REVIEW OF OPTOMETRY • VOL. 159, NO. 10 • OCTOBER 15, 2022 • Comanaging Systemic Disease • Hypertension and Stroke • Diabetes Complications • Ocular Effects of Sleep Disorders • COVID and the Eye • Thyroid Eye Disease

THERAPEUTIC REVIEW: How to Handle GCA, *p. 90* • SURGICAL MINUTE: When You See RCE, *p. 100*

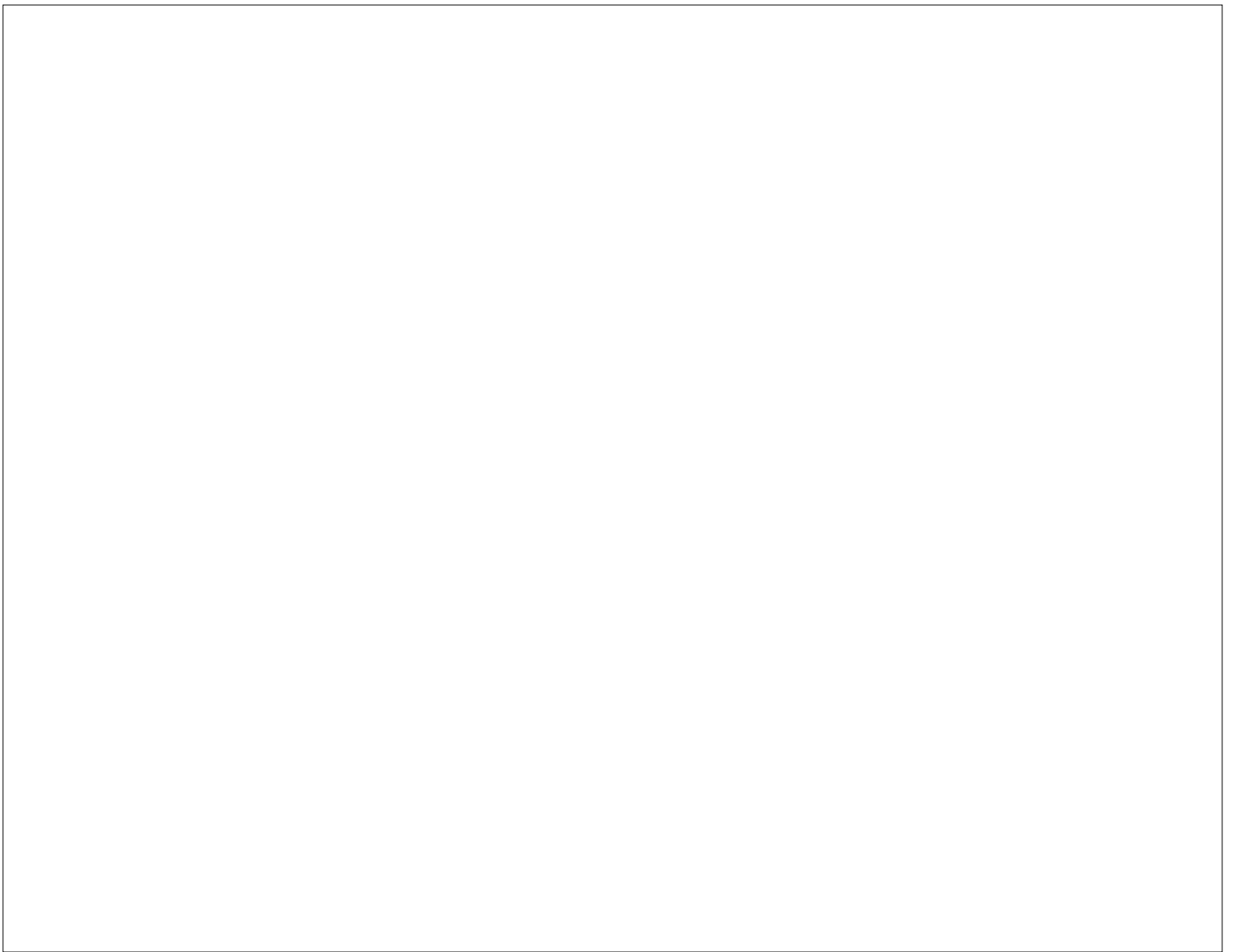
REVIEW of OPTOMETRY®

October 15, 2022 • reviewofoptometry.com

Leadership in clinical care

IN MEMORIAM
Remembering Art Epstein, OD
PAGE 5

SEEING SYSTEMIC DISEASE WITHIN THE EYE

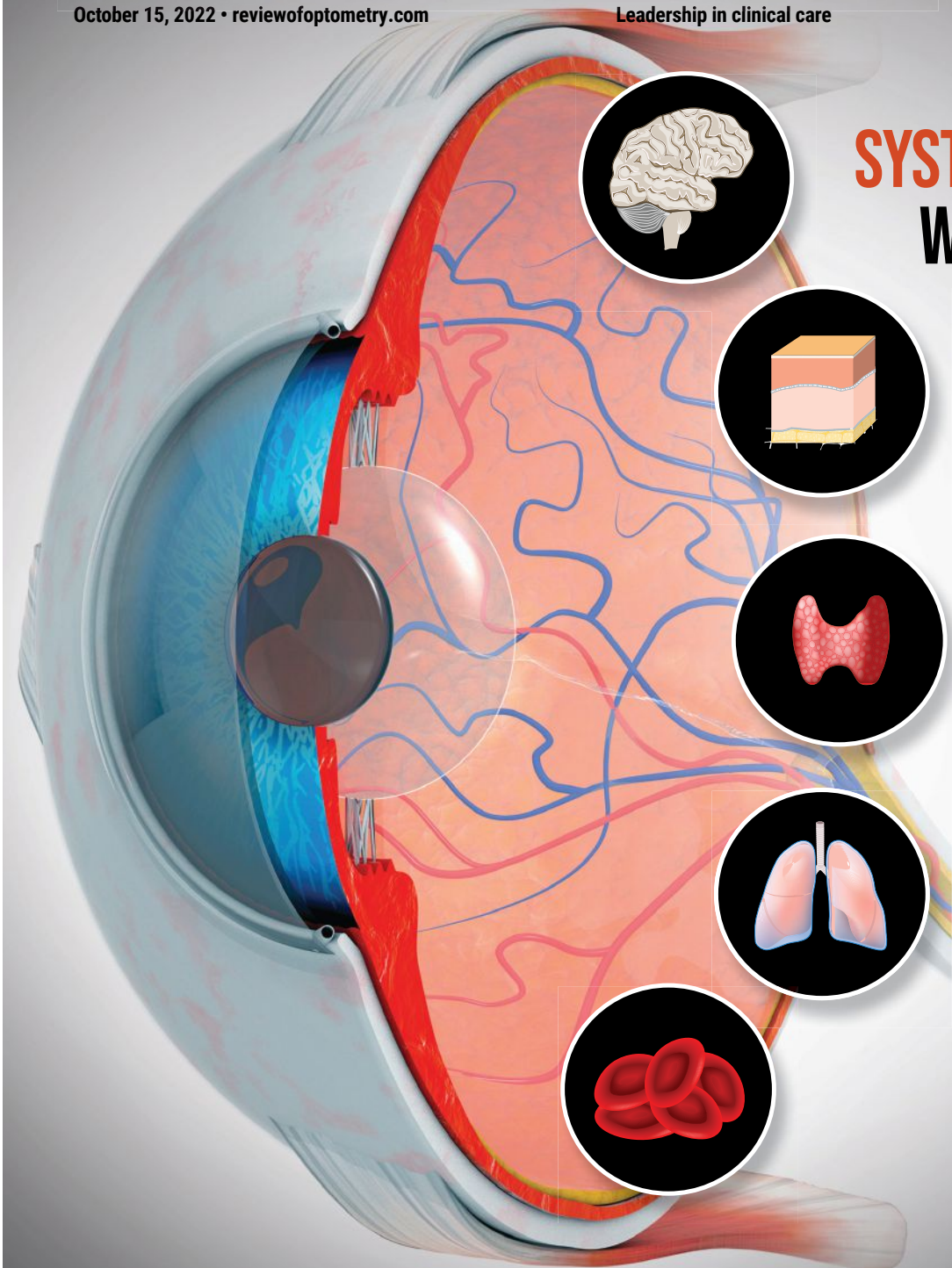


REVIEW® of OPTOMETRY

October 15, 2022 • reviewofoptometry.com

Leadership in clinical care

IN MEMORIAM
Remembering Art Epstein, OD
PAGE 5



SEEING SYSTEMIC DISEASE WITHIN THE EYE

What to look for, what to do.

REVIEW OF OPTOMETRY • VOL. 159, NO. 10 • OCTOBER 15, 2022 • Comanaging Systemic Disease • Hypertension and Stroke • Diabetes Complications • Ocular Effects of Sleep Disorders • COVID and the Eye • Thyroid Eye Disease

Vuity®
(pilocarpine HCl ophthalmic solution) 1.25%

AN EYE DROP FOR PRESBYOPIA?[1,2]

Go ahead. Read the fine print.

VUITY® MAY BE ABLE TO HELP.[1,2]

In studies, VUITY® improved the ability to read an additional 3 lines or more on a near vision eye chart.†

Improved near and intermediate vision without compromising distance vision†[1]

INDICATION
VUITY® (pilocarpine hydrochloride ophthalmic solution) 1.25% is indicated for the treatment of presbyopia in adults.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS
VUITY is contraindicated in patients with known hypersensitivity to any ingredient in the formulation.

WARNINGS AND PRECAUTIONS
Miotics, including VUITY, may cause accommodative spasm. Patients should be advised not to drive or operate machinery if vision is not clear (e.g., blurred vision). In addition, patients may experience temporary dim or dark vision with miotics, including VUITY. Patients should be advised to exercise caution in night driving and other hazardous activities in poor illumination.

Rare cases of retinal detachment and retinal tear have been reported with miotics, including VUITY. Individuals with pre-existing retinal disease are at increased risk. Therefore, examination of the retina is advised in all patients prior to the initiation of therapy. Patients should be advised to seek immediate medical care with sudden onset of flashing lights, floaters, or vision loss.

VUITY is not recommended to be used when iritis is present because adhesions (synechiae) may form between the iris and lens.

Contact lens wearers should be advised to remove their lenses prior to the instillation of VUITY and to wait 10 minutes after dosing before reinserting their contact lenses.

To prevent eye injury or contamination, care should be taken to avoid touching the dispensing bottle to the eye or to any other surface.

ADVERSE REACTIONS
The most common adverse reactions (>5%) reported in clinical trials were headache and conjunctival hyperemia.

Please see Brief Summary of full Prescribing Information on the accompanying page or reverse side.

† Primary endpoint was the proportion of participants gaining ≥3 lines in mesopic, high-contrast, binocular, distance-corrected near visual acuity (DCNVA) without losing more than 1 line (5 letters) of corrected distance visual acuity (CDVA) with the same refractive correction at Day 30, Hour 3.[1]

Change from baseline in photopic, high-contrast, binocular, DCIVA at Day 30, Hour 3 was a prespecified secondary endpoint.[3]

References:
1. VUITY Prescribing Information.
2. Price FW, et al. Ophthalmol Sci. 2021; doi: https://doi.org/10.106/j.xops.2021.100065.
3. Data on File, ABVRRTI73127.

VuityPro.com/efficacy

Allergan™
an AbbVie company

VUITY™ (pilocarpine hydrochloride ophthalmic solution) 1.25%, for topical ophthalmic use

PROFESSIONAL BRIEF SUMMARY
CONSULT PACKAGE INSERT FOR FULL PRESCRIBING INFORMATION

INDICATIONS AND USAGE

VUITY is indicated for the treatment of presbyopia in adults.

CONTRAINDICATIONS

VUITY is contraindicated in patients with known hypersensitivity to the active ingredient or to any of the excipients.

WARNINGS AND PRECAUTIONS

Blurred Vision

Miotics, including VUITY, may cause accommodative spasm. Patients should be advised not to drive or operate machinery if vision is not clear (e.g., blurred vision).

In addition, patients may experience temporary dim or dark vision with miotics, including VUITY. Patients should be advised to exercise caution in night driving and other hazardous activities in poor illumination.

Risk of Retinal Detachment

Rare cases of retinal detachment and retinal tear have been reported with miotics, including VUITY.

Individuals with pre-existing retinal disease are at increased risk. Therefore, examination of the retina is advised in all patients prior to the initiation of therapy.

Patients should be advised to seek immediate medical care with sudden onset of flashing lights, floaters, or vision loss.

Iritis

VUITY is not recommended to be used when iritis is present because adhesions (synechiae) may form between the iris and the lens.

Use with Contact Lenses

Contact lens wearers should be advised to remove their lenses prior to the instillation of VUITY and to wait 10 minutes after dosing before reinserting their contact lenses.

Potential for Eye Injury or Contamination

To prevent eye injury or contamination, care should be taken to avoid touching the dispensing bottle to the eye or to any other surface.

ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in labeling:

- Hypersensitivity *[see Contraindications]*

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.

VUITY was evaluated in 375 patients with presbyopia in two randomized, double-masked, vehicle-controlled studies (GEMINI 1 and GEMINI 2) of 30 days duration. The most common adverse reactions reported in >5% of patients were headache and conjunctival hyperemia. Ocular adverse reactions reported in 1-5% of patients were blurred vision, eye pain, visual impairment, eye irritation, and increased lacrimation.

Postmarketing Experience

The following adverse reactions have been identified during postapproval use of VUITY. 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 VUITY exposure.

Eye disorders: vitreous detachment, vitreomacular traction, retinal tear, retinal detachment.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no adequate and well-controlled studies of VUITY administration in pregnant women to inform a drug-associated risk. Oral administration of pilocarpine to pregnant rats throughout organogenesis and lactation did not produce adverse effects at clinically relevant doses.

Data

Human Data

No adequate and well-controlled trials of VUITY have been conducted in pregnant women. In a retrospective case series of 15 women with glaucoma, 4 patients used ophthalmic pilocarpine either pre-pregnancy, during pregnancy or postpartum. There were no adverse effects observed in patients or in their infants.

Animal Data

In embryofetal development studies, oral administration of pilocarpine to pregnant rats throughout organogenesis produced maternal toxicity, skeletal anomalies and reduction in fetal body weight at 90 mg/kg/day (approximately 970-fold higher than the maximum recommended human ophthalmic dose [MRHOD] of 0.015 mg/kg/day, on a mg/m^2 basis).

In a peri-/postnatal study in rats, oral administration of pilocarpine during late gestation through lactation increased stillbirths at a dose of 36 mg/kg/day (approximately 390-fold higher than the MRHOD). Decreased neonatal survival and reduced mean body weight of pups were observed at ≥18 mg/kg/day (approximately 200 times the recommended human daily dose of VUITY).

Lactation

Risk Summary

There is no information regarding the presence of pilocarpine in human milk, the effects on the breastfed infants, or the effects on milk production to inform risk of VUITY to an infant during lactation.

Pilocarpine and/or its metabolites are excreted in the milk of lactating rats. Systemic levels of pilocarpine following topical ocular administration are low, and it is not known whether measurable levels of pilocarpine 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 VUITY and any potential adverse effects on the breastfed child from VUITY.

Data

Animal Data

Following a single oral administration of ^{14}C-pilocarpine to lactating rats, the radioactivity concentrations in milk were similar to those in plasma.

Pediatric Use

Presbyopia does not occur in the pediatric population.

Geriatric Use

Clinical studies of VUITY did not include subjects aged 65 and over to determine whether they respond differently from younger subjects. Other reported clinical experience with ophthalmic pilocarpine solutions have not identified overall differences in safety between elderly and younger patients.

OVERDOSAGE

Systemic toxicity following topical ocular administration of pilocarpine is rare, but occasionally patients who are sensitive may develop sweating and gastrointestinal overactivity. Accidental ingestion can produce sweating, salivation, nausea, tremors and slowing of the pulse and a decrease in blood pressure. In moderate overdosage, spontaneous recovery is to be expected and is aided by intravenous fluids to compensate for dehydration. For patients demonstrating severe poisoning, atropine, the pharmacologic antagonist to pilocarpine, should be used.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis

Pilocarpine did not induce tumors in mice at any dosage level studied (up to 30 mg/kg/day; approximately 160-times the MRHOD). In rats, an oral dose of 18 mg/kg/day (approximately 200 times the MRHOD), resulted in a statistically significant increase in the incidence of benign pheochromocytomas in both male and female rats, and a statistically significant increase in the incidence of hepatocellular adenomas in female rats.

Mutagenesis

Pilocarpine did not show any potential to cause genetic toxicity in a series of studies that included: 1) bacterial assays (Salmonella and E. coli) for reverse gene mutations; 2) an in vitro chromosome aberration assay in a Chinese hamster ovary cell line; 3) an in vivo chromosome aberration assay (micronucleus test) in mice; and 4) a primary DNA damage assay (unscheduled DNA synthesis) in rat hepatocyte primary cultures.

Impairment of Fertility

Pilocarpine oral administration to male and female rats at a dosage of 18 mg/kg/day (200 times the recommended human daily dose) resulted in impaired reproductive function, including reduced fertility, decreased sperm motility, and morphologic evidence of abnormal sperm. It is unclear whether the reduction in fertility was due to effects on males, females, or both. In dogs, exposure to pilocarpine at a dosage of 3 mg/kg/day for 6 months resulted in evidence of impaired spermatogenesis (approximately 110 times the recommended human daily dose).

PATIENT COUNSELING INFORMATION

Night Driving

VUITY may cause temporary dim or dark vision. Advise patients to exercise caution with night driving and when hazardous activities are undertaken in poor illumination. *[see Warnings and Precautions]*

Accommodative Spasm

Temporary problems when changing focus between near and distant objects may occur. Advise patients not to drive or use machinery if vision is not clear (e.g., blurred vision). *[see Warnings and Precautions]*

When to Seek Physician Advice

Advise patients to seek immediate medical care with sudden onset of flashing lights, floaters, or vision loss. *[see Warnings and Precautions]*

Contact Lens Wear

Contact lens should be removed prior to the instillation of VUITY. Wait 10 minutes after dosing before reinserting contact lenses. *[see Warnings and Precautions]*

Avoiding Contamination of the Product

Do not touch dropper tip to any surface, as this may contaminate the contents. *[see Warnings and Precautions]*

Concomitant Topical Ocular Therapy

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

Distributed by: Allergan, an AbbVie Company
Manufactured for:
AbbVie Inc.
North Chicago, IL 60064 USA
Allergan is an affiliate of AbbVie Inc.

Ref: v2.0USPI7098 Revised: August 2022

LAB-7764 **MASTER**

US-VUI-220399

abbvie

California Governor Vetoes Optometric Laser Bill

Rationale relies on spurious claims of shortcomings in training, say OD supporters of expansion.

Advocates for greater patient access to eyecare services received some upsetting news in late September. After a long battle to get California's optometric scope expansion bill, AB 2236, to pass the state Senate, it was announced on Sept. 28 that Gov. Newsom has chosen to veto the bill. Had it been signed, the legislation would've granted the state's ODs authority to perform several advanced procedures including three types of laser surgery (SLT, capsulotomy, peripheral iridotomy), lesion removal, multiple types of injections and corneal crosslinking. The law also would have made California the 11th laser state and doubled the number of ODs in the country currently able to pursue such responsibilities.

In the governor's letter defending his decision to veto the bill, he offered the following rationale: "I am not convinced that the education and training required is sufficient to prepare optometrists to perform the surgical procedures identified." He wrote that AB 2236 would have allowed ODs to perform the same procedures with one year of training as ophthalmologists perform after three years of training.

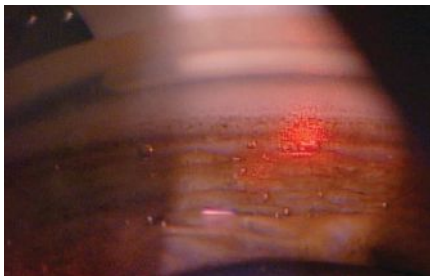


Photo: Nathan Lighthizer, OD

SLT is one of several procedures that the veto of AB 2236 prevents California ODs from offering to patients in need.

However, Paul Karpecki, OD, associate professor at Kentucky College of Optometry at the University of Pikeville, points out that this simply doesn't ring true for the specific procedures outlined in the bill.

"It appears the governor was misinformed," says Dr. Karpecki. "While ophthalmology residents do spend three years in ophthalmic and surgical training, they don't spend three years learning to perform non-invasive procedures like SLT. The bill was not attempting to have optometrists perform cataract surgery or other invasive intraocular surgeries" that comprise the bulk of residency and optional fellowship training. Dr. Karpecki adds, "I and many doctors of optometry in 10 states have provided these same procedures that California's House and Senate chose to approve, without harm and while greatly helping a significant unmet medical need."

OFFICE OF THE GOVERNOR

SEP 28 2022

To the Members of the California State Assembly:

I am returning Assembly Bill 2236 without my signature.

This bill would authorize optometrists to perform ocular surgical procedures currently performed by ophthalmologists after completing specified education and training.

I am not convinced that the education and training required is sufficient to prepare optometrists to perform the surgical procedures identified. This bill would allow optometrists to perform advanced surgical procedures with less than one year of training. In comparison, physicians who perform these procedures must complete at least a three year residency program.

For this reason, I cannot sign this bill.

Sincerely,

Gavin Newsom

Governor Newsom argues in his letter defending the veto that the bill would've allowed ODs to train for a third of the time as OMDs to perform the same procedures.

Nathan Lighthizer, OD, associate dean at NSU Oklahoma College of Optometry, also pushes back on Gov. Newsom's argument against the bill. "Optometrists have four to five years of rigorous classroom, laboratory and clinical training on these procedures—not 'less than one year of training' as was stated in the governor's veto announcement."

The California Optometric Association, which has worked alongside lawmakers for several years to push the laser bill forward, is also feeling the frustration of the loss.

"We are devastated by the veto," says Kristine Shultz, executive director of COA. "The public safety concerns are nonsense. AB 2236 contains the nation's strictest standards for education and certification when optometrists seek to perform these procedures," she points out. Like Dr. Karpecki, Ms. Shultz also notes that, "Other states have already expanded the list of procedures optometrists can perform without safety concerns materializing."

The purpose of AB 2236, sponsored by Assemblymember Evan Low, was to expand eyecare access and services for thousands of residents in the

(Continued on p. 6)

IN MEMORIAM

Optometry Remembers Charismatic Icon Art Epstein

The dry eye pioneer advanced the profession through education, advocacy and mentorship.

Arthur Epstein, OD, who died on Sept. 27, left an indelible mark on optometry, and the news of his unexpected passing has left many in the profession beside themselves. Dr. Epstein was a stalwart figure in the field who challenged colleagues and institutions to aim higher and always adapt to changing circumstances. His following and relationships within the profession and in industry had led him to become a sought-after speaker and lecturer on many hot topics and emerging trends in eye care. He was 71.

A child of the Bronx and Long Island in New York, Dr. Epstein received his optometry degree from the SUNY State College of Optometry, where he also served as the college's first resident in ocular disease. Jerome Sherman, OD, of SUNY recalls that Dr. Epstein was his first resident at the fledgling institution during its earliest years and was a commanding presence even then. "Art demonstrated perseverance very early on," says. Dr. Sherman. "During his residency, he somehow learned to perform procedures including BIO efficiently even with one arm in a cast because of an unfortunate injury!"

An expert in dry eye and ocular surface disease, Dr. Epstein participated in the seminal TFOS DEWS II report. After a move to Phoenix, AZ, he cofounded Phoenix Eye Care with his wife Shannon Steinhäuser, OD. There, he was director of clinical research at the practice's dry eye and ocular surface disease center.

He was a past chair of the Contact Lens & Cornea Section of the American Optometric Association and a founder of the Optometric Dry Eye Society. As chair, Dr. Epstein addressed the United States Congress on the subject of contact lens safety. In 2021, Dr. Epstein was ranked #1 in the US, according to *Newsweek's* America's Best Eye Doctors. He was commended for the quality and continuity of care he provided.

"It's very sad when a colleague dies, and even worse when the colleague was a former student and resident, and a friend for decades," says Dr. Sherman. "I am beyond sad: grief-stricken."

Dr. Epstein had been a longtime contributor to *Review of Optometry*, a member of its Editorial Advisory Board as well as founder and chief medical editor of the weekly e-newsletter *Optometric Physician*.

"He was one of the first optometrists I met when I started on the editorial staff back in 2007," notes *Review of Optometry* Publisher Michael Hoster. "He always took the time to call me and thoroughly explain ocular anatomy and pathology in an effort to make me a better editor and medical writer."

Dr. Epstein, a longtime advocate for the continued empowerment of optometrists, challenged his peers to aim higher and inspired countless doctors from several generations.

Many credit Dr. Epstein for his incisive commentary on the state of optometry. "Art never shied away from voicing his opinion about all matters of the optometric profession—no matter how potentially controversial," Mr. Hoster says. "He always emphasized what he thought was best for eyecare providers, their practices and their patients—without any fear of repercussion."

Mr. Hoster specified that that level of steadfast conviction, dedication and passion rarely is on display in public forums today and was a signature characteristic of Dr. Epstein's personal and professional complexion. "He's going to be missed tremendously."

"Art always pushed us to be better, at whatever we were doing, by questioning conventional wisdom and challenging the way things were," says Marc Ferrara, CEO of Information Services at Jobson Medical Information, the publisher of *Review of Optometry* and other eyecare titles. "He led the profession forward through his determined example and strong point of view."

Hearing Dr. Epstein's take on the events of the day was a fixture of the weekly routine for thousands of ODs and others in the profession, says Joseph Shovlin, OD, of Scranton, PA. "Every weekend, I looked forward to reading his weekly missive in *Optometric Physician*. Even when I didn't agree with what he had to say, I always knew his motives were in the best interest of our profession. In many respects, he was our conscience."

An Outspoken Mentor and Trailblazer

In person and online, optometrists and colleagues have been sharing memories and tributes to Dr. Epstein, an advocate for the continued empowerment and betterment of optometry.

(Continued on p. 6)

Scope Expansion Off the Table for Now in California

(Continued from p. 4)

Golden State. In a press release published by the COA following the loss, COA president Amanda K. Dexter, OD, wrote, "California optometrists sponsored AB 2263 to address a real and growing concern for our patients, particularly Medi-Cal enrollees, who face long waits for specialty care or go without needed health procedures."

She continued, "While we are deeply disappointed in this veto, we will keep pressing forward on a policy solution because the shortage of healthcare providers serving Californians with low incomes, rural communities and people of color will only grow worse without action."

Despite the frustration felt by advocates of optometric scope expansion, encouragement for the bill's future can be gained from its recent triumph in the Senate. "We thank Asm. Low for his leadership and Asm. Wood, a strong voice for patient access," Dr. Dexter wrote in the COA press release. "Thanks to these leaders, a strong, bipartisan majority of legislators of both parties agreed: highly trained optometrists can safely deliver advanced eye procedures our patients need, in their communities, from the providers they trust and who speak their language."

As scope expansion battles for optometrists continue in many states, ongoing effort must be put forward to educate and inform people and politicians on the safe and legitimate nature of these procedures, as well as on the ability of these laws to increase eye care access to underserved communities nationwide.

"I encourage the COA and its members to contact their legislators and continue to educate them on the importance of this bill," says Dr. Lighthizer.

Colleagues Mourn the Passing of Dr. Art Epstein

(Continued from p. 5)

"He was as passionate about optometry as anyone I've ever known and, more than anything else, he wanted to see our profession move forward," says Alan Kabat, OD, Medical Director at Oyster Point Pharma.

Dr. Kabat notes, "How appropriate that this memorial is being published in *Review of Optometry*. My relationship with Art began because of my involvement with *Review*, and my best and fondest memories of Art involve working together with and for *Review*," whether it was roundtable discussions on emerging drug therapies, continuing education meetings or social events like the publication's annual SECO dinner. "Art was a friend, a mentor, a foil and a confidant," he said.

Dr. Kabat, who held academic positions before transitioning to industry, also said of Dr. Epstein, "I can still hear him greeting me across a crowded room, "*Professor!*"—his pet name for me. I like to think that Art took pride not only in his own successes, but also those of his close friends," Dr. Kabat notes. "Rest in peace, my friend. You left an indelible mark on the hearts and minds of so many, and we will miss you terribly."

According to Christine Sindt, OD, a clinical professor at the University of Iowa, Dr. Epstein taught her the value of mentorship. "He provided me with countless opportunities—the opportunity to work harder, the opportunity to be of service to others, the opportunity to disagree until I actually understood my 'why,'" she says. "Art is in everything I do professionally, and I am so grateful."

"Art and I shared a friendship that started early in my career, and although he was sometimes considered fiery and provocative, Art always had the profession at heart," says noted educator and clinician Paul Karpecki, OD. "Those who knew him will remember him for his kindness, loyalty and caring personality. Although he has incredible professional accomplishments to his name, it's the person we'll miss the most."

Review of Optometry will continue to honor Dr. Epstein and his legacy of expertise and passion. A celebration of Dr. Epstein's life will be held at a later date to be announced.

IN BRIEF

Stroke Associated with Increased Prevalence of Ocular Disease. Significant **associations between visual impairment and major ocular disease with stroke were observed** in a recent cross-sectional study of 4,570 people.

With an odds ratio of 5.54, **ocular disease was associated with stroke, most notably cataract (30.8% prevalence among stroke patients vs. 13.4% without), AMD (19.6% vs 7.2%) and diabetic retinopathy (DR; 26.6% vs 11.6%).** An odds ratio of 9.61 was observed among stroke patients with DR. Additionally, odds ratios for mild to moderate and severe visual impairment were 6.79 and 9.46, respectively.

The authors noted that the associations were limited to mild visual impairment, mild to moderate and severe visual impairment and any ocular disease. The data also revealed **associations between DR and any ocular disease in diabetic participants**. The researchers identified a close relationship between stroke and mild to moderate and severe visual impairment among individuals with hypertension.

"Despite impaired central vision, which is the most common visual impairment in stroke patients, eye movement disorders, visual field loss and visual perceptual disorders are also usually found among stroke patients, and most patients have a combination of several visual problems," the authors wrote in their paper for the journal *Eye*.

"[This study] shows that stroke is associated with increased prevalence of ocular diseases," they conclude."These findings highlight the importance of ocular screening among stroke patients."

Li HY, Yang Q, Dong L, et al. Visual impairment and major eye diseases in stroke: a national cross-sectional study. Eye. September 21, 2022.

More Moisture[4] for Your Contact Lens Patients

Biotrue® Hydration Plus Multi-Purpose Solution

More Moisture for Contact Lenses[4]

- **25% MORE hyaluronan (HA)** means **MORE MOISTURE** to lenses in the first 12 hours of wear[1,2]

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

Study Finds 10 Factors Tied to Abnormal Pupil Size

Most involve age, medication use, refractive status and systemic health.

A new study on pupil size distribution reported on several associated conditions, including diabetes, that authors recommended ODs consider when examining patients.

"Sufficient pupil width is essential in ophthalmologic diagnostics to assess the periphery of the retina and to achieve adequate imaging quality in screening examinations, such as diabetic retinopathy screening," the researchers wrote in their paper. They studied 18,335 eyes of 9,559 participants aged 40 to 80 who had valid pupil size measurements.

They reported that the median pupil diameter was 4.19mm in patients' right eyes and 4.12mm in left eyes. They also found that a smaller pupil was associated with older age, hyperopic refractive error, previous cataract surgery, diabetes, obesity and ACE inhibitor use, whereas wider pupils were associated with female sex, arterial hypertension, tricyclic antidepressant use and SNRI and tetracyclic antidepressant use. Smoking and socioeconomic status weren't associated with pupil size.

Most prior studies found no gender difference in pupil size, the authors noted, but this one showed (small) differences in male and female pupil size. "The results are at odds with previous publications and need to be clarified by future studies," they wrote. One new finding the authors touted is the association with ACE inhibitors in their work, which was previously unknown.

They concluded that the associated risk factors with smaller pupils—older age, hyperopia, ACE inhibitor use and diabetes—"should be considered when developing and assessing the feasibility of screening using nonmydriatic fundus photography, as a sufficiently large pupil is required to achieve adequate image quality, especially when aiming to use AI algorithms for screening."

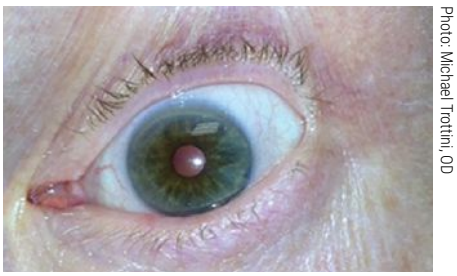


Photo: Michael Trottini, OD

Two factors not found to affect pupil size were smoking and socioeconomic status.

Kiel M, Grabitz SD, Hopf S, et al. Distribution of pupil size and associated factors: results from the population-based Gutenberg Health Study. Hindawi J Ophthalmol. September 9, 2022. [Epub ahead of print].

Microperimetry Looks Promising for Predicting AMD Progression

A recent study suggests that microperimetry—and mean retinal sensitivity value specifically—could help predict the two-year risk of progression to stage-four AMD.

This multi-center, prospective, non-comparative, open-label study included patients with one eye at stage four of the AREDS classification and the other eye at stage three (study eye). The researchers performed microperimetry at baseline and every six months during the two-year follow-up. At the end of this period, each eye was classified as either "progressive" (AREDS stage four) or "nonprogressive" (stage three).

The study analyzed 147 patients. Of these, 30.6% progressed from AREDS stage three to four. Data showed that the microperimetry criterion mean retinal sensitivity was significantly different at baseline between nonprogressive and progressive eyes. Lower values were observed for progressive eyes.

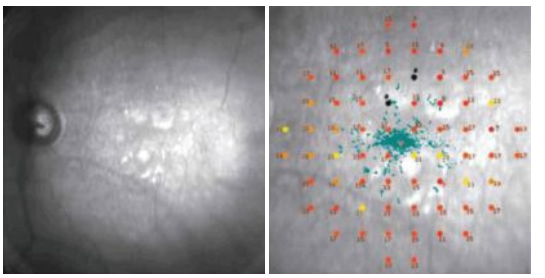


Photo: Topcon

The imaging biomarkers detected by the study group may help with earlier recognition of GA or nAMD development.

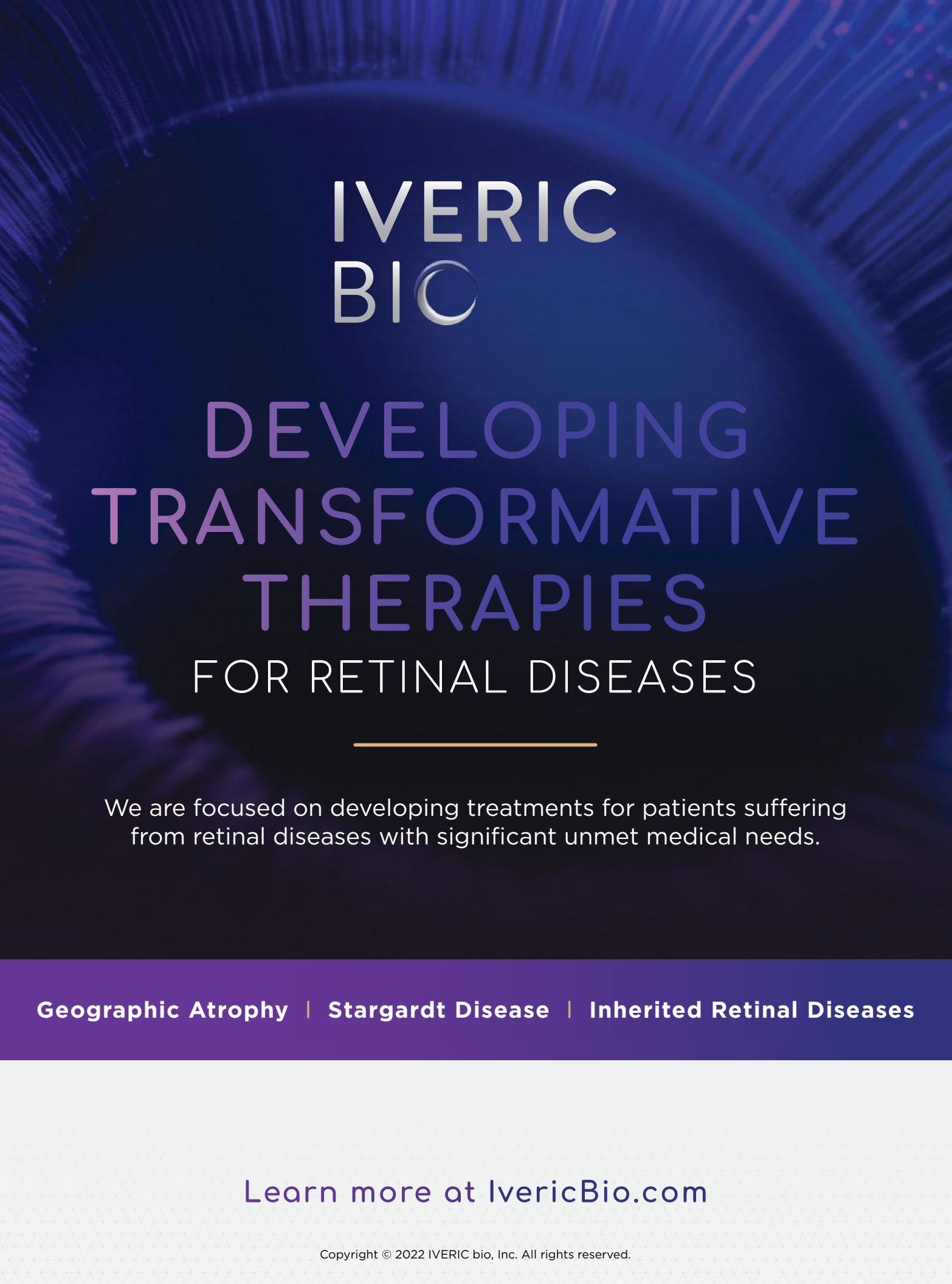
With a threshold for mean retinal sensitivity set at 24.7dB, diagnostic sensitivity was 80%. Specificity was 30.4%, positive predictive value was 33.6% and negative predictive value was 77.5%.

Mean retinal sensitivity was the only predictive parameter statistically associated with progression, according to the multivariate analysis which included microperimetry parameters and other routine ophthalmologic factors.

"Given the lack of biomarkers for predicting disease progression in AMD, this result seems promising and could be used in routine practice in contralateral eyes of the AREDS stage four eye to evaluate the risk of progression when mean retinal sensitivity is below 24.7dB," the study authors concluded in their paper. "Recognition of precursor lesions, or biomarkers of AMD progression to geographic atrophy or neovascular AMD, will be of great interest for developing future therapeutic approaches in intermediate AMD (*i.e.*, AREDS stage three). Identifying these biomarkers may help in selecting patients for clinical trials and defining better endpoints."

The authors acknowledged further studies will be needed to confirm the promising role of microperimetry.

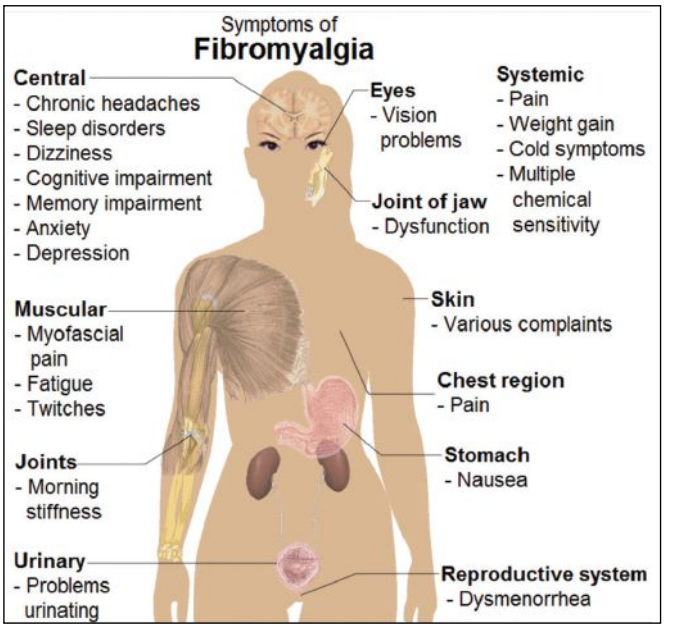
Kodjikian L, Creuzot-Garcher C, Korobelnik JF, et al. Microperimetry to predict disease progression in eyes at high risk of age-related macular degeneration disease: the PREVISION study. Acta Ophthalmol. September 19, 2022. [Epub ahead of print].



Fibromyalgia Signs Visible in Retina, Study Says

The pathophysiology of fibromyalgia isn't fully understood, but digital imaging of the neuroretina may shed some light on the condition. Researchers recently found OCT-observable retinal changes in fibromyalgia patients; in a separate study, the same group then calculated two different linear discriminant functions (LDFs)—a way to measure variance—to improve the specificity of OCT retinal parameters in fibromyalgia diagnosis.

Photo: Wikimedia Commons



OCT was able to effectively differentiate between healthy patients and those with fibromyalgia.

The study included 50 patients with fibromyalgia and 232 sex- and age-matched healthy controls. All participants underwent retinal evaluation using swept-source OCT angiography (Triton Plus) and spectral-domain OCT (Spectralis). All scans were done by the same operator who was blind to patient psychiatric and ophthalmologic evaluations.

They reported that the Spectralis was able to differentiate between controls and fibromyalgia patients. The researchers observed no significant differences in the macular vascular plexus between fibromyalgia patients and controls, but they did note that the vascular density in the superior sector showed strong inverse correlation with the duration of disease.

With Triton OCT, fibromyalgia patients demonstrated significant peripapillary RNFL thinning in the temporal sector. With Spectralis OCT, patients demonstrated significantly decreased peripapillary RNFL in the superonasal, nasal, inferonasal, temporal and inferotemporal sectors. The researchers noted in their paper that the LDF calculated for the Spectralis showed an area under the curve (a measure of predictive accuracy) of 0.968.

They concluded that fibromyalgia patients present with observable RNFL thinning on swept-source and spectral-domain OCT, but they also demonstrate a macular vascular density similar to that of healthy controls. The researchers wrote in their paper that this suggests "retinal structural changes aren't due to retinal hypoperfusion" and that the observation also supports the hypothesis that neurodegeneration is present in fibromyalgia.

