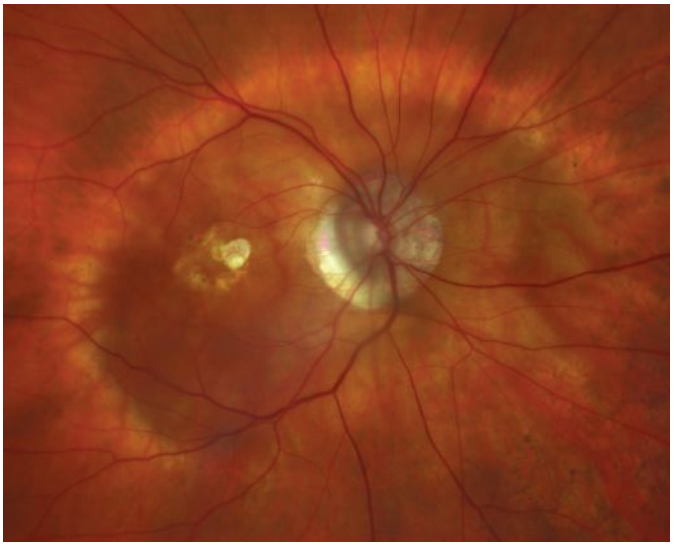


Fig. 1. Zeiss Clarus fundus photograph of the right eye.

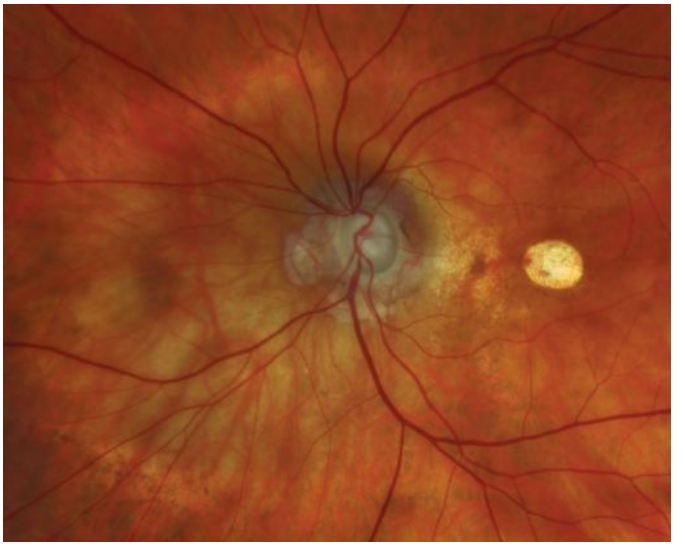
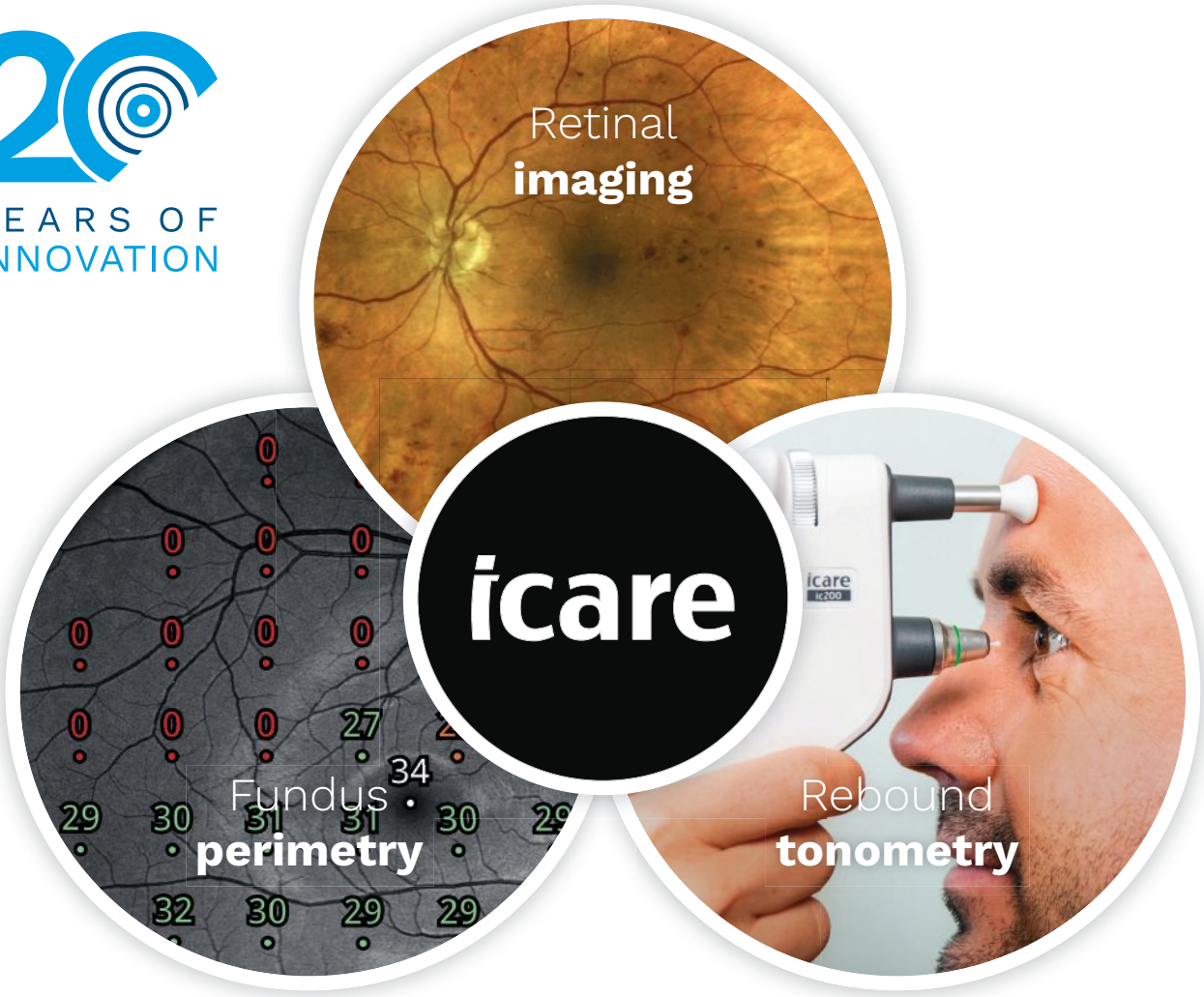


Fig. 2. Zeiss Clarus fundus photograph of the left eye.

About Dr. Aboumourad **Dr. Aboumourad** currently practices at Bascom Palmer Eye Institute in Miami. He has no financial disclosures.

20 YEARS OF INNOVATION



You know us for tonometry.

Get to know iCare for imaging and perimetry.

Discover the next level of eye care with our full line of devices.

Scan or visit www.icare-world.com/USA

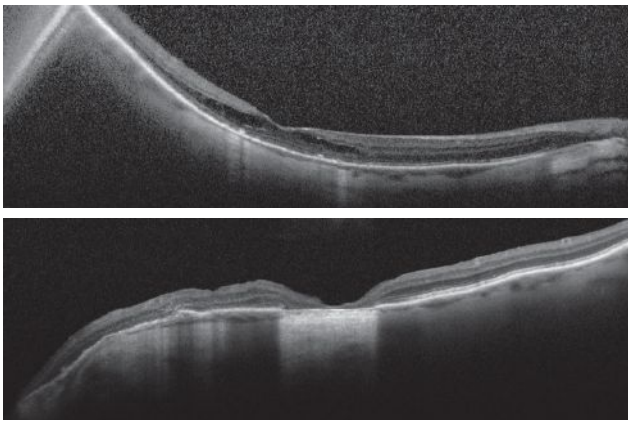
macular thickening with outer retinoschisis OD and central retinal pigment epithelial (RPE) atrophy with nasal outer-retinal disruption and loss of typical macular architecture OS (*Figures 3 and 4*). It is important to acknowledge the absence of macular hole and that the retina is flat. The patient was diagnosed with myopic foveoschisis OD and central RPE atrophy involving the fovea OS following macular hole repair.