The research group also noted that based on Spectralis' area under the curve, "The LDF that combines several RNFL parameters obtained with Spectralis OCT gives this device a powerful ability to differentiate between healthy individuals and individuals with fibromyalgia."

Garcia-Martin E, Tello A, Vilades E, et al. Diagnostic ability and capacity of optical coherence tomography-angiography to detect retinal and vascular changes in patients with fibromyalgia. J Ophthalmol. 2022;3946017:1-8.

IN BRIEF

New Data Strengthens the Case for SLT as First-line Therapy. An extension of the LiGHT trial in the UK further documents how **selective laser trabeculoplasty (SLT) can result in better outcomes than commonly used IOP-lowering eye drops.** This prospective study compared open-angle glaucoma and ocular hypertension patients after six years of treatment with either of the two methods.

The initial three-year trial included 692 patients, of which 524 completed another three years. **The SLT arm of the extension study had 69.8% of eyes remain at the target IOP** or even below the target without any need for further medical or surgical intervention. **The SLT group also saw a lower rate of disease progression at 19.6%, compared to the drops group at 26.8%.**

The drops group additionally needed more trabeculectomies and cataract surgeries than patients who underwent trabeculoplasty. For those who did need trabeculectomy in the SLT group, none were needed after the first three years and the rate was almost three times lower than the drops group after the entire six-year period. Cataract surgery was needed in at least 50% more eyes in the drops group over six years than the SLT group. This particular finding reflects evidence found by the Early Manifest Glaucoma Trial indicating eyes treated with IOP lowering drops display a greater need for surgical cataract removal.

After three years, 78% of eyes in the SLT arm did not need topical therapy. The almost 70% that did not need topical therapy after six years indicates that the drop-off in efficacy is not too large; from this, the researchers conclude that **SLT is an important part of long-term management of glaucoma and hypertension.**

While those in the SLT group were permitted a third round of the procedure after the three-year mark, **90% of subjects only needed one or two total treatments. Even further, over half (55.5%) needed only a single treatment in six years.**

Gazzard G, Konstantakopoulou E, Garway-Heath D, et al. LiGHT trial: 6-year results of primary selective laser trabeculoplasty versus eye drops for the treatment of glaucoma and ocular hypertension. Ophthalmology. 2022. [Epub ahead of print].

NANODROPPER

First we made smaller drops.

Then we revolutionized the standard of care.

Hundreds of clinics nationwide have improved their standard of care. Are you ready to better serve your patients?

Use discount code ROM10 for 10% off your first order!

The Nanodropper is the only FDA-listed, volume-reducing adaptor for eyedrop bottles designed to deliver precisely the amount of fluid the eye can absorb. Smaller drops have been shown to reduce the waste and cost of in-clinic and Rx formulations while minimizing local and systemic side effects.

nanodropper.com/ReviewOpt | pro@nanodropper.com | (507) 405-5676

Insurance Policies Discriminate Against Optometrists

Results of a recent AOA survey found that 60% of ODs were denied from a health plan and 30% from a vision plan, often for reasons that don't apply to their ophthalmology counterparts.

Optometrists have long fought to be seen and treated with the same respect as other medical doctors, especially ophthalmologists. Unfortunately, a recent survey by the American Optometric Association (AOA) Health Policy Institute revealed that discrimination still exists against doctors of optometry, specifically from insurance companies. Sixty percent of OD respondents reported that they have faced denied participation in a health plan's network.

The AOA distributed the survey to optometrists across the country and received 485 qualified responses from doctors in 47 states and the District of Columbia as well as from 42 state affiliate executive directors. Nearly two-thirds (64%) of respondents reported that health plans required them to credential with a vision plan, a policy that doesn't translate to ophthalmologists.

The results also suggested locational differences in insurance discrimination. For ODs practicing in metropolitan regions, the AOA wrote in their paper on the survey results that "84% reported denial to a medical plan's panel, while only 48% of doctors not practicing in a metropolitan statistical area reported a denial to a medical plan panel."[1] The paper also noted that "29 responding affiliates were aware of doctors in their state being denied participation in a health plan network."

While the rate of vision plan denial among optometrists certainly represents discrimination, it was only half that of health plan denial. "Thirty percent of respondents reported being denied participation in a vision plan network, while twice as many respondents reported being denied participation in a medical or health plan," the survey authors wrote.

There were several reasons for vision plan participation denial, including the plan's provider network was full (55%), the plan did not contract with private practice doctors (25%), proximity to other plan providers (18%) and the plan required an in-house optical (18%). For health plan denial, the survey authors wrote, "In contrast to their experience with vision plan denials, doctors of optometry found that only 40% of denials to medical plans was based upon the network of providers being full. Alarmingly, one-third reported that the denial was based upon the health plan's policy not to incorporate doctors of optometry into the medical provider panel."

Additionally, an online article by the AOA on the findings also stated, "A third of doctors of optometry reported being paid differently than ophthalmologists for the same procedure by the health plan, a differential accounted for by quality or performance measures only 7% of the time."[2]

It's clear from these survey results that discriminatory policies exist against optometrists throughout the country. What can be done to initiate change?

"Educating the plans and the patients on optometry's scope of practice can often help," Steven Eiss, OD, chair of the AOA Third Party Center, says in the article. "Many times, it can just be related to ignorance of what optometry can do. Also, the AOA, through the Third Party Center, has dedicated a lot of resources to battle this discrimination. Any time we are informed of a plan that is denying optometry, we make every effort to reach out to those plans to educate them on the value of having optometry as part of their provider panel."

These discriminatory policies not only affect optometrists but also their patients. They place a barrier between patients receiving accessible and affordable care from their trusted eyecare provider. In order for these laws to change, ODs and their advocates must continue to grow in these efforts to educate and earn the respect of patients, insurers and lawmakers.

Photo: Getty Images

Several discriminatory policies have prevented nearly two in three ODs from joining insurance plans.

1. Survey confirms insurance discrimination remains widespread. American Optometric Association Health Policy Institute. Published September 12, 2022. www.aoa.org/aoa/documents/advocacy/hpi/hpi_survey_confirms_insurance_discrimination_remains_widespread.pdf. Accessed on September 15, 2022.

2. AOA survey finds discrimination by health and vision plans. American Optometric Association. Published September 15, 2022. www.aoa.org/news/advocacy/third-party/aoa-survey-finds-discrimination-by-health-and-vision-plans?sso=y. Accessed on September 15, 2022.

LOMBART

YOUR OPHTHALMIC PARTNER

YOUR ONE-STOP EQUIPMENT SOLUTION

- NEW & PRE-OWNED EQUIPMENT
- SUPPLIES & ACCESSORIES
- EQUIPMENT REPAIRS & MAINTENANCE
- COMPREHENSIVE PROTECTION PLANS
- HASSLE-FREE FINANCING

VIRTUAL FIELD

TOPCON
MAESTRO2
OCT & FUNDUS
CAMERA

CORE LANE
PACKAGE

ATTENDING ACADEMY 2022 SAN DIEGO?
VISIT US AT BOOTH 404

800-LOMBART | LOMBARTINSTRUMENT.COM

LOMBART IS A DIVISION OF ADVANCING EYECARE™

HAAG-STREIT • HEINE • KEELER • MARCO • REICHERT • RELIANCE • S4OPTIK • TOPCON • WELCH-ALLYN • & MORE

Refractive Error, Strabismus Top Headache Causes in Kids

These, along with more serious ocular conditions, are likely the culprit in about a quarter of cases.

While ocular issues potentially resulting in headaches is well known, this problem is less documented in kids. New research aimed to clarify how prevalent this may be for children who complain of headaches.

The retrospective study included 1,878 children who underwent sensorimotor, anterior segment and dilated funduscopic examinations (either with or without cycloplegic refraction). The researchers found that nearly a quarter of the children had at least one new ocular finding upon examination, suggesting that headaches or an intracranial disease may be caused by an ophthalmologic source. Ocular findings included refractive issues, strabismus, optic nerve elevation, uveitis and glaucoma.

The most common condition presented was refractive issues, present in 18.2% of the children. This is consistent with prior literature that indicates associations do exist between refractive errors and headaches. Among the kids who had a full cycloplegic refraction, 6.9% presented a significant change in spherical equivalent refractive error. Additionally, 12.9% displayed an astigmatic change greater than 1D, while 8.0% displayed an anisometropic change greater than 1D.

The researchers point out that recent refraction in children may then need to be evaluated, considering refractive issues as a potential cause if they complain of new onset headaches. With a relatively high percentage of refractive errors observed, the researchers pose that the children likely are suffering from asthenopia, characterized by chronic headache and eye fatigue; the condition is either caused by uncorrected refractive errors or convergence impairment. It is important to consider that children may also describe asthenopia more akin to headache if they do not know how to describe eye strain. Subsequently, practitioners should think in broad terms what a child may mean when they describe their symptoms, in this case, head pain.

Photo: Brenda Montecalvo, OD

An ocular condition, most likely either strabismus or refractive error, is the cause of headaches in a quarter of children who experience them.

Researchers did report finding more serious ocular disorders, although their incidence was much lower. Included in this category are uveitis, glaucoma and extra ocular inflammatory conditions like episcleritis, orbital inflammatory syndrome and orbital cellulitis. All these are documented causes of ocular pain and headaches and are even listed for periorbital headaches as part of the differential diagnosis.

Despite the low prevalence of these conditions amongst children, an ophthalmologic exam plays a crucial role in intervention and treatment of the diseases, especially for some that may threaten the patient's vision.

Based on the research, the authors conclude that "a full ophthalmologic examination, including cycloplegic refraction, is indicated in the diagnostic workup of children with headache." They reiterate the importance of testing because "while complaints of nausea/vomiting, visual changes or morning headache should raise concern, generally the presence or absence of coincident visual, ocular or systemic symptoms are not reliable predictors of the likelihood of ocular pathology in a child with headache, and the absence of such symptoms does not obviate the need for an ophthalmologist examination."

Lin LY, Pan W, Ying GS, Binenbaum G. Ocular findings in children with headache. Ophthalmol Epidemiology. September 20, 2022. [Epub ahead of print].

IN BRIEF

■ ***MMP Concentrations May Affect Corneal Erosion Healing.*** Researchers believe **certain matrix metalloproteinases (MMPs) may be to blame for defective corneal re-epithelization in patients with recurrent corneal erosions.** MMPs degrade the junctional complexes that epithelial cells rely on in order to adhere to the basement membrane. In the study, **MMP-2 and MMP-3 were found to dissolve the basement membrane and accumulate in the epithelium, possibly inducing erosion recurrence.**

Patients were divided into two groups: a control group of 65 healthy patients with stable epithelial-stromal interface who qualified for epi-Bowman keratectomy (EBK) and a study group of phototherapeutic keratectomy (PTK) patients with recurrent corneal erosions and either Cogan's microcystic dystrophy (n=22) or posttraumatic corneal erosions (n=34).

The researchers analyzed the corneal epithelium collected during PTK and EBK procedures and determined the samples' MMP concentrations using an immunohistochemical assay. **They found statistically significantly higher concentrations of MMP-2 and MMP-3 in the study group compared with the control group.** The differences in concentrations of MMP-2 and MMP-3 in the recurrent corneal erosion subgroups weren't statistically significant.

"Knowledge of MMP concentrations in the corneal epithelium of recurrent corneal erosion patients might substantially contribute to the optimization of treatment strategies," the researchers wrote in their paper.

Jadczyk-Sorek K, Garczorz W, Bubała-Stachowicz B, et al. Increased matrix metalloproteinase-2 and matrix metalloproteinase-3 concentrations in corneal epithelium of patients with recurrent corneal erosions. Hindawi J Ophthalmol. September 25, 2022. [Epub ahead of print].

Smoking Associated With Increased Risk of Eyelid Cancer

Findings also identified basal cell carcinoma as the most common eyelid malignancy in the US.

Recent research estimating the prevalence of eyelid cancers in the American Academy of Ophthalmology IRIS Registry and examining associated factors revealed a previously unreported association between active smoking and eyelid cancer as well as specific subtypes, including basal cell carcinoma (BCC), squamous cell carcinoma (SCC) and malignant melanoma (MM).

The retrospective study enrolled IRIS patients with ICD-9/10 codes for eyelid cancers. These included BCC, SCC, MM, sebaceous carcinoma/other specified malignant neoplasm (SBC), melanoma *in-situ* (MIS) and unspecified malignant neoplasm (UMN).

The researchers estimated overall prevalence for each cancer type as well as age group, sex, race, ethnicity and smoking status. They then examined associations between or each type and possible risk factors.

In this analysis, 82,136 patients with eyelid cancer were identified. Data showed that the prevalence of any eyelid cancer was 145.1 per 100,000. The following cancer-specific prevalences per 100,000 people were reported: 87.9 (BCC), 25.6 (UMN), 11.1 (SCC), 5.0 (SBC), 4.1 (MM) and 0.4 (MIS).

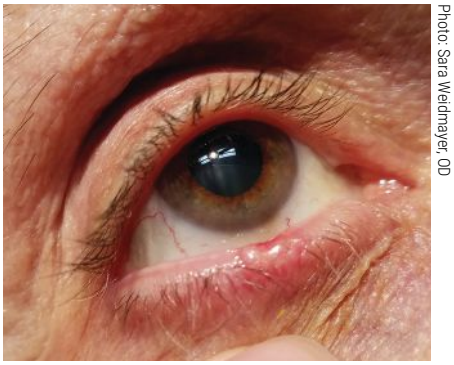


Photo: Sara Weidmayer, OD

BCC of the lower lid margin. Note the ulceration of the superior aspect, pearly elevated margins and madarosis.

The study authors observed that the prevalence increased with older age for any eyelid cancer as well as for each cancer type. They also found a higher prevalence among males for any eyelid cancer and BCC, SCC, MM and MIS. Compared with other races, prevalence was highest in whites for BCC, SCC, MM, SBC and any eyelid cancer.

A regression model revealed that any eyelid cancer was associated with older age groups, male sex and white race. Additionally, active smoking was correlated with any eyelid cancer, BCC, SCC and MM.

"Our findings support that BCC is the most common eyelid cancer in the United States, representing 61% of all eyelid cancers. This study also showed that eyelid cancers were associated with older age group, particularly those >60 years of age, male sex and white race," the team concluded in their recent *Ophthalmology Science* paper. "Healthcare providers should maintain a high index of suspicion for possible eyelid cancer when examining high-risk patients, such as older white non-Hispanic men who are active smokers." The researchers say they feel the data could aid in earlier detection and planning of healthcare policies for eyelid cancer prevention.

Baş Z, Sharpe J, Yaghy A, et al. Eyelid cancer prevalence and associated factors in the American Academy of Ophthalmology IRIS Registry. Ophthalmol Science. September 27, 2022. [Epub ahead of print].

Ortho-K Improves Chorioretinal Blood Flow in Myopia, Study Finds

It's known that high myopes have relatively thinner choroids, so it stands to reason that efforts to curtail myopia development might impact the choroidal vasculature in a positive way. A recent study documented just this phenomenon. Upon observing potential alterations in fundus microcirculation and retinal thickness in adolescent myopic orthokeratology (ortho-K) wearers, researchers recently found that these lenses improved retinal blood flow while controlling myopia.

A total of 48 patients were enrolled and divided into two groups based on the presence or absence of astigmatism: toric ortho-K and spherical ortho-K. OCT-A was used to measure the superficial and deep retinal vessel densities at the macular region, radial peripapillary capillary (RPC) density, foveal avascular zone (FAZ) area and choriocapillaris (ChC) perfusion area before and after ortho-K for three months.

After three months of toric ortho-K wear, superficial vessel density in the fovea and parafovea had significantly increased, and deep vessel density in the whole area and fovea were significantly elevated. In the spherical group, superficial vessel density was significantly higher in the parafovea, and the deep vessel density in the whole area and parafovea was significantly higher.

RPC density in the two groups increased after three months of ortho-K in the whole area and inside the disc area. Three months after toric ortho-K wear was initiated, the FAZ area was significantly reduced by 0.05mm^2, while the ChC perfusion area was enlarged by 0.06mm^2. The FAZ area in the spherical group significantly decreased by 0.01mm^2, whereas the ChC perfusion area increased by 0.06mm^2. Retinal thickness in both groups increased after three months of ortho-K in the whole area and parafoveal area.

While ortho-K didn't improve astigmatism in myopia patients, the researchers concluded that it affects retinal blood flow and warrants further study to clarify the association.

Wang XQ, Chen M, Zeng LZ, Liu LQ. Investigation of retinal microvasculature and choriocapillaris in adolescent myopic patients with astigmatism undergoing orthokeratology. BMC Ophthalmol. September 23, 2022. [Epub ahead of print].

Smart System® | VR Headset

Developed by the industry leader in vision testing for over 30 years

AAO 2022
San Diego
Booth #820

The Only VR Headset with Time-Tested Software

M&S takes vision testing to new heights. The programmable VR Headset with Surface Pro 7 Tablet is powered by our trusted M&S Smart System® software for fast and accurate vision testing. Our years of experience and service continue to help your clinic shine.

Reliable Results
Trust data accuracy with *Active Eye Tracking* technology that continuously monitors patient fixation and pauses the test when fixation is lost

Speed and Efficiency
Our proven testing protocols reduce patient fatigue by providing *Quick*Screen results in 45 seconds and full threshold test results in under 3 minutes per eye

Patient and Practice Friendly
Comfortable design with easy set up, audio and visual cues to your technician and patient, the ability to test without a wifi connection and results that can be immediately exported to your EMR

Schedule a demo at: MSTech-Eyes.com/vr-headset

M&S TECHNOLOGIES®

The First Choice in Vision Testing Systems

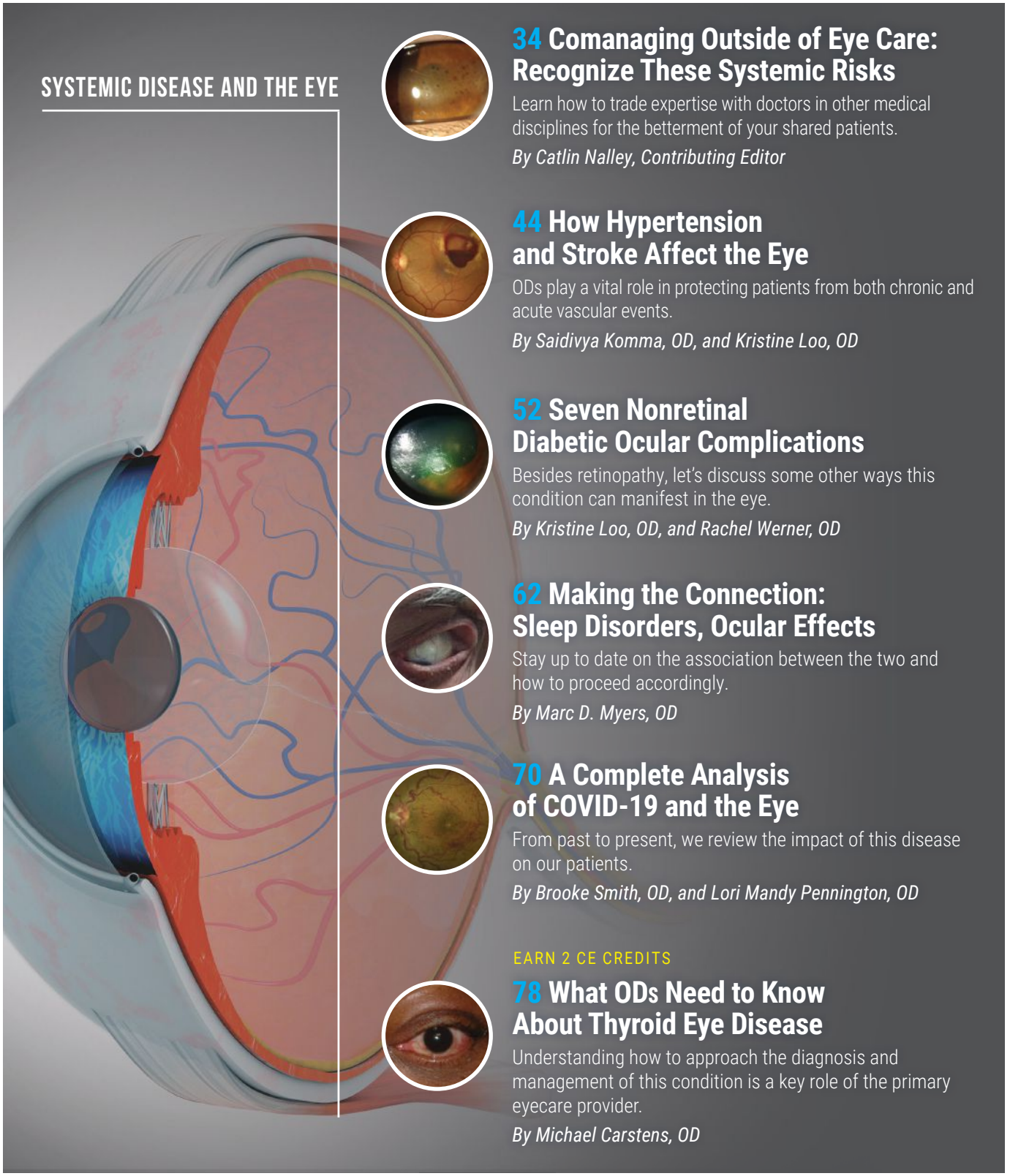
A HILCO VISION COMPANY

847-763-0500
mstech-eyes.com

FEATURES

REVIEW OF OPTOMETRY • Vol. 159, No. 10 • OCTOBER 15, 2022

SYSTEMIC DISEASE AND THE EYE



xiidra® (lifitegrast ophthalmic solution) 5%

When Selecting an Rx Treatment for Dry Eye Disease

DON'T MAKE HER WAIT. CHOOSE XIIDRA.

Because lasting symptom relief can start as early as 2 weeks[1*†]

*Xiidra reduced symptoms of eye dryness at 2 weeks (based on Eye Dryness Score [EDS] compared to vehicle) in 2 out of 4 studies, with improvements observed at 6 and 12 weeks in all 4 studies.[1]

Access to Xiidra is better than ever.[2]
Scan to see coverage in your area.

Indication

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of signs and symptoms of dry eye disease (DED).

Important Safety Information

- Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients.
- In clinical trials, the most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.
- To avoid the potential for eye injury or contamination of the solution, patients should not touch the tip of the single-use container to their eye or to any surface.

NOVARTIS

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080


Not an actual patient.

Important Safety Information (cont)

- Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.
- Safety and efficacy in pediatric patients below the age of 17 years have not been established.

For additional safety information about XIIDRA®, please refer to the brief summary of Prescribing Information on adjacent page.

†Pivotal trial data

The safety and efficacy of Xiidra were assessed in four 12-week, randomized, multicenter, double-masked, vehicle-controlled studies (N=2133). Patients were dosed twice daily. **Use of artificial tears was not allowed during the studies.** The study end points included assessment of signs (based on Inferior fluorescein Corneal Staining Score [ICSS] on a scale of 0-4) and symptoms (based on patient-reported EDS on a visual analogue scale of 0-100).[1]

Effects on symptoms of dry eye disease: A larger reduction in EDS favoring Xiidra was observed in all studies at day 42 and day 84. Xiidra reduced symptoms of eye dryness at 2 weeks (based on EDS) compared to vehicle in 2 out of 4 clinical trials.[1]

Effects on signs of dry eye disease: At day 84, a larger reduction in ICSS favoring Xiidra was observed in 3 of the 4 studies.[1]

References: 1. Xiidra [package insert]. East Hanover, NJ: Novartis Pharmaceuticals Corp. **2.** Data on file. Fingertip Formulary® as of 07/2022. Novartis Pharmaceuticals Corp; July 2022.

XIIDRA® (lifitegrast ophthalmic solution), for topical ophthalmic use
Initial U.S. Approval: 2016

BRIEF SUMMARY: Please see package insert for full prescribing information.

1 INDICATIONS AND USAGE

Xiidra® (lifitegrast ophthalmic solution) 5% is indicated for the treatment of the signs and symptoms of dry eye disease (DED).

4 CONTRAINDICATIONS

Xiidra is contraindicated in patients with known hypersensitivity to lifitegrast or to any of the other ingredients in the formulation *[see Adverse Reactions (6.2)]*.

6 ADVERSE REACTIONS

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

- Hypersensitivity *[see Contraindications (4)]*

6.1 Clinical Trials Experience

Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in 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 five clinical trials of DED conducted with lifitegrast ophthalmic solution, 1401 patients received at least one dose of lifitegrast (1287 of which received lifitegrast 5%). The majority of patients (84%) had less than or equal to 3 months of treatment exposure. One hundred-seventy patients were exposed to lifitegrast for approximately 12 months. The majority of the treated patients were female (77%). The most common adverse reactions reported in 5%-25% of patients were instillation-site irritation, dysgeusia, and reduced visual acuity.

Other adverse reactions reported in 1%-5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus, and sinusitis.

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Xiidra. 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.

Rare serious cases of hypersensitivity, including anaphylactic reaction, bronchospasm, respiratory distress, pharyngeal edema, swollen tongue, urticaria, allergic conjunctivitis, dyspnea, angioedema, and allergic dermatitis have been reported. Eye swelling and rash have also been reported *[see Contraindications (4)]*.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

There are no available data on Xiidra use in pregnant women to inform any drug-associated risks. Intravenous (IV) administration of lifitegrast to pregnant rats, from premating through gestation day 17, did not produce teratogenicity at clinically relevant systemic exposures. Intravenous administration of lifitegrast to pregnant rabbits during organogenesis produced an increased incidence of omphalocele at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the recommended human ophthalmic dose [RHOD], based on the area under the curve [AUC] level). Since human systemic exposure to lifitegrast following ocular administration of Xiidra at the RHOD is low, the applicability of animal findings to the risk of Xiidra use in humans during pregnancy is unclear *[see Clinical Pharmacology (12.3) in the full prescribing information]*.

Data

Animal Data

Lifitegrast administered daily by IV injection to rats, from premating through gestation day 17, caused an increase in mean pre-implantation loss and an increased incidence of several minor skeletal anomalies at 30 mg/kg/day, representing 5,400-fold the human plasma exposure at the RHOD of Xiidra, based on AUC. No teratogenicity was observed in the rat at 10 mg/kg/day (460-fold the human plasma exposure at the RHOD, based on AUC). In the rabbit, an increased incidence of omphalocele was observed at the lowest dose tested, 3 mg/kg/day (400-fold the human plasma exposure at the RHOD, based on AUC), when administered by IV injection daily from gestation days 7 through 19. A fetal no observed adverse effect level (NOAEL) was not identified in the rabbit.

8.2 Lactation

Risk Summary

There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lifitegrast from ocular administration is low *[see Clinical Pharmacology (12.3) in the full prescribing information]*. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for Xiidra and any potential adverse effects on the breastfed child from Xiidra.

8.4 Pediatric Use

Safety and efficacy in pediatric patients below the age of 17 years have not been established.

8.5 Geriatric Use

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

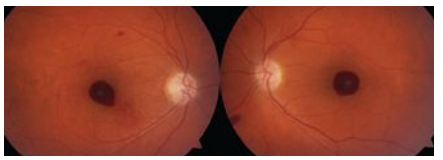
Distributed by:
Novartis Pharmaceuticals Corporation
One Health Plaza
East Hanover, NJ 07936

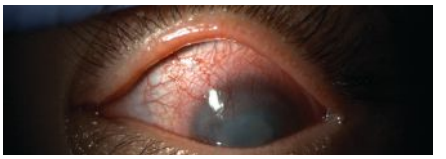
T2020-87

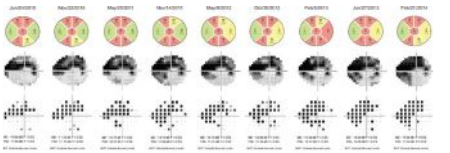
DEPARTMENTS

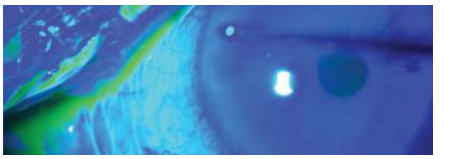
VISIT US ON SOCIAL MEDIA

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









We Welcome Your Comments

Feedback from the community provides important insights about clinical practice. If you would like to share your thoughts on the topics discussed in this issue—or the wider field of optometry at large—please write to: ***editor@reviewofoptometry.com***

REVIEW of OPTOMETRY
Leadership in clinical care

Business Offices
19 Campus Boulevard, Suite 101
Newtown Square, PA 19073
Subscription inquiries (877) 529-1746 (USA only)
outside USA, call (847) 763-9630

PUBLISHER
MICHAEL HOSTER
(610) 492-1028
mhoster@jobson.com

SENIOR MANAGER, STRATEGIC ACCOUNTS
MICHELE BARRETT
(610) 492-1014
mbarrett@jobson.com

REGIONAL SALES MANAGER
JONATHAN DARDINE
(610) 492-1030
jdardine@jobson.com

PRODUCTION MANAGER
FARRAH APONTE
(212) 274-7057
faponte@jobson.com

PRODUCTION MANAGER
KAREN LALLONE
(610) 492-1010
klallone@jobson.com

DIGITAL MARKETING MANAGER
MATT EGGER
(610) 492-1029
megger@jobson.com

CLASSIFIED ADVERTISING
(888) 498-1460

SUBSCRIPTIONS
$63 PER YEAR, $99 (US) IN CANADA,
$158 (US) IN ALL OTHER COUNTRIES
revoptometry@cambeywest.com

CIRCULATION
PO BOX 71, CONGERS, NY 10920-0071
(877) 529-1746
OUTSIDE USA: (845) 267-3065

SENIOR CIRCULATION MANAGER
HAMILTON MAHER
(212) 219-7870
hmaher@jhihealth.com

CEO, INFORMATION GROUP SERVICES
MARC FERRARA

SENIOR VICE PRESIDENT, OPERATIONS
JEFF LEVITZ

VICE PRESIDENT, HUMAN RESOURCES
TAMMY GARCIA

VICE PRESIDENT, CREATIVE SERVICES & PRODUCTION
MONICA TETTAMANZI

CORPORATE PRODUCTION DIRECTOR
JOHN ANTHONY CAGGIANO

VICE PRESIDENT, CIRCULATION
JARED SONNERS

Jobson Health Information/WebMD
395 Hudson Street, 3rd Floor, New York, NY 10014

REVIEW OF OPTOMETRY (ISSN 0147-7633) IS PUBLISHED MONTHLY, 12 TIMES A YEAR BY JOBSON MEDICAL INFORMATION LLC, 395 HUDSON STREET, 3RD FLOOR FLOOR, NEW YORK, NY 10014. PERIODICALS POSTAGE PAID AT NEW YORK, NY 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.

NEW

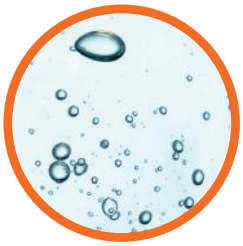
HELP YOUR PATIENTS GO FROM

DRY EYES

TO EXTRA LONG-LASTING

HYDRATION[1-8]

Introducing blink® triple care — the first and only over-the-counter eye drop with both hyaluronate and a nano-emulsion lipid within the unique formula.[9-10] Here's how our **DUAL ACTION MOISTURE SEAL TECHNOLOGY**[5-8] works:



HYALURONIC ACID
binds moisture and helps boost hydration[3-5]

LIPID NANO EMULSION
helps protect against tear evaporation[11] to lock in moisture[5-8]

The result is **3-in-1 Extended Relief**[1-8] for both Aqueous-Deficient and Evaporative Dry Eyes[12]:

- **Instantly Soothes**[1-8]
- **Extra Long-Lasting Hydration**[1-8]
- **Locks in Moisture**[5-8]

References: 1. Wasmanski AD and Kislan T. Cross-Over Evaluation of Polyethylene Glycol 400 (PEG-400) 0.4% and 0.25% Artificial Tears in Mild Dry Eye Patients. Invest. Ophthalmol. Vis. Sci. 2010;51(13):6263. 2. Montani G. Intrasubject Tear Osmolarity Changes with Two Different Types of Eye Drops. Optom. Vis. Sci. 2013;90(4): 372-377. doi: 10.1097/OPX.0b013e318288bdbe 3. Laurent TC. Structure of Hyaluronic Acid. In: EA Balazs (Ed.), Chemistry and Molecular Biology of Intracellular Matrix. Academic Press, London. 1970:703-732. 4. Aragona P, Papa V, Micali A, et al. Long Term Treatment with Sodium Hyaluronate-Containing Artificial Tears Reduces Ocular Surface Damage in Patients with Dry Eye. Br. J. Ophthamol. 2002;86(2):181-184. doi: 10.1136/bjo.86.2.181. 5. Prabhasawat P, Tesavibul N, Kasetsuwan K. Performance Profile of Sodium Hyaluronate in Patients with Lipid Tear Deficiency: Randomised, Double-Blind, Controlled, Exploratory Study. Br. J. Ophthalmol. 2007;91(1):47-50. doi: 10.1136/bjo.2006.097691. 6. Zheng X, Goto T, Shiraishi A, et al. In vitro efficacy of ocular surface lubricants against dehydration. Invest. Ophthalmol. Vis. Sci. 2013;32(9):1260-1264. doi: 10.1097/j.ico.0b013e31829cfd44. 7. Maissa C, Guillon M, Simmons P, et al. Effect of castor oil emulsion eyedrops on tear film composition and stability. Contact Lens Anterior Eye. 2010;33(2):76-82. doi: 10.1016/j.clae.2009.10.005. 8. Craig JP, Nichols KK, Akpek EK, et al. TFOS DEWS II Definition and Classification Report. The Ocular Surface. 2017;15(3):276-283. 9. US Dry Eye OTC Product Comparison. 10. IRI US 2020 Dry Eye Share Competitive Report. 11. JJV Data on File 2020. Blink Triple Care Lubricating Eye Drops - Consolidated, Approved Claims List. 12. 2012. Lemp, Miachael A. Distribution of Aqueous-Deficient and Evaporative Dry Eye in a Clinic-Based Patient Cohort: A Retrospective Study

Important Safety Information: Blink® Tears, Blink GelTears® and Blink® Triple Care drops are for the temporary relief of burning, irritation and discomfort due to dryness of the eye or exposure to wind or sun, and may be used as a protectant against further irritation. Patients should stop use and contact their eye care practitioner if they experience eye pain, changes in vision, continued redness or irritation of the eye, or if the condition worsens or persists for more than 72 hours.

REVIEW of OPTOMETRY

Founded 1891

Editorial Offices

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

Jobson Medical Information/WebMD
395 Hudson Street, 3rd Floor, New York, NY 10014

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

Printed in USA

BY JACK PERSICO
EDITOR-IN-CHIEF
OUTLOOK

Honoring Art Epstein

Fiercely loyal to optometry, he often led the way by starting much-needed conversations. We each can continue that tradition.

It's hard to process the loss of someone as singular as Art Epstein. I'm just one of thousands doing that now, in these first few days following his untimely passing. So much has already been said about his impact on the optometry profession, including the heartfelt comments we share in our news section this month from some of his friends, that I worry I can hardly add very much. But one of the things I think the optometry profession will miss most is Dr. Epstein's outspoken advocacy for change.

Art always had the courage of his convictions. Week in and week out, his "Off the Cuff" commentaries in *Optometric Physician* either took aspects of the profession to task for various shortcomings or highlighted some new direction he exhorted us to explore. Professional societies, optometric colleges, CE providers, product manufacturers—no one escaped Art's gaze if he had a bone to pick with them.

It's not easy to identify the fault lines in our institutions that create vulnerabilities for practicing optometrists. It's harder still to call out their leaders for inaction. Art did both effortlessly. In this he was almost a one-man Fourth Estate—the old-fashioned term for the press to describe its role in holding those in power to account.

In short, we need people like Art Epstein as a bulwark against complacency. Perhaps Joe Shovlin said it best: "In many respects, he was our conscience." That voice will be sorely missed in the months ahead.

Optometry is in the midst of another of its periodic transitions, with many states agitating for an expanded scope of practice that would encompass minor surgical procedures. The effort has seen much success in 2022, with Virginia and Colorado gaining such privileges and other states crafting legislation for their own upcoming runs at it.

Unfortunately, the day after Art Epstein passed away came the news that California's governor shot down the state's scope expansion bill. Had it been signed, this would have opened up new opportunities for motivated ODs to better serve the public good, filling a hole in the provision of eye care particularly for low-income people who rely on the state's Medi-Cal plan.

Man, how I wish we could've heard Art skewer the facile arguments against the bill put forth by the governor and the lobbyists that fed the words to him.

It's easy for opponents of scope expansion to hide behind (unsubstantiated) claims of hazards to public safety, as the medical lobby did once again in sinking the California bill, but the facts will bear us out in time. I watched the floor debate on the bill in the state Assembly when the vote took place in late August. Let's just say that was not a conversation where accuracy was a priority for the bill's detractors.

If I'm sounding a little fed up about the matter, I'll thank Art for that. As a longtime member of the *Review* editorial board, he often encouraged me privately to take a stand, to go out on a limb, to develop a voice for myself and this publication.

If Art Epstein's legacy can be to instill an abiding sense of responsibility in each of us—to call out hypocrisy, to challenge the norms and most of all *to act*—then I think we can fairly say we'll have honored his memory. Let's get to it. ■

Prevent AMD Vision Loss with Digital Healthcare

IRIS REGISTRY

20/83 VA

Average at wet AMD diagnosis according to IRIS Registry real-world data[1]

HOME STUDY

≥20/40 VA

Average at wet AMD diagnosis with ForeseeHome[2]

Early Detection Helps Preserve Vision

ForeseeHome is a **remote monitoring** program for at-risk dry AMD patients that helps **detect wet AMD earlier** and alerts you of changes.

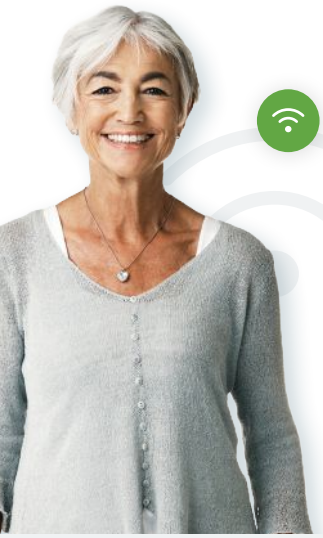
ForeseeHOME™
AMD Monitoring Program

Remote patient monitoring

leads to better outcomes and stronger optometric practices

- FDA Cleared
- Medicare Covered

- Plug and play digital health solution for your patients
- Solidify long-term relationships with your patients
- No cost to your practice
- Strengthen your referral relationships with qualified wet AMD referrals



The Key to Successful Home Monitoring

NOTAL VISION MONITORING CENTER

- Engagement & Education
- Benefits Verification & Authorization
- Continuous Monitoring
- Practice Workflow Implementation
- Remote Patient Management
- Vision Alert Management

References: 1. Rao P et al. *Ophthalmology*. 2018;125(4):522-528. **2.** Domalpally A, Clemons TE, Bressler SB, et al. *Ophthalmol Retina*. 2019;3(4):326-335.

See website for FDA Indication for Use.

SM-169.2

GET STARTED TODAY

1-855-600-3112

Mon-Fri, 8 AM to 6 PM EST

www.foreseehome.com/doctor

BY PAUL M. KARPECKI, OD
CHIEF CLINICAL EDITOR

Why Pricey Prescriptions are Here to Stay

The Inflation Reduction Act doesn't address the main cause: PBMs.

Patients and prescribers have no interaction with pharmacy benefit managers (PBMs), yet these administrators usually take home more than half of the money generated from each Rx filled. They serve as middlemen to "negotiate" with pharmaceutical companies for placement on an insurance formulary. Three PBMs have an oligopoly, accounting for more than 80% of the category: CVS Caremark, Express Scripts and OptumRx.

While these groups claim to help lower drug costs, prices continue to escalate. Why? To capitalize on their position, PBMs will pay and work incestuously with insurance companies, which sometimes even own the PBMs.

How Does the Scheme Work?

These middlemen collect billions of dollars in rebates for prioritizing pharmaceutical agents on tiered formularies. Then, they pay the insurance companies and hospitals, being sure to keep a sizable share for themselves. This pay-to-play approach fails to take drug efficacy or patient needs into account.

If drug companies refuse to pay these fees—which can constitute 60% of the entire cost of the drug—the PBM will exclude them from the formulary entirely or assign them to a lower tier that challenges patient access, leaving overworked physicians to petition for them. This happens despite the fact that pharmaceutical companies are the ones spending billions on research and development for potentially life- and vision-saving treatments and fighting to have these drugs passed by the FDA. Greater transparency of the profit flow within this system would help shed light on its need for reformation.

> **"The system's pay-to-play approach fails to take drug efficacy or patient needs into account."**

PBMs Tied to Inflation

Here's an example to illustrate how a patient may end up paying more for their drugs than the insurance companies do (thanks to PBMs). Let's say a drug company provides a rebate of 80% on a drug priced at $500; thus, the company keeps $100. The logical move would be to charge $1,000, so that they can take home $200. Although the manufacturer might appear greedy, it's the PBM receiving the much larger monetary portion of $800. The insurance companies then purchase and upcharge these drugs to get their cut, and so the cycle continues.

United Health Group's 2022 second quarter revenues grew $9 billion, or 13%, to over $80 billion year-over-year, and its earnings exceeded $7 billion over the last three months. Fewer drugs are covered, making it harder for pharmacies to maintain profitability. Insurance companies create barriers that oblige pharmacies to increase prices, such as by denying drug coverage, mandating prior authorizations or requiring step-edits that order the use of a generic or cheaper drug first. This system often prevents patients from receiving a medication that would be superior or essential to their health.

We Can't Ignore the Middlemen

The Inflation Reduction Act calls for policy improvements such as allowing Medicare to negotiate prices and help prevent PBMs from charging rebates on a few select drugs. However, the document doesn't require PBMs to be transparent about what they make.

While it's true we must address costs at every level, failing to include PBMs in the commercial payer space will continue to stand in the way of reducing inflation of drug prices. If PBMs decide they want an 85% rebate or more, drug companies won't have the means to lower prices and continue developing drugs that save vision and lives.

Calling for Creative Solutions

If the government isn't willing to require transparency, other avenues to dodge the middlemen need to be sought out. One company, RVL Pharmaceuticals, has eliminated PBMs, insurance companies and pharmacies. The maker of Upneeq for ptosis offers a prescription at a set price through RVL Pharmacy, which also ensures the patient doesn't encounter surprises (*e.g.*, insurance denials, pre-authorizations or inflated costs).

Another creative solution that removes the middleman is allowing doctors to dispense medications from their offices, which is legal for optometrists and ophthalmologists in most states.

It's time to look at the true reason for inflation in health care. Understanding the behind-the-scenes world of PBMs is essential to help keep medications accessible and affordable. ■

About Dr. Karpecki

Dr. Karpecki is the director of Cornea and External Disease for Kentucky Eye Institute, associate professor at KYCO and medical director for the Dry Eye Institutes of Kentucky and Indiana. He is also chair of the New Technologies & Treatments conferences. 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.

HIGH-PERFORMANCE LENS

PLUS

HIGHEST PATIENT REBATES[1]

Offer your patients the **highest rebates available**[1] with Bausch + Lomb INFUSE®.
New wearers can save $300* when they purchase an annual supply
and existing wearers can save $200!*

Up to **$300** **IN SAVINGS*** with purchase

SEE DETAILS

IT'S FAST AND EASY TO REDEEM

Rebates approved in as little as 48 hours on BauschRewards.com†
Can also be redeemed with convenient text option!

*Rebate amount is dependent on product and quantities purchased and whether the patient is a new or existing wearer as defined in the terms and conditions. Terms and conditions apply. Please see BauschRewards.com
†From the time of submission validation.

REFERENCE: 1. Data on file. Bausch & Lomb Incorporated. Rochester, NY.

BAUSCH+LOMB

BY MONTGOMERY VICKERS, OD

CHAIRSIDE

Take the Road Less Traveled

You don't need to be like everyone to be someone.

"Ain't no cure for the summertime blues." These timely lyrics were written and performed by the great Eddie Cochran in 1958. I was five years old. The song was subsequently recorded and performed by the Beach Boys, Blue Cheer, the Who, T. Rex, Rush, Brian Setzer, Jimi Hendrix and, one of my favorites, Alan Jackson. I'm sure many more have played this song to appreciative audiences all over the world. I wouldn't even be shocked if the Beatles ran it by the folks in Hamburg, Germany, pre-Ringo Starr.

But not every musician performed "Summertime Blues." It wasn't on any of the Three Tenors albums, although I suspect they would have killed it.

Oh, I forgot. This is an optometry column. Well, the point is this: just because a rock star (or doctor) who you respect does something that seems awesome, that does not mean you have to do it, too. You have to be you. When I was in school, the esteemed Dr. Burt Hooten made this point when he said the following cringeworthy statement: "Your patients will be like you. If you're fat and ugly, your patients will be fat and ugly, too."

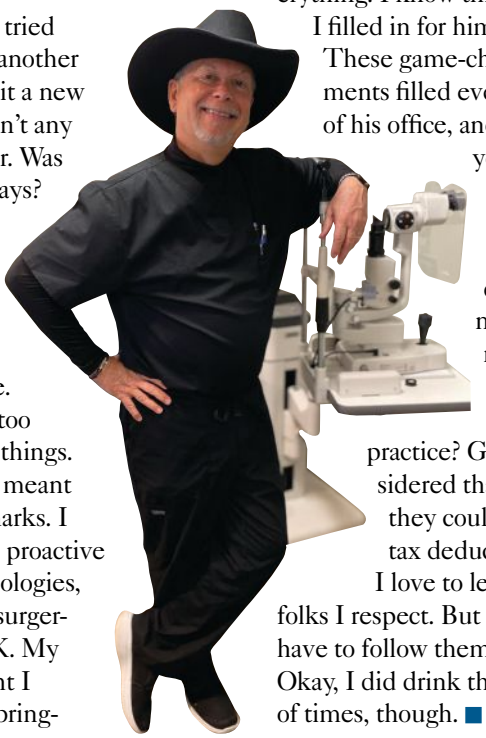
This explains why all my patients are crusty old goats. Enough about that though, more about how I got to this point in the first place.

Low vision is very important and can definitely add a wonderful and necessary service to your practice plus a new (and mostly non-insurance) profit stream. I tried it. I have tried everything. I was not good at it. Therefore, it did not really benefit my patients or my practice. Selling and installing new nose pads for $1.00 worked better for me.

Same for vision therapy: you have to love it or you won't do it well. Me? Also not my forte. I am more than happy to send these cases to doctors who actually know what they are doing and will help my patients. You never lose patients when you do something that will help them.

Okay, that's not 100% true; sometimes, the patient has 20/20 eyes and a 20/200 attitude.

What have you tried because you saw another doctor do it? Was it a new vision plan? I wasn't any good at that either. Was it working Saturdays? A total bust for me. Was it a senior citizen discount? We did that and called it Medicare.



Now don't get too scared to try new things. That's not what I meant by my earlier remarks. I have always been proactive with newer technologies, lens designs and surgeries such as LASIK. My colleagues thought I must be nuts for bringing up LASIK before we had anyone nearby in West Virginia performing it. My theory was I wanted my patients to hear about these advances from me, their trusted eye doctor, not from their hairdresser or cousin Larry, who still thinks he made a good decision to have a radial keratotomy back in the day. You know Larry, right? His right cornea is shaped like the Matterhorn. His left? A pristine +7.00 -5.00x132 and he says he's as happy as a clam. Thank goodness for radial keratotomies, right Larry? Sure is better than when you were -2.00 OU.

The lesson: even though you are indeed the best resource about new technologies for your patients, you don't have to recommend every single new thing. A plumber is paid to plumb. You are paid to think.

I know a very successful doctor who bought every single new instrument that he could possibly afford. He always wanted to be the first to have everything. I know this for a fact because I filled in for him a couple of times. These game-changing new instruments filled every nook and cranny of his office, and you could write your name with your finger in the dust that covered them. Maybe you should decide how each new fancy instrument would benefit, first, the patient and, second, your practice? Guess he never considered that, but, who knows, they could've all been good tax deductions.

I love to learn new stuff from folks I respect. But that doesn't mean I have to follow them blindly over a cliff. Okay, I did drink the Kool-Aid a couple of times, though. ■

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.

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

Covering the spectrum of *Dry Eye Relief*

Introducing preservative-free iVIZIA™ lubricant eye drops for the comprehensive combination of lasting relief and ocular surface protection.[1-6]

- Trehalose provides bioprotection, osmoprotection, and rehydration[1-4]
- Hyaluronic acid (HA) and povidone deliver lubrication with long-lasting relief[5-6]
- Increased tear film thickness for up to 240 minutes[7]
- Preservative free
- Proprietary multi-dose bottle design for calibrated dosing and contamination protection
- Suitable for all dry eye sufferers, including contact lens wearers†

Help patients see dry eye relief differently. Recommend iVIZIA OTC.

Request samples and learn more by scanning the QR code or visiting iVIZIA.com/ECP.

*Prescription market data, Sept. 2021 – S01K without cyclosporine.
†To limit blurriness when using contact lenses, remove contacts, apply drops, then insert contacts.

References: 1. Chen W, Zhang X, Liu M, et al. Trehalose protects against ocular surface disorders in experimental murine dry eye through suppression of apoptosis. *Exp Eye Res*. 2009;89(3):311-318. **2.** Aragona P, Colosi P, Rania L, et al. Protective effects of trehalose on the corneal epithelial cells. *ScientificWorldJournal*. 2014;2014:717835. **3.** Chiambaretta F, Doan S, Labetoulle M, et al. A randomized, controlled study of the efficacy and safety of a new eyedrop formulation for moderate to severe dry eye syndrome. *Eur J Ophthalmol*. 2017;27(1):1-9. **4.** Liu Z, Chen D, Chen X, et al. Trehalose induces autophagy against inflammation by activating TFEB signaling pathway in human corneal epithelial cells exposed to hyperosmotic stress. *Invest Ophthalmol Vis Sci*. 2020;61(10):26. **5.** US FDA Department of Health and Human Services. Ophthalmic drug products for over-the-counter human use. Updated October 21, 2021. Accessed January 19, 2022. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=349. **6.** Jones L, Downie LE, Korb D, et al. TFOS DEWS II management and therapy report. *Ocul Surf*. 2017;15(3):575-628. **7.** Schmidl D, Schmetterer L, Witkowska KJ, et al. Tear film thickness after treatment with artificial tears in patients with moderate dry eye disease. *Cornea*. 2015;34(4):421-426.

Made by Théa let's open our eyes | Brought to you by Similasan™ EVIDENCE-BASED EYE CARE

Valsalva Salvo

This type of retinopathy presents with dramatic preretinal hemorrhages and sudden, painless vision loss.

Q A patient just released from the hospital after a bout of pneumonia presented with blurred vision and bilateral retinal hemorrhages. What is the best way to manage this case?

A "A thorough medical history is critical," advises Jason Guo, OD, of the Eye Clinic of University Village in Seattle. This patient had just been placed in an induced coma on a ventilator for a week with pneumonia, a history of hypertension and a recent diagnosis of liver damage and anemia. Her medication list included furosemide for liver damage, nadolol and spironolactone for hypertension and prednisone for pneumonia.

"When you see bilateral preretinal hemorrhages, start ruling out diabetic retinopathy (DR), retinal arterial macroaneurysm, hemorrhagic posterior vitreous detachment (PVD) or Terson syndrome," Dr. Guo advises.

There was no history of diabetes or signs of DR. Bilateral symmetrical arterial microaneurysms typically look very different than this patient's presentation. There were no signs of a PVD or any vitreous hemorrhage. Terson syndrome was unlikely due to the lack of any associated neurological disease or increased intracranial pressure. Medical eye examination revealed best-corrected acuity of 20/80 OD and 20/200 OS. All other findings were normal except for the fundus.

Don't Hold it In

The macula revealed large preretinal hemorrhages OD and OS that obscured the fovea. There was a small retinal hemorrhage noted two disc diameters superior to the macula, and the left eye showed a larger retinal hemorrhage inferior nasal to the optic nerve. OCT confirmed preretinal/subhyaloid hemorrhage over the foveae, and delineation was appreciated between blood and inner retina OU (*Figure 1*).

Valsalva retinopathy made the most sense; it can occur unilaterally or bilaterally in an otherwise healthy patient.

A Valsalva maneuver is an effort to exhale without letting air escape through the nose or mouth. People often use a Valsalva maneuver during common activities, such as straining to have a bowel movement or blowing a stuffy nose. While Valsalva retinopathy is more commonly seen in males, there is actually no predilection between sex, age or race.[1] It is described as a venous vasculopathy caused by a rise in the intrathoracic or intra-abdominal pressure against a closed glottis that ruptures small superficial capillaries.[2] It produces a high influx of pressure against the venous system and allows the pressure to pass the thoracic and abdominal pressures into the vessels supplying the eye.[3] This increase in pressure in the eye leads to the perifoveal superficial retinal capillaries rupturing, causing a detachment of the internal limiting membrane (ILM).

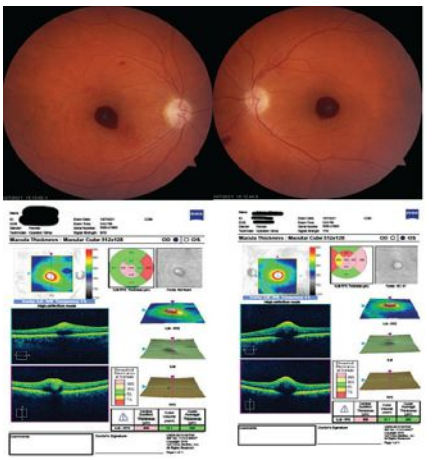


Fig. 1. Fundus exam revealed bilateral preretinal hemorrhages, and corresponding OCT imaging.

Don't Panic

Monitor the hemorrhages, as they usually resolve on their own. That occurred in this patient, with visual acuity of 20/25 OD and OS almost three months after the initial presentation.

If the patient is symptomatic or if the hemorrhage does not improve or resolve within three months, using neodymium:YAG laser can disrupt the ILM or posterior hyaloid, leading to the drainage of blood into the inferior cavity and producing a faster resolution.[4,5] A second intervention is pars plana vitrectomy, but this is risky and should be avoided if possible.

While Valsalva retinopathy is a rare side effect of intubation and mechanical ventilation, do not overlook it. Although this patient was on a ventilator for pneumonia and not COVID-19, understanding the ocular effects of intubation can help prepare optometrists for unintended consequences. Patients undergoing general anesthesia of any kind are also at risk.[6] ■

1. Simakurthy S, Tripathy K. Valsalva retinopathy. In: StatPearls [Internet]. Treasure Island, FL: StatPearls Publishing. Last updated June 27, 2022.

2. Duane TD. Valsalva hemorrhagic retinopathy. Trans Am Ophthalmol Soc. 1972;70:298-313.

3. Pstras L, Thomaseth K, Waniewski J, et al. The Valsalva manoeuvre: physiology and clinical examples. Acta Physiol (Oxf). 2016;217(2):103-19.

4. Sahu DK, Namperumalsamy P, Kim R, Ravindran RD. Argon laser treatment for premacular hemorrhage. Retina. 1998;18(1):79-82.

5. Schulz-Key S, Carlsson JO, Crafoord S. Long-term follow-up of pars plana vitrectomy for vitreous floaters: complications, outcomes and patient satisfaction. Acta Ophthalmol. 2011; 89(2):159-65.

6. Sunny ACL. Bilateral Valsalva retinopathy after general anesthesia: a case report. J Acute Dis. 2020;9:131-3.

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.

200° of iCare

iCare EIDON

Eidon Ultra-Widefield:
200 degrees of **imaging**

iCare's unique combination of sharpness and TrueColor offers now an even wider view of the retina. From 120˚ with a single shot, up to 200˚, helps detect subtle signs of pathologies in the periphery using a mosaic function.*

+ Rich in details from center to periphery
+ Imaging through media opacities

* Ultra-Widefield imaging is available with the optional EIDON UWF Module.

JUST LAUNCHED

iCare HOME2

24-hour at home
tonometry

+ **NEW!** Supine, reclined & seated positions
+ **NEW!** New smart light guide for easy positioning
+ **NEW!** Interactive display screen
+ **NEW!** Comprehensive IOP reports

For more information, scan, call 888.422.7313, or email infoUSA@icare-world.com
www.icare-world.com/USA

For better perception icare

CHRISTIAN, real DB patient
and ophthalmologist

We're willing to bet most eye care professionals don't realize just how prevalent *Demodex* blepharitis is.[1]

In fact, ~**25 million eye care patients** are affected by *Demodex* blepharitis (DB).[2,3]

DON'T BELIEVE US?
LEARN HOW EASILY DB CAN FLY UNDER THE RADAR AT

LOOK at the LIDS.COM

@LookAtTheLids

tarsus

References: 1. Data on file, Tarsus Pharmaceuticals, Inc. June 2022. **2.** Trattler W, Karpecki P, Rapoport Y, et al. The prevalence of *Demodex* blepharitis in US eye care clinic patients as determined by collarettes: a pathognomonic sign. *Clin Ophthalmol.* 2022;16:1153-1164. **3.** Saydah SH, Gerzoff RB, Saaddine JB, Zhang X, Cotch MF. Eye care among US adults at high risk for vision loss in the United States in 2002 and 2017. *JAMA Ophthalmol*. 2020;138(5):479-489.

TARPRE-DB-0043 8/22

COMANAGING OUTSIDE OF EYE CARE: RECOGNIZE THESE SYSTEMIC RISKS

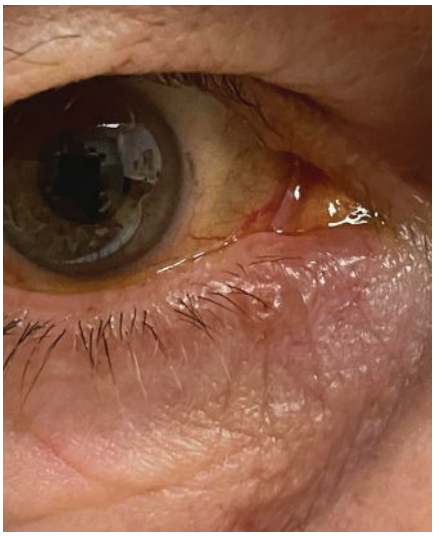
Learn how to trade expertise with doctors in other medical disciplines for the betterment of your shared patients.

BY CATLIN NALLEY
CONTRIBUTING EDITOR

Optometrists are tasked with managing the ocular health of patients, but the role of the OD does not end there. As primary eye care providers, you play a critical role in the overall health and well-being of your patients. Quite often, this means comanaging systemic conditions such as diabetes and hypertension with primary care and specialty physicians.

"None of us are ever going to see a pair of eyes in clinic that aren't attached to the rest of the body," notes James Fanelli, OD, of Cape Fear, NC. "What we are seeing in the eye is oftentimes just a manifestation of something happening elsewhere." Some scenarios are obvious, as when a patient comes in with a known diagnosis, he explains, but frequently "they may not have a systemic diagnosis and we find something in the eye that indicates, for example, that they could be diabetic or have elevated cholesterol levels," he continues. "As optometrists, we can then work very closely with the appropriate internal medicine specialist to get their condition under control to mitigate the risk of ophthalmic and systemic complications."

Photo: Marc Myers, OD



Suspicious non-healing, ulcerated skin lesion along the lower lid margin that the patient reported as becoming slightly larger over several months. Referral was made to oculoplastic surgeon to confirm diagnosis and necessary treatment of malignancy vs. benign lesion.

Given the wide range of systemic conditions an OD may encounter in their practice, navigating this aspect of patient care is not a simple undertaking. In this article, we will delve into the nuances of comanaging common systemic diseases with providers outside of eye care as well as what the optometrist needs to know to provide comprehensive care for the whole patient.

The OD's Role in Systemic Disease

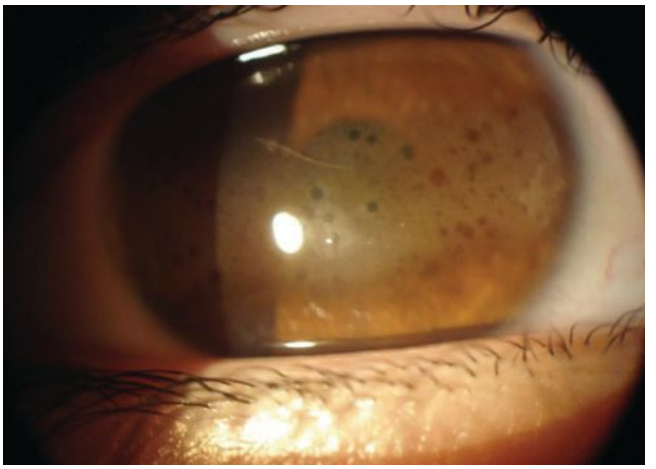
Dozens of systemic diseases are associated with ocular findings, and ODs are a key component of the diagnosis and comanagement of these conditions, given their role on the front lines of care. Virtually every portion of the optometric exam may provide clues to some sign of systemic disease, according to Joseph Shovlin, OD, of Scranton, PA, who notes that some signs and symptoms are subtle and can go undiagnosed without careful scrutiny.

Dr. Shovlin recommends starting with a detailed ocular and systemic history that should include attention to family history then moving through the typical optometric exam sequence. There are a number of commonly seen ocular signs that may signal systemic conditions.

"Starting with an external examination that may show eyelash ptosis/floppy eyelid syndrome, you'll want to consider if additional evidence points to sleep apnea," Dr Shovlin says. "Special attention may be indicated to seemingly benign conditions," he advises. For instance, simple myokymia that spreads beyond the lid warrants imaging to rule out a compressive lesion at the stylomastoid foramen. Facial involvement may signal Lyme disease.

"The cornea and conjunctiva may hold a treasure trove of valuable information that can lead to a systemic query," Dr. Shovlin continues. "Quite commonly seen is band keratopathy, suggesting a phosphorous renal clearance decrease specifically pointing to kidney problems or even parathyroid (PTH) dysfunction, necessitating PTH testing."

Photo: Joseph Shovlin, OD



Band keratopathy seen in a patient with kidney disease.

Optometrists must be able to detect the tell-tale signs or symptoms both in patients who have been diagnosed with a systemic disease as well as those who have not. "As primary healthcare providers, we should take an active role in management of patient's systemic conditions and lifestyle choices," says Mohammad Rafieetary, OD, of Germantown, TN.

The first step, he explains, is to not just ask questions like, "Do you have diabetes?" and wait for a "yes" or a "no" answer and go to the next question. "If the answer is a 'yes,' we need to ask about level of management, adherence to the regimen and follow-ups with other healthcare providers," Dr. Rafieetary explains. "If the answer is a no, then we need to investigate thoroughly."

This includes, according to Dr. Rafieetary, asking questions like these: "When was the last time you had a physical? What was the doctor's name? Did you follow-up for your test results? Do you know what your blood sugar numbers were?"

While he acknowledged these questions can sound obtrusive, their responses will help ODs better understand the patient and how involved they are with their health. A major component of managing any condition is education the patient. This is an area ODs can—and should—take an active role.

Below, we will discuss a few systemic conditions and the role an optometrist can play in their diagnosis and management.

• *Cardiovascular diseases.* Conditions such as hypertension, hyperlipidemia, carotid occlusive disease and related issues can manifest in a variety of ways in the eye. This may be as basic as corneal arcus, hypertensive vascular changes in the retina, various presentations of retinopathy or ocular ischemic syndrome, or include issues such as artery or vein occlusion, ischemic optic neuropathy or cranial nerve palsies, according to Sara Weidmayer, OD, of Ann Arbor, MI.

"We also commonly hear of transient monocular vision loss (TMVL): this is a form of transient ischemic attack (TIA)," she says. "Around 25% of patients with TMVL also had a concomitant stroke, and the highest risk of having a stroke after TIA is within 48 hours, so our swift and appropriate action in getting these patients emergency stroke workups and subsequent stroke risk management is crucial."

These patients can sometimes have giant cell arteritis (inflammatory source), carotid stenosis or aortic valve calcification (embolic source) or atrial fibrillation (thromboembolic source), so directing a cardiovascular workup is key, according to Dr. Weidmayer.

Kelly Malloy, OD, of Philadelphia also emphasized the importance of checking blood pressure. "As you know, blood pressure is analogous to intraocular pressure (IOP). If you are seeing a patient for their yearly eye exam, you would always check IOP, even if they are followed every three months by a glaucoma specialist." If you found the IOP to be elevated, she argues, you would communicate that to the glaucoma specialist.

"We need to think about blood pressure in the same way. It should be measured on every patient encounter and we should be communicating with the primary care physician (PCP)/ specialist who is managing their blood pressure if we find it to be poorly controlled," she recommends.

Optometrists will often see patients on medicine for blood pressure and cholesterol, notes Dr. Fanelli. "This will clearly manifest, completely asymptomatic and very normally, as atherosclerotic retinopathy or perhaps very mild hypertensive retinopathy, but with both of those conditions, as the disease progresses the ophthalmic retinal findings and the retinal vascular become much more pronounced," he explains, while emphasizing the importance of retinal photography in these cases.

"This can make a significant difference for our patients long term," he elaborates. "Even in those who are currently managed for hyperlipidemia, evidence of disease progression in the end organ we examine—the eye—warrants a conversation with their internist to perhaps drive lipids down even further. That is a valuable piece of information for the internist to know."

"A careful evaluation of the retina and specifically its vasculature may identify acute or longstanding hypertension concerns," adds Dr. Shovlin. "Of course, diabetic eye related changes may be evident as well even in undiagnosed diabetics. Early hypertensive retinopathy shows retinal arteriole narrowing/focal constriction and can show exudate, edema and even optic nerve swelling in more advanced disease."

• Diabetes and other retinal manifestations. ODs should be on the lookout for signs of the systemic component in patients with negative history, Dr. Rafieetary recommends. "For those with known diagnosis, historical perspectives, such as duration of disease, level of management, presence of complications and comorbidities such as renal failure, past CVA, hypertension, lipid disorders, sleep apnea, cardiovascular disease, obesity and smoking are all important in the risk assessment of presence of diabetic retinopathy, as well as potential progression and prognosis."

One out of every 10 patients you see have diabetes and three or four out of 10 are pre-diabetic, according to Dr. Rafieetary, who notes that diabetes can also have non-retinal ocular effects such as refractive shift. This should raise the suspicion to further dissect the issue.

While patients may be resistant to dilation, Dr. Rafieetary underscores the importance of performing a dilated fundus exam on all patients. This, he notes, becomes even more imperative among patients with certain symptoms or conditions with potential retinal involvement.

"Use of imaging technologies plays a critical role as well," Dr. Rafieetary adds. "However, ODs should keep in mind the limitations, sensitivity and specificity of these tests. For example, OCT is an excellent test for detection of diabetic macular edema. However, it is not to be substituted for a comprehensive retinal examination."

• Neurologic conditions. There are a number of neurologic diseases that can affect vision and cause various symptoms ranging from dry eye and double vision to blindness. Systemic neurologic conditions such as Parkinson's and Alzheimer's can have ocular manifestations and, following a stroke, patients often face visual problems that stem from neurologic damage.

"Be sure to use the tools in your toolbox to your full capacity," says Dr. Malloy. "As the eye doctor, you are the only member of the patient's health care team to have and be able to access visual fields and OCT. Remember that these are not just for glaucoma." When patients complain of new-onset headaches or subjective visual disturbances, run visual fields and OCTs, Dr. Malloy advises. "This should be done before referring to the PCP or neurologist for headache management."

Abnormalities on these tests, she adds, could help identify an underlying issue that may otherwise be incorrectly labeled as migraine. "For example, uncovering a subtle homonymous hemianopia in such a patient could demonstrate that this person needs neuroimaging that might uncover a brain mass," says Dr. Malloy, who recommends all optometrists refamiliarize themselves with performing a cursory neurologic examination.

"You test cranial nerves II, III, IV, and VI or a regular basis, but how often do you check the other eight cranial nerves? Your ability to do so may help identify and localize a causative etiology for a patient's symptoms or clinical presentation," she advises. "Do you ever test a patient's strength and sensation, or assess their gait? These can not only help localize an etiology for their ocular signs and symptoms but also help you identify non-ocular issues for which the patient would benefit from neurologic consultation."

Dr. Malloy also emphasizes the importance of assessing a patient's mental status. When it's warranted, a simple, mini-mental status exam—in addition to the other aspects of a neurological examination—can help determine when a neurologic referral may be indicated for early neurodegenerative disease or other causes of dementia.

"Be sure to look at the patient as a whole and not just a pair of eyes," she says. "Work to your capability of being an integral part of the patient's health care team. This is applicable to all areas of systemic disease, not just neurologic issues."

• Autoimmune and inflammatory diseases. There are a number of autoimmune and inflammatory diseases that can impact the eyes and vision, such as lupus and rheumatoid arthritis. Other conditions an OD may come across in the clinic include spondyloarthropathies, sarcoidosis, Sjögren's syndrome and inflammatory bowel disease.

These conditions can present with a variety of ocular manifestations. For instance, lupus can lead to eye-related conditions such as optic neuropathy

DETERMINING REFERRAL URGENCY

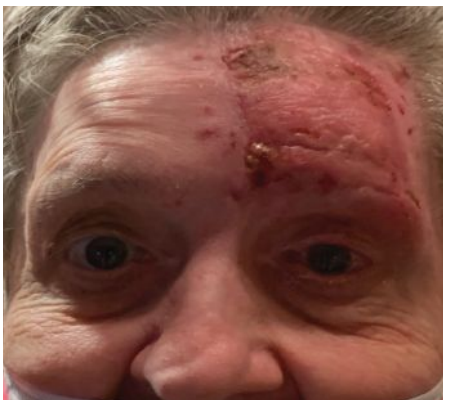
As discussed, optometrists should be prepared to refer to a specialist when deemed necessary. However, most specialists, and especially neurologists, are often booked out at least three months, if not longer. It is up to the OD, according to Dr. Malloy, to determine the urgency of the referral.

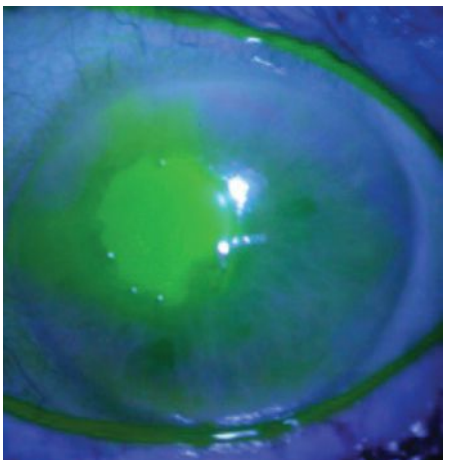
"Keep in mind that there is a difference between wanting your patient to be seen sooner so you feel better about shouldering the responsibility and needing your patient to be seen sooner because you know they have something of legitimate concern," she advises. "However, if your patient does have that more urgent issue, you will need to call the office and speak with a nurse or doctor to explain why you feel your patient needs to be seen more urgently."

As your patient's advocate, if you feel they are not receiving the necessary care in the appropriate timeframe, be persistent, Dr. Malloy urges. "When needed, you can call the hospital emergency department and discuss the possibility of sending the patient to them to initiate any emergent work-up and/or treatment if you know what is needed."

This is why keeping up with the literature and new practice guidelines is critical. "For example, the latest practice guidelines now clearly state that we should be managing all patients with acute vision loss (even if transient) or acute retinal artery occlusion the same as we would manage any new-onset stroke, with immediate referral to an emergency department at a hospital with a dedicated stroke center," Dr. Malloy notes.

Photo: Joseph Shovlin, OD





Neurotrophic keratopathy secondary to herpes zoster infection.

and vascular lesions. Patients may present with symptoms such as dry eyes, blurred vision and light sensitivity. A common symptom of rheumatoid arthritis is dry eye. Other conditions associated with this condition include scleritis and uveitis. In fact, there is about a 50% chance that patients with scleritis have an associated autoimmune condition.

As always, it's important to keep a patient's medical history in mind throughout the entirety of your exam as well as recognize the signs of any potentially underlying conditions.

• *Other conditions.* There are a plethora of other conditions that ODs will likely see in their practice. One example is obstructive sleep apnea, an often underdiagnosed condition, according to Dr. Rafieetary, who notes that this condition has ocular and non-ocular signs that ODs should know about and have a conversation with the patient if suspected. "This is associated with floppy eyelid syndrome, and it's remarkable how even a very basic eye exam and symptom screening can prompt a sleep study and obstructive sleep apnea diagnosis," adds Dr. Weidmayer.

Another area where optometrists can have an impact is dermatologic conditions, notes Philadelphia's Marc Myers, OD. "We see our patients, hopefully, on a routine basis, and by doing so we can follow up on skin diagnoses and skin cancers. Most skin cancers affect people above the shoulder."

When Dr. Myers examines a patient, he is not only assessing their eyes, but also looking at the skin of their head and neck. He will ask questions such as, "Do you have a history of involvement with a dermatologist? When was the last time you were there? Are you using sun-safe techniques like staying out of the sun and using sunscreen?" Dr. Myers will then communicate with the dermatologist directly if he finds anything suspicious that could warrant further examination and testing.

Dr. Shovlin, who recently had a patient with a suspicious nose lesion that turned out to be basal cell carcinoma, emphasizes the importance of looking under the face mask.

Regardless of the condition, an optometrist must feel comfortable to pick up the phone and call the appropriate provider, whether that is the PCP or a specialist, Dr. Myers says. "We have to share clear and detailed findings, so that our comanagement partner understands the severity and needs of the patient," he notes. "This also helps confirm that the importance of following through with the recommended care has been communicated to the patient."

Patient Care Across Disciplines

Effectively comanaging systemic conditions with healthcare providers outside of eye care requires strong relationships based on mutual respect and trust. Taking the time to foster connections with local PCPs and specialists will go a long way when the need for collaborations arises.

Communication is key. When the OD is the first to suspect a systemic condition, it is important to reach out directly to the appropriate provider.

Dr. Shovlin prefers a phone call. If you are referring to a specialist, the PCP should always be kept in the loop, he advises.

"In some cases," says Dr. Rafieetary, "it is best to send the patient to the local ER with a call to the ER physician ahead of time," particularly if dealing with acute and life-and vision-threatening situations such as malignant hypertension, central retinal artery occlusion, papilledema or ischemic optic neuropathy with suspicious of giant cell arteritis. "It may not even be unreasonable to call EMT to transport the patient," he advises.

In cases where specialty care hasn't been established, ODs shouldn't hesitate to make a referral to a specialist or subspecialist, according to Dr. Rafieetary. However, he notes, there are instances where a PCP referral may be required.

"In our area, most rheumatologists do not accept patients from our office if we suspect an autoimmune disease," he explains. "They want an internist to at least evaluate the patient and try to manage their care. We have had to establish working relationships with a handful of our area rheumatologists to be able to send the patient directly to them."

How you communicate with other providers is also crucial. "Although EHRs have made it simpler to send a report to other healthcare providers (HCPs) and we should take advantage of this, you cannot always trust that the note or the report gets into the hands of the HCP you were trying to send information to," advises Dr. Rafieetary. "Sometimes it is easier to make the patient an appointment or rely on them to make an appointment for themselves, or present to a pre-existing appointment with a copy of your test results or a note you need to convey to other HCPs."

In Patients With Diabetic Eye Disease (DR and DME),

HELPING TO PROTECT VISION STARTS WITH YOU

IF YOU SEE OR SUSPECT DIABETIC RETINOPATHY

EDUCATE PATIENTS[1]

- Your early and frequent discussions about progression of disease, timely referral, and potential treatment options can empower patients[1]

REFER APPROPRIATE PATIENTS[1]

- The AOA recommends referring patients with severe NPDR and PDR within 2 to 4 weeks, and patients with higher-risk PDR with or without macular edema within 24 to 48 hours[1]

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.
- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.
- There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

Please see Important Safety Information throughout and Brief Summary of the full Prescribing Information on the following page.

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

Brought to you by **REGENERON®**

FOLLOW UP WITH PATIENTS

- Encourage referred patients to promptly visit a retina specialist

CONTINUE TO MONITOR PATIENTS[1]

- The AOA recommends frequent monitoring of patients[1]
  - At least every 6 to 9 months in patients with moderate NPDR and more frequently for patients with greater disease severity

The more you know about anti-VEGF agents and other potential treatments for DR, the better you can help inform your patients. Find out more by visiting diabeticretinaldisease.com.

ADVERSE REACTIONS

- Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.
- The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.
- Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

INDICATIONS

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

anti-VEGF, anti–vascular endothelial growth factor; AOA, American Optometric Association; NPDR, nonproliferative diabetic retinopathy; PDR, proliferative diabetic retinopathy.

Reference: 1. Eye care of the patient with diabetes mellitus. American Optometric Association. Accessed April 2, 2021. http://aoa.uberflip.com/i/1183026-evidence-based-clinical-practice-guideline-eye-care-of-the-patient-with-diabetes-mellitus-second-edition/

07/2021
EYL.21.03.0229

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

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

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

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

4 CONTRAINDICATIONS

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

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

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

5 WARNINGS AND PRECAUTIONS

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

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

8 USE IN SPECIFIC POPULATIONS

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

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

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

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

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

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

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

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

REGENERON

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

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

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

EYL.20.09.0052

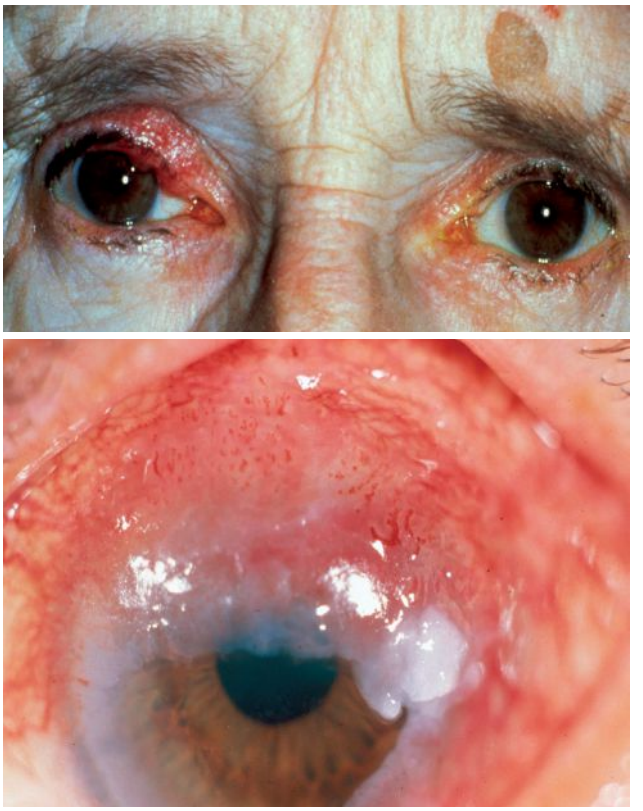
Working with other providers can sometimes be challenging, and Dr. Shovlin notes that there will be occasions where you may be met with some resistance, especially if you are recommending specific testing. "Don't be deterred," he says. Recalling a recent case, he explains, "I sent an elderly woman who experienced an artery occlusion for a stroke protocol to the ED along with a note for obtaining an ESR and CRP, in addition to what would normally be done on ED presentation." About four hours later, Dr. Shovlin received a phone call at home from a first-year emergency physician admonishing him for suggesting such testing on "her" patient.

"She refused to do a simple sed rate and when I called the ED the next morning, I spoke to another physician who obtained the necessary test only to report a sed rate of 82 later that day," he continues. "Steroids were immediately started and a temporal artery biopsy was done in our ambulatory surgery center later that week showing inflammation consistent with giant cell arteritis."

Effectively comanaging with other physicians requires confidence as well as willingness to learn and ask questions, when needed. "Very clear and specific referrals are key. Remember that you are the eye specialist, and other healthcare providers in different specialties depend on you to communicate what is happening with the patient, why you referred them and what specifically you want them to look for," Dr. Weidmayer, says.

"If you have a specific problem that requires a specific test, state exactly what needs to be done. If you don't know exactly what to do, that's OK—but talk to somebody who does," she adds. "We should all know enough to understand the level of urgency of the condition at hand. Don't be afraid to pick up the phone and talk to someone to ensure you're making the appropriate decisions."

Photo: Joseph Shovlin, OD



Experts advise optometrists to be vigilant for clinical signs of sebaceous gland carcinoma.

ODs must also recognize that providers outside of eye care don't always understand what optometry is and the full scope of what the specialty is capable of, notes Dr. Fanelli. "Having confidence in—and clearly articulating—your expertise is an important aspect of comanagement," he says. "Building relationships and mutual trust in one another's abilities is the key component of success. You want to work the providers who understand and value what you bring to the table as an optometrist."

Systemic Meds and the Eye

Another key component of systemic disease comanagement is medication. For the OD, that means contending with potential ocular side effects. However, given the growing list of drugs that can affect the eye and vision, this can prove challenging.

"There are many medications that have an effect on the eye. Unfortunately, some have potential to cause irreversible vision loss," according to Dr. Shovlin, who advises ODs to "always alert any provider who has any direct effect in prescribing such medication with any concerns you have after you have examined your patient."

Quite often, Dr. Weidmayer explains, the need for the systemic medication is greater than the risk of ophthalmic side effects. "However, we certainly still have a say and can communicate that with the prescribing physician."

One example Dr. Weidmayer gives is Plaquenil use. She finds that patients on this medication are taking a dose that exceeds the maximum recommended 5mg/kg/day in regard to retinal toxicity risk. "This typically happens as elderly patients lose weight and their dose is not adjusted accordingly," she says. "I regularly talk with our rheumatologists and ask them to trim the dose—which usually gets trimmed from 200mg BID to 300mg/day equivalent (either 300mg/day or 400/200 per day alternating for a 300mg/day equivalent).

"Another nuance I tend to run into in Plaquenil monitoring is pre-existing or developing macular disease," she continues. "I ask the rheumatologist to explore alternatives to Plaquenil when there are any macular issues present that would make it difficult for me to discern whether the patient was developing Plaquenil toxicity over time."

Any evidence of early macular toxicity is a hard stop for Plaquenil, according to Dr. Weidmayer. "Rheumatology has never given me pushback on that, since permanent central vision loss would be the end result if the patient remained on it," she explains.

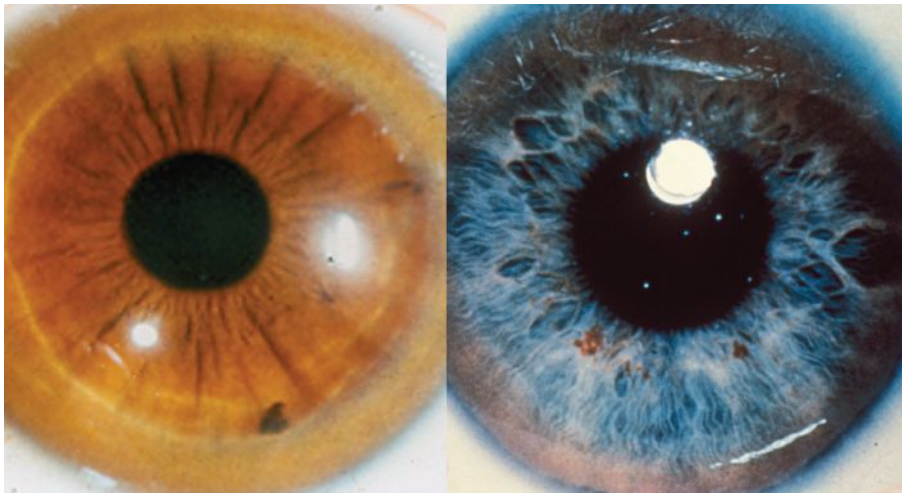


Photo: Joseph Showlin, OD

The genetic disorder Wilson's disease manifests in the eye as a Kayser-Fleischer ring.

Patients with pachychoroid spectrum disease (*e.g.*, CSCR) should avoid systemic steroids if possible, Dr. Weidmayer advises, while acknowledging that this cannot always reasonably be avoided, since steroids are used for such a wide range of conditions.

"In patients with a CSCR history, I typically alert the healthcare team that steroids of any kind should be avoided if possible and ask that they refer the patient to me if any are started so I can evaluate them," Dr. Weidmayer explains, while noting that this is similar to the approach she takes when managing steroid-sensitive IOP patients.