Discussion

Myopic foveoschisis is when highly myopic patients develop macular retinoschisis with or without an associated localized retinal detachment or secondary macular hole.[1,2] When there are preretinal proliferative membranes causing traction on the retina, the term *myopic traction maculopathy* (MTM) can be more broadly applied.[3] While initially described in 1959, the term *myopic foveoschisis* was first coined in 1999 and further expanded upon with the advent of OCT technology, which improved our ability to better understand and identify this disease.[1,2]

The prevalence of myopic foveoschisis has been reported to be approximately 0.8% of the general population, but can be as high as 32.9% of high myopes in the general population and 62% of high myopes in tertiary care settings.[4] High myopia is generally regarded as an axial length greater than 26mm to 26.5mm or a spherical equivalent refractive error greater than -6D or -8D, depending on the study.[2-5]

Pathophysiology is thought to be largely related to variations in elasticity of the inner and outer retina, which may be accompanied by preretinal fibrous proliferations that can induce anteroposterior traction on the retinal surface, thereby exacerbating inequalities of retinal flexibility.[1,2] The degree of tangential and anteroposterior traction exerted on the retina is probably related to the shape, diameter and depth of posterior staphylomas.[3,4] To that end, it has been proposed that developing myopic foveoschisis may be more related to staphyloma progression.[2] Interestingly, histopathologic studies have identified a disproportionate presence of collagen fibers, cellular debris and fibrous glial cells as compared with idiopathic nonmyopic macular holes[1,2] Risk factors for development of myopic foveoschisis include spherical equivalent > -8D, axial length > 31mm, presence of posterior staphyloma, abnormal vitreoretinal interfaces (including ERM) and increasing age (typically over 50 years of age).[1,2]



Figs. 3 and 4. Heidelberg Spectralis OCT of the right eye (top) and left eye (bottom).

Due to the subtle clinical nature of slight macular elevations within staphylomas, it is felt that OCT is the most useful diagnostic tool.[1] Rapid advancements over the last few decades have allowed for high resolution structural analysis of the macula, aiding our ability to detect more subtle myopic foveoschisis or ERM/ILM detachments (*i.e.*, macular schisis of the inner retina).[1] MTM is a spectrum of disease in the setting of high myopia and often with posterior staphyloma, where patients may present with ERM, ILM detachment, myopic foveoschisis, foveal or macular detachment, lamellar or full-thickness macular hole (FTMH) and subsequent retinal detachment.[1-3]

Surgical Intervention

The natural history is evolution along the MTM spectrum, which often begins as inner or compound inner and outer macular schisis that progresses to primarily outer retinal macular schisis. Eventually, lamellar and FTMH may form, and a localized foveal detachment can progress to retinal detachment.[5,6] The earlier stages of MTM with inner, outer or compound inner and outer macular schisis are often observed, though surgery can be considered based on severity and patient needs.[1,5] Foveal detachment portends a high risk of macular hole formation, and surgical intervention is generally indicated within one to two months.[1,5] Of patients with myopic foveoschisis, between 31% and 50% have been reported to develop FTMH alone within three years and FTMH with retinal detachment within two years, respectively.[1]

Goals of surgery are to release any abnormal vitreoretinal or preretinal traction and to tamponade the retina to restore the retinal architecture.[5] Cases of FTMH repair in high myopes carry a worse single-surgery success rate than idiopathic nonmyopic macular holes due the greater mechanical tension of the globe wall within the staphyloma.[1] Initial techniques were aimed at reinforcing the sclera of the posterior globe with donor tissue in the 1930s and subsequently the macular buckle in the 1950s.[5] Once PPV was developed, it provided an intraocular approach to releasing vitreoretinal and preretinal traction and was later combined with ILM peeling.[1,2,5] Long-acting tamponade (*e.g.*, silicone oil or C_3F_8 gas) is preferred to promote restoration of retinal architecture and reattachment of the photoreceptors and RPE.[1,5]

Our patient was observed over three years with overall stability. Should she develop worsening of her schisis with foveal detachment, lamellar or full-thickness macular hole, surgical intervention may be indicated. ■

1. Ryan SJ, Davis JL, Flynn HW, et al. Retina, Fifth ed. London; New York: Saunders/Elsevier, 2013.

2. Gohil R, Sivaprasad S, Han LT, et al. Myopic foveoschisis: a clinical review. Eye (Lond). 2015;29(5):593-601.

3. Panozzo G, Mercanti A. OCT findings in myopic traction maculopathy. Arch Ophthalmol. 2004;122(10):1455-60.

4. Cheong KX, Xu L, Ohno-Matsui K, et al. An evidence-based review of the epidemiology of myopic traction maculopathy. Surv Ophthalmol. 2022;67(6):1603-30.

5. Frisina R, Gius I, Palmieri M, et al. Myopic traction maculopathy: diagnostic and management strategies. Clin Ophthalmol. 2020;14:3699-708.