For example, she has a patient with very steroid-responsive IOP who gets semi-regular intra-articular steroid injections. His orthopedic/physical medicine and rehabilitation physician has been made well aware that his IOP is steroid-sensitive, so Dr. Weidmayer is alerted several weeks before any scheduled injection.

"I send the patient some Cosopt and he comes in at scheduled intervals for IOP checks thereafter until we can stop the Cosopt again," she says. "This is not an unmanageable situation, we just all need to be on the same page."

There are a plethora of other medications that an OD may come across in their practice. One example is sildenafil (Viagra). "This and other PDE-5 inhibitors have been associated with dose-dependent, reversible color vision abnormalities, but also with more concerning non-arteritic anterior ischemic optic neuropathy (NAION)," according to Dr. Weidmayer. Risk vs. benefit calculations should be discussed with such patients on an individual basis and include considerations of possible comorbid health conditions (*e.g.*, hypertension, diabetes, hyperlipidemia) and relevant ocular history (*e.g.*, prior NAION in the other eye, binocular/monocular status, other eye disease), she notes.

"I will typically simply alert the prescribing physician that PDE-5 inhibitors are associated with an increased risk for NAION and summarize the discussion I had with the patient as a launching point for the PCP to consider discussing risks/benefits with the patient," Dr. Weidmayer explains.

Another medication ODs should be aware of is pentosan polysulfate (Elmiron), which is used for patients who have interstitial cystitis. This medication can cause irreversible central vision loss, so close monitoring is necessary. "Pre-emptively communicating with urologists in your local community about the ocular risks of this medication is a great idea; that way, prescribers will send patients to eyecare providers for appropriate screening," suggests Dr. Weidmayer.

Recent evidence has shown that antibody-drug conjugates (ADCs)—a newer class of targeted cancer therapy—can cause corneal deposits and microcysts, keratitis, conjunctivitis and optic neuropathy.

"With the explosion of the systemic therapies for almost every condition, it is impossible to remember or keep up with indications and adverse reactions of all things in the market. We also must keep in mind interaction with medications that we may prescribe," Dr. Rafieetary says.

"In years past," he notes, "we used to rely on PDR books, but once again the worldwide web and various apps have made it much easier for us to search or verify this information. One of my favorite apps is Medscape."

Take a Holistic Approach to Practicing Eye Care

With a host of systemic conditions and associated medications, it can feel daunting to play an active role in the diagnosis and management of these diseases. However, optometrists are in the perfect position to do so.

"So many systemic diagnoses have a bearing on how the eye works and can have direct consequences on ocular health," notes Dr. Myers. "Sharing your knowledge and positioning yourself as a provider invested in your patients' overall health is beneficial both for the community and your own practice—opening the door for future comanagement and referrals to the practice."

An aging population that has a growing need for primary eye care coupled with a looming shortage of ophthalmologists will make this even more important moving forward. "We're going to be the gatekeepers that have to be aware of these medical diagnoses both for early detection of ophthalmic complications as well as ocular manifestations that indicate a systemic issue," Dr. Myers says. "As optometrists, we have a multifaceted part to play to ensure our patients receive optimal and comprehensive care." ■

DIGITAL DEVICES ARE IMPACTING YOUR PATIENTS

By
Courtney Dryer, OD
and
Jennifer Palombi, OD, FAAO

Introduction

Digital eye strain is defined as visual disturbance and/or ocular discomfort related to the use of digital devices.[1] Digital eye strain was previously called computer vision syndrome but was renamed to include all digital devices. Each week, Americans spend 60 hours on digital devices,[1] and 50 to 90% of users report symptoms of digital eye strain.[2] Since the start of the pandemic, the reported number of screen time hours increased from 10.09 in 2019 to 13.28 hours in 2022.[3] With increased usage of digital devices across all continents and age groups, all device users are at risk for developing symptoms of digital eye strain.

Patients who suffer from digital eye strain report a variety of symptoms including headaches, ocular discomfort, dry eye, diplopia, and blurred vision at near and far after prolonged computer use.[4] Digital eye strain studies show a significant impact on both visual comfort and productivity after only 4 hours of screen time.[5] By identifying the symptoms of digital eye strain and recommending appropriate management strategies, an eye care practitioner (ECP) can readily address patient complaints from digital device use.

Symptoms of Digital Eye Strain

Eye strain or asthenopia is the feeling of pain, ache, and tired eyes.[6] Irritation, burning, redness, and double vision are also reported.[7] In studies conducted in countries across the globe including India,[8] Italy,[9] Australia,[10] and Mexico,[11] asthenopia was a common symptom among computer operators. Frequent breaks and proper workspace ergonomics reduced those with symptoms from 63.4% to 25.2%.[10] It is unclear whether age is a factor, but asthenopia seems to be more prevalent in women.[12] Headache frequency increased in correlation with the duration of computer work and decreased when screen distance was lengthened beyond 50 cm.[13]

Initial studies divided digital eye strain symptoms into two groups: external and internal symptoms.[14] External symptoms relate more to dry eye and include burning, irritation, ocular dryness, and tearing. Internal symptoms may include eye strain, headache, eye ache, diplopia, and blur and may be caused by refractive, accommodative or vergence abnormalities.[15] External symptoms should be managed with dry eye treatment, while internal symptoms of digital eye strain can be alleviated with proper spectacle and/or contact lens corrections. Extraocular symptoms have been added as a mechanism of digital eye strain and include neck stiffness, neck pain, shoulder pain, headache, and backache. These symptoms are due to improper computer screen placement resulting in muscle strain.[7]

Understanding Accommodative Response with Digital Device Use

Accommodative micro-fluctuations (AMF) are states of temporal ocular instability due to spasms of the ciliary body when viewing a near target.[16] AMF is divided into a low (less than 0.6 Hz) and high frequency (1.0-2.3 Hz) component. The low frequency component may have a neurological component while the high frequency component may be related to arterial pulse frequency. If the ciliary muscles tire, the slight increase in accommodative load triggers the high frequency component of AMF to rise. AMF can be measured by changes in the refractive power of the eye over time with an auto-refractor. These micro-fluctuations are indicative of eye strain.

The Digital Zone Optics® lens design found in Biofinity Energys® consists of multiple aspheric curves across the front surface of the optic zone, which may ease asthenopia without impacting distance vision. In evaluating the potential effectiveness of the Digital Zone Optics® lens design found in Biofinity Energys® for reducing high frequency AMF, investigators in a 2020 study demonstrated the relationship between a higher AMF response and increased asthenopia, as well as a reduction in high frequency AMF with the Digital Zone Optics® lens design when compared to a spherical lens. Reducing the AMF response may help alleviate eye strain[17*] for Biofinity Energys® wearers.

Dry Eye Evaluation

Dry eye is a multi-factorial disease of the ocular surface characterized by a loss of homoeostasis of the tear film.[18] Dry eye can be the result of either decreased lacrimal tear secretion or excessive evaporation. Conditions such as Sjogren's syndrome, obstruction of the lacrimal glands, reduced sensory input from the trigeminal nerve, or damage to the facial nerve can reduce tear output. Evaporation can result from increased corneal exposure, meibomian gland dysfunction, low blink rate, or ocular surface disorders. Decreased blink rate, incomplete blinking, corneal exposure, contact lens wear, environmental factors, systemic disease, and medication usage are contributing factors to digital eye strain secondary to dry eye. Recognizing the presence and cause of dry eye symptoms in managing the patient with digital eye strain improves decision-making and outcomes for those patients.

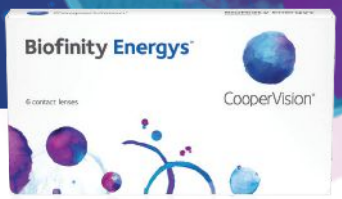
Blink Rate

Blinking is vital to maintaining the tear film and ocular health. Blinking expresses and spreads lipids across the ocular surface, minimizing tear evaporation. Decreased blink rate or incomplete blinking may play a role in digital eye strain. Studies show that blink rate is reduced during computer use (3.6-11.6 blinks/minute) compared to normal blinking (17-26 blinks/minute).[1] Blink rates also decrease as cognitive tasks increase and as font size and contrast are reduced. Squinting is common during computer work to improve concentration, increase focus, and reduce glare.[6] When compared to a book, study participants describe electronic text as more blurred, which may lead to squinting and adversely affect blink rate.[13]

Workspace Configuration and Other Strategies

Proper ergonomics should be discussed with patients. The global pandemic has many patients working from home. Office setups and device usage have changed. Many patients have shifted to laptop use over office desktops. Poor workstation or improper ergonomics may be a cause for symptoms such as back, neck, shoulder, and wrist pain. The United States Occupational Safety and Health Administration (OSHA) recommends a desktop viewing distance between 50 to 100 cm. The center of the computer monitor should be 15-20 degrees below eye level.[4] The contrast of the word to the background, office lighting, and glare from the screen should also be evaluated.[7]

All patients should be educated on quality blinking with complete lid closure, the 20-20-20 rule for visual breaks, and proper ergonomics. Frequent breaks allow the accommodative system to relax and reduce the symptoms of digital eye strain.[7] A humidifier may reduce the symptoms of dry eye associated with environmental factors.[19] In addition, consider a contact lens option like Biofinity Energys® that may help address two key symptoms associated with digital eye strain for contact lens wearers: dryness and tiredness.**



Comfort

Maintaining comfortable lens wear in digital device users is crucial. Aquaform® Technology used in all Biofinity® lenses allows for a naturally wettable silicone hydrogel material without the need for surface treatment. In the matrix of long silicone chains, hydrogen bonds form to lock water molecules within the lens for a comfortable lens-wearing experience. In fact, in a recent market assessment of 150 wearers, patients rated Biofinity Energys® almost 9 out of 10 for initial comfort.[20] Patients new to Biofinity Energys® not only found the lens initially very comfortable, they also reported that they continued to find the lens comfortable at follow up.[21] At the conclusion of the assessment, all participating patients rated Biofinity Energys® 9 out of 10 for overall comfort.[22]

Vision

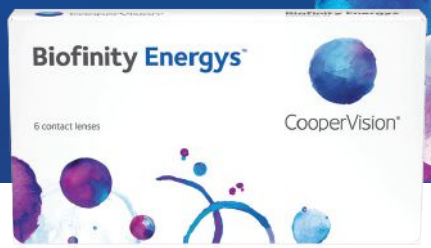
In addition to the comfort benefits of the Biofinity® family, Biofinity Energys® lenses feature the Digital Zone Optics® lens design, which helps with eye tiredness caused by focusing on digital devices. Multiple front-surface aspheric curves distribute power evenly to simulate positive power across the entire optic zone, so wearers can change focus from on-screen to off-screen and back with less effort. This eases accommodative burden and may help reduce ciliary stress.[17*] Distance vision is not adversely impacted by the unique Digital Zone Optics® lens design, and fitting Biofinity Energys® in practice is no different to fitting a standard, spherical, single vision, soft lens. ECPs agree that Biofinity Energys® provides excellent vision for their patients[23] and that Biofinity Energys® is their first choice when fitting monthly replacement lenses.[24]

Patient Satisfaction

Rather than asking patients if they use digital devices, perhaps the more useful route in today's world is to ask how many types of screens they use regularly and for how long each day. Patients sometimes assume that eye strain and fatigue are expected side effects of sustained screen viewing. Fitting Biofinity Energys® allows ECPs to proactively address some of the symptoms of digital eye strain for greater wearer satisfaction. Patients experiencing symptoms of digital eye strain have high overall satisfaction when wearing Biofinity Energys®.[25] In fact, patients new to Biofinity Energys® in the aforementioned assessment rated the lens 9 out of 10 for overall satisfaction and expressed satisfaction specifically with their levels of eye tiredness[25] and dryness.[26] Finally, patients who are satisfied with their contact lens experience are likely to become a rich referral source for the practice, as evidenced by the fact that 4 in 5 patients experiencing symptoms of digital eye strain reported that they would recommend Biofinity Energys® to friends or family after trialing the lens themselves.[27]

Conclusion

Insights shared here illustrate that patients benefit when ECPs take the time to provide general advice for the management of digital eye strain and that relief from accommodative stress is possible. Biofinity Energys® has been designed to meet the visual demands of patients' modern lifestyles and may benefit both existing and new contact lens wearers who routinely use digital devices.



Learn more about digital device use and contact lens wear.

Author Bios:

Jennifer Palombi, OD, FAAO joined CooperVision in 2017 and currently serves as the Senior Manager of Professional Education and Development for the U.S. In her role, she provides clinical insights to cross functional teams and manages internal and external professional communication and education programs related to CooperVision's broad portfolio of products and services.

Clinically, she has a particular interest in specialty contact lenses, as well as neuro-ophthalmic and orbital disease. She is a graduate of The Ohio State University College of Optometry in Columbus, Ohio and is a Fellow of the American Academy of Optometry. Dr. Palombi lectured extensively on both ocular disease and contact lens topics during her 20 years of clinical practice, which included private practice, hospital-based and OD/MD practice settings. In 2020, Dr. Palombi was named to Vision Monday's "Most Influential Women in Optical" in the Mentors category.

Courtney Dryer, OD earned her doctorate from Southern College of Optometry, Memphis, Tennessee in 2011. She opened her own practice Autarchic Spec Shop in 2013 in Charlotte, North Carolina. She has had the privilege of writing for numerous optometric publications and serving in various industry capacities. In 2015, Vision Monday named her a "Rising Star" and one of the "Most Influential Women in Optical." Her optometric passions include practice management, specialty contact lenses, and dry eye management.

Footnotes

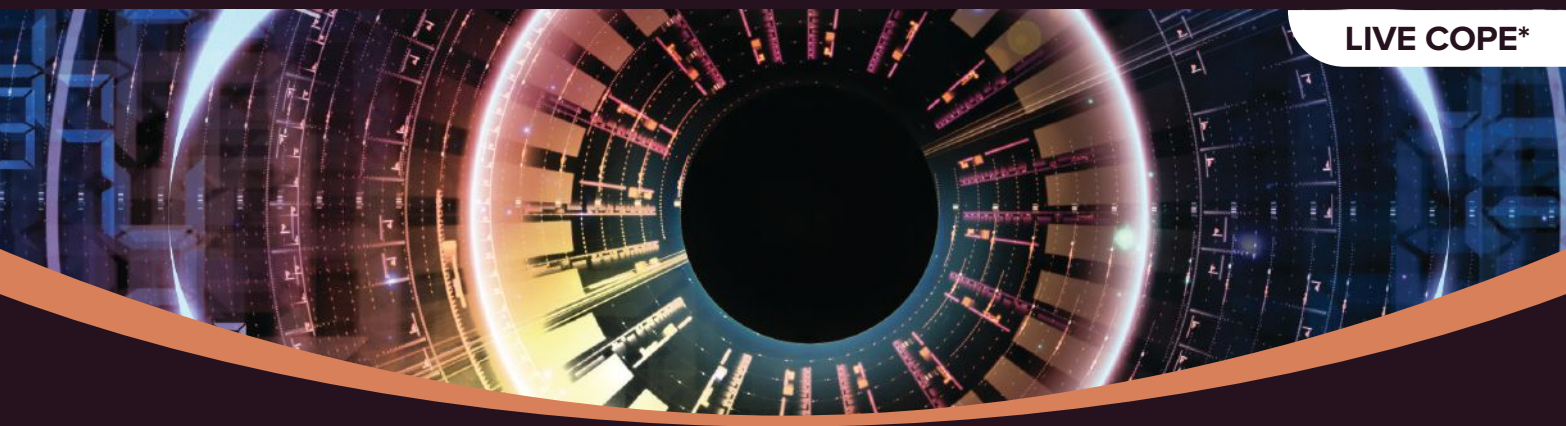
* Based on a statistically significant difference of the mean change in Accommodative Microfluctuations and when compared to Biofinity sphere after reading on an iPhone for 20 minutes at a distance of 25 cm.
** US monthly single vision lens.

References

1. Coles-Brennan C, Sulley A, Young G. Management of digital eye strain. Clin Exp Optom. 2019;102(1):18-29. doi:10.1111/cxo.12798 **2.** Computer Vision Syndrome. 2022. https://www.aoa.org/healthy-eyes/eye-and-vision-conditions/computer-vision-syndrome?sso=y **3.** COVID-19: Screen Time spikes to over 13 hours per day according to Eyesafe Nielsen estimates. Eyesafe. Accessed 19 Aug 2022, https://eyesafe.com/covid-19-screen-time-spike-to-over-13-hours-per-day/ **4.** Rosenfield M. Computer vision syndrome: a review of ocular causes and potential treatments. Ophthalmic Physiol Opt. 2011;31(5):502-15. doi:10.1111/j.1475-1313.2011.00834.x **5.**Rossignol AM, Morse EP, Summers VM, Pagnotto LD. Video display terminal use and reported health symptoms among Massachusetts clerical workers. J Occup Med. 1987;29(2):112-8. **6.** Sheedy JE, Hayes JN, Engle J. Is all asthenopia the same? Optom Vis Sci. 2003;80(11):732-9. doi:10.1097/00006324-200311000-00008 **7.** Loh K, Redd S. Understanding and preventing computer vision syndrome. Malays Fam Physician. 2008;3(3):128-30. **8.** Bhanderi DJ, Choudhary S, Doshi VG. A community-based study of asthenopia in computer operators. Indian J Ophthalmol. 2008;56(1):51-5. doi:10.4103/0301-4738.37596 **9.** Mocci F, Serra A, Corrias GA. Psychological factors and visual fatigue in working with video display terminals. Occup Environ Med. 2001;58(4):267-71. doi:10.1136/oem.58.4.267 **10.** Dain SJ, McCarthy AK, Chan-Ling T. Symptoms in VDU operators. Am J Optom Physiol Opt. 1988;65(3):162-7. doi:10.1097/00006324-198803000-00004 **11.** Sánchez-Román FR, Pérez-Lucio C, Juárez-Ruíz C, Vélez-Zamora NM, Jiménez-Villarruel M. [Risk factors for asthenopia among computer terminal operators]. Salud Publica Mex. 1996;38(3):189-96. Factores de riesgo para la astenopía en operadores de terminales de computadoras. **12.** Shima M, Nitta Y, Iwasaki A, Adachi M. [Investigation of subjective symptoms among visual display terminal users and their affecting factors--analysis using log-linear models]. Nihon Eiseigaku Zasshi. 1993;47(6):1032-40. doi:10.1265/jjh.47.1032 **13.** Chu C, Rosenfield M, Portello JK, Benzoni JA, Collier JD. A comparison of symptoms after viewing text on a computer screen and hardcopy. Ophthalmic Physiol Opt. 2011;31(1):29-32. **14.** Portello JK, Rosenfield M, Chu CA. Blink rate, incomplete blinks and computer vision syndrome. Optom Vis Sci. 2013;90(5):482-7. doi:10.1097/OPX.0b013e31828f09a7 **15.** Sheppard AL, Wolffsohn JS. Digital eye strain: prevalence, measurement and amelioration. BMJ Open Ophthalmology. 2018;3(1):e000146. doi:10.1136/bmjophth-2018-000146 **16.** Campbell FW, Robson JG, Westheimer G. Fluctuations of accommodation under steady viewing conditions. J Physiol. 1959;145(3):579-94. doi:10.1113/jphysiol.1959.sp006164 **17.** Kajita M, Muraoka T, Orsborn G. Changes in accommodative micro-fluctuations after wearing contact lenses of different optical designs. Cont Lens Anterior Eye. 2020;43(5):493-496. doi:10.1016/j.clae.2020.03.003 **18.** Buckley RJ. Assessment and management of dry eye disease. Eye (Lond). 2018;32(2):200-203. doi:10.1038/eye.2017.289 **19.** Tsubota K. Tear dynamics and dry eye. Progress in Retinal and Eye Research. 1998/10/01/ 1998;17(4):565-596. doi:https://doi.org/10.1016/S1350-9462(98)00004-4 **20.** CooperVision. CVI data on file 2022. US in market assessment survey conducted by ECPs: N=150, patients wearing Biofinity Energys contact lenses. New wearers wore them for one week. Initial comfort 8.9/10. **21.** CooperVision. CVI data on file 2022. US in market assessment survey conducted by ECPs: N=83, habitual contact lens patients refit and new contact lens patients fit into Biofinity Energys contact lenses after one week of wear. Initial comfort 8.5/10, overall comfort 8.9/10. **22.** CooperVision. CVI data on file 2022. US in market assessment survey conducted by ECPs: N=150, patients wearing Biofinity Energys contact lenses. **23.** CooperVision. CVI data on file 2022. US in market assessment survey conducted by 15 ECPs: N=150, Patients wearing Biofinity Energys contact lenses. New wearers wore contact lenses for one week. ECP's Top 2 Box: 100%. **24.** CooperVision. CVI data on file 2022. US in market assessment survey conducted by 15 ECPs: N=150, Patients wearing Biofinity Energys® contact lenses. New wearers wore contact lenses for one week. ECPs post-IMA Top 2 Box: 87%. **25.** CooperVision. data on file 2022. US in market assessment survey conducted by ECPs: N=62, habitual contact lens patients refit and new contact lens patients fit into Biofinity Energys contact lenses after one week of wear and currently experiencing digital eye strain. Average Rate 8.7/10. **26.** CooperVision. CVI data on file 2022. US in market assessment survey conducted by ECPs: N=62, habitual contact lens patients refit and new contact lens patients fit into Biofinity Energys contact lenses after one week of wear and currently experiencing digital eye strain. Average Rate 8.5/10. **27.** CooperVision. CVI data on file 2022. US in market assessment survey conducted by ECPs: N=62, habitual contact lens patients refit and new contact lens patients fit into Biofinity Energys contact lenses after one week of wear and currently experiencing digital eye strain. 84% went on to recommend to family and friends.

CooperVision®

A Medscape LIVE! CONFERENCE



LIVE COPE*

NEW TECHNOLOGIES & TREATMENTS IN EYE CARE

NOVEMBER 11–13, 2022

HILTON ORLANDO BUENA VISTA PALACE | 1900 E. BUENA VISTA DRIVE
ORLANDO, FLORIDA

IN-PERSON EVENT

PROGRAM CHAIR

Paul M. Karpecki, OD, FAAO
Kentucky Eye Institute
Director of Cornea &
External Disease
Associate Professor
University of Pikeville
Kentucky College
of Optometry
Lexington, Kentucky

PRESENTING FACULTY

Douglas Devries, OD
Co-founder
Eye Care Associates of Nevada
Associate Clinical Professor
of Optometry
Sparks, Nevada

Mark Dunbar, OD, FAAO
Director of Optometry
University of Miami
Miami, Florida

Brianna Rhue, OD, FAAO
West Broward
Eyecare Associates
Tamarac, Florida

Eric Schmidt, OD, FAAO
President and Founder
Omni Eye Specialists
Wilmington, North Carolina

Earn up to 20 LIVE COPE credits*
8 hours of TQ**

For more information and to register, visit:
www.reviewedu.com/ntt-orlando

REGISTER

COPE | UAB SCHOOL OF OPTOMETRY The University of Alabama at Birmingham | PIM Postgraduate Institute for Medicine

*COPE approval pending
*Florida Board of Optometry approval pending
**8 hours of TQ approval is pending for optometrists licensed in Florida or other states requiring "Transcript Quality" courses for re-licensure.

Partially supported by an unrestricted educational grant from Bausch + Lomb.

REVIEW Education GROUP

HOW HYPERTENSION AND STROKE AFFECT THE EYE

ODs play a vital role in protecting patients from both chronic and acute vascular events. Here's what to look for and how to react.

BY SAIDIVYA KOMMA, OD, AND KRISTINE LOO, OD
KERNERSVILLE, NC

Hypertension affects 47.3% of the adult United States population, with one in five of these individuals unaware of their condition and only one in four having it under control.[1] Meanwhile, one stroke occurs every 40 seconds and one death from stroke every 3.5 minutes in the US.[2] It is no coincidence that hypertension is the leading cause of stroke.[3]

Given the prevalence of these conditions, optometrists in a primary care setting encounter affected patients daily. When primary eyecare providers examine the blood vessels of the eyes, it yields clues to systemic vascular status. As a result, it is important to address and manage the ocular manifestations of hypertension and stroke, which could potentially save lives.

First and foremost, the patient's symptoms on an initial intake or history form may elevate level of suspicion. Risk factors for hypertension and stroke that can be gathered from the history form alone include the following:[3]

- Age >65 years old
- African-American race
- Male sex
- Obesity
- Tobacco/alcohol consumption
- (+) Family history
- Comorbidities:
  - Diabetes
  - Cardiovascular disease
  - High cholesterol
  - Sleep apnea
  - Kidney disease

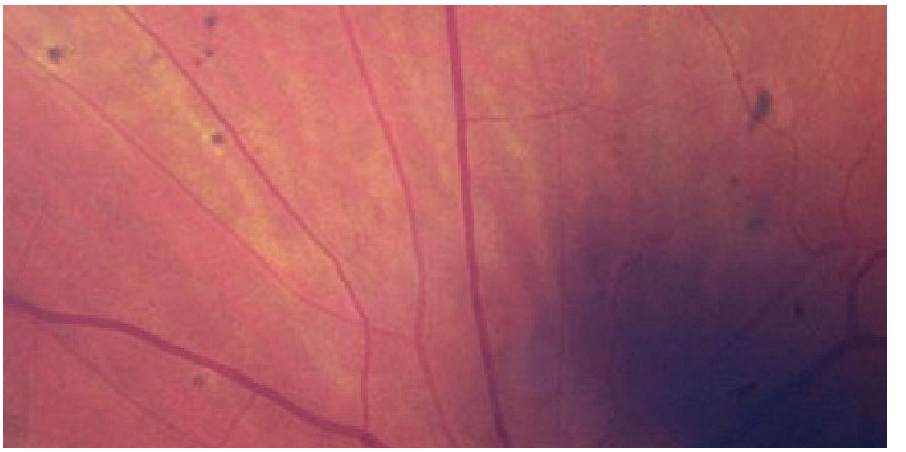


Fig. 1. Elschnig spots seen in a patient with hypertensive retinopathy.

Hypertension on Routine Exam

In addition to taking a thorough history, make blood pressure (BP) measurement a part of the routine exam for patients with the above-mentioned risk factors. Not only is this the best way to assess for control in existing hypertensive patients, but it can also alert them about undiagnosed hypertension, as the condition is largely asymptomatic in nature.

The diagnosis of hypertension is made through serial BP readings taken throughout the day, so having

About the authors

Dr. Komma serves as an externship coordinator and staff optometrist at the Kernersville VA Health Care Center. She graduated from the Pennsylvania College of Optometry and completed her ocular disease residency at the Salisbury VA Medical Center. **Dr. Loo** is a staff optometrist and eye clinic section chief at the Kernersville VA Health Care Center. She graduated from the Illinois College of Optometry and completed her residency in primary care/ocular disease at the Salisbury VA Medical Center. They have no financial interests to disclose.

more information may aid the patient or their primary care provider in the diagnosis. In 2017, the American College of Cardiology and American Heart Association (AHA) lowered the threshold blood pressure reading for the diagnosis of hypertension to ≥130/80, as studies found that doing so reduced the risk of mortality by 27%.[4]

In patients with elevated BP readings in-office (the aforementioned ≥130/80), it is important to assess for headaches, arrhythmia, vision loss, tinnitus, fatigue, nausea, vomiting, confusion, chest pain, tremors, muscle weakness and tingling or numbness, as these are all common signs and symptoms of a stroke requiring urgent evaluation.[2] If a patient presents with hypertensive crisis (>180/120), even without symptoms, at the least an attempt should be made to call the general physician; with no other alternative, the patient should be advised to seek immediate care at an emergency room.

In asymptomatic patients with stage 1 or stage 2 hypertension, dilation without phenylephrine is indicated due to the drop's potential to elevate blood pressure as a vasoconstrictor (*Table 1*). If phenylephrine is required to gain access to the retinal periphery, punctal occlusion can be used to prevent systemic absorption.

The pathophysiology of benign essential hypertension, which accounts for 95% of hypertensive patients, is complex.[1,3] No single identifiable cause accounts for elevated BP in these patients but rather a combination of lifestyle and genetic risk factors. The other 5% of hypertensive patients have a direct, underlying renal or adrenal disease.[1,3] BP elevates when normal cardiac output is met by increased peripheral resistance in the arterioles due to vasoconstriction. The main culprit behind excess vasoconstriction is an overactive sympathetic nervous system.[5] This causes endothelial cell dysfunction in medium- to large-sized arteries, which leads to thrombus formation and turbulent blood flow, and ultimately increases the risk for clot formation.[5]

Table 1. Staging of Hypertension[4]

BLOOD PRESSURE STAGING	SYSTOLIC	AND/OR	DIASTOLIC
Normal	<120	and	<80
High Normal	120-129	and	<80
Stage 1 Hypertension	130-139	or	80 to 89
Stage 2 Hypertension	>140	or	>90
Hypertensive Crisis	>180	and/or	>120

Source: American Heart Association

Table 2. Staging of Hypertensive Retinopathy *(Keith-Wagener-Barker Classification)*

Grade	Characteristics
Grade 1	Mild, generalized arteriolar narrowing
Grade 2	A/V nicking (at the arteriovenous crossing, the artery lies over the vein and shares the same outer sheath—increased sclerosis can lead to compression of the vein and thrombus formation)
Grade 3	Changes from breakdown of the blood-retina barrier due to acute elevations in BP: retinal edima, cotton wool spots and exudates, hemorrhages.
Grade 4	· Malignant hypertension (>180/120) · Papilledema and macular star

The inner retinal vasculature is autoregulated—meaning that there is an absence of sympathetic nerve supply, unlike the choroidal vasculature that only has a sympathetic nerve supply.[6] Elevated BP in the background of autoregulation initially causes vasoconstriction, but persistent elevation overrides this compensatory mechanism, leading to vasospasms, thickening of the vessel layers and endothelial damage.[7] As a result, chronic hypertension leads to retinal arteriolar narrowing and, eventually, the breakdown of the blood-retinal barrier.

These changes can be observed funduscopically as increased arterial light reflexes, artery-vein compression, cotton wools spots or inner retinal hemorrhages with exudates.[7,8] Meanwhile, hypertensive choroidopathy will present as areas of focal infarcts, seen funduscopically as Siegrist streaks and Elschnig spots.[9] Although these are changes that may be seen on routine exam in hypertensive patients, the presence of grade 2 hypertensive retinopathy and beyond increases the long-term risk for stroke and suggests the need for tighter BP control (*Table 2*).[10]

Keep an Eye Out

Transient monocular vision loss (TMVL), transient ischemic attacks (TIA), branch retinal artery occlusions (BRAO) and central retinal artery occlusions (CRAO) are all forms of acute retinal arterial ischemia that are considered ocular and systemic emergencies requiring proper and immediate diagnosis and management by the eyecare provider.[13] While the signs, symptoms and visual outcomes may be different between each entity, their overall systemic and neurologic significance and management are the same and should be reviewed.

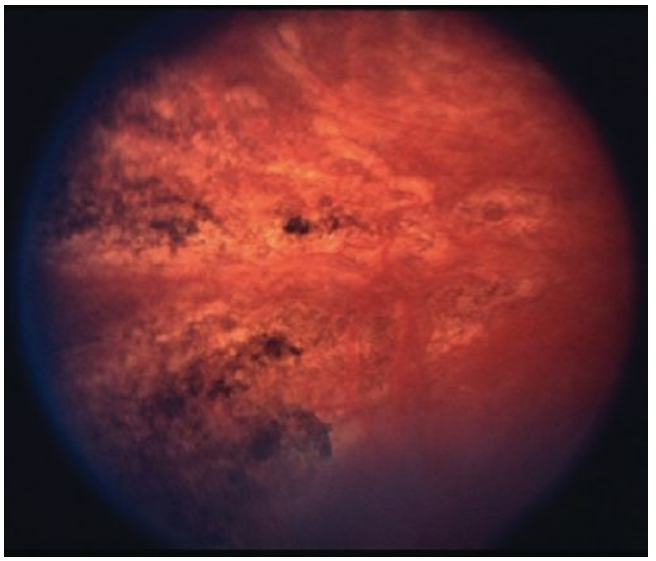


Photo: Retina Image Bank

Fig. 2. Siegrist streaks, a rare manifestion of hypertensive choroidopathy.

Understanding the protocols for timely referral of these patients may be lifesaving, as risks for stroke are at the greatest within the first few days of onset of these signs or symptoms.[13]

• *TMVL* is a temporary episode of vision loss in one eye that can last a few minutes to hours followed by spontaneous recovery. TMVL of an ischemic or vascular nature is caused by impaired blood flow to the retina due to either a vaso-occlusive or embolic event from atherosclerotic plaques; this is sometimes referred to as a retinal TIA.[11,12] The term amaurosis fugax (from the Greek meaning fleeting darkness) is often used interchangeably with TIA to describe interrupted vision.[11]

TIAs usually last less than one hour and have a high risk of subsequent cerebral ischemia and stroke—at its highest during the 14 days following initial onset of symptoms.[11] It has been reported that 10% to 15% of patients with a TIA will have a stroke within 90 days, with approximately half occurring within 48 hours. Patients who survive the initial high-risk phase have a 10-year stroke risk of approximately 19%. Considered along with other related conditions, these patients present a 43% risk over 10 years of experiencing a stroke, myocardial infarction or vascular death.[13]

Common causes of TMVL include an embolus of the internal carotid artery or from the heart, atherosclerosis, giant cell arteritis (GCA) and carotid artery dissection.[12] Cases of TMVL deserve emergent referral for neurologic imaging for stroke prevention and to confirm a diagnosis. Symptoms of vascular TMVL due to a retinal source include episodes of painless blurring of vision (transient visual obscuration) described as a veil, shade or haze that either ascends or descends vertically and darkening or blacking out of vision, lasting seconds to minutes, that spontaneously resolve. Complaints of "zig-zag lines," "colors," "heat waves" or "sparkles," known as scintillating scotomas, are visual symptoms of aura more commonly associated with vasospastic migraines than with ischemia.[11]

TMVL can occur secondary to arteritic vascular disease, thus it is important to order blood work to test for GCA in patients over the age of 50.[11] Those with elevated inflammatory markers, such as elevated c-reactive protein (CRP) or elevated erythrocyte sedimentation rate (ESR) and elevated platelets along with new-onset headaches, jaw claudication and scalp tenderness should be referred immediately for temporal artery biopsy and started on high doses of corticosteroids.[11]

• *Retinal artery occlusions.* BRAO and CRAO are caused by acute occlusions of the retinal vasculature that can lead to sudden painless vision loss and result in retinal infarctions.[14,15] The main cause of these artery occlusions has been identified and suggested to be emboli from the carotid arteries or the heart, with a range from 3% to 96% from ipsilateral carotid artery disease and 24% to 72% from emboli from cardiac sources.[14] Additionally, one study reported that of 375 patients with nonarteritic retinal arterial occlusion, one third had ipsilateral internal carotid stenosis of at least 50% and half had an abnormal echocardiogram.[16]

The ophthalmic artery branches from the distal internal carotid artery at a perpendicular angle and the diameter of the ophthalmic artery is approximately one third of the internal carotid artery. Hence, it is possible for an emboli that causes an artery occlusion to also enter into cerebral circulation, and can therefore lead to cerebral

Patients at Risk for Stroke: The Role of the OD

1. Identify and establish a relationship with the nearest certified stroke center open 24/7.

2. Offer same-day appointments for patients with acute painless monocular vision loss (transient or permanent).

3. If confirmed diagnosis of vascular TMVL, BRAO, CRAO or Malignant Hypertensive Retinopathy, check blood pressure in office, inquire about additional systemic symptoms, consider GCA.

4. Send patient immediately to nearest stroke center or rapid-TIA ED with a note indicating "Ocular TIA" or "Ocular Stroke." Inform and educate patient on the urgency of referral. Call the center to warn them that "a stroke patient is on the way."

Workups in the ED to include:

- Blood work (*e.g.*, CBC with platelets, hA1C, PT, PTT, lipid panel, ESR, CRP)
- Electrocardiography
- MRI, including DWI of brain
- MRA, CTA or carotid ultrasound/transcranial Doppler

Time well spent.

With Chronos Automated Binocular Refraction System, spend more time on what matters most, your patients.

Transform the time you spend on refraction into quality time with your patients. Topcon enables stronger patient consultations, conversations, and loyalty. Simply delegate the upfront binocular autorefraction, keratometry and subjective acuity testing to a technician with the help of the SightPilot guided refraction software.

Discover the true value of Chronos.
Visit us at Academy 2022 - Booth #510.
topconhealthcare.com/chronos

TOPCON Healthcare
SEEING EYE HEALTH DIFFERENTLY

Table 3. Identifying a Patient with TIA[29,30]

ABCD2 Score: a risk assessment tool for patients at risk for a stroke after a TIA. Scores greater than 4 had a statistically significant predictive value for stroke. However, it is recommended that additional information such as brain imaging and carotid ultrasound should be evaluated along with the score assessment to improve diagnostic accuracy.

Risk Factor	Points
Age ≥ 60 years	1
Blood Pressure: initial systolic BP ≥140mm Hg OR diastolic BP ≥ 90mm Hg	1
Clinical features of TIA (choose one): · Unilateral weakness with or without speech impairment OR · Speech impairment without unilateral weakness	 2 1
Duration: · TIA duration >60 minutes · TIA duration 10-59 minutes	 2 1

Table 4. Identifying a Patient with a Stroke[14,31,32]

Be Sure to "Act FAST" *(Adapted from the American Stroke Association)*	Suggested Revisions that Include Ocular Involvement
Warning signs to spot a stroke: • **F**ace drooping. Does one side of the face droop? Ask the patient to smile. Is the patient's smile uneven? • **A**rm weakness. Is one arm weak or numb? Ask the patient to raise both arms. Does one arm drift downward? • **S**peech difficulty. Is speech slurred? • **T**ime to call 911 if signs above are present. Early treatment leads to higher survival rates.	Include symptoms of painless sudden vision loss, TIA or TMVL as a main symptom of stroke: · Act Very FAST: **V**ision, **F**ace, **A**rm, **S**peech, **T**ime[8] · BE FAST: **B**alance, **E**yes, **F**ace, **A**rm, **S**peech, **T**ime[9]

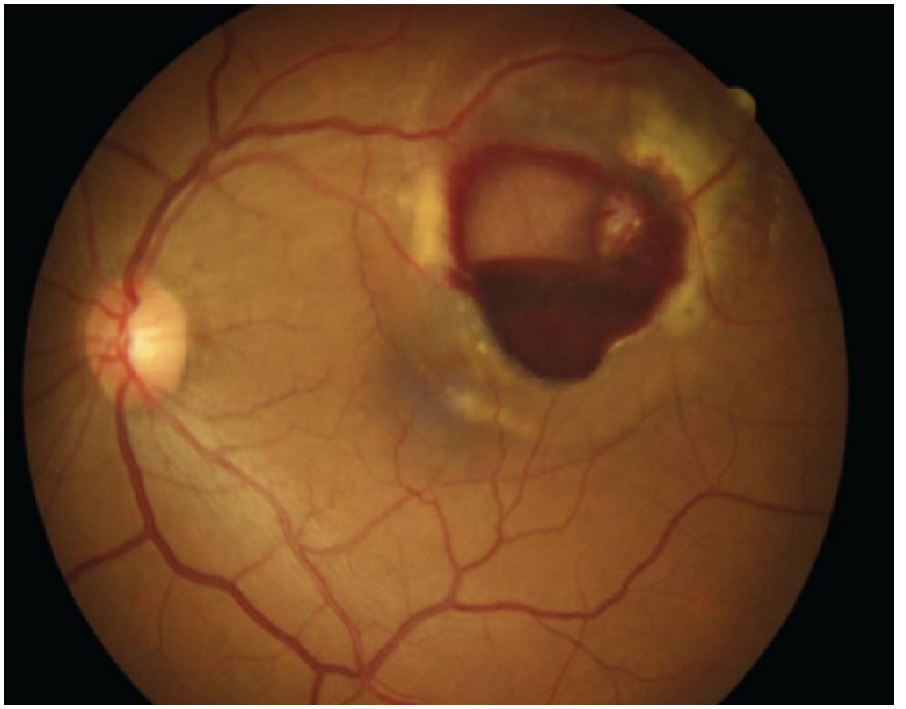


Fig. 3. Retinal arterial microaneurysm.

infarctions.[14] Consequently, studies have shown that acute cerebral infarctions are frequently observed on diffusion-weighted brain imaging in patients with acute retinal artery occlusions.[15]

Acute ocular treatment for visual recovery may only be possible within a short time window, reported to be within hours of symptom onset.[17] The main goal of acute treatment is to attempt to reverse retinal ischemia and restore retinal perfusion.[17] This can be done by increasing the blood oxygen content to the retina through vasodilation, such as carbogen inhalation, or reducing intraocular pressure to help increase the retinal artery perfusion through digital ocular massage, anterior chamber paracentesis or IOP lowering medication.[17,18] Unfortunately, these acute in-office treatments may not result in significant visual recovery, are widely divergent, do not have strong evidence-based data supporting them and do not treat the underlying, more emergent causes.[17,18]

Role of the OD

In 2011 and 2013, the addition of retinal cell death, along with brain and spinal cord cell death as attributable factors to ischemia, was included in the definition of a stroke by the American Stroke Association and the AHA.[14] Since then, several studies have reported the presence of multiple small cerebral infarctions in up to 31% of patients with vascular TMVL, acute BRAO and CRAOs, further emphasizing that acute retinal arterial ischemia is equivalent to a stroke and must be addressed emergently.[14,15,19-23] Findings from the Atherosclerosis Risk in Communities study found that hypertensive retinopathy increases the risk of a stroke two- to threefold, with the Blue Mountains Eyes Study showing a higher risk of combined stroke events in patients with hypertensive retinopathy.[24-27]

For patients presenting with severe BP elevation (commonly >200/120mm Hg) with associated

Menicon

PROGENT

Biweekly cleaning for gas permeable lenses

ORDER ONLINE

www.meniconwebstore.com

Say **goodbye** to protein and deposits

IN 30 MINUTES

NO mechanical rubbing

NO abrasive cleaners

NO wasted time

Biweekly use of **Menicon PROGENT** removes protein build up and helps maintain deposit-free lenses without the mechanical rubbing or abrasive cleaners that can damage plasma treated lenses or complex surface geometries.

Menicon

meniconamerica.com

Photo: Diana Mah, OD

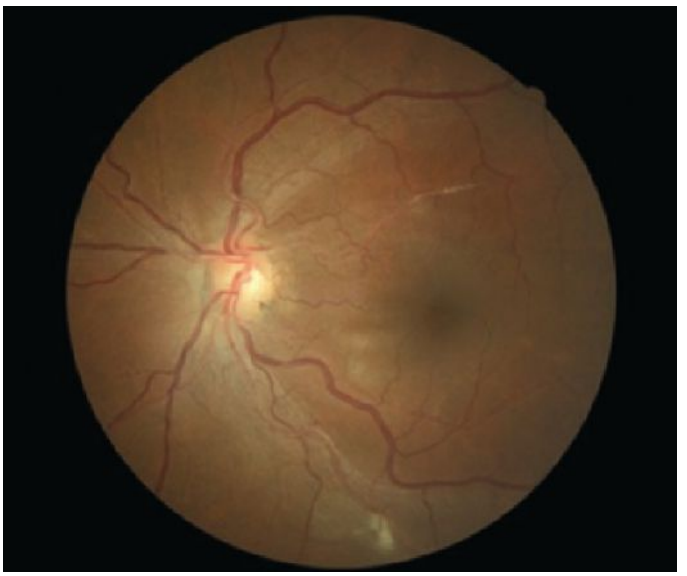


Fig. 4. A patient with grade 3 hypertensive retinopathy.

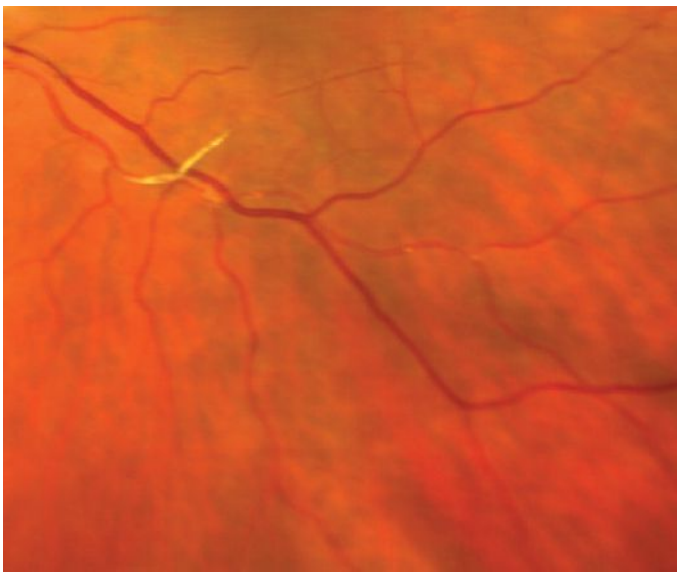


Fig. 5. Platelet-fibrin emboli.

bilateral malignant hypertensive retinopathy, an immediate referral to the emergency department is crucial for diagnostic workup and immediate blood pressure reduction to avoid progressive organ failure.[28]

Identifying a patient with TIA, including vascular TMVL, can be difficult but the use of clinical scores such as the ABCD2 can help those at highest risk of subsequent strokes. Higher scores are associated with a higher risk of stroke (*Table 3*).[29,30]

Using the mnemonic "Act FAST," adapted from the American Stroke Association, can also help identify a patient with a stroke or TIA (Table 4). However, some studies have suggested to add the ocular symptom of sudden vision loss in the acronym to read, "Act VFAST" (act very fast), or to include balance and eyes ("BE-FAST"), either of which could increase screening accuracy and sensitivity (*Table 4*).[14,31,32]

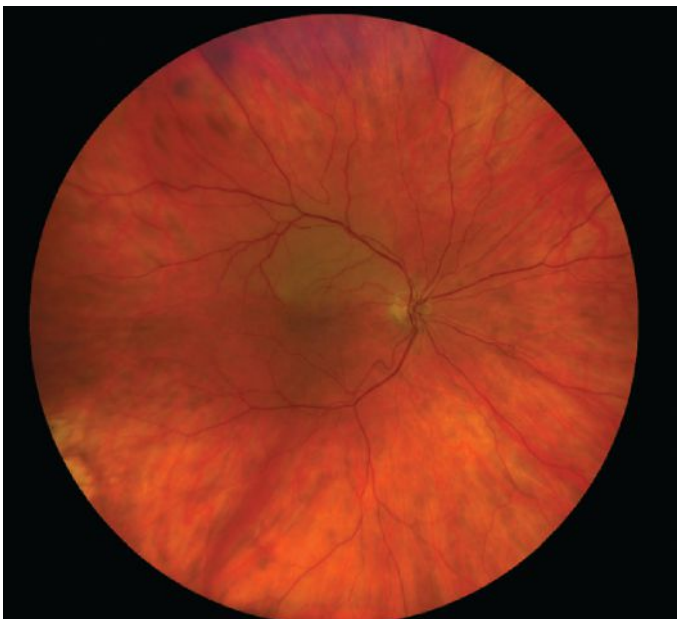


Fig. 6. BRVO is a form of acute retinal arterial ischemia that is considered both ocular and systemic emergencies requiring proper and immediate diagnosis and management.

Once the diagnosis of TIA or vascular TMVL, BRAO or CRAO has been confirmed, an immediate referral to the closest emergency department with a stroke center or a rapid-access TIA clinic should be conducted. Immediate brain imaging, vascular imaging, cardiac monitoring and lab work should all be completed to rule out GCA. MRI with diffusion-weighted imaging sequences is the preferred brain imaging modality because of its most sensitive and specific modality for detection of early ischemic changes in the brain.[15] Multiple small infarctions have been reported to frequently occur ipsilateral to the involved eye on diffusion-weighted MRI of the brain within days of vision loss from acute retinal ischemia.[33] Many of these findings were seen in patients with no neurologic symptoms, further reinforcing the importance of immediate brain imaging and stroke work-up in patients with suspected retinal ischemia.[15]

Takeaways

Eyecare providers can play a pivotal role in proper diagnosis and management for patients at highest risk of a stroke by accurately identifying patients who present to an eye exam with an acute TIA, TMVL, BRAO or CRAO. Following guidelines in concurrence with the AHA/American Stroke Association ensures patients will get fast referral to a stroke center and undergo immediate brain imaging.[14,15] These quick actions provide the opportunity for early preventative treatments that reduce the risk of subsequent life-threatening stroke or cardiovascular events.[14,15]

1. Centers for Disease Control and Prevention. Hypertension prevalence in the US: million hearts. www.millionhearts.hhs.gov/data-reports/hypertension-prevalence.html. March 22 2021. Accessed September 1, 2022.

2. Centers for Disease Control and Prevention. Stroke. www.cdc.gov/stroke/index.htm. June 14, 2022. Accessed September 1, 2022.

3. Centers for Disease Control and Prevention. Facts about hypertension. www.cdc.gov/blood-pressure/facts.htm. July 17, 2022. Accessed September 1, 2022.

4. American College of Cardiology. New ACC/AHA high blood pressure guidelines lower definition of hypertension. www.acc.org/latest-in-cardiology/articles/2017/11/08/11/47/mon-5pm-bp-guideline-aha-2017. November 13, 2017. Accessed September 1, 2022.

5. Saxena T, Ali AO, Saxena M. Pathophysiology of essential hypertension: an update. Expert Rev Cardiovasc Ther. 2018;16(12):879-87.

6. Kiel JW. The Ocular Circulation. Chapter 2, anatomy. San Rafael, CA: Morgan & Claypool Life Sciences; 2010.

7. Hayreh SS. Hypertensive retinopathy. Introduction. Ophthalmologica. 1989;198(4):173-7.

8. Tso MO, Jampol LM. Pathophysiology of hypertensive retinopathy. Ophthalmology. 1982;89(10):1132-45.

9. Pierro L, Pece A, Camesasca F, Brancato R. Hypertensive choroidopathy: a case report. Int Ophthalmol. 1991;15(1):9-14.

10. Ong YT, Wong TY, Klein R, et al. Hypertensive retinopathy and risk of stroke. Hypertension. 2013;62(4):706-11.

11. Jeeva-Patel T, Kabanovski A, Margolin E. Transient monocular visual loss: when is it an emergency? J Emerg Med. 2021;60(2):192-6.

12. Ahmed R, Foroozan R. Transient monocular visual loss. Neurol Clin. 2010;28(3):619-29.

13. Heath Jeffery RC, Chen FK, Lueck CJ. Blackout: Understanding transient vision loss. Aust J Gen Pract. 2021;50(3):136-40.

14. Biousse V, Nahab F, Newman NJ. Management of acute retinal ischemia: follow the guidelines. Ophthalmology. 2018;125(10):1597-1607.

15. Lee J, Kim SW, Lee SC, et al. Co-occurrence of acute retinal artery occlusion and acute ischemic stroke: diffusion-weighted magnetic resonance imaging study. Am J Ophthalmol. 2014;157(6):1231-8.

16. Hayreh SS, Podhajsky PA, Zimmerman MB. Retinal artery occlusion: associated systemic and ophthalmic abnormalities. Ophthalmology. 2009;116(10):1928-36.

17. Cugati S, Varma DD, Chen CS, Lee AW. Treatment options for central retinal artery occlusion. Curr Treat Options Neurol. 2013;15(1):63-77.

18. Chronopoulos A, Schutz JS. Central retinal artery occlusion-A new, provisional treatment approach. Surv Ophthalmol. 2019;64(4):443-51.

19. Tanaka K, Uehara T, Kimura K, et al. Japan TIA Research Group 2009-2011. Features of patients with transient monocular blindness: a multicenter retrospective study in Japan. J Stroke Cerebrovasc Dis. 2014;23(3):e151-5.

20. Lauda F, Neugebauer H, Reiber L, Jüttler E. Acute silent brain infarction in monocular visual loss of ischemic origin. Cerebrovasc Dis. 2015;40(3-4):151-6.

21. Cho KH, Kim CK, Woo SJ, et al. Cerebral small vessel disease in branch retinal artery occlusion. Invest Ophthalmol Vis Sci. 2016 ;57(13):5818-24.

22. Golsari A, Bittersohl D, Cheng B, et al. Silent brain infarctions and leukoaraiosis in patients with retinal ischemia: a prospective single-center observational study. Stroke. 2017;48(5):1392-6.

23. Tanaka K, Uehara T, Kimura K, et al. PROMISE-TIA study Investigators. Comparison of clinical characteristics among subtypes of visual symptoms in patients with transient ischemic attack: analysis of the PROspective Multicenter registry to Identify Subsequent cardiovascular Events after TIA (PROMISE-TIA) Registry. J Stroke Cerebrovasc Dis. 2018;27(6):1711-6.

24. Henderson AD, Bruce BB, Newman NJ, Biousse V. Hypertension-related eye abnormalities and the risk of stroke. Rev Neurol Dis. 2011;8(1-2):1-9.

25. The Atherosclerosis Risk in Communities (ARIC) Study: design and objectives. The ARIC investigators. Am J Epidemiol. 1989;129(4):687-702.

26. Mitchell P, Wang JJ, Wong TY, et al. Retinal microvascular signs and risk of stroke and stroke mortality. Neurology. 2005;65(7):1005-9.

27. Wong TY, Klein R, Couper DJ, et al. Retinal microvascular abnormalities and incident stroke: the Atherosclerosis Risk in Communities Study. Lancet. 2001;358(9288):1134-40.

28. Unger T, Borghi C, Charchar F, et al. 2020 international society of hypertension global hypertension practice guidelines. Hypertension. 2020; 75(6):1334-57.

29. Quinn TJ, Cameron AC, Dawson J, et al. ABCD2 scores and prediction of noncerebrovascular diagnosis in an outpatient population: a case-control study. Stroke. 2009;40(3):749-53.

30. Fothergill A, Christianson TJ, Brown RD Jr, Rabinstein AA. Validation and refinement of the ABCD2 score: a population-based analysis. Stroke. 2009;40(8):2669-73.

31. Lawlor M, Perry R, Plant GT. Is the 'Act FAST' stroke campaign lobeist? The implications of including symptoms of occipital lobe and eye stroke in public education campaigns. J Neurol Neurosurg Psychiatry. 2015;86(7):818-20.

32. El Ammar F, Ardelt A, Del Brutto VJ, et al. BE-FAST: a sensitive screening tool to identify in-hospital acute ischemic stroke. J Stroke Cerebrovasc Dis. 2020;29(7):104821.

33. Biousse V. Acute retinal arterial ischemia: an emergency often ignored. Am J Ophthalmol. 2014;157(6):1119-21.

SEVEN NONRETINAL DIABETIC OCULAR COMPLICATIONS

Besides retinopathy, let's discuss some other ways this condition can manifest in the eye.

BY KRISTINE LOO, OD, AND RACHEL WERNER, OD
KERNERSVILLE, NC

Diabetes, as described by the Centers for Disease Control (CDC), is a chronic condition that affects how your body turns food into energy. It's mainly characterized by elevated blood sugar. The disease occurs when the body does not make any insulin (type 1) or is unable to properly use insulin or produce sufficient insulin (type 2). As a result, blood sugar (glucose) builds up in the blood, giving rise to several complications within the body including of the eyes, kidneys and limbs.[1]

The National Diabetes Statistic Report from the CDC reports that a total of 37.3 million people have diabetes, which is roughly 11.3% of the US population.[2] The condition can lead to several additional medical problems including high blood pressure, high cholesterol, heart disease, stroke, kidney failure, leg and foot amputation and early death.[1] According to the CDC, diabetes is the leading cause of new cases of blindness among adults 18 to 64 years old. Data from 2019 revealed that among US adults 18 and older diagnosed with diabetes, 11.8% reported severe vision difficulty or blindness.[2]

When evaluating a patient with diabetes, there are two critical factors to remember for proper management. First, it is important to obtain the patient's full history of diabetes, as it can contribute to their risk of disease complications. Important risk factors to consider and ask patients about include family history of diabetes, history of viral exposure that may have triggered autoimmune destruction of islet cells (for type 1, examples include Epstein-Barr and cytomegalovirus), autoimmune disease, BMI, age, ethnic background, gestational diabetes, prediabetes, hypertension, cholesterol levels and amount of physical activity (*Table 1*).[3]

Patients with longer durations of diabetes, higher levels of glycemia, greater BMI, higher blood pressure and presence of nephropathy are at greater risk of vision loss from diabetic ocular complications.[4]

Second, it is important to familiarize yourself with the ocular manifestations from diabetes that can be detected early in the disease process to help prevent severe complications, most notably blindness.

Surveillance for diabetic retinopathy is an integral part of eye exams in patients with diabetes largely due to it being one of the most common causes of severe visual impairment. Diabetic retinopathy can be classified broadly as nonproliferative and proliferative retinopathy. Nonproliferative diabetic retinopathy is classified into categories depending on prognostic value of lesion severity and may show microaneurysms, hemorrhages, lipids and/or soft exudates.[5] This stage of the disease occurs early, and patients are most often asymptomatic in the absence of significant macular edema. Progression to proliferative diabetic retinopathy involves advanced damage to the retinal capillaries resulting in the development of hypoxia, ischemia and neovascularization that could lead to vitreous hemorrhage and/or tractional retinal detachment and consequent severe vision loss.[5]

Diabetic macular edema can occur at any stage of retinopathy and is the most common cause of vision loss

About the authors

Dr. Loo is a staff optometrist and eye clinic section chief at the Kernersville VA Health Care Center. She graduated from the Illinois College of Optometry and completed her residency in primary care/ocular disease at the Salisbury VA Medical Center. **Dr. Werner** is a staff optometrist at the Kernersville VA Health Care Center. She graduated from Southern College of Optometry and completed her residency in primary care/low vision rehabilitation at the VA Boston Healthcare System. They have no financial interests to disclose.

Table 1. Risk Factors for Diabetes[3]

Type 1 Diabetes Mellitus	Type 2 Diabetes Mellitus
· Family history of diabetes: having a parent or sibling with type 1 diabetes (child has a 10% risk if one parent has type 1 diabetes or a 20% to 30% risk if both parents have the disease) · Viral exposure: exposure to Epstein-Barr virus, coxsackievirus, mumps virus or cytomegalovirus may trigger the autoimmune destruction of islet cells or directly inject the islet cells · Autoimmune conditions: Hashimoto's disease, Graves' disease, Addison's disease, celiac disease, Crohn's disease or rheumatoid arthritis	· Family history of diabetes: first degree relatives of individuals with type 2 diabetes are three-times more likely to develop the disease · Being overweight or obese: having a BMI ≥25kg/m^2 (risk of diabetes at low BMI may be higher in some ethnic groups, such as in Asians) · Age: 45 years and older · Ethnic background: African American, Hispanic/Latino, American Indian, Alaska Native, Asian American or Pacific Islander · Gestational diabetes: diabetes while pregnant · Prediabetes: patients with impaired glucose tolerance or impaired fasting glucose

in those with diabetic retinopathy.[6] Macular edema results from a buildup of intraretinal fluid within the macula and may present with or without the presence of lipid exudates.[3]

While diabetic retinopathy and/or diabetic macular edema may be the most common manifestation of diabetes in the eye, it is important to remember that all ocular structures can be affected by diabetes and can be evident without the presence of diabetic retinopathy.

Diagnosing these nonretinal ocular complications can also help with early diagnosis and management of diabetes to prevent sight- and life-threatening results.

There are seven nonretinal ocular diabetes complications to remember when evaluating a patient with diabetes: prescription and vision changes, cranial nerve palsies, dry eye, neurotrophic cornea, cataracts, vitreous degeneration or detachment and optic neuropathies (*Figure 1*).

In this article, we're going to discuss the signs, symptoms, risk factors and potential management and treatment options of each nonretinal complication to look out for and consider when evaluating patients with diabetes.

1. Prescription/Vision Changes

One of the first measurements we perform in an eye exam involves the assessment of the patient's visual acuity and refractive status; consequently, detected or patient-reported changes in vision are often the first signs or symptoms of undiagnosed or uncontrolled diabetes.

More specifically, transient changes or fluctuations in vision and prescription can be a key sign of impaired glucose control and may also occur after introduction of diabetes treatment with rapid improvement of glucose control.[7]

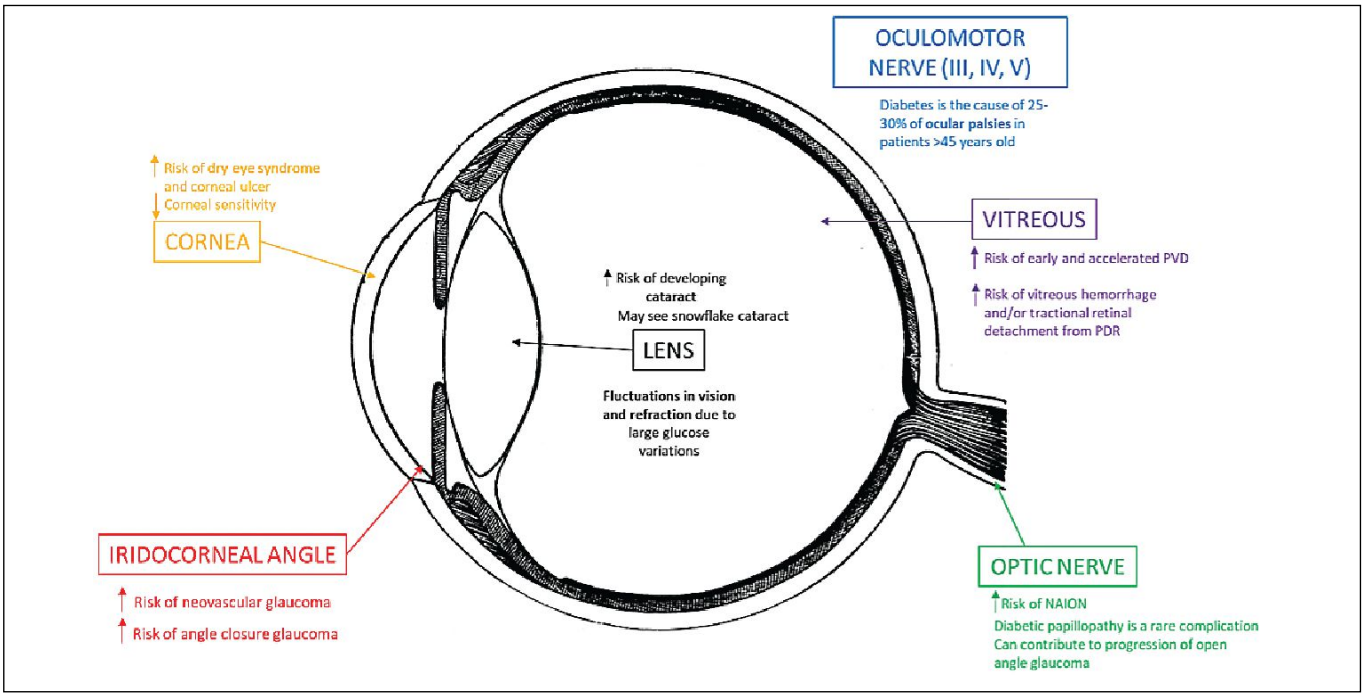


Fig. 1. Shown here are several nonretinal ocular complications that may present in patients with diabetes.[3,7]

These fluctuations can be hyperopic or myopic due to excess glucose entering via the aqueous humor, which then leads to excess fluid absorption of glucose by the crystalline lens.[7] A myopic shift occurs from lens swelling due to the activation of the aldose reductase pathway inducing the intracellular accumulation of sorbitol.[7] On the other hand, a hyperopic shift occurs when there is a significant reduction of the concentration of glucose in the aqueous humor.[7] It is also important to note that a hyperopic shift may also happen with the development of diabetic macular edema from artificially reducing axial length or from cortical cataract formation that is more common in diabetes.[7] These refractive shifts can be several diopters or more; therefore, it is not recommended to finalize the prescription until these large glycemic variations are normalized and stable.

Patients with poorly controlled or long-term diabetes may also present with acquired color vision changes including blue-yellow and/or red-green deficiencies.[3] The development of color vision changes can precede the development of diabetic retinopathy or present in patients who have already been diagnosed with the condition and/or macular edema.[3] The degree of color vision impairment increases with the severity of the macular edema.[3,7]

Additionally, altered accommodative dysfunction, visual field changes and decreased contrast sensitivity may present in patients with uncontrolled blood sugar or with a history of diabetic retinal disease and treatment with panretinal laser photocoagulation.[3]

When patients present with vision fluctuations and changes because of hyperglycemia, it is important to fully assess the eye with a dilated exam to rule out retinal involvement and refer to a retinal specialist for treatment in cases involving more advanced disease. Educating patients about inconsistent refractive status due to uncontrolled blood sugar is important to encourage stability. A follow-up exam for a more accurate refraction is recommended after glucose control has been stabilized for at least several weeks.[7]

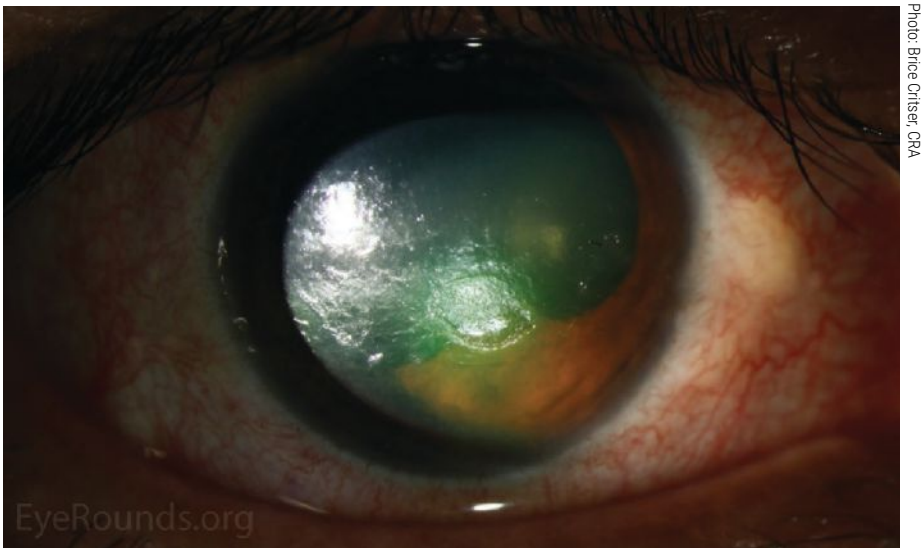


Photo: Brice Critser, CRA

Fig. 2. This image shows a patient with a neurotropic corneal ulcer, a finding that may present in some patients with poorly controlled diabetes.

2. Cranial Nerve Palsies

Ocular motility disorders can develop secondary to diabetic neuropathies involving the third, fourth or sixth cranial nerves often with binocular diplopia but pupillary-sparing signs and symptoms.[7] Diabetes is the cause of 25% to 30% of ocular palsies in patients older than 45 with isolated sixth nerve palsy being five-times more frequent in patients with diabetes compared with nondiabetic patients.[7] Third nerve palsies are also among the more common diabetes-related neuropathies with patients presenting with signs of eyelid ptosis, exotropia and hypotropia of the affected eye with or without acute pain.[3]

Here are some notes on the variations between third, fourth and sixth nerve palsies:

- Usually, third nerve palsies associated with diabetes do not involve the pupil, which is an important diagnostic feature to help rule out other neurological disorders, including compressive lesions or intracranial aneurysms.[3] This can also be confirmed with an MRI of the head.
- Patients with fourth nerve palsies present with complaints of sudden-onset vertical diplopia with the deviation worsening with downward or lateral gaze away from the affected muscle and with the head tilted to the side of the affected muscle.[3]
- Patients with sixth nerve palsies may complain of horizontal diplopia with the affected eye being esotropic.[3] Patients may also turn their heads in the direction of paralysis to reduce the diplopia.[3]

Recovery from these ocular motility palsies can take two to six months without sequalae with the management of other systemic and vascular risk factors including blood sugar and pressure control; however, recurrences are common, especially with recurrent hyperglycemia.[3,7]

Although most diabetic neuropathies are pupil sparing, diabetes can affect the sympathetic innervation of the iris resulting in sluggish pupillary reflexes.[3] Pupils therefore may be more miotic and have a weaker reaction to topical mydriatic drops.[3] Furthermore, patients with a history of panretinal photocoagulation may have an increased pupillary size due to potential damage to the short and long ciliary nerves.[3]

Careful assessment of the pupils and ocular motilities in multiple positions

For the treatment of all stages of neurotrophic keratitis (NK)

NOT JUST ANY SOLUTION

A RESOLUTION

Complete and long-lasting resolution of NK for most patients*[1-4]

- **Up to 72% of patients** achieved complete corneal healing in clinical trials*†[1-3]
- **80% of these patients** remained healed at 1 year (REPARO trial)*[4]

oxervate® (cenegermin-bkbj ophthalmic solution) 0.002% (20 mcg/mL)

* Resolution was evaluated in clinical trials as complete corneal healing, defined as the absence of staining in the lesion area and no persistent staining in the rest of the cornea after 8 weeks of treatment and as <0.5-mm lesion staining at 48-week follow-up.[1-3]

† Key study findings were after 8 weeks of treatment, 6 times daily. REPARO (Study NGF0212): 52 European patients with neurotrophic keratitis (NK) in 1 eye per group; 72% of patients completely healed; vehicle response rate 33.3%. Study NGF0214: 24 US patients with NK in 1 or both eyes per group; 65.2% completely healed; vehicle response rate 16.7%.[2,3]

Important Safety Information

WARNINGS AND PRECAUTIONS

Use with Contact Lens

Contact lenses should be removed before applying OXERVATE because the presence of a contact lens (either therapeutic or corrective) could theoretically limit the distribution of cenegermin-bkbj onto the area of the corneal lesion. Lenses may be reinserted 15 minutes after administration.

Eye Discomfort

OXERVATE may cause mild to moderate eye discomfort such as eye pain during treatment. The patient should be advised to contact their doctor if a more serious eye reaction occurs.

ADVERSE REACTIONS

In clinical trials, the most common adverse reaction was eye pain following instillation which was reported in approximately 16% of patients. Other adverse reactions occurring in 1% to 10% of OXERVATE patients and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation and tearing.

USE IN SPECIFIC POPULATIONS

Pregnancy

There are no data from the use of OXERVATE in pregnant women to inform any drug associated risks.

Lactation

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

Pediatric Use

The safety and effectiveness of OXERVATE have been established in the pediatric population. Use of OXERVATE in pediatric patients 2 years of age and older is supported by evidence from adequate and well-controlled trials of OXERVATE in adults with additional safety data in children.

INDICATION

OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) is indicated for the treatment of neurotrophic keratitis.

DOSAGE AND ADMINISTRATION

Instill one drop of OXERVATE in the affected eye(s), 6 times a day at 2-hour intervals for eight weeks.

To report ADVERSE REACTIONS, contact Dompé U.S. Inc. at 1-833-366-7387 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.

Please see the Brief Summary of full Prescribing Information for OXERVATE on the following page.

References: 1. OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% (20 mcg/mL) [US package insert]. Boston, MA; Dompé U.S. Inc.; 2019. **2.** Bonini S, et al. *Ophthalmology*. 2018;125:1332-1343. **3.** Pflugfelder SC, et al. *Ophthalmology*. 2020;127:14-26. **4.** Data on File. Clinical Study Report (NGF0212). Dompé U.S. Inc., 2016.

See more clinical data
OXERVATE.com/hcp

Dompé

oxervate®
(cenegermin-bkbj ophthalmic solution) 0.002% (20 mcg/mL)

Brief Summary of full Prescribing Information

Consult the full Prescribing Information for complete product information, available at www.oxervate.com/prescribing-information.

INDICATIONS AND USAGE

OXERVATE® (cenegermin-bkbj) ophthalmic solution 0.002% is indicated for the treatment of neurotrophic keratitis.

DOSAGE AND ADMINISTRATION

General Dosing Information

Contact lenses should be removed before applying OXERVATE and may be reinserted 15 minutes after administration.

If a dose is missed, treatment should be continued as normal, at the next scheduled administration.

If more than one topical ophthalmic product is being used, administer the eye drops at least 15 minutes apart to avoid diluting products. Administer OXERVATE 15 minutes prior to using any eye ointment, gel or other viscous eye drops.

Recommended Dosage and Dose Administration

Instill one drop of OXERVATE in the affected eye(s), 6 times a day at 2-hour intervals for eight weeks.

WARNINGS AND PRECAUTIONS

Use with Contact Lens

Contact lenses should be removed before applying OXERVATE because the presence of a contact lens (either therapeutic or corrective) could theoretically limit the distribution of cenegermin-bkbj onto the area of the corneal lesion. Lenses may be reinserted 15 minutes after administration.

Eye Discomfort

OXERVATE may cause mild to moderate eye discomfort such as eye pain during treatment. The patient should be advised to contact their doctor if a more serious eye reaction occurs.

ADVERSE REACTIONS

Clinical Studies Experience

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

In two clinical trials of patients with neurotrophic keratitis, a total of 101 patients received cenegermin-bkbj eye drops at 20 mcg/mL at a frequency of 6 times daily in the affected eye(s) for a duration of 8 weeks. The mean age of the population was 61 to 65 years of age (18 to 95). The majority of the treated patients were female (61%). The most common adverse reaction was eye pain following instillation which was reported in approximately 16% of patients. Other adverse reactions occurring in 1-10% of OXERVATE patients and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation and tearing.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no data from the use of OXERVATE in pregnant women to inform any drug associated risks.

Administration of cenegermin-bkbj to pregnant rats or rabbits during the period of organogenesis did not produce adverse fetal effects at clinically relevant doses. In a pre- and postnatal development study, administration of cenegermin-bkbj to pregnant rats throughout gestation and lactation did not produce adverse effects in offspring at clinically relevant doses.

Lactation

Risk Summary

There are no data on the presence of OXERVATE in human milk, the effects on 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 OXERVATE, and any potential adverse effects on the breastfed infant from OXERVATE.

Pediatric Use

The safety and effectiveness of OXERVATE have been established in the pediatric population. Use of OXERVATE in this population is supported by evidence from adequate and well-controlled trials of OXERVATE in adults with additional safety data in pediatric patients from 2 years of age and older.

Geriatric Use

Of the total number of subjects in clinical studies of OXERVATE, 43.5 % were 65 years old and over. No overall differences in safety or effectiveness were observed between elderly and younger adult patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Carcinogenesis and Mutagenesis

Animal studies have not been conducted to determine the carcinogenic and mutagenic potential of cenegermin-bkbj.

Impairment of fertility

Daily subcutaneous administration of cenegermin-bkbj to male and female rats for at least 14 days prior to mating, and at least 18 days post-coitum had no effect on fertility parameters in male or female rats at doses up to 267 mcg/kg/day (1709 times the MRHOD).

In general toxicology studies, subcutaneous and ocular administration of cenegermin-bkbj in females was associated with ovarian findings including persistent estrus, ovarian follicular cysts, atrophy/reduction of corpora lutea, and changes in ovarian weight at doses greater than or equal to 19 mcg/kg/day (119 times the MRHOD).

Dompé

of gaze is crucial when evaluating cranial palsies. After ruling out other life-threatening and neurological etiologies, counseling patients about the importance of blood sugar control and the length of time for resolution is recommended. Providing an eye patch for temporary relief of diplopia may also be warranted.

3. Dry Eye

Symptoms of dry eye are a common reason why patients seek eye care, and the condition has been linked to diabetes. Patients often present to the clinic with symptoms of ocular discomfort, irritation, grittiness or foreign body sensation with accompanying fluctuating vision changes. However, some patients with diabetes may not have any symptoms due to corneal sensory neuropathy; thus, an evaluation of the cornea for epithelial defects is important.[3]

Studies have shown a higher prevalence of dry eye syndrome resulting from tear film abnormalities in patients with diabetes compared with the general population.[7] One study found that 53% of people with diabetes reported symptoms of dry eye compared with 9% of individuals without diabetes.[5] Common dry eye findings in patients with diabetes include meibomian gland dysfunction and reduced corneal sensitivity. The latter is due to the neuropathy of the ophthalmic division of the trigeminal nerve leading to reduced reflex tear secretion and increased risk of neurotrophic keratitis.[3] Damage to the microvascular supply to the lacrimal gland can also occur in patients with a long history of diabetes thereby impairing lacrimation.[3] The reduced tear production and impaired corneal sensitivity delays corneal healing, so patients should be closely monitored to assess for infection.[5]

Management of patients with dry eye includes the use of lubricating eye drops and proper eyelid disease treatment. Close monitoring of patients with abrasions, recurrent corneal erosion, nonspecific keratitis (NK) and/or corneal ulceration is important, and treatment with the use of bandage contact lens or patching, sodium chloride solutions/ointments, corticosteroids, antibiotic drops or other types of ocular surface treatment may be warranted.[3,5] Educating patients on the importance of diabetes control will also aid in the management of dry eye disease (are you detecting a pattern yet with that advice?).

4. Neurotrophic Keratitis

As mentioned, patients with diabetes may have decreased corneal sensation from neuropathy of the ophthalmic division of the trigeminal nerve, putting them at risk for NK.[3] There are also structural changes that occur within the cornea that can predispose patients with diabetes to NK. Chronic hyperglycemia results in a thickened basement membrane, resulting in poor adhesion between the basement membrane and the stroma.[8,9] This poor adhesion along with delayed wound healing can make neurotrophic corneal ulcers difficult to manage in patients with diabetes (*Figure 2*).

NK should be suspected in patients who have epithelial defects without significant symptoms. Corneal nerve sensitivity testing with a cotton swab wisp, dental floss or corneal esthesiometer should be performed to confirm the diagnosis, and four corneal quadrants should be tested and compared between the eyes. Early NK may look like epithelial staining, which can be managed with copious preservative-free artificial tears and lubricating ointment at night. If there is a large epithelial defect without stromal involvement, a bandage contact lens should be placed on the eye, and prophylactic antibiotic eyedrops should be added. The addition of an amniotic membrane or autologous serum can be used for persistent cases.

If the epithelial defect progresses to an ulcer with stromal involvement, the recommended treatment is tarsorrhaphy with the addition of oral tetracyclines and vitamin C. Corneal neurotization can be performed on patients with recurrent or nonhealing corneal ulcers. Corneal neurotization is the process of grafting healthy nerve tissue onto the distal portion of the damaged corneal nerve to re-establish the neuronal pathway.[10]

5. Cataracts

Patients with type 2 diabetes are four-times more likely to have cataracts than patients without diabetes.[11] It's thought that cataracts progress faster in patients with diabetes due to an increased deposition of advanced glycation end products.[12] The incidence of cataract formation and progression also increases with increased duration of diabetes and poorer blood glucose control.[12] There is an association with increased incidence of posterior subcapsular cataracts, nuclear sclerotic cataracts and cortical cataracts in patients with diabetes.[12]

A rare type of cataract that can occur in uncontrolled diabetes is the snowflake cataract (*Figure 3*). These are generally seen in patients with type 1 diabetes who have poor blood sugar control. A snowflake cataract is described as anterior and posterior cortical opacities with a snowflake-like pattern.[13] There have been case

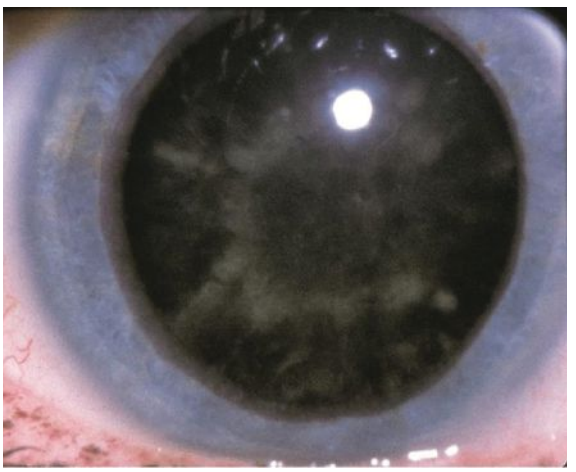


Photo: American Academy of Ophthalmology

Fig. 3. This patient has what's been coined a "snowflake cataract," a rare complication mainly seen in patients with poorly controlled type 1 diabetes.

reports describing the reversal of the cataract with improved blood sugar control.[13]

The mainstay treatment for cataracts in patients with diabetes is cataract surgery. It's important to note that cataract surgery may cause diabetic retinopathy or diabetic macular edema to progress.[11] Consider the implications cataract surgery may have on your patient's visual outcome before referring them. It may be prudent to wait until more severe diabetic retinopathy or any macular edema is appropriately managed by retina providers before thinking about a surgical evaluation of cataract.

6. Vitreous

Elevated blood glucose levels can affect the structural components of the vitreous.[14] Studies have detected non enzymatic glycation of the vitreous collagen in diabetic patients from elevated vitreous glucose levels.[14,15] This can then lead to early and accelerated vitreous degeneration or partial posterior vitreous detachments.[14] Partial posterior vitreous detachments can play a role in proliferative diabetic retinopathy. As new blood vessel growth on the retina expands into the posterior vitreous cortex, it can increase the incidence of vitreous hemorrhage and/or tractional retinal detachment from vitreous traction on these new vessels.[3]

7. Optic Neuropathies

Patients with diabetes are at increased risk for the following forms of optic neuropathy:

Diabetic papillopathy. This is a rare complication of diabetes with an incidence rate of 0.5% (*Figure 4*).[11] The pathogenesis of diabetic papillopathy is not fully understood but thought to be a consequence of limited vascular supply to the peripapillary area and is associated with rapid reductions in blood glucose level.[9]

Patients with diabetic papillopathy generally present with mildly reduced visual acuity. They will have unilateral or bilateral hyperemic nerve swelling and may not present with an afferent pupillary defect (APD) or dyschromatopsia. Typically, they will present with some form of diabetic retinopathy, but not always. The visual field may only show an enlarged blind spot without any other defects.

Diabetic papillopathy is a diagnosis of exclusion. Head imaging and labs should be ordered to rule out other, more ominous forms of optic neuropathy. Diabetic papillopathy tends to resolve within a few months to a year, and the vision will go back to normal or near-normal. There is no current treatment for diabetic papillopathy other than blood sugar control.

Photo: Columbia Eye

Fig. 4. Diabetic papillopathy, pictured here, is an atypical form of NAION causing no physical symptoms.

Non-arteritic anterior ischemic optic neuropathy (NAION). This occurs when microvascular changes lead to ischemia of the anterior portion of the optic nerve. Although diabetes is not a direct cause of NAION, it can increase a patient's risk of developing the condition.[16] One study showed that up to 25% of patients with NAION also have diabetes.[12]

NAION presents as unilateral vision loss with a swollen optic nerve. There is typically an APD present, and visual field testing may show an altitudinal defect. The contralateral eye will show a "disc at risk" with a small cup-to-disc ratio. Immediate testing for ESR, CRP and platelet count must be ordered to rule out giant cell arteritis, especially in patients older than 55.

There is currently no treatment for NAION. It's important to stress the benefits of blood pressure, blood sugar and cholesterol control to these patients. They should also discuss with their primary care physician about potentially avoiding blood pressure medications at night to prevent nocturnal hypotension, which may be a predisposing factor. However, you will need to weigh the pros and cons in this situation, as taking blood pressure medications in the morning rather than the evening has been shown to increase the risk of stroke and heart-related death.

Finally, patients should be counseled on the risk of occurrence to the contralateral eye.

Glaucoma. There is conflicting evidence showing diabetes is a risk factor for glaucoma and it's thought that diabetes can contribute to the progression of open-angle glaucoma. One study showed that open-angle glaucoma patients with diabetes have lower retrobulbar flow in the central retinal artery, suggesting that diabetes influences the vasculature of the optic nerve and can therefore contribute to disease progression.[17] The study also found that open-angle glaucoma patients with diabetes appear to have more impairment of vascular regulation compared with open-angle glaucoma patients without diabetes.[17]

With this in mind, you may want to consider targeting a lower intraocular pressure in your patients with diabetes to further reduce the stress

on the optic nerve and help prevent glaucoma progression.

Patients with diabetes are at higher risk for other types of glaucoma as well. Neovascular glaucoma is a well-known complication of proliferative diabetic retinopathy that can lead to angle closure.[7] This patient population may also be at increased risk for angle-closure glaucoma due to increased prevalence and progression of cataract formation.[7]

Summary

Although retinopathy is a significant part of diabetic eye disease, it is important to remember that diabetes can affect all portions of the eye. Being familiar with these complications can help with early diagnosis and management of the disease to prevent further ocular or vision damage. Take the time to evaluate your patients' eyes from front to back.