6. Parolini B, Palmieri M, Finzi A, et al. The new myopic traction maculopathy staging System. Eur J Ophthalmol. 2021;31(3):1299-312.

Merchandise Offered

Practice For Sale

PRODUCT REVIEW

New items to improve clinical care and strengthen your practice.

ONLINE FIRST:
GET THE LATEST
PRODUCT NEWS AT
www.reviewofoptometry.com

▶ CONTACT LENSES

Alcon Adds Multifocal Option to Total30 Line

The modality of monthly contact lens replacement has gotten a boost in recent years from Alcon's Total30 line, which—in addition to single vision and toric options—now offers a lens for presbyopia. Like the others in the Total30 line, the multifocal lens features the company's "water gradient" design concept to aid in moisture retention. This allows the water content of the lens to gradually increase to nearly 100% at the lens surface to promote on-eye comfort from day one through 30, Alcon says. The Total30 multifocal lens is now available in the US and in select international markets.

▶ DIAGNOSTIC EQUIPMENT

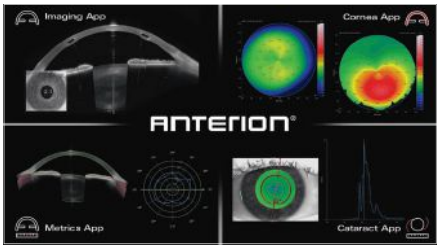
Three Apps Added to Heidelberg AS-OCT Platform

ODs who use a Heidelberg OCT can now upgrade to the newest version of the device's Anterion platform to beef up their anterior segment assessments. The system now has two additional modules ODs may find useful—the Cornea app and the Metrics app—as well as a third for cataract surgery planning.

The Cornea app combines OCT imaging, tomography maps and wavefront analysis to give clinicians a more complete picture of a patient's corneal geometry. It can also provide both curvature and elevation maps of the anterior and posterior corneal surfaces. Doctors can also toggle between display options (*i.e.*, single or multi-view) to allow for comparison of both eyes, as well as a follow-up layout with progression analysis. Pupil and corneal diameter measurements can also be completed.

The Metrics app organizes and illustrates data from OCT scans, with the anterior chamber displayed in a radial view, Heidelberg says. To customize assessment for individual patients, the module offers the option to determine predefined angle parameters and perform freehand measurements. Along with more common parameters (anterior chamber depth, ACA, AOD, TISA, ACA distance, spur-to-spur distance, central corneal thickness and white-to-white), Metrics can also provide data on anterior chamber volume, lens thickness and vault.

More suited for ophthalmology practices, the Cataract app can aid in surgical planning and intraocular lens selection by combining corneal measurements with monofocal and toric IOL calculators.



▶ PHARMACEUTICALS

FDA Approves Second Presbyopia Drop

And then there were two… drugs for presbyopia, that is. Soon to join Allergan's Vuity (pilocarpine 1.25%) on the market is another pilocarpine drop, this one at a lower concentration of 0.4%. Called Qlosi (pronounced "CLOH-see"), the drop is now FDA-approved for daily or BID dosing as needed for patients with presbyopia. Given Qlosi's lower concentration, clinicians will be curious to see whether it results in fewer adverse effects than Vuity. Another plus: The formula is preservative-free, Orasis says.

In the drug's two Phase III clinical trials (n=>600), the pupil-constricting drop showed efficacy 20 minutes after administration and—with the benefit of a second dose two to three hours after the first—can last up to eight hours, as measured on day 15. Both trials also met their primary and secondary endpoints on day eight, achieving a gain of at least three lines in distance-corrected near VA without losing one line or more in distance VA.

Headache (6.8%) and instillation site pain (5.8%) were among the most common treatment-related adverse events (AEs). Moderate AEs were reported by 1.3% of participants, and all other AEs were mild, the company reports. Optometrists and their patients can expect the drug to be commercially available in the first half of 2024, Orasis says.

New Drug Hastens Reversal of Mydriasis

For patients who complain about lingering visual disturbances after dilation, eye doctors will soon be able to instill a drop that cuts the recovery time down significantly, according to Viatris and Ocuphire Pharma, the drug's developers. Last month, the FDA approved Ryzumvi (phentolamine ophthalmic solution 0.75%) for the treatment of pharmacologically induced mydriasis produced by adrenergic agonists (*e.g.*, phenylephrine) or parasympatholytic (*e.g.*, tropicamide) agents, and said they expect it to be available in the first half of 2024.