Remember that most of the issues related to diabetic eye disease can be managed with consistently improved glucose control from the time of diagnosis. Educate your patients about your exam findings and how they relate to diabetes. Encourage them to regulate their blood sugar not only through prescribed medications, but also through lifestyle modifications, mainly diet and exercise. Lastly, be sure to congratulate your patients who have achieved better blood sugar control, as this is not an easy feat! ■

1. Diabetes report card 2021. CDC. https://www.cdc.gov/diabetes/library/reports/reportcard.html. Accessed July 2022.

2. National Diabetes Statistics Report: Coexisting Conditions and Complications. CDC. https://www.cdc.gov/diabetes/data/statistics-report/coexisting-conditions-complications.html. Accessed July 2022.

3. Evidence-based clinical practice guideline: eye care of the patient with diabetes mellitus. second edition. American Optometric Association. Published October 2019. https://aoa.uberflip.com/i/1183026-evidence-based-clinical-practice-guideline-eye-care-of-the-patient-with-diabetes-mellitus-second-edition/3?m4=. Accessed July 2022.

4. Klein R, Klein BEK. Epidemiology of ocular functions and diseases in persons with diabetes. In: Cowie CC, Casagrande SS, Menke A, et al. Diabetes in America. 3rd ed. Bethesda (MD): National Institute of Diabetes and Digestive and Kidney Diseases (US). 2018.

5. Seewoodhary M. An overview of diabetic retinopathy and other ocular complications of diabetes mellitus. Nurs Stand. 2021;36(7):71-76.

6. Browning DJ, Stewart MW, Lee C. Diabetic macular edema: Evidence-based management. Indian J Ophthalmol. 2018;66(12):1736-50.

7. Feldman-Billard S, Dupas B. Eye disorders other than diabetic retinopathy in patients with diabetes. Diabetes Metab. 2021;47(6):101279.

8. Cousen P, Cackett P, Bennett H, Swa K, Dhillon B. Tear production and corneal sensitivity in diabetes. Journal of Diabetes and its Complications. 2007;21(6):371-73.

9. Sayin N, Kara N, Pekel G. Ocular complications of diabetes mellitus. World Journal of Diabetes. 2015;6(1):92-108.

10. American Academy of Ophthalmology. Corneal neurotization for neurotrophic keratitis. June 27, 2022. EyeWiki. https://eyewiki.aao.org/Corneal_Neurotization_for_Neurotrophic_Keratitis. Accessed August 2, 2022.

11. Skarbez K, Priestley Y, Hoepf M, Koevary SB. Comprehensive Review of the Effects of Diabetes on Ocular Health. Expert Rev Ophthalmol. 2010;5(4):557-77.

12. Jeganathan VS, Wang JJ, Wong TY. Ocular associations of diabetes other than diabetic retinopathy. Diabetes Care. 2008;31(9):1905-12.

13. Jin YY, Huang K, Zou CC, Liang L, Wang XM, Jin J. Reversible cataract as the presenting sign of diabetes mellitus: Report of two cases and literature review. Iran J Pediatr. 2012;22(1):125-28.

14. Sebag J, Ansari RR, Dunker S, Suh KI. Dynamic light scattering of diabetic vitreopathy. Diabetes Technol Ther. 1999;1(2):169-76.

15. Sebag J. Diabetic vitreopathy. Ophthalmol. 1996;103(2):205-6.

16. Lee MS, Grossman D, Arnold AC, Sloan FA. Incidence of nonarteritic anterior ischemic optic neuropathy: increased risk among diabetic patients. Ophthalmol. 2011;118(5):959-63.

17. Shoshani Y, Harris A, Shoja MM, et al. Impaired ocular blood flow regulation in patients with open-angle glaucoma and diabetes. Clinical & Experimental Ophthalmol. 2012;40(7):697-705.


Phoroptor® VRx
DIGITAL REFRACTION SYSTEM
Reichert
TECHNOLOGIES
AMETEK

MORE **EFFICIENT.**
BETTER **CARE.**

Refract safely and efficiently from across the room or across the Internet with Reichert's complete line of digital refraction devices, featuring **Phoroptor® VRx,** the most advanced Phoroptor® and **ClearChart® 4**, the pixel-perfect Digital Acuity System.

Improve glaucoma care with **Ocular Response Analyzer® G3** featuring Corneal Hysteresis + IOPcc and **Tono-Pen AVIA®**, the most trusted handheld tonometer.

WATCH NOW AT
REICHERT.COM

Reichert®
AMETEK®

passionate about eye care

MAKING THE CONNECTION: SLEEP DISORDERS, OCULAR EFFECTS

Stay up to date on the association between the two and how to proceed accordingly.

BY MARC D. MYERS, OD
COATESVILLE, PA

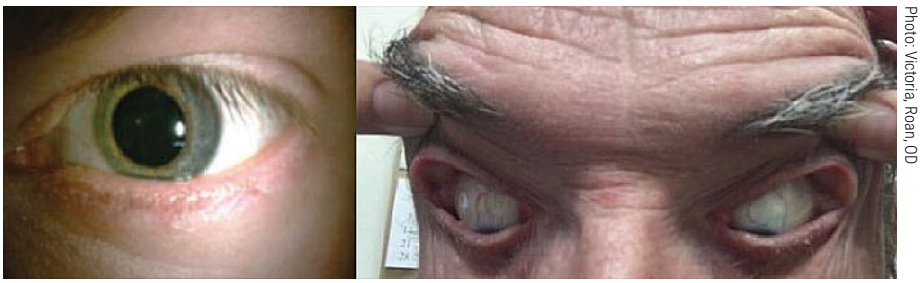


Photo: Victoria Roan, OD

Patients with OSA may develop lash ptosis (left) and/or floppy eyelid syndrome (right).

Consider that one-third of the average human's lifetime is spent sleeping. Sleep is a universal function of living species. Its restorative functions include memory consolidation, hormone regulation, growth and sympathetic/parasympathetic balance.[1] Sleep disorders can interfere with normal physical, mental, social and emotional functioning. Insufficient quality or quantity of sleep is associated with system dysfunctions including endocrine, metabolic, higher cortical function and neurological disorders.[2,3] Every day, new research helps us learn more about the direct and indirect consequences sleep disorders may have on ocular health.

The biological process of sleep is a reversible state of unconsciousness in which metabolism and motor activity is reduced.[4] There are two different kinds of sleep: rapid eye movement (REM) and non-rapid eye movement (NREM).[4] NREM typically follows a drowsy state and involves dreamless sleep. It is divided into three stages of sleep: the first (N1) is characterized by a transition from wakefulness to sleep, the second (N2) comprises the largest percentage of total sleep and the third (N3) involves a period of approximately 70 to 80 minutes of deep sleep. Following N3, deep sleep lightens, and REM follows. This part of the cycle is customarily associated with active dreaming and body movements.[4]

Sleep disorders consist of conditions that are attributed to the disruption of normal sleep patterns.[3,4] Although sleep disorders are more common in adults, they can occur during childhood.[3] Considered to be most prevalent during childhood, parasomnias are unusual behaviors that one may experience during the course of sleep. Included are sleepwalking, confusional arousals, sleep terrors, sleep talking and nightmares.[3,4] Parasomnias are generally not associated with complaints of insomnia or sleepiness but can be associated with possible injury (due to irregular movements and mobility) and negative psychosocial effects.[5]

Disorders of sleep are associated with complaints of insufficient sleep, altered amounts of perceived sleep or abnormal movements during sleep.[2] The physical examination of a patient suspected of having a sleep disorder may include signs of poor concentration, reported drowsiness, slowed reaction time, hypertension (HTN), enlarged tonsils and a narrowed airway. The major causes of sleep disorders are medical and psychological conditions.[4]

About the author **Dr. Myers** is an optometrist at the Coatesville Veterans Affairs Medical Center in Coatesville, PA. He lectures in academia and throughout North America and Europe on ocular disease. He has no relevant financial interests to disclose.

Medical Conditions and Sleep Disorders

There are many medical conditions that have been associated with sleep disorders. Cardiovascular disease may cause the patient to wake during sleep due to the feeling of shortness of breath.[2-4] Neurologic diagnoses including stroke, hypnic jerk (sudden, involuntary muscle contractions that occur as you are falling asleep) and restless leg syndrome (RLS) are associated with unwanted movements that disrupt sleep.[2-4,6-9] Other neurologic diagnoses that cause sleep disruption include central sleep apnea, headache and central degenerative disorders such as Alzheimer's disease, Parkinson's disease, dementia and amyotrophic lateral sclerosis.[4,10]

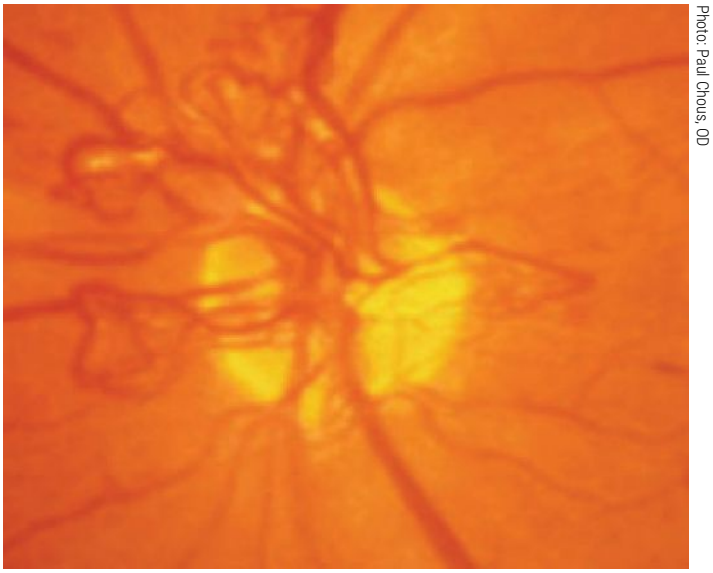


Photo: Paul Chous, OD

Sleep apnea has been linked to diabetes-related ocular conditions.

Endocrine disorders, including metabolic syndromes, may disrupt the sleep-wake cycle as hormone regulation is altered. Hyperthyroidism, diabetes mellitus and vitamin D deficiency are among these common disorders.[2-4] Pregnancy and menopause also affect hormone regulation and may impact sleep.

Chronic obstructive pulmonary disease and asthma are common pulmonary diseases that affect sleep due to difficulty breathing or compromised breathing patterns. Obstructive sleep apnea (OSA) is a pulmonary disorder associated with the collapse of the upper airway during sleep.[2-4,11]

The gastrointestinal diagnosis, gastroesophageal reflux disease, is often associated with the disruption of sleep due to the flareup of symptoms when a patient lays down to go to sleep.[2-4] When laying down, gravity no longer assists in keeping stomach acids contained, causing reflux into the esophagus. Symptoms of heart burn and chest pain can develop and awaken patients from sleep.[4]

Musculoskeletal conditions causing acute or chronic pain, such as an acute injury, arthritis and fibromyalgia, cause patients to wake more during the course of sleep resulting in reduced quality and quantity of sleep. Patients who live with pain learn how to position themselves when sleeping to avoid uncomfortable posture.[4]

Psychological Conditions and Sleep Disorders

Sleep disorders are common among patients who suffer from depression and result in both insomnia (trouble falling and/or staying asleep) and hypersomnia (episodes of excessive daytime sleepiness or prolonged nighttime sleep).[2,3] Anxiety also predisposes patients to insomnia as they may have trouble falling asleep, staying asleep and feeling rested upon awakening. Panic attacks may occur during both light and deep sleep, resulting in sleep disruption.[4]

Medications used to treat psychological conditions may cause patients to have difficulty falling asleep and have an impact on sleep patterns.[3] Antidepressant medications can disrupt REM sleep patterns. Most commonly associated with treatment in elderly patients, benzodiazepines can cause rebound insomnia if a dosage change is made or a medication is discontinued.[4]

Other Conditions and Sleep Disorders

Environmental factors that disrupt the typical sleep cycle, such as night shifts or jet lag, may also impact quality and quantity of sleep. Other factors such as loud noises and extreme temperatures can result in sleep deprivation as well.[12-14]

In addition to the psychiatric medications mentioned earlier, there are other types of medications that can disrupt sleep.[2-4,6,10] Corticosteroid medications can cause "jitters" that may result in difficulty falling asleep and disrupted REM sleep. Diuretic medications cause increased urination, depleting the body of fluids and sodium, potassium, calcium and magnesium. As a result, sleep is disrupted due to the urge to use the bathroom and the painful effects of cramps.[4]

It is safe to assume that as we age, our level of physical activity is reduced, resulting in less fatigue and the perception of the need to "get some sleep." Sleep disorders are very common in the elderly population, with patients reporting difficulty falling asleep (increased sleep latency), frequent overnight awakenings and early morning awakening.[2-4]

Classification of Sleep Disorders

Sleep disorders that occur in adults manifest as complaints of insufficient sleep, excessive perceived sleep or abnormal movements during sleep.[1,5,8] Transient insomnia is very common and may present in one-third of adults. In many instances, insomnia becomes a more chronic and persistent problem if behavioral, emotional, cognitive and/or medical issues are also present.[2-4]

There is a belief that sleep is primarily controlled by two regulatory mechanisms: a circadian mechanism that determines the timing of sleep and wakefulness and a homeostatic mechanism that determines the need for sleep and sleep intensity.[6] The homeostatic mechanism is thought to determine the need for sleep, or sleep propensity, based on prior wake time, or how long someone has gone without sleep. Circadian rhythm sleep disorders are influenced by homeostatic factors as well as the circadian system.[2,4,6]

The circadian rhythm in humans is thought to be an endogenously generated system that lasts approximately 24 hours in duration.[12-14] The suprachiasmatic nucleus (SCN) is located in the anterior part of the hypothalamus and is considered the pacemaker of the circadian timing system. Efferent projections from the SCN innervate structures including the pineal gland, producing melatonin. Normally, the sleep phase of the circadian rhythm occurs about two hours after the onset of melatonin secretion.[12-14] Sleep-wake phase disorders may occur when society-driven sleep times delay (sleep occurs later than needed) or advance (sleep occurs sooner than needed) the sleep phase of the circadian cycle.

Sleep-related breathing disorders are associated with insufficient patterns of sleep.[2-4,11,15] There are three types of sleep apnea: obstructive, central and complex. OSA occurs when there is a cessation of air flow for at least 10 seconds and is the result of the collapse of the upper airway during sleep. The prevalence of diagnosed OSA has been increasing in the United States due to increasing rates of obesity and overall awareness of the disorder.[11,15]

Central sleep apnea is the interruption of air flow that occurs due to a lack of effort to breathe, most commonly originating from the brain respiratory centers and flowing to the muscles that control breathing. Complex sleep apnea occurs as a result of the combination of both obstructive and central apnea.[11,15]

Photo: Brad Sutton, OD

NTG has been a fairly common report in sleep apnea.

Sleep-related movement disorders include RLS and periodic limb movement disorder (PLMD). RLS, also known as Willis-Ekbom disease, is described as an irresistible restlessness and urge to move the legs, and less commonly the arms and trunk, due to painful and uncomfortable sensations.[7,8] The principal abnormality in RLS is identified as a dopamine deficiency and dysregulation of iron by the brain. RLS is thought to affect 5% to 8% of the general population, with women and adults over 40 more likely to experience the condition.[7,8]

PLMD is also referred to as sleep-related myoclonus syndrome or nocturnal myoclonus syndrome.[9] Although the pathogenesis of PLMD is not clearly defined, dopamine deficiency could be an underlying factor that triggers the spinal flexor pathways resulting in increased limb movements during sleep. Patients commonly complain of disturbed sleep due to repetitive lower extremity movements in the form of extension of the big toe and flexion of the ankle, knee and hip.[9] These movements may be associated with autonomic arousal resulting in a change in heart rate and blood pressure or cortical arousal causing frequent nocturnal awakenings. Patient-reported symptoms also include complaints of non-restorative sleep and daytime sleepiness and fatigue affecting their overall livelihood.[2,9]

Ocular Sequelae of Sleep Disorders

Sleep disorders and their treatment may directly and indirectly compromise ocular health.[2-4] The pathophysiologic mechanisms of sleep disorders are thought to influence extracerebral physiologic functions that when compromised result in cardiovascular disease, cerebrovascular disease and metabolic imbalances (increasing the risk of obesity and diabetes).[16] In addition, lifestyle modifications, pharmacologic therapies and therapeutic modalities such as continuous positive airway pressure (CPAP) are associated with ocular disease.[16]

Prolonged eyelid closure during sleep serves as a mechanical barrier between the ocular surface and the external environment.[16,17] It also reduces tear production. REM promotes the transfer of aqueous humor, increasing nutrient supply to the cornea and compensating for the reduction in tear production and oxygen to the cornea. Frequent nocturnal awakenings due to a sleep disorder may result in a patient developing signs and symptoms of dry eye as the result of a compromised ocular surface.[16,17]

OSA is an independent risk factor for the development of HTN and cardiovascular and cerebrovascular diseases such as obesity, diabetes, ischemic heart disease and psoriasis. Considering the consequences these systemic diseases have on the vascular system, it is no surprise that

LUMIFY®

BRIMONIDINE TARTRATE OPHTHALMIC SOLUTION 0.025%
REDNESS RELIEVER EYE DROPS

A redness reliever like no other*

- **Unique method of action**† that selectively targets redness
- **Virtually no rebound redness** and no tachyphylaxis in clinical trials[1‡]
- **Clinically proven safe and effective** in 6 clinical trials with over 600 patients

Actual results. No retouching. Consistent with average clinical trial results.

*Low-dose OTC brimonidine. †Low-dose brimonidine is an α2-AR agonist that primarily constricts the venule. [1]McLaurin E, et. al. *Optom Vis Sci*. 2018;95(3):264-271. ‡In clinical trials, one case of rebound redness was reported. §In Home Use Test, March 2018. n=301.
LUMIFY is a trademark of Bausch & Lomb Incorporated or its affiliates.

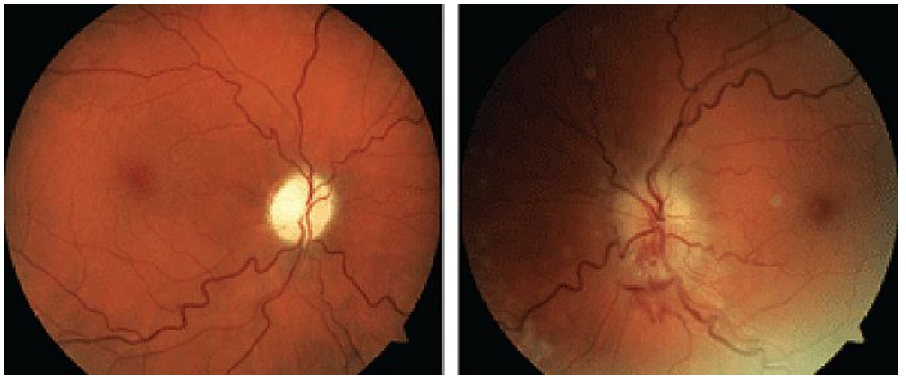
To learn more about LUMIFY visit: **LUMIFYDrops.com/Professional**

Call 1-833-4-LUMIFY (1-833-458-6439)
for samples and patient resources

Call 1-800-828-9030
to start selling LUMIFY in your office

BAUSCH+LOMB

Photo: Brad Sutton, OD



NAION and sleep apnea share a significant association.

several ophthalmologic diseases are linked to OSA.[2,3,11] These diagnoses include floppy eyelid syndrome, primary open-angle glaucoma (POAG), normal-tension glaucoma (NTG), nonarteritic anterior ischemic optic neuropathy (NAION), papilledema and dry eye, as well as CPAP-associated eye complications.[2,11,16-18]

The signs of floppy eyelid syndrome include easily everted floppy eyelids, eyelash ptosis and papillary conjunctivitis due to spontaneous eyelid eversion. Patients may present with symptoms that include watering, stickiness, discomfort and blurred vision that is usually bilateral and most oftentimes worse upon awakening in the morning.[16-19] Clinical presentation may include ptosis, misdirected (most often downward) or inverted eyelashes, papillary conjunctivitis and corneal involvement. Corneal findings can include punctate keratopathy, epithelial defect, surface scarring, neovascularization, keratoconus and infectious keratitis, among others.[16-19]

The exact pathophysiology of floppy eyelid syndrome is not completely understood. Studies have suggested the role of mechanical stress, alternating periods of ischemia and reperfusion causing tissue inflammation and loss of elastin fibers in the tarsal plate. An increase in the immunoreactivity of the eyelid elastolytic processes, in particular an increase in matrix metalloproteinase, likely accounts for the loss of elastin fibers.[19]

CPAP-associated eye complications are thought to arise from two possible mechanisms. Most commonly, air leaks around the superior portion of the mask causing air to blow onto the ocular surface. The other mechanism involves retrograde movement of air and mucus from the nasal passage through the nasolacrimal duct and onto the ocular surface. Consequences of these mechanisms include dry eye, increased mucoid discharge on the ocular surface, blepharitis and episodes of bacterial conjunctivitis.[11,20] It is best to avoid sleeping in an extended-wear contact lens when using CPAP.

In addition to ocular surface complications, patients often present with skin irritation and breakdown due to a poorly fit mask or dry air flow. Most often adjustments made to the fit of the mask and/or to the humidity of air flow solve these skin issues. Switching to a nasal interface may be required to eliminate areas of pressure on the skin or to reduce the flow of air that escapes the superior border of the mask.[16]

Treatment of ocular complications associated with CPAP use includes nocturnal lubrication with a viscous artificial tear or ointment.[2-4,11,16] Additional daytime lubrication may be needed to quell symptoms reported upon awakening. As with complications involving the nasal passages or facial skin, the health of the ocular surface can be improved by adjusting the fit of the mask or increasing the humidity of the flow of air.[11,16]

POAG and OSA were reported in 1982 to occur in the same family of diagnoses.[21] The number and duration of apneic episodes in cases of OSA correlated directly with the severity of POAG. Since initial reports, NTG has also been associated with OSA. The prevalence of OSA and glaucoma ranges from 2% to 27% vs. the expected 2% in the general population.[16]

Additional direct correlations that have been identified between patients with moderate to severe OSA and glaucoma include increased incidence of visual field defects and decreased retinal nerve fiber layer thickness.[16] The proposed physiologic mechanisms linking OSA to glaucomatous optic nerve damage include direct hypoxic injury, disrupted autoregulation of blood flow due to periods of hypoxia and hypercapnia (excessive carbon dioxide in the blood stream due to inadequate respiration) and blood flow disruption due to periods of HTN that occur during apneic episodes.[22]

Interestingly, POAG has also been associated with circadian rhythm sleep disorders and endogenous melatonin levels. POAG is considered a causal factor for circadian disruption. Glaucoma causes retinal ganglion cell (RGC) damage. Intrinsically photosensitive RGCs (ipRGCs) convey non-image-forming photic information via the retinohypothalamic tract to the SCN.[12,18] As ipRGCs are progressively damaged, photic information to the SCN is adversely altered, disrupting circadian rhythms and causing impaired sleep and altered mood. Other neurodegenerative pathologies associated with disruption of circadian rhythms include Alzheimer's disease, Parkinson's disease and Huntington's disease.[12,18]

Altered circadian rhythms impact endogenous melatonin production, causing deregulation of circadian intraocular pressure (IOP). Melatonin is a hormone produced by the pineal gland in response to darkness, playing a key role in the body's

The Only Source for a Factory Certified Pre-Owned Santinelli International Edger

Sold only by Santinelli, these refurbished edgers are restored back to their original specifications by our team of expert technicians and must pass a comprehensive 150-point inspection.

BUY IT STRAIGHT FROM THE SOURCE:

— Refurbished by the experts

— Includes installation, training, and phone support

— 1-Year warranty backed by factory-trained technicians




CONTACT US TO LEARN ABOUT EXCLUSIVE SAVINGS

800.644.EDGE (3343) | SANTINELLI.COM

Santinelli® INTERNATIONAL
A DIVISION OF ADVANCING EYECARE™

PERFECTING THE ART INSIDE THE FRAME™

PROUD WINNER FOR 13 CONSECUTIVE YEARS
2021 EYEVOTE 20/20 VM

sleep-wake cycle. Its production is reduced in bright light conditions, and melatonin production decreases with age.[16-18] Variability in melatonin levels can obscure circadian IOP rhythms, resulting in less consistent control of IOP and potential progression of glaucoma. The altered "rhythm" of IOP may account for some resistance to IOP-lowering therapy. Studies support the use of endogenously administered melatonin in the management of glaucoma (and in neurodegenerative diseases) to better synchronize circadian rhythms, perhaps improving the efficacy of IOP-lowering therapy. For adults, 0.5mg to 5mg of melatonin taken one hour before bed is considered to be a safe and effective therapy.[16-18]

Sleep apnea has been documented to be 1.5 to two times more likely to be associated with NAION than HTN or diabetes.[2,11,16] Mechanisms believed to explain this associated risk include impaired optic nerve head blood flow autoregulation secondary to the effects of apneic episodes, apnea-induced blood pressure variations or an imbalance between vasodilator (nitric oxide) and vasoconstrictor (endothelin) blood pressure variations. Also, episodic increases in intracranial pressure (ICP) associated with hypercapnia during apneic episodes may impact optic nerve head health as a result of direct compression or impaired circulation.[11,16]

Care of NAION concentrates on systemic disease management to ultimately reduce the risk of recurrence in the ipsilateral or contralateral eye.[16,23] It is recommended to include screening for physical features of OSA in this patient population and to conduct diagnostic testing as well. Sleep study screening (polysomnography) should be performed to identify those patients who would benefit from intervention such as treatment via CPAP and initiate the appropriate therapy accordingly and in a more timely fashion.[16,23]

Papilledema, bilateral optic disc swelling in the presence of increased intracranial pressure, has been identified as having an association with OSA.[16,17,24] A report hypothesized that papilledema in patients with OSA was secondary to transient hypercapnia and the resultant transient increases in ICP. Hence, some patients with OSA may present with normal daytime intracranial pressure. CPAP should be used to treat OSA and may contribute to the effect of acetazolamide in reduced ICP and improved signs and symptoms of papilledema.[16,17,24]

> **Sleep apnea has been documented to be 1.5 to two times more likely to be associated with NAION than HTN or diabetes.[2,11,16]**

Takeaways

The improvement in diagnosis and treatment of sleep disorders has been in part due to patient education and public awareness of the prevalence of these disorders.[2-4,16-19] Wearable technologies available commercially in the form of wristbands, watches and rings may aid in recognizing and monitoring potentially problematic sleep patterns.

Providers are more aware of early signs and symptoms of sleep disorders and the association with systemic diseases such as HTN, diabetes, obesity and mood disorders. In addition, care has become more efficacious as medical treatments and surgical interventions have improved.[2-4,16-19]

Over the past several decades, significant gains have been made in understanding the relationship that sleep disorders have with ocular disease.[16-20] More timely diagnosis and treatment of these disorders will hopefully occur as the pathophysiologic mechanisms linking these disorders are better understood. Optimally, the coordination of care will flourish between primary care providers, sleep specialists (most frequently pulmonologists) and eyecare providers. ■

1. DelRosso LM, Silvestri R, Ferri R. Restless sleep disorder. Sleep Med Clinic. 2021;16:381-7.
2. Pavlova MK, Latreille V. Sleep disorders. Am J Med. 2019;132(3):392-9.
3. Holder S, Narula NS. Common sleep disorders in adults: diagnosis and management. Am Fam Phys. 2022;105(4):397-405.
4. Karna B, Gupta V. Sleep disorder. StatPearls [Internet]. Treasure Island (FL). 2022.
5. Proserpio P, Terzaghi M, Manni R, et al. Drugs used in parasomnia. Sleep Med Clinic. 2020;15:289-300.
6. McDermott M, Brown D, Chervin RD. Sleep disorders and the risk of stroke. Expert Rev Neurother. 2018;18(7):523-31.
7. Bollu PC, Yelum A, Thakkar MM. Sleep medicine: restless leg syndrome. Missouri Medicine. 2018;115(4):380-7.
8. Gossard TP, Trotti LM, Videnovic A, et al. Restless legs syndrome: contemporary diagnosis and treatment. Neurotherapeutics. 2012;18:140-55.
9. Joseph V, Nagalli S. Periodic limb movement disorder. StatPearls [Internet]. Treasure Island (FL). 2022.
10. Jee HJ, Shin W, Jung HJ, et al. Impact of sleep disorder as a risk factor for dementia in men and women. Biomol Ther. 2020;28(1):58-73.
11. Rundo JV. Obstructive sleep apnea basics. Cleveland Clinic Journal of Med. 2019;86(sup1):2-9.
12. Ma MA, Morrison EH. Neuroanatomy, nucleus suprachiasmic. StatPearls [Internet]. Treasure Island (FL). 2022.
13. Kim MJ, Lee JH, Duffy JF. Circadian rhythm sleep disorders. J Clin Outcomes Manag. 2013;20(11):513-28.
14. Frank MG. Challenging sleep homeostasis. Neurobiol Sleep Circadian Rhythms. 2021;10(1):1-3.
15. Huon LK, Liu SYC, Camacho M, et al. The association between ophthalmologic diseases and obstructive sleep apnea: a systemic review and meta-analysis. Sleep Breath. 2016;20:1145-54.
16. Waller EA, Bendel RE, Kaplan J. Sleep disorders and the eye. Mayo Clin Proc. 2008;83(11):1251-61.
17. Lee SSY, Nilagiri VK, Mackey DA. Sleep and eye disease: a review. Clin Experiment Ophthalmol. 2022;50(3):334-44.
18. Gubin D, Weinert D. Melatonin, circadian rhythms and glaucoma: current perspective. Neural Regeneration Research. 2022;17(8):1759-80.
19. Mojon DS, Goldblum D, Fleischhauer J, et al. Eyelid, conjunctival and corneal findings in sleep apnea syndrome. Ophthalmology. 1999;106(6):1182-5.
20. McNab AA. Floppy eyelid syndrome and obstructive sleep apnea. Ophthal Plast Reconstr Syrg. 1997;13(2):98-114.
21. Walsh JT, Montplaisir J. Familial glaucoma with sleep apnea: a new syndrome? Thorax. 1982;37(11):845-9.
22. Gerghel D, Hosking SL, Orgul S. Autonomic nervous system, circadian rhythms, and primary open angle glaucoma. Surv Ophthalmol. 2004;49(5):491-508.
23. Mojon DS, Mathis J, Zulauf M, et al. Optic neuropathy associated with sleep apnea syndrome. Ophthalmology. 1998;105(5):874-7.
24. Sugita Y, Iijima S, Teshima Y, et al. Marked episodic elevation of cerebrospinal fluid pressure during nocturnal sleep in patients with sleep apnea hypersomnia syndrome. Electroencephalogy Clin Neurophysiol. 1985;60(3):214-9.

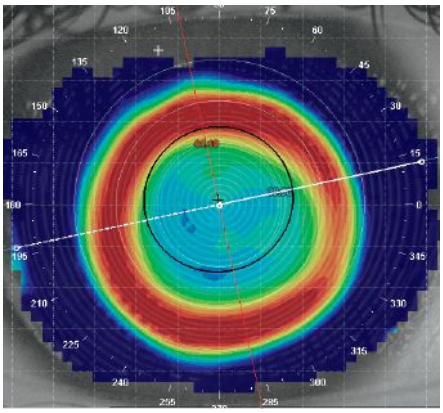
FOR OVERNIGHT ORTHOKERATOLOGY

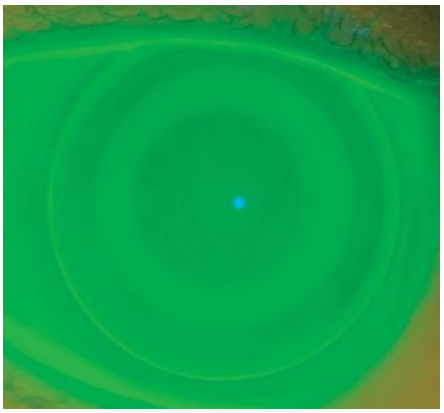
REM LENS®

RAPID EYE MOLDING

Changing Sight, Overnight™

Giving you the control to treat your myopic afflicted patients.





- NCLE certified consultation experts to guide you through the entire fitting process
- Highly adjustable parameters
- Dynamic Edge Profile™ delivers remarkable comfort
- Diameter & optic zone options for myopia management patients, along with standard Orthokeratology patients
- 89% First fit success rate*
- Simplified lens design, and ease of ordering
- Online lens design calculator
- 24-hour turnaround time
- Competitive pricing and hassle free, no return warranty

Vision Shaping Treatment VST®

Scan to learn more about REMLens®!

X-CEL SPECIALTY CONTACTS

800.241.9312 | xcelspecialtycontacts.com/remlens

A COMPLETE ANALYSIS OF COVID-19 AND THE EYE

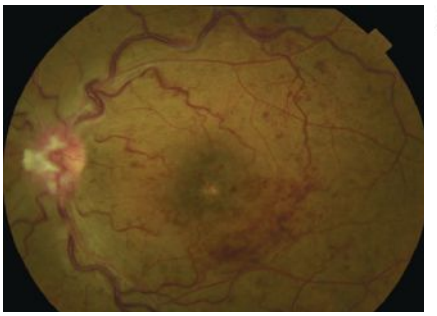
From past to present, we review the impact of this disease on our patients.

BY BROOKE SMITH, OD, AND LORI MANDY PENNINGTON, OD
HAMPTON, VA

Since the announcement of the first confirmed cases of COVID-19 in Wuhan, China at the end of 2019, this coronavirus disease continues to be a global health crisis. According to the World Health Organization, as of August 5, 2022, there have been almost 600 million confirmed cases of COVID-19, including 6.47 million deaths.[1]

COVID-19 is characterized by fever and severe respiratory illness or pneumonia, but it can also affect the ophthalmic, neurological, cardiovascular, gastroenterological and nephrological systems.[2] COVID-19 is a multisystem disease and can present with a wide array of clinical manifestations, ranging from asymptomatic to symptomatic with mild, moderate or severe disease.

SARS-CoV-2 is mainly spread via the respiratory tract through respiratory droplet transmission when an infected host sneezes, talks or coughs.[3] It enters a cell by binding its spike protein with the cell's angiotensin-converting enzyme 2 (ACE2) receptor.[3-5] Transmembrane protease serine 2 proteins (TMPRSS2) prime the spike protein on SARS-CoV-2 for contact with ACE2, which enables infection of cells. The ACE2 receptor is found throughout the body which allows the virus to infect multiple organs. In the human eye, ACE2 is found in the retina and choroid tissues.[3] One study demonstrated ACE2 expression in conjunctival, limbic and corneal cells and TMPRSS2 expression in the conjunctiva.[5] While the presence of ACE2 receptors and TMPRSS2 proteins on the ocular surface seems convincing, there remains discussion on whether the tear film of infected COVID-19 patients contains viral particles.[3]



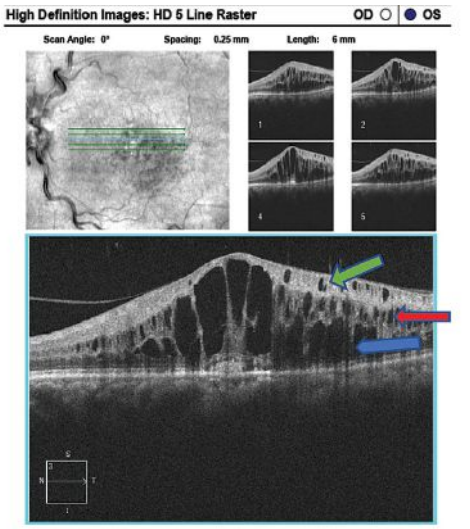


Fig. 1. Fundus photography demonstrating an ischemic retinal vein occlusion with, at right, SD-OCT illustrating the presence of cystoid macula edema with cysts located in the outer nuclear layer (blue arrow), inner nuclear (red arrow) and ganglion cell layer (green arrow).

Ocular Transmission and Complications

There are two different philosophies on COVID-19 transmission through the eye. The first considers the conjunctiva as a direct inoculation site of infected droplets. The second centers around the nasolacrimal duct as a way for viral

About the Authors

Dr. Smith is a staff optometrist at the Hampton VA Medical Center, where she is the externship director and adjunct faculty for The Ohio State University. She is an active Fellow of the American Academy of Optometry where she lectures and currently sits on the fellowship committee advisory board. **Dr. Pennington** is a staff optometrist at the Hampton VA Medical Center, where she is adjunct faculty for The Ohio State University College of Optometry. She is the president of the Tidewater Optometric Society and a member of the board of trustees for the Virginia Optometric Association. Neither has any financial disclosures.

Table 1. Covid-19 Orbital and Anterior Segment Complications[2,4,6]

Orbital	Anterior Segment
Dacryoadenitis	Follicular conjunctivitis
Retro-orbital pain	Viral keratoconjunctivitis
Orbital cellulitis	Hemorrhagic and pseudomembranous conjunctivitis
Sinusitis	Episcleritis
Mucormycosis	Keratitis
Orbital histiocytic lesion	Conjunctival chemosis

movement to enter the gastrointestinal and respiratory tracts.[3,6] One recent study showed that even though conjunctival cells expressed SARS-CoV-2, an infection did not result.[7] A study published in July 2022 determined that SARS-CoV-2 was detectable with a conjunctival sac swab by polymerase chain reaction (PCR) testing in patients who had a PCR-positive nasopharyngeal swab, but the positivity rate was only about 12%.[8]

The prevalence of ophthalmic manifestations among COVID-19 patients ranges from 2% to 32%.[4] Conjunctivitis has been the chief ophthalmic diagnosis identified in COVID-19 patients in the literature.[2,4,6] Patients can present with numerous symptoms including ocular redness, soreness, foreign body sensation, light sensitivity, tearing, mucoid discharge, eyelid swelling and chemosis.[2,4,6] These symptoms more commonly affect patients with severe systemic symptoms of COVID-19, although they can rarely present as an initial manifestation of the disease.

The onset of ocular symptoms typically occurs at the same time as systemic symptoms (47.5%), and 12.6% report symptoms lasting ≥14 days.[9] *Table 1* lists the most common orbital and anterior segment findings.[2,4,6] Patients on ventilators or using respiratory masks in the ICU may also develop exposure keratopathy and ultimately severe corneal infections. Adequate ocular lubrication and closure of the eyelids may help prevent these ocular surface problems.[2] As with other ocular viral infections, COVID-19 conjunctivitis is typically self-limiting and can be generally managed with symptomatic care. In the absence of significant ocular pain, decreased vision or light sensitivity, many patients can be managed with preservative-free artificial tears, cold compresses and lubricating ophthalmic ointment. In severe cases, a prophylactic antibiotic may be prescribed to minimize secondary opportunistic bacterial infections.

As seen in *Table 2*, the majority of COVID-19 posterior segment complications are retinal in nature but can manifest in the vitreous and/or choroid too.[10] Posterior segment involvement has varied manifestations that are vascular, inflammatory and/or neuronal in response to viral COVID-19.[11] These complications may occur within a week after the onset of COVID-19 symptoms up to more than six weeks after.[12] Researchers believe that the retinal endothelium via the ACE2 receptors are affected from the virus. This causes compromise to the blood-retinal barrier, allowing a greater immune response.[13] It can also cause severe endothelial disruption, complement activation and generalized inflammation.[12] The choroid is highly vascularized, making it susceptible to systemic conditions, especially ones that affect the blood vessels.[10]

The most described non–vision threatening retinal findings in patients with COVID-19 are microvascular in nature, such as retinal hemorrhages and cotton wool spots.[10,12] By contrast, the most common vision threatening manifestation is retinal vein occlusion with associated macular edema (*Figure 1*).[11,12] Paracentral acute middle maculopathy and acute macular neuroretinopathy are rare microvascular diseases that involve the deeper retinal vessels. Their symptoms include acute painless diminution of vision, faintly colorful paracentral scotoma and dyschromatopsia.[11] OCT testing in COVID+ patients shows hyperreflective lesions in different retinal layers and can include the posterior vitreous hyaloid, inner plexiform layer and ganglion cell layer with disruption of the ellipsoid zone.[11,14]

Neurological complications were initially known to include headache (6.5% to 70.3%) and olfactory disturbances. Today, severe neurological complications can present in up to 36% of patients as ocular manifestations and/or stroke.[15-17] A range of symptoms have been reported: anosmia, ageusia, headache, dizziness, myalgias, diplopia, focal neurologic deficits and encephalopathy.[16,18] In the setting of COVID-19 infection, an abnormal immune response contributes to neurologic dysfunction. Studies have shown that COVID infection can cause increased levels of cytokines in the plasma, creating a "cytokine storm" that can cause immunologic upregulation, vasodilation, vascular permeability, endothelial dysfunction, coagulopathy and direct viral neurotropism.[16]

Current neuro-ophthalmic COVID anomalies can be classified into afferent and efferent visual pathway complications (*Table 3*).[16] One of the most common noted afferent neurological complication is optic neuritis, often found in individuals with systemic inflammatory or autoimmune disorders.[15] It is not uncommon for patients with optic neuritis and COVID to develop myelin oligodendrocyte glycoprotein antibody-associated optic neuritis or optic neuritis in the setting of acute disseminated encephalomyelitis.[16] Efferent neurological complications commonly include pupillary and eye movement disorders with the sixth cranial nerve most affected.[16] Systemic involvement can also include the loss of tendon reflexes and acute ataxia as seen in Miller Fisher syndrome.[16]

Ischemic stroke, rather than hemorrhagic, accounts for about 2% to 4.6% patients with COVID-19 and

Table 2. COVID-19 Posterior Segment Complications[10]

Retina	Vitreous	Choroid
Intra-retinal hemorrhages	Vitritis	Chorioretinitis
Cotton wool spots	Posterior uveitis	White dot syndromes:
Retinal vein occlusions	Endophthalmitis	· acute posterior multifocal placoid pigment epitheliopathy
Arterial occlusions		· acute zonal occult outer retinopathy
Vasculitis		
Vascular dilatation		
Paracentral acute middle maculopathy		
Acute macular neuroretinopathy		
Panuveitis		
Acute retinal necrosis		

has been one of the most notable and devastating neurological complications of COVID-19.[16,19,20] Although stroke is more common in the younger male population, early outcome is worse in women with a higher in-hospital mortality, longer hospital stays and more long-term disability. Patients requiring hospitalization for COVID-19 have a three- to four-fold greater risk of stroke.[21] Despite gender differences, many ischemic stroke patients with COVID-19 have shared vascular risk factors, such as hypertension, hyperlipidemia and diabetes. In women, obesity, atrial fibrillation and heart disease are more prevalent.

Although the cause of ischemic stroke associated with COVID-19 is unclear, studies have hypothesized that it is due to an immune-mediated etiology, particularly related to an inflammatory response and hypoxemia. This promotes the occurrence of embolic event and increased blood viscosity, which causes a hypercoagulable state and thromboembolism.[20]

Visual complications from COVID-19 related ischemic stroke can result in vision and/or field loss and visual snow syndrome.[19] These issues are the results of acute temporal, parietal or occipital infarct due to vasodilation and vascular permeability or due to endothelial dysfunction and/or coagulopathy.[16] For example, our 51-year-old diabetic female patient who acquired COVID-19 in January 2022 with hospitalization later developed secondary blood clots and two ischemic strokes, one under hospitalization and another two months later. Although the patient's visual acuity was 20/20 OU, it was confirmed on a Humphrey 120-point screener visual field analysis that she suffered a left-sided homonymous hemianopia field defect (*Figure 2*). Therefore, the risk of ischemic stroke must be taken into consideration when a patient has been admitted with COVID-19. Patients may benefit from the early initiation of anti-inflammatory and anticoagulant therapy. However, further clinical trials are needed for verified evidence.[20]

Vaccine Complications

In December 2020, the Food and Drug Administration approved the first COVID-19 vaccine for emergency use authorization. There are currently four approved or authorized COVID-19 vaccines in the United States: Pfizer-BioNTech, Moderna, Johnson & Johnson's Janssen and, most recently, Novavax. As of September 1, 2022, a total of almost 12.45 billion vaccine doses have been administered worldwide.[1]

A 2022 study looked at the adverse ocular events reported to the Vaccine Adverse Event Reporting System following vaccination against COVID-19 between December 2020 and December 2021. The most-reported events were eye swelling, ocular hyperemia, conjunctivitis (33.33%), blurred vision (26.69%) and visual impairment (19.77%). These conditions accounted for more than 70% of all complications.[22] All of the different vaccine types administered in the USA were associated with ocular adverse events.

More severe anterior segment complications after COVID-19 vaccination include uveitis, scleritis, herpes zoster ophthalmicus, herpes stromal keratitis and corneal graft rejections.[23] The underlying pathophysiology for vaccine-related uveitis is mostly unknown but has been hypothesized to be an autoimmune reaction triggered by the vaccines. Vaccination activates a cytokine cascade of pro-inflammatory type 1 interferon expression, which results in a defensive immune response. It can also trigger the production of autoantibodies responsible for an autoimmune response. Specifically for mRNA vaccines, mRNA can bind to Toll-like receptors that also activates a pro-inflammatory cytokine cascade.[24]

COVID-19 vaccinations may reactivate herpetic keratitis in patients with a previous herpetic keratitis or keratouveitis infection. Changes in immune status, including lymphocyte depletion, are thought to trigger the reactivation.[25,26] Prophylactic antiviral treatment with oral valacyclovir should be considered, at least for high-risk patients with several previous episodes of herpetic uveitis.[25,26]

Corneal graft rejection has been reported following administration of COVID-19 vaccines. Most cases had additional risk factors associated with rejection. Vaccination increases circulation of proinflammatory cytokines, CD4+ and CD8+ T-cell responses that may contribute to graft rejection. A patient's risk of rejection varies depending on the transplant type (most commonly penetrating keratoplasty), the time elapsed since transplant and other associated risk factors.[27,28] Prophylactic topical corticosteroids before and after vaccination may lessen the risk of rejection after vaccination but more research needs to be done. It is important to note that corneal graft rejection has also been reported following COVID-19 illness.[27]

TIGHT BUDGET?

We'll fit it.

Purchase TelScreen equipment for quick & comprehensive patient education with great image quality.

EyeRes™
Digital Imaging Systems
by TelScreen

www.TelScreen.com

@telscreen

@telscreen

Table 3. COVID-19 Neuro-Ophthalmic Complications[16]

Afferent	Efferent
Optic neuritis	Cranial neuropathies
Papillophlebitis	Miller Fisher syndrome
Papilledema and pseudotumor cerebri	Adie's tonic pupils
Visual disturbance associated with posterior reversible encephalopathy syndrome	Ocular myasthenia gravis
Vision loss caused by stroke	Nystagmus
Homonymous hemianopia	Eye movement disorders
	Guillain-Barré syndrome

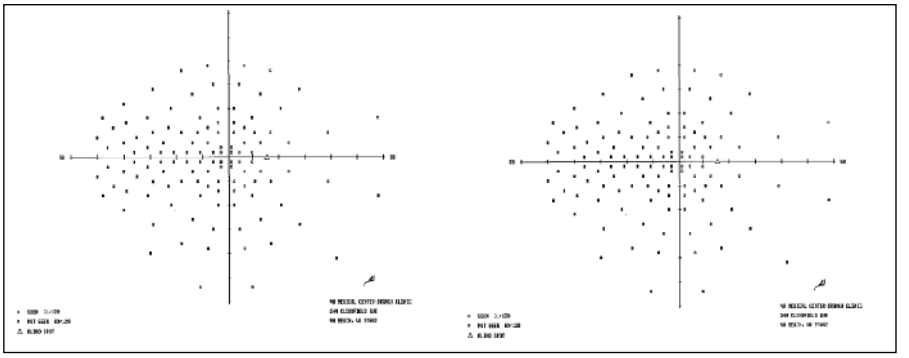


Fig. 2. Humphrey visual field analysis with 120-point screen demonstrating a left-sided homonymous hemianopia visual field defect secondary to ischemic stroke from COVID-19.

Adverse neuro-ophthalmological complications related to vaccines against COVID-19 are shown in *Table 4*.[29] At this time, optic neuritis is the most common. Most complications are mild and transient and have been clinically observed between four and 10 days post-vaccine.[21,29] Seventeen days after receiving a second COVID-19 vaccination, a 65-year-old male suffered a right pupil-sparing third nerve palsy with external ophthalmalgia. MRI imaging was remarkable for edema and enhancement of the right oculomotor nerve. These clinical findings improved on day 30 and entirely resolved on day 71.[30] Although, it has been hypothesized to be related to thrombosis and thrombocytopenia, cerebrovascular complications are rare.[21] These immune-mediated events are respondent to high-dose steroids for treatment and have a favorable clinical outcome.[30]

Eyecare providers must be able to identify potential, although rare, post-COVID-19 vaccination adverse reactions. It should be kept in mind that ocular adverse events are not exclusive to COVID-19 vaccines and have been reported in many other vaccines, such as influenza, zoster, tetanus and pneumococcal vaccines.[31] Overall, the benefits of COVID-19 vaccination outweigh the risks of ocular complications.

Face Mask Complications

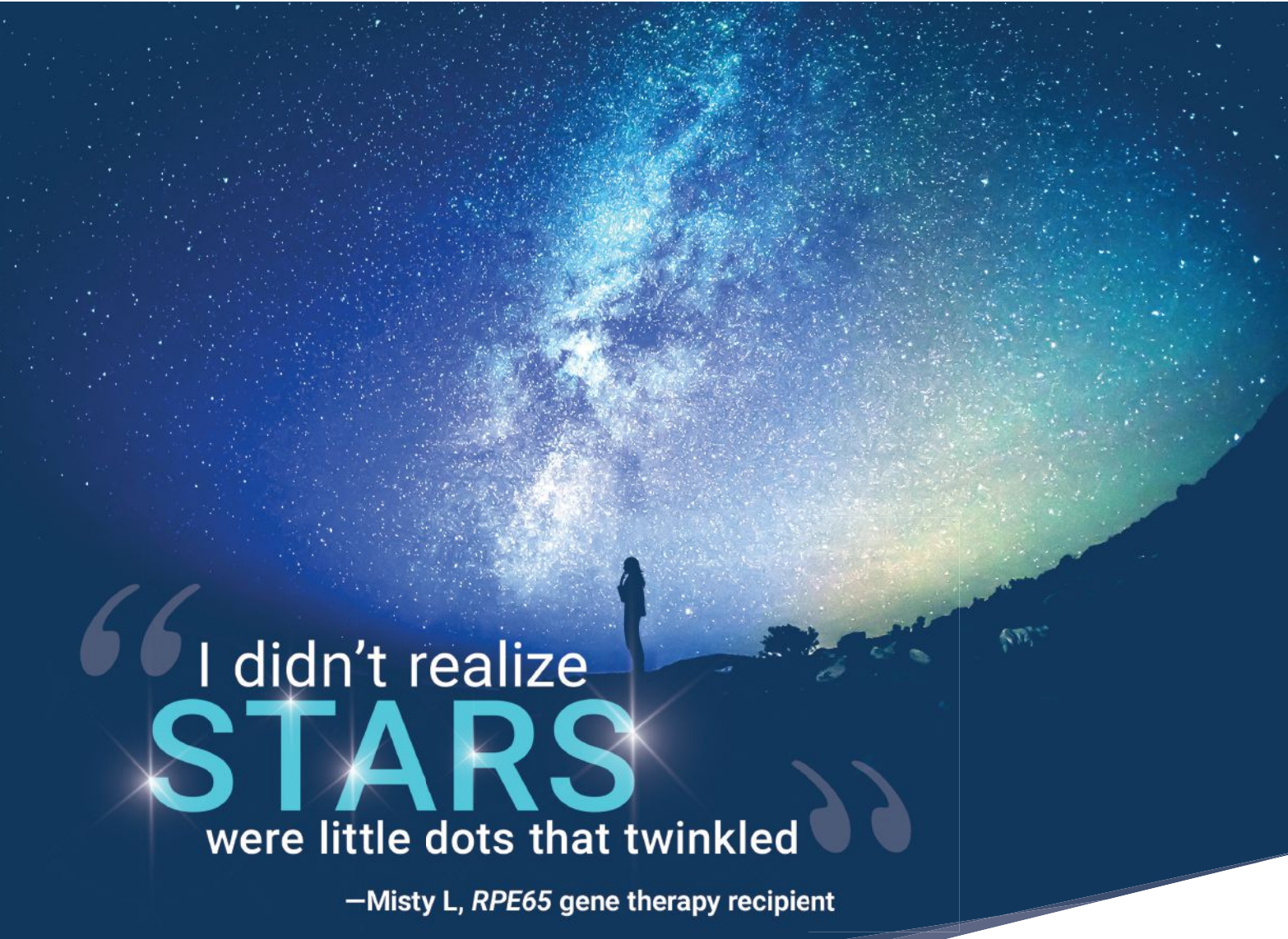
During the COVID-19 pandemic, the prevalent use of face masks was recommended to protect against the spread of SARS-CoV-2. Mask-associated dry eye was first mentioned in literature in June 2020.[32] Since then, several articles have investigated mask-associated dry eye in the general population as well as in the healthcare workplace. A survey found that mask-associated dry eye risk factors may include longer mask wearing time, improper wearing of face masks, dry environment, older age, female sex, higher education and less outdoor time.[33] Mask wearing has also be associated with meibomian gland dysfunction. One study noted that increased mask wear appears to correlate to an increased incidence of chalazion.[34] Another determined that wearing masks decreased tear break-up time and increased ocular surface temperature and blood flow. A tightly fitting mask or taping the top of the mask may reduce the risk of dry eye symptoms associated with mask wear.[12]

Endophthalmitis, a purulent inflammation of the vitreous and aqueous material, has been known to manifest from exogenous or endogenous origin. Initially, it was hypothesized that wearing a face mask while receiving an intravitreal injection (IVI) may be associated with a higher risk of endophthalmitis due to the possibility of the increased chance of contamination by *Streptococcus* via oropharyngeal droplet transmission.[35] A multicenter large-scale retrospective study found that universal masking during intravitreal injections did not alter the risk of post-injection endophthalmitis or post-IVI endophthalmitis; 0.020% vs. 0.035% in pre-COVID and COVID periods.[35,36] Current standards of facial draping and 0.25% povidone-iodine ocular surface irrigation are successful prophylactic measures to reduce case incidences.[35]

The Future of COVID

As we continue to understand COVID, what future outcomes are on the horizon? Present long-term complications include cardiovascular, neurological, psychological, hematological, pulmonary and dermatological problems.[37] Current studies are delving into the most common "long-COVID" complaints, pulmonary and neurologic symptom-complex.[38] Rapidly changing variants also complicate long-term studies of viral complications. Larger, published studies are needed to classify long-term symptom presentations and patient follow-up trends.[37]

The new mRNA vaccines must still overcome several challenges to meet worldwide market needs. The inability to control the virus has led to development of new variants that have shown a reduction in the effectiveness of therapeutics and vaccinations.[37,39] Upcoming research and development for future variants rely on immunological vaccine



WE'RE SEEING AMAZING RESULTS. AND SO ARE THEY.

At the Foundation Fighting Blindness our mission is everybody's vision. Our work shines a light on the darkness of inherited retinal diseases (IRDs).

We're the world's leading organization searching for treatments and cures. We need your help to fuel the discovery of innovations that will illuminate the future for so many. We have robust disease information, a national network of local chapters and support groups, local educational events, and our My Retina Tracker® Registry to help keep your patients connected with clinical and research advancements.

Help accelerate our mission by donating at ECPs4Cures.org.

FOUNDATION FIGHTING BLINDNESS

FightingBlindness.org

Table 4. COVID-19 Vaccine Neuro-Ophthalmic Complications[29]

Optic neuritis
Uveitis
Herpes zoster ophthalmicus
Acute macular neuroretinopathy
Optic disc edema as an atypical presentation of Guillain-Barré syndrome
Arteritic anterior ischemic optic neuropathy
Abducens nerve palsy

design, total number of doses needed, dosing intervals and approaches to achieve safe, durable vaccine immunity in both children and adults.[39] Further development is needed to find an adjustable formulation platform resulting in less or no adverse effects, access to low-income countries and tackling previous racial discrepancies.[37,40]

The success of mRNA vaccines in COVID-19 highlighted the potential for future disease management in infectious diseases, cancer and protein replacement therapies.40 Traditional administration routes of mRNA therapies are limited to intramuscular and intravenous in delivery, but forthcoming researchers are evaluating intranasal and oral delivery options.[40] Patients with COVID-19, especially those with severe cases with multiorgan failure, have been shown to have markedly elevated inflammatory markers and proinflammatory cytokines. Multiple trials are underway to evaluate blocking these proinflammatory pathways to ease disease progression.

As we continue to learn more about COVID-19 variants and "long COVID," it is likely that there are other ophthalmic manifestations that are still unknown. Clinicians must be aware of related complications of ocular disease with or without a formal COVID diagnosis and/or receipt of vaccinations. Future research will allow for better understanding of underlying mechanisms of disease variants, accurate treatments and the ability to prevent unwanted consequences of the infection or the vaccines.[22,41]

The CDC-supported COVID Data Tracker (covid.cdc.gov/covid-data-tracker/#datatracker-home) provides daily epidemiologic updates for the US regarding COVID-19. Also, one can further delve into local communal transmission data with trending variants and travel guidance recommendations.

Nonetheless, as more of the population is vaccinated, we are hopeful that systemic suffering and ocular complications will soon cease. ■

1. World Health Organization. WHO coronavirus (COVID-19) dashboard. Last updated August 31, 2022. covid19.who.int. Accessed September 1, 2022.

2. Leung EH, Fan J, Flynn Jr. HW, Albini TA. Ocular and systemic complications of COVID-19: impact on patients and healthcare. Clin Ophthalmol. 2022;16:1-13.

3. Davis G, Li K, Thankam FG, et al Ocular transmissibility of COVID-19: possibilities and perspectives. Mol Cell Biochem. 2022;477(3): 849-64.

4. Hu K, Patel J, Swiston C, et al. Ophthalmic manifestations of coronavirus (COVID-19). In: StatPearls [Internet]. Treasure Island (FL): StatPearls Publishing. Updated May 24, 2022. ncbi.nlm.nih.gov/books/NBK556093/. Accessed September 1, 2022.

5. Zhou L, Xu Z, Castiglione GM, et al. ACE2 and TMPRSS2 are expressed on the humanocular surface, suggesting susceptibility to SARS-CoV-2infection. Ocul Surf. 2020;18:537-44.

6. Baj J, Forma A, Teresińska B, et al. How does SARS-CoV-2 affect our eyes-what have we learnt so far about the ophthalmic manifestations of COVID-19? J Clin Med. 2022;11(12):3379.

7. Jackson RM, Hatton CF, Spegarova JS, et al. Conjunctival epithelial cells resist productive SARS-CoV-2 infection. Stem Cell Reports. 2022;17(7):1699-713.

8. Furdova A, Vesely P, Trnka M, et al. Conjunctival swab findings in 484 COVID-19 patients in four hospital centers in Slovakia. Vision (Basel). 2022;6(3):46.

9. McHarg M, Wang Y, Yakin M, et al. Ocular symptoms In COVID-19 infection: a survey study. Res Sq. June 1, 2022. [Preprint].

10. Zhang Y, Stewart JM. Retinal and choroidal manifestations of COVID-19. Curr Opin Ophthalmol. 2021;32(6):536-40.

11. Sen M, Honavar SG, Sharma N, Sachdev MS. COVID-19 and eye: a review of ophthalmic manifestations of COVID-19. Indian J Ophthalmol. 2021;69(3):488-509.

12. Sen S, Kannan NB, Kumar J, et al. Retinal manifestations in patients with SARS-CoV-2 infection and pathogenetic implications: a systematic review. Int Ophthalmol. 2022;42(1):323-36.

13. Sutandi N, Lee F. Vitreoretinal abnormalities in corona virus disease 2019 patients: what we know so far. Taiwan J Ophthalmol. 2021;11(3):232-43.

14. Abrishami M, Daneshvar R, Emamverdian Z, et al. Spectral-domain optical coherence tomography assessment of retinal and choroidal changes in patients with coronavirus disease 2019: a case-control study. J Ophthalmic Inflamm Infect. 2022;12(1):18.

15. Landis BC, Brooks AE, Digre KB, Seay MD. Coronavirus disease 2019, eye pain, headache and beyond. J Neuroophthalmol. 2022;42(1):18-25.

16. Tisdale AK, Dinkin M, Chwalisz BK. Afferent and efferent neuro-ophthalmic complications of coronavirus disease 19. J Neuroophthalmol. 2021;41(2):154-65.

17. Douedi S, Naser H, Mazahir U, Hamad AI, Sedarous M. Third cranial nerve palsy due to COVID-19 infection. Cureus. 2021;13(4):e14280.

18. Marsiglia M, Chwalisz BK, Maher M. neuroradiologic imaging of neurologic and neuro-ophthalmic complications of coronavirus-19 infection. J Neuroophthalmol. 2021;41(4):452-60.

19. Gold DM, Galetta SL. Neuro-ophthalmologic complications of coronavirus disease 2019 (COVID-19). Neurosci Lett. 2021;742:135531.

20. Luo W, Liu X, Bao K, Huang C. Ischemic stroke associated with COVID-19: a systematic review and meta-analysis. J Neurol. 2022;269(4):1731-40.

21. De Michele M, Kahan J, Berto I, et al. Cerebrovascular complications of COVID-19 and COVID-19 vaccination. Circ Res. 2022;130(8):1187-1203.

22. Nyankerh CNA, Boateng AK, Appah M. Ocular complications after COVID-19 vaccination, vaccine adverse event reporting system. Vaccines (Basel). 2022;10(6):941.

23. Wang MTM, Niederer RL, McGhee CNJ, Danesh-Meyer HV. COVID-19 vaccination and the eye. Am J Ophthalmol. 2022;240:79-98.

24. Chew MC, Wiryasaputra S, Wu M, et al. Incidence of COVID-19 vaccination-related uveitis and effects of booster dose in a tertiary uveitis referral center. Front Med (Lausanne). 2022;9:925683.

25. Bolletta E, Iannetta D, Mastrofilippo V, et al. Uveitis and other ocular complications following COVID-19 vaccination. J Clin Med. 2021;10(24):5960.

26. Ortiz-Egea JM, Sánchez CG, López-Jiménez A, Navarro OD. Herpetic anterior uveitis following Pfizer-BioNTech coronavirus disease 2019 vaccine: two case reports. J Med Case Rep. 2022;16(1):127.

27. Dugan SP, Mian SI. Impact of vaccination on keratoplasty. Curr Opin Ophthalmol. 2022;33(4):296-305.

28. Sen M, Honavar SG. After the Storm: Ophthalmic manifestations of COVID-19 vaccines. Indian J Ophthalmol. 2021;69(12):3398-420.

29. Lotan I, Lydston M, Levy M. Neuro-ophthalmological complications of the COVID-19 vaccines: a systematic review. J Neuroophthalmol. 2022;42(2):154-62.

30. Kubota T, Hasegawa T, Ikeda K and Aoki M. Case Report: Isolated, unilateral oculomotor palsy with anti-GQ1b antibody following COVID-19 vaccination. F1000Res. 2022;10:1142.

31. Cheng JY, Margo CE. Ocular adverse events following vaccination: overview and update. Surv Ophthalmol. 2022;67(2):293-306.

32. White DE. Blog: MADE: a new coronavirus-associated eye disease. June 22, 2020. www.healio.com/news/ophthalmology/20200622/blog-a-new-coronavirusassociated-eye-disease. Accessed September 1, 2022.

33. Fan Q, Liang M, Kong W, et al. Wearing face masks and possibility for dry eye during the COVID-19 pandemic. Sci Rep. 2022;12(1):6214.

34. Charters, Linda. Taping surgical masks to the skin decreases risk of ocular surface damage during the COVID-19 pandemic. Ophthalmology Times. May 2, 2022. www.ophthalmologytimes.com/view/taping-surgical-masks-to-the-skin-decreases-risk-of-ocular-surface-damage-during-the-covid-19-pandemic. Accessed September 1, 2022.

35. Tanaka K, Shimada H, Mori R, et al. Safety measures for maintaining low endophthalmitis rate after intravitreal anti-vascular endothelial growth factor injection before and during the COVID-19 pandemic. J Clin Med. 2022;11(3):876.

36. Mirghorbani M, Bazvand F, Riazi-Esfahani H, et al. Post-intravitreal injection endophthalmitis pattern during the COVID-19 pandemic with implementation of patients' masking. Graefes Arch Clin Exp Ophthalmol. June 9, 2022. [Epub ahead of print].

37. Desai AD, Lavelle M, Boursiquot BC, Wan EY. Long-term complications of COVID-19. Am J Physiol Cell Physiol. 2022;322(1):C1-11.

38. Robinson PC, Liew DFL, Tanner HL, et al. COVID-19 therapeutics: challenges and directions for the future. Proc Natl Acad Sci USA. 2022;119(15):e2119893119.

39. Altmann DM, Boyton RJ. COVID-19 vaccination: The road ahead. Science. 2022;375(6585):1127-32.

40 Szabó GT, Mahiny AJ, Vlatkovic I. COVID-19 mRNA vaccines: platforms and current developments. Mol Ther. 2022;30(5):1850-68.

41. Baj J, Forma A, Teresińska B, et al. How does SARS-CoV-2 affect our eyes-what have we learnt so far about the ophthalmic manifestations of COVID-19? J Clin Med. 2022;11(12):3379.

For patients with Graves' disease (GD), Thyroid Eye Disease (TED) may be hiding in plain sight.[1,2]

Up to 50% of patients with GD may develop TED, a separate and distinct disease which can progress if left untreated. Look out for the early signs and symptoms[3-7]:

- **Proptosis**[1]
- **Diplopia**[3]
- **Dry eyes**[8-11]
- **Sensitivity to light**[12]
- **Grittiness**[8-11]
- **Pain or pressure behind the eyes**[1,13]

If you identify new or changing signs or symptoms, consult with an eye doctor who specializes in TED right away.[1,14]

Visit TEDimpact.com to find a TED specialist or contact a Horizon Representative at 1-855-950-2076.

References: 1. Barrio-Barrio J, Sabater AL, Bonet-Farriol E, Velázquez-Villoria Á, Galofré JC. Graves' ophthalmopathy: VISA versus EUGOGO classification, assessment, and management. *J Ophthalmol*. 2015;2015:249125. **2.** Bothun ED, Scheurer RA, Harrison AR, Lee MS. Update on thyroid eye disease and management. *Clin Ophthalmol*. 2009;3:543-551. **3.** Bahn RS. Graves' ophthalmopathy. *N Engl J Med*. 2010;362(8):726-738. **4.** Bartalena L, Krassas GE, Wiersinga W, et al. Efficacy and safety of three different cumulative doses of intravenous methylprednisolone for moderate to severe and active Graves' orbitopathy. *J Clin Endocrinol Metab*. 2012;97(12):4454-4463. **5.** Patel A, Yang H, Douglas RS. A new era in the treatment of thyroid eye disease. *Am J Ophthalmol*. 2019;208:281-288. **6.** Ponto KA, Pitz S, Pfeiffer N, Hommel G, Weber MM, Kahaly GJ. Quality of life and occupational disability in endocrine orbitopathy. *Dtsch Arztebl Int*. 2009;106(17):283-289. **7.** Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med*. 2017;376(18):1748-1761. **8.** Bartley GB, Fatourechi V, Kadrmas EF, et al. Long-term follow-up of Graves ophthalmopathy in an incidence cohort. *Ophthalmology*. 1996;103(6):958-962. **9.** Terwee C, Wakelkamp I, Tan S, Dekker F, Prummel MF, Wiersinga W. Long-term effects of Graves' ophthalmopathy on health-related quality of life. *Eur J Endocrinol*. 2002;146(6):751-757. **10.** Bartley GB. The epidemiologic characteristics and clinical course of ophthalmopathy associated with autoimmune thyroid disease in Olmsted County, Minnesota. *Trans Am Ophthalmol Soc*. 1994;92:477-588. **11.** Estcourt S, Hickey J, Perros P, Dayan C, Vaidya B. The patient experience of services for thyroid eye disease in the United Kingdom: results of a nationwide survey. *Eur J Endocrinol*. 2009;161(3):483-487. doi:10.1530/EJE-09-0383. **12.** Dolman PJ. Grading severity and activity in thyroid eye disease. *Ophthalmic Plast Reconstr Surg*. 2018;34(4S suppl):S34-S40. **13.** Phelps PO, Williams K. Thyroid eye disease for the primary care physician. *Dis Mon*. 2014;60(6):292-298. **14.** Ross DS, Burch HB, Cooper DS, et al. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid*. 2016;26(10):1343-1421.

HORIZON

Earn 2 CE Credits
(COPE APPROVED)

WHAT ODs NEED TO KNOW ABOUT THYROID EYE DISEASE

Understanding how to approach the diagnosis and management of this condition is a key role of the primary eyecare provider.

BY MICHAEL CARSTENS, OD
DURHAM, NC

Thyroid eye disease (TED) has been called many names such as thyroid-associated orbitopathy, dysthyroid orbitopathy and thyrotoxic exophthalmos. TED is commonly associated with Graves' disease (GD), which is used synonymously with Graves' orbitopathy and Graves' ophthalmopathy in the literature.

GD or Graves' hyperthyroidism is a relatively common autoimmune disease affecting somewhere between 1% and 3% of the adult population. The onset of GD is typically between the ages of 30 and 50. It's more common in women than men; however, males and those over 50 tend to develop more severe disease.[1] Around 20% to 50% of GD patients will develop ophthalmologic signs, usually within two years of diagnosis of thyroid disease. Approximately 90% of TED patients will have hyperthyroidism, and the remainder will be euthyroid or have TED associated with Hashimoto's disease or secondary to primary hyperthyroidism.[1] Around 40% will present clinical signs before or at the time of diagnosis.[1,2]

As an optometrist, you are likely to encounter several patients with TED over the course of your career. Familiarizing yourself with the clinical signs and symptoms and diagnostic testing as well as the latest management strategies can significantly improve your patients' outcomes and quality of life.

Pathogenesis of TED

Erroneous and excessive orbital fibroblast (OF) activity has been identified as the primary mechanism in Grave's orbitopathy. Fibroblasts, derived from mesenchymal stem cells in the bone marrow, can reside in connective tissue or can be found circulating throughout the body. They are most commonly associated with structural maintenance and produce extracellular matrix proteins such as collagen and glycosaminoglycans. However, OF also play a significant role in the immune response to tissue injury. They are capable of activating T-cells through antigen presentation and cytokine secretion; in turn, T-cells engage in regulating OF activity and differentiation.

The link between the thyroid and OF is not well understood. However, distinct populations of orbital fibroblasts of GD patients have been identified, and these cells vary in their capacities for gene expression, cytokine release and differentiation.[3] Orbital fibroblasts, especially those from GD patients, can be hyper-responsive when compared with fibroblasts from other anatomical locations.[4]

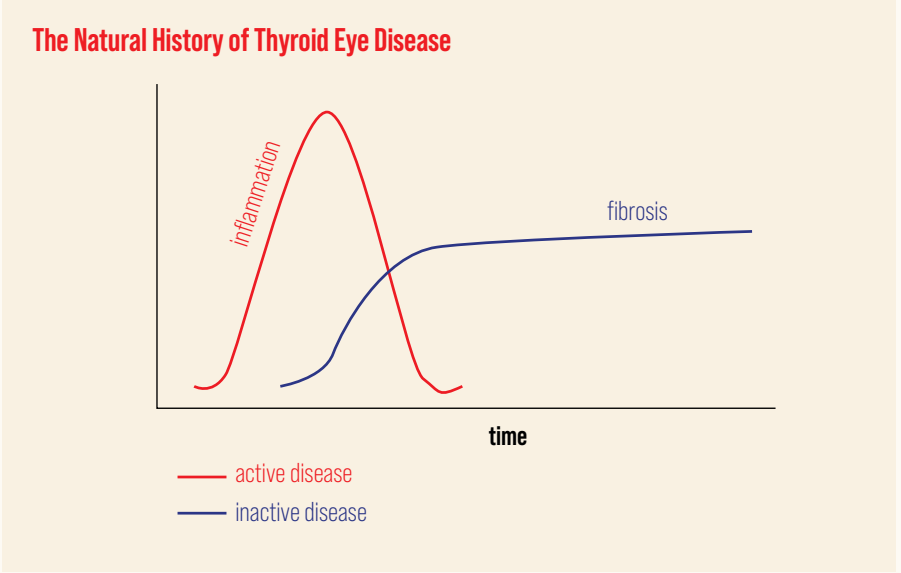
It has recently been shown that orbital fibroblasts, especially those of GD patients, display both thyrotropin (TSH) and insulin-like growth factor-1 receptors (IGF-1). These receptors reside in close proximity of one another on the cell surface,

About the author **Dr. Carstens** is a clinical supervisor and director of optometric education at the Durham VA Medical Center in North Carolina. He has no relevant financial interests to disclose.

and physical scaffolds between them enable cross-talk.[5] Stimulation of this TSH-IGF-1 receptor complex results in the secretion of hyaluronic acid and cytokines. Thus, the IGF-1 receptor has also been implicated in the pathogenesis of TED. Teprotumumab exploits the IGF-1 receptor pathway in its mechanism of action and will be discussed later.

During the inflammatory phase of GD, excessive production of extracellular matrix proteins, notably the highly hydrophilic HA, from activated fibroblasts leads to connective tissue and extraocular muscle edema and dysfunction. Muscle swelling along with an increase in adipogenesis (by way of fibroblast differentiation) results in an overall increase in orbital tissue volume. Due to the rigid confines of the bony orbital walls, the increase in volume pushes the globe forward and creates congestion at the orbital apex.

As the acute inflammatory phase resolves, tissue remodeling and fibrosis proceeds while the orbital fibroblasts continue to differentiate into adipocytes and myofibrocytes. The result can be permanent motility dysfunction and disfigurement and should be avoided at all costs.



TED has two different phases: an active and an inactive.

Natural History

This can be categorized by two phases: the initial inflammatory phase, or active phase, followed by an inactive or fibrotic phase. During the active phase, clinical signs and symptoms can progress rather rapidly before quieting spontaneously after six to 18 months. Although inflammation subsides, patients rarely return to their baseline in the inactive state. It's important to understand the different management strategies for both phases of the disease, as treatment and monitoring vary greatly.

Two subtypes of TED have been described, and their clinical courses can differ substantially. Type I tends to be found in younger patients with a whiter and quieter presentation, less muscle involvement and more fat deposition in the orbit. As a result, these patients are less likely to develop diplopia and dysthyroid optic neuropathy (DON). Type II is more likely to occur in older patients with more overt anterior segment inflammation such as conjunctival injection, eyelid edema and chemosis. These patients tend to have more muscle involvement and are at higher risk of DON. Smokers are more likely to fall into the type II category.

TED in the Clinic

Evaluation of a patient with suspected TED should start with a detailed

Release Date: October 15, 2022

Expiration Date: October 15, 2025

Estimated Time to Complete Activity: two hours

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

JOINTLY ACCREDITED PROVIDER™ INTERPROFESSIONAL CONTINUING EDUCATION

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

- Identify thyroid eye disease among their patients.
- Determine when and how they should use clinical activity scores.
- Determine the best treatment approach for their patients.
- Recognize when to get additional labs and/or imaging, or when to refer.

Target Audience: This activity is intended for optometrists engaged in thyroid eye disease management.

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.

Reviewed by: Salus University, Elkins Park, PA SALUS UNIVERSITY

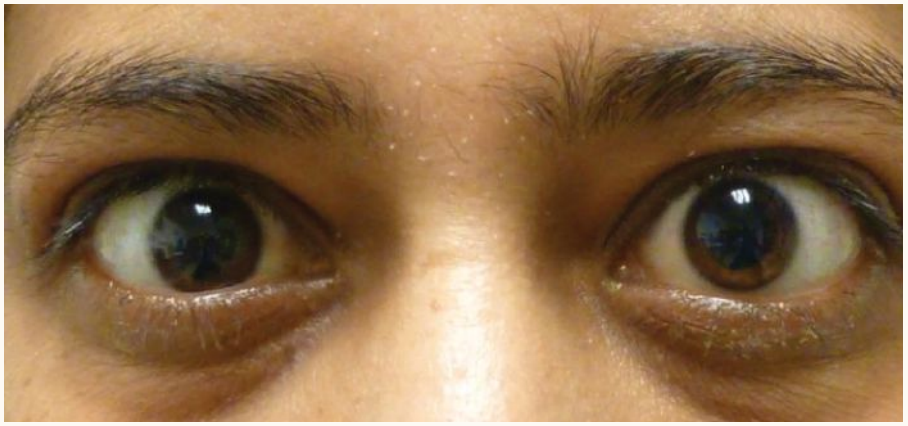
Faculty/Editorial Board: Michael Carstens, OD

Credit Statement: This course is COPE-approved for two hours of CE credit. Activity #124729 and course ID 80840-SD. Check with your local state licensing board to see if this counts toward your CE requirement for relicensure.

Disclosure Statements: 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 healthcare 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: *Author:* Dr. Carstens has no relevant financial interests to disclose. *Managers and Editorial Staff:* The PIM planners and managers have nothing to disclose. The Review Education Group planners, managers and editorial staff have nothing to disclose.

Photo: Michael Richard, MD



Mild lid retraction with temporal flare.

history including a review of systems with specific questions relating to thyroid disfunction. For hyperthyroidism, ask about recent weight loss, increased sweating, heat intolerance, hair loss, diarrhea, heart palpitations, anxiety and muscle weakness. Conversely, hypothyroidism can cause weight gain, cold intolerance, fatigue, dry skin, depression, change in menses and/or muscle cramps. Risk factors for TED such as smoking or a positive family history should also be assessed.

For those with known thyroid disease, history of planned, current and past therapies should be documented. This is especially important for those with a history of or planned radioactive iodine therapy, as this has been shown to exacerbate or trigger the onset of TED.

The clinical exam should be comprehensive, as TED can present with various clinical signs and symptoms. Patients may complain of dry eyes, pressure or pain behind the eyes and sandy or gritty sensations. Blurred vision, double vision and excessive tearing are also common. They may have an increase in redness or fullness to the eyelids. Some may even notice a change in their physical appearance and report that their eyes look bigger or that they just look different. Diurnal variation is common, with symptoms typically worse in the morning.

Assessment of the patient outside of the slit lamp can provide the first clue of thyroid dysfunction. Facial asymmetry can be subtle and is usually lost behind the magnification of the slit lamp. Attention should be given to the relative positions of the upper and lower eyelids. Upper eyelid retraction is one of the hallmark signs of hyperthyroidism, but it can oftentimes be subtle and overlooked.

This retraction is often characterized as having a "temporal flare," where the lateral aspect of the lid margin is higher than the medial. Retraction can be due to one or a combination of factors including proptosis, levator/Müller's muscle hypertrophy and increased sympathetic tone.[6] The margin to reflex distance (MRD) can be used to quantify upper eyelid retraction. MRD1 is the distance from the pupillary light reflex to the upper eyelid margin. MRD2 is that to the lower eyelid margin. You can also measure the amount of "superior scleral show" or 12:00 limbus to upper eyelid margin at the slit lamp in primary gaze. A value greater than 5mm or asymmetry greater than 1mm is considered abnormal. Von Graefe's sign (superior lid lag on downgaze) can also be observed in TED.

A basic sensory motor exam should always be performed. Extraocular motility and alignment defects can come from infiltration/inflammation of the extraocular muscles (EOMs). This most commonly involves the inferior and medial recti, followed by the superior and lateral recti and oblique muscles. Keep in mind that motility issues in TED are restrictive and do not improve with forced duction testing. This can be useful in differentiating TED from neurogenic causes such as a cranial nerve palsy or myasthenia gravis. A relative afferent pupillary defect is specific for optic nerve dysfunction but is not particularly sensitive when there is bilateral and symmetric disease.

Any patient suspected of having TED should be evaluated for proptosis. This can be easier to detect clinically from a "worm's eye view," with the patient chin-up or laid back while the clinician views their eyes tangentially from below. Displacement of the globe anteriorly can be measured with an exophthalmometer or by radiologic imaging. Hertel exophthalmometry is a quick, easy and reliable test that is found in most comprehensive eye clinics. Normal values vary by race and gender. For Asian patients, 16mm to 18mm is considered normal, whereas 18mm to 20mm is normal for Caucasian and 20mm to 22mm is normal for Black patients.[7] Proptosis reduction can be a primary measure for treatment outcomes and should be recorded at baseline and follow-up visits consistently.

Anterior examination at the slit lamp can reveal evidence of inflammation of the conjunctiva with injection and chemosis. Swelling and injection of the caruncle and muscle insertions are also associated with TED. The tear film and cornea should be evaluated with fluorescein dye. A decreased tear meniscus, shorter tear breakup time and punctate epithelial erosions are suggestive of exposure issues. More advanced cases of TED can have corneal thinning and ulcerations.

The posterior exam should include careful assessment of the optic nerve. Approximately 3% to 7% of patients with TED will have optic neuropathy.[8] The mechanism of DON is thought to be the result of inflammation, compression and ischemia. DON is rarely seen in Graves' orbitopathy patients without significant muscle enlargement. In fact, medial

rectus volume as measured with CT imaging has been shown to be the greatest predictor of DON.[9]

Since optic nerve compression usually occurs from congestion at the orbital apex, visible changes at the optic nerve head can be subtle or absent. Ancillary testing can help support the clinical suspicion of DON. Automated visual fields can show various defects, the most common being altitudinal, arcuate and paracentral.[7] Color vision has been shown to be reduced in 77% of eyes with DON and should be assessed in patients suspected of having TED.[10] More specifically, a 2021 study showed that a tritan (blue-yellow), rather than a protan (red-green) test, was more sensitive for DON.[11]

Studies looking at RNFL thickness have been conducted with variable results. One case-controlled observational study showed an overall increase in superior, nasal and inferior RNFL thickness values in TED patients compared with controls.[12] A prospective longitudinal study showed that RNFL thinning can occur even in mild or subclinical TED.[13] Both studies excluded those with clinically evident DON. The differences in outcomes of these studies can probably be explained by differences in methodology and patient demographics.

Furthermore, the pathogenesis of DON is believed to involve both compression and inflammation, the two of which will have different effects on RNFL thickness. Where active inflammation can increase RNFL thickness values, compression results in thinning of the RNFL. Several studies, including the aforementioned, have supported the finding that macular and ganglion cell layer-inner-plexiform layer thickness may be a more sensitive test for optic neuropathy in TED patients.[14]

Macular OCT can also be useful in identifying more subtle retinal changes that can occur with TED. For instance, choroidal thickness can vary in patients with TED.[15] Macular OCT angiography has also been used to show changes in retinal and choroid blood flow.[16,17] Chorioretinal folds caused by posterior flattening of the globe can be more easily visualized on OCT as well.

Making the Diagnosis

The diagnosis of TED can be made when two of three criteria are met: 1) clinical signs and symptoms as discussed previously, 2) laboratory tests and 3) radiologic signs consistent with thyroid orbitopathy.

Laboratory testing. The three primary tests used to assess thyroid function are TSH, T3 and FreeT4. With the vast majority of TED cases being secondary to GD, it's helpful to include tests for thyroid-stimulating immunoglobulins (TSI) or TSH receptor antibodies. A thyroid antibody panel is sometimes available and will also include thyroid peroxidase antibodies that can be positive in Hashimoto's disease. A strong correlation exists between TSI levels and TED activity scores. Monitoring with TSI levels can sometimes be useful when trying to determine a patient's clinical activity.

Radiologic imaging. When unilateral, equivocal moderate-to-severe clinical disease or DON is suspected, orbital imaging is necessary. Although MRI may be better for soft tissue differentiation, non-contrast CT is preferred due to its lower cost, widespread availability and rapid acquisition time. In most cases, adequate assessment of the EOMs can be achieved without a contrast medium due to the vastly different densities of muscle and fat. CT also allows for the evaluation of the orbital walls and sinuses which can be helpful when planning orbital decompression surgery. MRI allows for better resolution of soft tissue and can be useful for cases where the clinical diagnosis is uncertain, atypical or unilateral. It may also be helpful in assessing clinical activity.