In two Phase III pivotal trials, a total of 553 subjects aged 12 to 80 years with drug-induced mydriasis received two drops of Ryzumvi in the study eye (and one drop in the fellow eye) one hour following instillation of the dilating agent. The percentage of study eyes returning to ≤0.2mm from baseline pupil diameter was statistically significantly greater at all time points measured from 60 minutes through 24 hours vs. placebo (vehicle), a press release explains. Efficacy was similar for all age ranges.

For patients aged 12 years and older, doctors are instructed to instill one to two drops in each dilated eye after an ophthalmic exam or procedure. For children aged three to 11, the dose should be only one drop. The drug should not be used in patients currently experiencing iritis.

The most common ocular AEs reported in >5% of subjects were instillation site pain, stinging and burning (16%) and conjunctival hyperemia (12%). The only non-ocular AE reported in >5% of subjects was dysgeusia (6%).

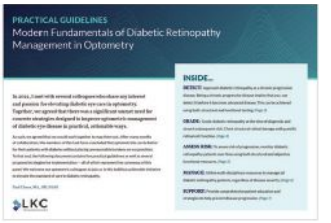
▶ DRY EYE

Bruder Launches Portable, Single-use Heat Mask

Developers of the popular Bruder moist heat mask recently added a product to their portfolio for patients who desire dry eye relief while on the go or when a microwave is unavailable. Called Eyedration, the mask contains a formula made of iron powder, activated carbon, water, inorganic salt and vermiculite; together, these ingredients generate moist heat once exposed to air, which Bruder says is warm enough to melt the meibum oil in eyelid glands and help maintain tear production. Once a mask is opened, the air-activated heat lasts up to 20 minutes, Bruder reports. The single-use masks can be ordered individually or as a 10-pack.

▶ CLINICAL EDUCATION

Report Aims to Simplify Optometric Approach to Diabetic Eye Disease



ODs who are interested in sharpening their ability to detect diabetic retinopathy (DR) early, track progress with greater precision and educate patients on their role in mitigating its effects may wish to download a new report commissioned by LKC Technologies, makers of the RetEval ERG device.

Called *Modern Fundamentals of Diabetic Retinopathy Management in Optometry,* the report presents a consensus statement from 14 optometric experts on the five pillars of care for DR patients: (1) detect, (2) grade, (3) assess, (4) manage and (5) support. The experts provide concise recommendations on the OD's role in each. The consensus statement also highlights the emerging role of ERG in detecting functional loss from DR that may precede structural damage and how to integrate this component into clinical protocols using RetEval.

The goal, says LKC in a press release, is to present a simplified framework for DR management that will allow ODs to confidently care for the growing population of individuals with diabetes. The report can be downloaded at the sponsor's website, www.lkc.com. LKC says the task force will provide further explanation and respond to FAQs in optometry's print publications and at CE venues in the coming months. ■

ADVERTISER INDEX

This index is published as a convenience and not as part of the advertising contract. Every care will be taken to index correctly. No allowance will be made for errors due to spelling, incorrect page number, or failure to insert.

BY ANDREW S. GURWOOD, OD

DIAGNOSTIC QUIZ

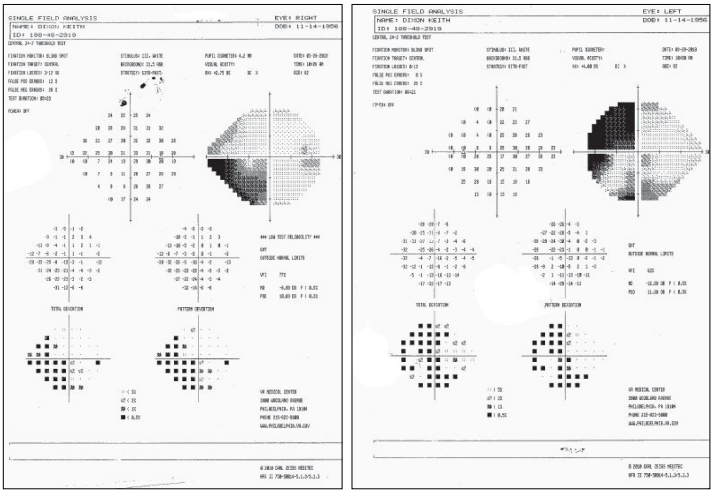
Seen and Unseen

A patient presents with good acuity but poor facial recognition. Recent MCA infarction makes you suspect which diagnosis?

A 62-year-old African-American male presented to the eye clinic for a glaucoma follow up. Additionally, the patient reported that distance and near vision seemed blurrier, even though at his last eye doctor visit he changed his spectacles. According to his wife, he had been acting confused, not recognizing people he knew well. His past medical history was remarkable for hypertension, vitamin D deficiency, traumatic brain injury, cerebrovascular accident (left middle cerebral artery infarction) and heart disease. He was considered a glaucoma suspect because of slightly increased cup disc ratios seen in both eyes.

Clinical Findings

The patient's best-corrected entering visual acuities were 20/20 OD and 20/20 OS at distance and near. His external examination was normal and there was no evidence of an afferent pupillary defect. Confrontation visual fields demonstrated restriction in the left inferior quadrant OD and restriction in the left superior quadrant OS. Biomicroscopy found unremarkable anterior segments, both eyes with Goldmann applanation pressures measuring 13mm Hg OU.



The patient's visual field results (OD at left, OS at right).

Additional studies included a glaucoma workup to rule out a conversion to the treatable form of the disease secondary to the slightly increased cup-disc ratios OU. This included optical coherence tomography OU and automated visual fields (see the printouts). The structural tests demonstrated normal nerve fiber layers, both eyes. Pachymetry was also completed, finding normal central corneal thickness (560µm).

Poor facial recognition was confirmed with photographs of family. Finally, a referral to neurology with the suggestion of neuroimaging to rule out new stroke was made.

Your Diagnosis

What would be your diagnosis in this case based on the findings presented? What's the likely prognosis? Which interventions, if any, would you recommend? To find out, read the online version of this article at www.reviewofoptometry.com. ■

Dr. Gurwood thanks Felicia Cicco for her contributions to this manuscript.

About Dr. Gurwood Dr. Gurwood is a professor of clinical sciences at The Eye Institute of the Pennsylvania College of Optometry at Salus University. He is a co-chief of Primary Care Suite 3. He is attending medical staff in the department of ophthalmology at Albert Einstein Medical Center, Philadelphia. He has no financial interests to disclose.

Retina Quiz Answers (from page 92)—Q1: d, Q2: b, Q3: c, Q4: a, Q5: c

REM LENS®

RAPID EYE MOLDING

Changing SIGHT Overnight.

Overnight Orthokeratology

1. NCLE certified consultation experts to guide you through the entire fitting process
2. Highly adjustable parameters with an online lens design calculator
3. Dynamic Edge Profile™ delivers remarkable comfort
4. Diameter & optic zone options for myopia management patients, along with standard Orthokeratology patients

Scan to learn more about REMLens®.

X-CEL SPECIALTY CONTACTS

800.241.9312
xcelspecialtycontacts.com/remlens

Vision Shaping Treatment VST®

MADE EXCLUSIVELY WITH BOSTON® EQUALENS® II LENS MATERIALS

More Moisture[4] for Your Contact Lens Patients

Biotrue® Hydration Plus Multi-Purpose Solution

More Moisture for Contact Lenses[4]

- **25% MORE hyaluronan (HA)**[1] means **MORE MOISTURE** to lenses in the first 12 hours of wear[2]

Ingredients Informed by TFOS DEWS II

- Essential electrolyte (potassium) found in natural tears
- Osmoprotectant/antioxidant[3] (erythritol) helps maintain ocular surface homeostasis under hyperosmotic stress[5]

Exceptional Cleaning and Disinfection

- Removes dirt and protein buildup for clear, clean lenses
- Kills 99.9% of germs tested[6]

Clinically Tested for Comfort

- Excellent patient ratings for overall comfort, cleanliness at removal and overall impressions

[1]Compared to Biotrue Multi-Purpose Solution.
[2]Based on a laboratory study.
[3]Antioxidant protects hyaluronan against free radicals.
[4]For 12 hours compared to Biotrue Multi-Purpose Solution, based on a laboratory study.
[5]Data on file. Bausch & Lomb Incorporated. Rochester, NY.
[6]Standardized Testing (ISO 14729) against *S. aureus, P. aeruginosa, S. marcescens, C. albicans, F. solani.*

Discover our extended line of Biotrue® products at

biotrue.com

BAUSCH+LOMB