EOM belly enlargement (with tendon sparing) and fat expansion are the hallmark radiologic findings of Graves' orbitopathy. The most common muscles involved are the inferior rectus and medial rectus, followed by the superior rectus, lateral rectus and oblique rectus. However, other findings such as fat stranding, anterior soft tissue swelling, lacrimal gland enlargement, exophthalmos and superior optic vein dilatation can also be observed.[18]

Clinical Grading Systems

Management of TED is based on clinical disease activity and severity of signs and symptoms. Accurate assessment of these parameters is critical when developing a treatment plan. There have been a handful of grading systems that have been created over the years to facilitate this process. The most common are the CAS, NOSPECS, VISA and EUGOGO classification systems.

CAS, first published in 2003, stands for Clinical Activity Score and has been widely used in evaluating treatment efficacy in clinical trials. It is based on four classic signs of inflammation (pain, redness, swelling and impaired function). One point is given for each clinical element (one through seven) present the initial

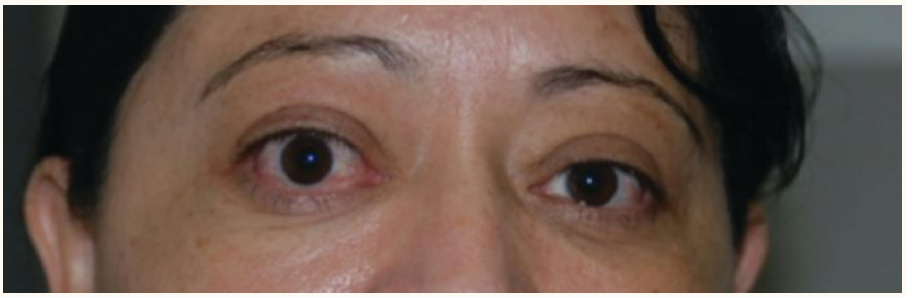


Photo: Michael Richard, MD

Mild proptosis, upper lid retraction and conjunctival injection evident the right eye.

Table 1. CAS Scoring

Pain	1	Pain behind the eye (in the last four weeks)
	2	Pain on eye movement (in the last four weeks)
Redness	3	Eyelid hyperemia
	4	Conjunctival hyperemia in more than one quadrant
Swelling	5	Eyelid edema
	6	Chemosis
	7	Swelling of the caruncle
Impaired function	8	Increase in proptosis ≥2mm over one to three months
	9	Decrease in motility in any direction ≥5° over one to three months
	10	Decrease in visual acuity ≥one line on Snellen

visit. Elements eight through 10 are used on follow-up to reflect disease progression. A CAS score of three or more is considered active disease. A score of four or more, when including elements eight through 10 at follow-up is indicative of progression.[19]

NOSPECS stands for No signs or symptoms, Only symptoms, Soft tissue involvement, Proptosis, EOM involvement, Corneal involvement and Sight loss. This system was developed in the late 60s and modified again in the late 70s. The mnemonic may be helpful to some clinicians or students as a reminder of the clinical signs and symptoms in TED, but its usefulness in monitoring progression and response to therapy is limited and has since fallen out of favor.

The VISA (Vision, Inflammation, Strabismus and Appearance) classification system was developed in 2006 and has been adopted by the International Thyroid Eye Disease Society (ITEDS). It attempts to quantify activity and severity levels while also making basic treatment recommendations. VISA uses a weighted point system to determine severity, and each parameter is graded independently. Activity is measured by progression within any of the categories as defined within each element. ITEDS has a clinical record form available online for download that can guide practitioners through the scoring and monitoring process. The VISA grading system incorporates both objective and subjective data to create its management plans.

The EUGOGO (European Group on Graves' Orbitopathy) protocol was developed in 2008 and revised in 2016 and again in 2021.[20] This is the most widely accepted system used today and attempts to provide grading of clinical activity and severity as well as provide guidance on treatment and management. It is the first system to include a GD-specific quality of life questionnaire (GO-QoL) in its algorithm. Disease activity scoring follows the CAS protocol where a score greater than three at the initial visit is active, and a score of four or higher at follow-up is considered active/progressive. Disease severity is broken down into three categories: mild, moderate-to-severe and sight-threatening.

Patient Management

For all patients with GD, the first step in management is to control risk factors for progression. Management of thyroid disfunction is crucial and will involve communication with the patient's primary care physician or endocrinologist. A referral to oculoplastics or neuro-ophthalmology should be made for those with clinically active moderate-to-severe or sight-threatening disease. A discussion about smoking cessation is imperative, as evidence suggests current smokers are twice as likely to develop TED and more likely to have severe disease and relapse than non-smokers.[21]

Mild disease. For mild Graves' orbitopathy, management focuses on local treatment of the ocular surface. Dry eye treatment options

Table 2. EUGOGO Scoring

Severity	Characteristics
Mild	Minor impact on daily life. May have one or more of the following: - Mild lid retraction (<2mm) - Mild soft tissue involvement - Exophthalmos <3mm above age- and gender-expected values - Intermittent or no diplopia - Corneal exposure that responds to topical lubricants
Moderate-to-severe	Non-sight-threatening Graves' orbitopathy with an impact on daily life significant enough to justify the risks of immunosuppression or surgery Often have two or more of the following: - Lid retraction ≥2mm - Moderate or severe soft tissue involvement - Exophthalmos ≥3mm above age- and gender-expected values - Intermittent or constant diplopia - Variable or constant diplopia
Sight-threatening	Patients with corneal breakdown or DON

are ever-expanding and are certainly in the wheelhouse of modern-day optometry. Ocular lubricants in the form of tears, gels and ointments are first-line options in exposure-related dry eye. Punctual occlusion can also be considered.

The role of topical immunomodulators like cyclosporin and lifitegrast has yet to be established in patients with active Graves' orbitopathy. One study on topical cyclosporine showed no benefit to those with inactive TED and dry eye disease already taking artificial tears four times a day.[22]

Intermittent diplopia can sometimes be managed with prismatic correction. The use of fresnel prism may be more appropriate as the magnitude and direction can change frequently.

Selenium supplementation (200µg/day) has been shown to reduce progression of Graves' orbitopathy and improve quality of life in those with mild disease; however, this benefit has only been shown in selenium-deficient areas.[20] Selenium supplementation can help achieve euthyroidism faster in those with GD and inadequate intake. Laboratory testing of serum selenium levels prior to initiating supplementation is recommended so that overdosing and toxicity can be avoided.[23]

Sometimes mild inactive disease can lead to cosmetic disfigurement and quality of life issues that can justify a surgical referral. An example would be when there is unilateral lid retraction or proptosis that does not meet the moderate-to-severe criteria.

Moderate-to-severe disease. The EUGOGO 2021 publication of clinical practice guidelines is a comprehensive manual on the treatment of moderate-to-severe and sight-threatening Graves' orbitopathy. Recommendations were made by a consensus of a 48-member task force, following a comprehensive review of published clinical trials. These recommendations will be reviewed later.

For active moderate-to-severe Graves' orbitopathy, first-line treatment is often with systemic corticosteroids. Intravenous methylprednisolone (IVMP) is given at either an intermediate dose (500mg once weekly for six weeks followed by 250mg weekly for six weeks) or a high dose (750mg weekly for six weeks followed by 250mg weekly for six weeks). High-dose IVMP is reserved for more severe disease as it carries a higher risk of liver toxicity and cardiovascular side effects. Intravenous administration of steroids is preferred due to increased efficacy and overall fewer side effects when compared with oral steroids.[20,24] A referral to an institution with the means and experience to manage dosing and side effects is suggested. The benefits of IVMP are maximized with earlier intervention, and delayed referral can affect clinical outcomes.

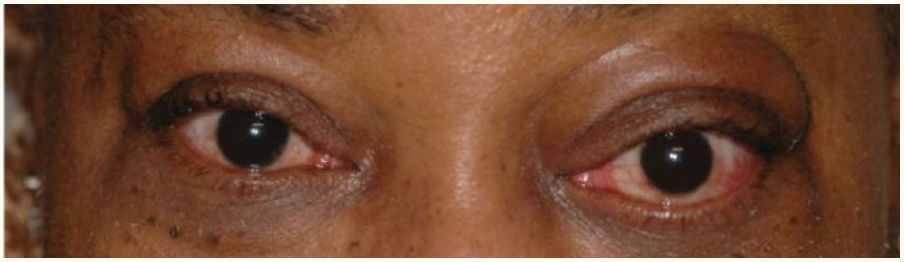


Photo: Michael Richard, MD

Proptosis, eyelid edema, mild upper lid retraction and lower lid lagophthalmos.

Contraindications for IVMP include recent hepatitis, liver dysfunction, cardiovascular morbidity, severe hypertension, inadequately managed diabetes and severe or uncontrolled glaucoma.[25] Prior to starting a corticosteroid, control of diabetes and hypertension should be optimized and there should be extensive discussion on patient expectations and outcomes. Although clinical and quality of life improvement following steroid treatment can be as high as 80%, it is unlikely that patients return to their pre-disease state, and additional treatment and sometimes surgery is required to manage residual complications of Graves' orbitopathy like strabismus and proptosis.

When there is an inadequate response to initial steroid therapy, secondary treatment options can be considered. Options are numerous, and decision-making is multifactorial.

Orbital radiotherapy is generally considered a safe and effective second-line therapy. It's most beneficial in reducing soft tissue swelling and can improve extraocular motility; however, it does not typically improve proptosis. It is more effective when combined with oral or IV steroids.[20] It should be avoided in patients with hypertensive or diabetic retinopathy due to the potential for radiation retinopathy.

There are several immune-modulators that have emerged in the last decade that can be used as an adjunct to steroids or sometimes as monotherapy. One of the more favorable is mycophenolate, a drug primarily used as an immunosuppressant following organ transplantation. Its popularity for use in other autoimmune disease has grown due to its safety and efficacy profile.[24] Mycophenolate is known to inhibit proliferation of B- and T-cells as well as fibroblasts.

As an adjunct, it has been shown to increase the efficacy of IVMP without increasing side effects. Thus, mycophenolate has been recommended with IVMP as a first-line option by the EUGOGO. It can also be used as a standalone option when steroids are contraindicated.[20] Mycophenolate sodium is taken orally at 0.72g/day.

Cyclosporine, another T-cell inhibitor, has been shown to be effective only in combination with steroids. When trialed as monotherapy, it was inferior to corticosteroids in both efficacy and relapse rate. The potential for renal toxicity makes cyclosporine less attractive than other second-line options. Azathioprine is another anti-proliferative agent that is similar to mycophenolate in mechanism but carries a higher risk of side effects.

The emergence of monoclonal antibody therapies (mAbs) has significantly changed the treatment landscape in nearly all areas of medicine over the last three decades. This class of medications can bind to their target with high specificity. Because mAbs do not undergo hepatic or renal metabolism, they also have a lower propensity for drug interactions. The evolution of mAbs from murine and chimeric antibodies to fully human mAbs has significantly helped to reduce the risk of developing an anti-antibody response.[26]

A handful of mAbs have been studied in clinical trials. The most notable are rituximab, tocilizumab and teprotumumab. Rituximab is a chimeric mAb against the CD20 surface antigen found on B-cells. Few randomized controlled trials of rituximab in patients with Graves' orbitopathy have been done, and the results have been conflicting.

Tocilizumab is a humanized mAb against the interleukin-6 receptor. Clinical trials with tocilizumab have only been done with steroid-resistant TED, and the results were favorable for CAS reduction and disease inactivation; however, proptosis reduction was modest, and there was no difference in quality of life measures compared with placebo.[20,24]

Teprotumumab, a fully human mAb, is the first FDA-approved treatment for Graves' orbitopathy. It is directed against the IGF-1 receptor, which, as discussed earlier, is coupled with the TSH receptor and overexpressed by OF, T- and B-cells in GD. Phase III trials of teprotumumab (OPTIC trials) showed a significant number of patients had ≥2mm reduction in proptosis when compared with placebo (83% vs. 10%, respectively). Inactivation of disease was 59% in the treatment group vs. 21% in the placebo group. A significant reduction in diplopia was achieved in 68% vs. 29% of cases, respectively.[27]

A follow-up and extension trial (OPTIC-X) included participants from the OPTIC trial that either were non-responders, experienced relapse or belonged to the placebo group. Naturally, these patients had a longer mean duration of active disease than the original OPTIC study participants (12.9 months vs. 6.3 months). Patient outcomes and adverse events were similar to the original study and were validated over a longer follow-up period (48 weeks vs. 24 weeks in the OPTIC trial).

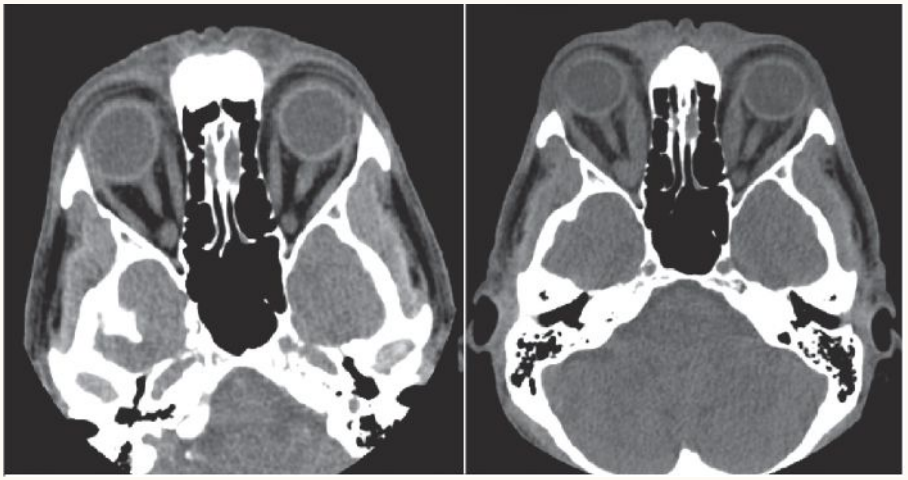
Results from the OPTIC-X trial suggest that response to treatment with teprotumumab is durable in most, and some non-responders can potentially benefit from a second treatment. It also raises the question of whether teprotumumab can be used in those with inactive disease, as a handful of patients who experienced proptosis reduction had a CAS score of zero or one at baseline.[29]

Teprotumumab is administered by infusion with a dose of 10mg/kg for the first dose, followed by seven infusions of 20mg/kg spaced three weeks apart for a total of 24 weeks. It is generally well-tolerated with most side effects being mild-to-moderate. The most common are muscle spasms, alopecia, nausea and fatigue. Less than 5% of patients in the clinical trials experienced hearing impairment and hyperglycemia. Patients with irritable bowel disease should be counselled, as a flareup is possible. Infusion reactions can occur and include transient increases in blood pressure, tachycardia, dyspnea, headache and muscular pain. Reactions are usually mild or moderate in severity and can usually be successfully managed with corticosteroids and antihistamines.[27,28]

Recommendations for use of teprotumumab in clinical practice were published by the OPTIC trial investigators in 2019.[29] The authors suggest that prior to starting teprotumumab, patients should undergo a complete physical exam (with measurements of height, weight and blood pressure), standard laboratory tests (including complete blood count, liver function tests, fasting glucose and hemoglobin A1c) and an electrocardiogram. A comprehensive eye exam should be performed and include measurements such as motility, strabismus and exophthalmometry.

Teprotumumab has not been compared head-to-head with steroids or other mAbs in clinical trials. The biggest barrier to treatment currently is cost, especially when compared with corticosteroids. A 24-week course can run close to $350,000. Prior authorization is needed for most insurance plans, and some may require a trial with steroids prior to approval.

Sight-threatening disease. Vision loss from DON or severe corneal comprise occurs in a small percentage of patients with TED. Prompt referral is necessary to ensure optimal out-



CT of orbits showing a patient in 2017 before the onset of GD (left) and in 2020 after onset (right). Note the medial rectus enlargement.

comes in these cases. Treatment of such sight-threatening disease usually involves a course of high-dose IVMP and is sometimes followed by orbital radiation and/or surgical decompression. Decompression is achieved by removing soft tissue and/or expanding the bony walls to decompress the optic nerve at the orbital apex.[30] There are different approaches to decompression surgery, and the choice can vary by the patient's needs and the surgeon's preference. Teprotumumab or other immunologic agents may play a role in treating sight-threatening TED especially in refractory cases or when surgery may be contraindicated.

Inactive disease. As noted, despite even the best attempts at controlling inflammation during the active phase of TED, very few patients return to their pre-disease state when it subsides. Dry eye, diplopia, lid retraction and proptosis are common sequelae. Some patients, especially those with concern for chronic exposure keratopathy and/or significant disfigurement, may require surgery. In extreme cases, multiple procedures may be necessary. Comanagement with strabismus and oculoplastic surgeons is not uncommon.

Patients may have to wait months for their disease to stabilize before they are eligible for surgery, and during that time temporary solutions may be necessary. For diplopia, Fresnel prism or patching may be needed. Taping lids and aggressively lubricating with gels and ointments can help protect the cornea from exposure. With or without rehabilitative surgeries, residual dry eye and diplopia can still occur. Various strategies exist in the management of these chronic conditions.

Summary

TED has the potential to be a sight-threatening and debilitating condition that can present with a wide variety of clinical signs and symptoms. It is characterized by an active phase of autoimmune driven orbital and soft tissue inflammation that lasts roughly six to 18 months in total, followed by an inactive phase of chronic tissue fibrosis. Disease relapse (or reactivation) is uncommon but not rare and may occur in about 15% of affected patients.[30]

A diagnosis of TED is made by a combination of clinical signs, laboratory testing and/or radiologic imaging. In order to optimize treatment outcomes, early recognition is necessary, and communication with primary care and/or endocrinology for the treatment of the underlying hyper or hypothyroidism is critical.

Clinical disease activity and severity grading should be assessed to help determine the best treatment strategy for the patient. Moderate-to-severe and sight-threatening active disease should be referred to subspecialists with experience treating TED. First-line treatment for these severity stages has historically involved intravenous steroids; however, newly developed and more targeted treatments are gaining popularity due to their potential for better clinical outcomes and safety profiles.

As a primary eyecare provider, a comprehensive understanding of the clinical signs of TED as well as the diagnostic testing and appropriate treatment and monitoring strategies is critical to ensure better outcomes for your patients with this condition. ■

1. Kendler DL, Lippa J, Rootman J. The initial clinical characteristics of Graves' orbitopathy vary with age and sex. Arch Ophthalmol. 1993;111(2):197-201.

2. Davies T, Burch H. Clinical features of Graves' orbitopathy (ophthalmology). UpToDate. Last updated Mar 19, 2021.

3. Koumas L, Smith TJ, Feldon S, et al. Thy-1 expression in human fibroblast subsets defines myofibroblastic or lipofibroblastic phenotypes. Am J Pathol. 2003;163(4):1291-1300.

4. Dik WA, Virakul S, van Steensel L. Current perspectives on the role of orbital fibroblasts in the pathogenesis of Graves' ophthalmopathy. Exp Eye Res. 2016;142:83-91.

5. Krieger CC, Boutin A, Jang D, et al. Arrestin-β-1 Physically Scaffolds TSH and IGF1 Receptors to Enable Crosstalk. Endocrinology. 2019;160(6):1468-79.

6. Small RG. Upper eyelid retraction in Graves' ophthalmopathy: a new surgical technique and a study of the abnormal levator muscle. Trans Am Ophthalmol Soc. 1988;86:725-93.

7. Denisova K, Barmettler A. Evaluating the thyroid eye disease patient. Int Ophthalmol Clin. 2021;61(2):33-52.

8. Blandford AD, Zhang D, Chundury RV, et al. Dysthyroid optic neuropathy: update on pathogenesis, diagnosis, and management. Expert Rev Ophthalmol. 2017;12(2):111-21.

9. Weis E, Heran MK, Jhamb A, et al. Quantitative computed tomographic predictors of compressive optic neuropathy in patients with thyroid orbitopathy: a volumetric analysis. Ophthalmology. 2012;119(10):2174-8.

10. McKeag D, Lane C, Lazarus JH, et al. Clinical features of dysthyroid optic neuropathy: a European Group on Graves' Orbitopathy (EUGOGO) survey. Br J Ophthalmol. 2007;91(4):455-8.

11. Garip Kuebler A, Halfter K, Reznicek L, et al. A pathological indicator for dysthyroid optic neuropathy: tritan color vision deficiency. Graefes Arch Clin Exp Ophthalmol. 2021;259(11):3421-6.

12. Blum Meirovitch S, Leibovitch I, Kesler A, et al. Retina and nerve fiber layer thickness in eyes with thyroid-associated ophthalmopathy. Isr Med Assoc J. 2017;19(5):277-81.

13. Mugdha K, Kaur A, Sinha N, et al. Evaluation of retinal nerve fiber layer thickness profile in thyroid ophthalmopathy without optic nerve dysfunction. Int J Ophthalmol. 2016;9(11):1634-7.

14. Guo J, Li X, Ma R, et al. The changes of retinal nerve fibre layer and ganglion cell layer with different severity of thyroid eye disease. Eye (Lond). 2022;36(1):129-34.

15. Gul A, Basural E, Ozturk HE. Comparison of choroidal thickness in patients with active and stable thyroid eye disease. Arq Bras Oftalmol. 2019;82(2):124-8.

16. Del Noce C, Vagge A, Nicolò M, et al. Evaluation of choroidal thickness and choroidal vascular blood flow in patients with thyroid-associated orbitopathy (TAO) using SD-OCT and Angio-OCT. Graefes Arch Clin Exp Ophthalmol. 2020;258(5):1103-7.

17. Yu L, Jiao Q, Cheng Y, et al. Evaluation of retinal and choroidal variations in thyroid-associated ophthalmopathy using optical coherence tomography angiography. BMC Ophthalmol. 2020;20(1):421.

18. Gonçalves AC, Gebrim EM, Monteiro ML. Imaging studies for diagnosing Graves' orbitopathy and dysthyroid optic neuropathy. Clinics (Sao Paulo). 2012;67(11):1327-34.

19. Mourits MP, Prummel MF, Wiersinga WM, et al. Clinical activity score as a guide in the management of patients with Graves' ophthalmopathy. Clin Endocrinol (Oxf). 1997;47(1):9-14.

20. Bartalena L, Kahaly GJ, Baldeschi L, et al. The 2021 European Group on Graves' orbitopathy (EUGOGO) clinical practice guidelines for the medical management of Graves' orbitopathy. Eur J Endocrinol. 2021;185(4):G43-G67.

21. Jain AP, Jaru-Ampornpan P, Douglas RS. Thyroid eye disease: redefining its management-a review. Clin Exp Ophthalmol. 2021;49(2):203-11.

22. Altiparmak UE, Acar DE, Ozer PA, et al. Topical cyclosporine A for the dry eye findings of thyroid orbitopathy patients. Eye (Lond). 2010;24(6):1044-50.

23. Dharmasena A. Selenium supplementation in thyroid associated ophthalmopathy: an update. Int J Ophthalmol. 2014;7(2):365-75.

24. Khong JJ, McNab A. Medical treatment in thyroid eye disease in 2020. Br J Ophthalmol. 2021;105(3):299-305.

25. Zang S, Ponto KA, Kahaly GJ. Clinical review: Intravenous glucocorticoids for Graves' orbitopathy: efficacy and morbidity. J Clin Endocrinol Metab. 2011;96(2):320-32.

26. Foltz IN, Karow M, Wasserman SM. Evolution and emergence of therapeutic monoclonal antibodies: what cardiologists need to know. Circulation. 2013;127(22):2222-30.

27. Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the Treatment of Active Thyroid Eye Disease. N Engl J Med. 2020;382(4):341-52.

28. Douglas RS, Kahaly GJ, Ugradar S, et al. Teprotumumab Efficacy, Safety, and Durability in Longer-Duration Thyroid Eye Disease and Re-treatment: OPTIC-X Study. Ophthalmology. 2022;129(4):438-49.

29. Douglas RS, Wang Y, Dailey RA, et al. Teprotumumab in clinical practice: recommendations and considerations from the OPTIC trial investigators. J Neuroophthalmol. 2021;41(4):461-8.

30. Patel P, Khandji J, Kazim M. Recurrent Thyroid Eye Disease. Ophthalmic Plast Reconstr Surg. 2015 Nov-Dec;31(6):445-8. doi: 10.1097/IOP.0000000000000371. PMID: 25621464.

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, LLC, Attn.: CE Processing, 395 Hudson Street, 3rd Floor New York, New York 10014. To be eligible, please return the card within three years of publication. You can also access the test form and submit your answers and payment via credit card 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. The incidence of GD in the adult population is approximately:
a. 10% to 15%.
b. 4% to 5%.
c. 0.1% to 0.2%.
d. 1% to 3%.

2. Which are implicated as the major player in the pathogenesis of TED?
a. Astrocytes.
b. Osteocytes.
c. Fibroblasts.
d. Endothelial cells.

3. Which of the following is true regarding the pathogenesis of TED?
a. The relationship between thyroid dysfunction and orbital disease is well understood.
b. Hyaluronic acid is secreted by T- and B-cells.
c. The IGF-1 receptor has recently been implicated as a key player in TED.
d. EOMs accumulate lactic acid that causes muscle edema.

4. Which of the following can reduce the risk of developing TED?
a. Radioactive iodine.
b. Smoking.
c. Achieving euthyroid status.
d. PO steroids.

5. Which of the following statements is false?
a. TED is characterized by an inflammatory phase followed by a fibrotic phase.
b. TED affects more men than women.
c. TED-associated inflammation typically lasts six to 18 months.
d. Smoking is a risk factor for developing TED.

6. Which of the following is not a common finding in TED?
a. Diplopia.
b. Lid retraction.
c. Proptosis.
d. Scleritis.

7. Which of the following is not a cause of vision loss in TED?
a. Maculopathy.
b. Optic neuropathy.
c. Dry eye.
d. Corneal ulcerations.

8. DON occurs in approximately what percentage of patients with TED?
a. 3% to 6%.
b. 6% to 10%.
c. 1% to 3%.
d. <1%.

9. The most common EOMs affected in TED are which of the following?
a. Superior and inferior rectus.
b. Medial and lateral rectus.
c. Superior and inferior oblique.
d. Medial and inferior rectus.

10. Which of the following is true regarding radiologic imaging in TED?
a. MRI is necessary to confirm a diagnosis of TED.
b. EOM tendon inflammation is a hallmark sign of TED.
c. CT without contrast is a good option for orbital imaging in TED.
d. Eyelid retraction is easily measured with CT.

11. Which of the following is not considered when assessing CAS?
a. Eyelid edema.
b. Pain with eye movement.
c. Cosmetic disfigurement.
d. Swelling of the caruncle.

12. Which of the following is true of TED?
a. Smoking increases the risk of more severe disease.
b. It is most common in African Americans.
c. CAS scoring involves a quality-of-life assessment.
d. Chronic diplopia from EOM fibrosis responds well to high-dose IV steroids.

13. Which of the following statements is true?
a. EUGOGO uses CAS grading for activity.
b. NOSPECS is a widely accepted clinical grading algorithm.
c. CAS scores of less than six are considered inactive.
d. VISA scoring only uses subjective data.

14. EUGOGO classification of mild disease includes all but which of the following?
a. Lid retraction less than 2mm.
b. Proptosis less than 3mm.
c. Diplopia in primary gaze.
d. Corneal exposure that responds to lubrication.

15. Which is not a treatment for mild TED?
a. Topical lubricants.
b. Selenium supplementation.
c. PO corticosteroids.
d. Punctal plugs.

16. For moderate-to-severe active disease, which is not recommended as a first-line therapy?
a. IV steroids.
b. PO steroids.
c. IV steroids + mycophenolate.
d. Teprotumumab.

17. Which of the following is not a second-line option for moderate-to-severe active TED?
a. Teprotumumab.
b. Orbital radiation and corticosteroids.
c. Radioactive iodine.
d. Azathioprine.

18. Which of the following statements is true regarding teprotumumab?
a. It acts exclusively on the thyrotropin receptor.
b. It is considered the best first-line option for those with sight-threatening disease.
c. It can be injected directly into the orbit for immediate relief of symptoms.
d. It has not been studied against IV corticosteroids in clinical trials.

19. Which of the following is a true statement?
a. Moderate-to-severe disease can be treated in most optometric offices and does not need to be referred.
b. Red desaturation is the most sensitive test for DON.
c. The pathophysiology of DON involves compression, ischemia and inflammation.
d. Vision loss in TED is common, occurring in nearly 50% of patients.

20. Which of the following is false?
a. Treatment of TED is a team effort, often involving primary care and endocrinology.
b. Early treatment in the active phase of TED is critical in achieving best possible outcomes.
c. Smoking cessation and control of underlying dysthyroidism is a first step in treatment of TED.
d. Early decompression surgery is warranted for moderate-to-severe active disease to help prevent crowding at the orbital apex.

Examination Answer Sheet

What ODs Need to Know About Thyroid Eye Disease

Valid for credit through October 15, 2025

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, Attn.: CE Processing, 395 Hudson Street, 3rd Floor New York, New York 10014.

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 80840-SD.

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

Jointly provided by PIM and the Review Education Group.
Salus University has sponsored the review and approval of this activity.

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. Identify thyroid eye disease among their patients. ① ② ③ ④ ⑤
22. Determine when and how they should use clinical activity scores. ① ② ③ ④ ⑤
23. Determine when and how they should use clinical activity scores. ① ② ③ ④ ⑤
24. Recognize when to get additional labs and/or imaging, or when to refer. 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 123198 RO-OSC-1022

Contact Contaminators

Acanthamoeba infections can be easily combated with stringent contact lens wear and care routines.

Q I'm worried about the risk of *Acanthamoeba* keratitis (AK) in my patients who wear contact lenses. Why are contact lens wearers at an increased risk? How significant is the reduction in safety and efficacy if they switch to daily disposable lenses?

A Since *Acanthamoeba* is ubiquitous, *i.e.*, present everywhere, and 50% to 100% of us have antibodies to this organism, why is *Acanthamoeba* keratitis not more common and why are contact lens wearers most at risk?[1] "The rate of AK is 20 times more common in contact lens wear than the general population," says Associate Professor Nicole Carnt, BOptom, PhD, of the School of Optometry and Vision Science, UNSW, Sydney in Australia.[2] In reusable lens wear, refraining from water activities such as swimming and showering can reduce risk by over 50%.[3]

Acanthamoeba is everywhere but predominately lives in water and soil.[4] It's been found in the United Kingdom and Australia that roughly a third of domestic bathroom sinks harbor the organism.[5,6] *Acanthamoeba* has even been isolated from a shower curtain.[7] Dr. Carnt notes that studies indicate that the same genotype of *Acanthamoeba* in a patient's home water can also be found in the eye, indicating a direct link between the two.[6,8]

Contact lenses act as a vector to transmit organisms to the eye. While 6% of contact lens cases harbor *Acanthamoeba*, there is not a direct correlation.[9] However, daily disposables are four times less likely to cause AK than reusables, likely related to contamination of the lens case and the reusable lenses, according to Dr. Carnt.[10] When compared with reusable lens bacterial keratitis, cases involving daily disposables display a smaller proportion of corneal isolates that are gram-negative (or environmental) and more gram-positive (endogenous) organisms, generally resulting in better outcomes.[11]

Contact lenses not only transmit organisms to the eye—they also retain them for a longer period of time. "We have different ways of protecting our corneas from infection, including our eyelids, blinking mechanism, tear film antimicrobials and sloughing of the ocular surface epithelial cells," Dr. Carnt explains.

A contact lens affects the homeostasis of all these defense mechanisms. "If you are in the shower without contact lenses and water gets in your eyes, blinking is enough to wash away or dilute the organisms because it will cause your eyes to water," says Dr. Carnt. With a contact lens in place, there is an opportunity for the organisms to stick on the front or back of the lens and get trapped underneath the lens, subsequently remaining on the eye longer.

Furthermore, *Acanthamoeba* contains a mannose-binding protein that can facilitate attachment to the cornea. This can happen when epithelial cells are irritated—for example, by microtrauma from the contact lens—causing the infective process to ensue.[12]

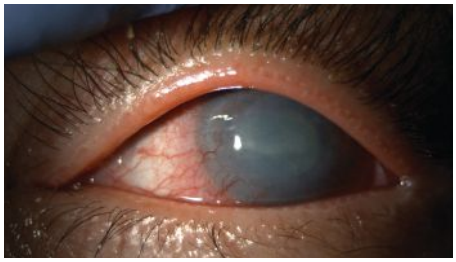
Photo: Hari Peguda, BOptom, UNSW Scientia PhD Scholar

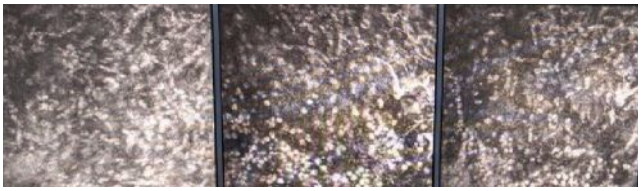
A contact lens with *Acanthamoeba* on the surface after 90 minutes of incubation (seen at 4x magnification).

About Dr. Shovlin

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

Photos: Suzanne Sherman, OD





Clinical presentation of *Acanthamoeba* keratitis (left) and *in vivo* confocal microscopy (above) of organism cysts in the cornea.

Acanthamoeba has a defense mechanism of its own. When it is threatened by lack of nutrients, temperature extremes or pH changes, it encysts into a double-walled inactive, sessile form that can exist for months to years.[4] This is one of the main reasons AK has such poor outcomes, with 50% of patients needing treatment for more than 12 months and subsequent reduced quality of life, impacting reading, mobility and emotional well-being.[13]

The best defense against AK is prevention. By switching all wearers from reusable soft to daily disposable lenses, cases of AK would halve.[10] However, daily disposables are not without risk themselves. The chance of AK in daily disposables can be further reduced by not reusing, sleeping or showering in the lenses.[10] The biggest reduction in risk is regularly seeing an eyecare practitioner.[10] "We are in a powerful position to educate wearers how to use contact lenses safely and enjoy the benefits of healthy contact wear," sums up Dr. Carnt. ■

1. Clarke DW, Niederkorn JY. The immunobiology of Acanthamoeba keratitis. Microbes and infection / Institut Pasteur. 2006;8(5):1400-5.

2. Radford CF, Minassian D, Dart JKG. Acanthamoeba keratitis in England and Wales: incidence, outcome and risk factors. Br J Ophthalmol. 2002;86:536-42.

3. Carnt N, Hoffman JM, Verma S, et al. Acanthamoeba keratitis: confirmation of the UK outbreak and a prospective case-control study identifying contributing risk factors. Br J Ophthalmol. 2018;102(12):1621-8.

4. Kilvington S, White DG. Acanthamoeba biology, ecology and human disease. Rev Med Microbiol. 1994;5:12-20.

5. Carnt NA, Subedi D, Lim AW, et al. Prevalence and seasonal variation of Acanthamoeba in domestic tap water in greater Sydney, Australia. Clinical & Exp Optom : J of the Austral Optometrical Assoc. 2020;103(6):782-6.

6. Carnt NA, Subedi D, Connor S, Kilvington S. The relationship between environmental sources and the susceptibility of Acanthamoeba keratitis in the United Kingdom. PloS One. 2020;15(3):e0229681.

7. Rayamajhee B, Subedi D, Won S, et al. Investigating domestic shower settings as a risk factor for Acanthamoeba keratitis. Water-Sui. 2020;12(12).

8. Kilvington S, Gray T, Dart J, et al. Acanthamoeba keratitis: the role of domestic tap water contamination in the United Kingdom. Invest Ophthalmol Vis Sci. 2004;45(1):165-9.

9. Larkin DFP, Kilvington S, Easty DL. Contamination of contact lens storage cases by Acanthamoeba and bacteria. Br J Ophthalmol. 1990;74:331-3.

10. Carnt NM, Dart J. Acanthamoeba keratitis risk factors for daily wear contact lens users: a case control study. Ophthalmology. 2022.

11. Stapleton F, Naduvilath T, Keay L, et al. Risk factors and causative organisms in microbial keratitis in daily disposable contact lens wear. PloS One. 2017;12(8):e0181343.

12. Clarke DW, Niederkorn JY. The pathophysiology of Acanthamoeba keratitis. Trends Parasitol. 2006;22(4):175-80.

13. Carnt NA, Man REK, Fenwick EK, Lamoureux EL, Keay LJ. Impact of Acanthamoeba keratitis on the vision-related quality of life of contact lens wearers. Cornea. 2022;41(2):206-10.

BY JOSEPH W. SOWKA, OD

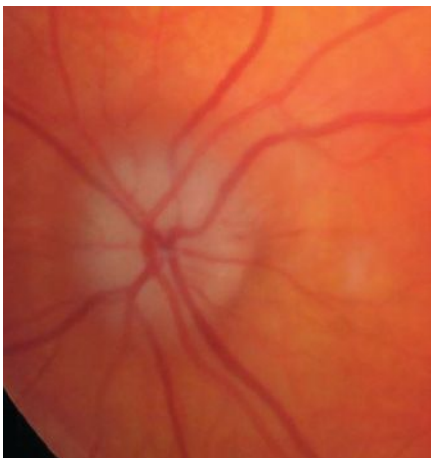
End-of-Day GCA

Cooperative care enhances outcomes in patients who present with this condition.

Three recent patients, all coming later in the day as emergencies, underscored a need for cooperative care to ensure the best outcome.

The first was a 64-year-old woman who noticed an obscuration in her right lower visual field. She was 20/400 in that eye from a longstanding macular scar, but she knew something was different. Threshold perimetry revealed an inferior arcuate defect and a slightly pale and swollen optic disc in that eye. When questioned, she mentioned some mild intermittent headache controlled by oral analgesics, loss of seven pounds over the past four weeks, mild loss of appetite and some mild malaise and fatigue. Otherwise, she felt well.

The second was a 63-year-old woman who had been sent from a local emergency room because she had woken up that morning completely blind in her left eye. When she presented, she stated that she had improved somewhat from complete blindness in that eye but felt that the vision was still terrible. Vision testing and perimetry revealed 20/30 acuity and a markedly constricted visual field with only central fixation remaining. She reported frontal and occipital headaches for several months. She also stated that her appetite was nil and that she had lost 15lbs over the past several months. She said that she had been generally unwell since contracting COVID several months earlier and reported fatigue, malaise and lethargy. Funduscopically, she had a pale, swollen optic disc.



A pale, swollen disc in arteritic AION.

The third patient was an 88-year-old man who had noted a sudden change of vision in his right eye five days previously. His visual acuity was counting fingers at 4ft with a dense inferior arcuate scotoma in that eye. Like the previous patients he manifested a pale, edematous optic disc in that eye. Upon detailed questioning, he denied any headache, jaw claudication, weight loss, appetite loss and had no constitutional symptoms to speak of.

Each of these three patients shared the same diagnosis of anterior ischemic optic neuropathy (AION) and based upon age and symptoms were suspected of having specifically arteritic AION and giant cell arteritis (GCA). Each was sent (or in the case of patient #2, sent back) to an emergency room with information about the presumptive diagnosis, and recommendations to obtain an erythrocyte sedimentation rate, C-reactive protein and platelet count. Additionally, I provided my cell phone number with instructions to call back with the results and consultation.

Discussion

One of the true emergencies in all of eye care is a patient suffering vision loss from GCA, coming in the form of ischemic optic neuropathy (anterior or posterior) or retinal artery occlusion. In many cases what begins as unilateral devastating vision reduction quickly progresses to bilaterality and total visual disability for the patient.[1,2]

Patients suffering from GCA are elderly, with a mean age of 71 at presentation.[3] This condition is generally considered only after 50, with women somewhat more likely to develop it.[4]

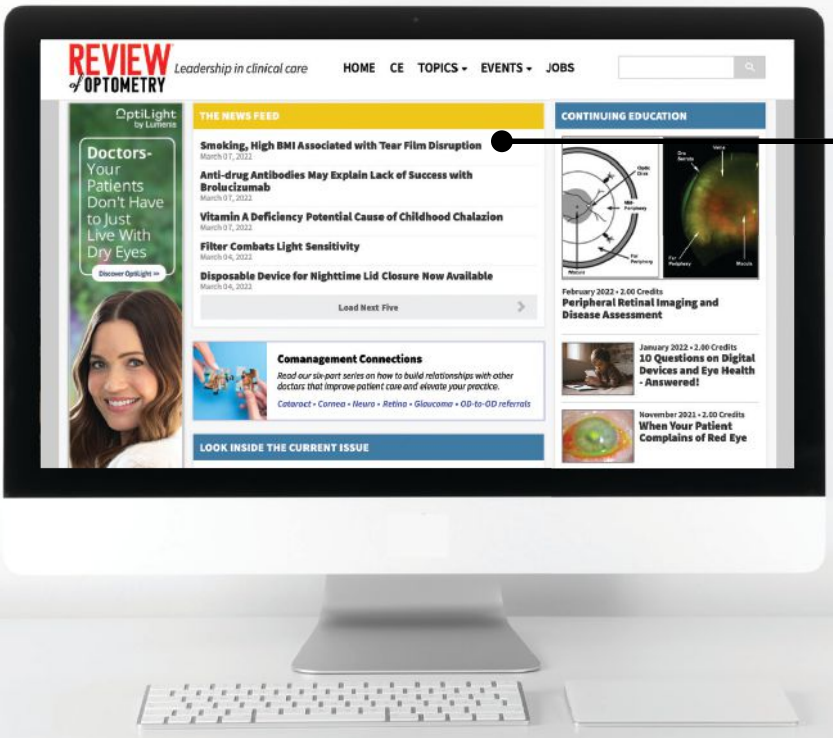
There are a multitude of systemic manifestations occurring in GCA including malaise, weight loss and anorexia, headache (typically in the temporal or occipital region), pulseless and indurated temporal arteries, night sweats, tongue necrosis and oral ulceration, dental abscess, scalp pain, scalp necrosis and jaw claudication when eating. There is also head and neck swelling, anemia, depression, mental disturbance, neck pain, low grade fever, transient ischemic attack and stroke, proximal myalgia, persistent flu-like illness, chronic pharyngitis, vertigo, muscle aches, cardiac arrhythmia, congestive heart failure and myocardial infarction.[5-13] There are patients who will show no or minimal systemic symptoms of this disease.

GCA is a granulomatous inflammation of medium- and large-sized arteries that have a defined internal and external elastic lamina.[5] The interleukin (IL)-6 pathway is upregulated in GCA. There is cellular infiltration of the muscular wall of these vessels by T lymphocytes, macrophages, histiocytes, plasma cells and multinucleate giant cells.[14,15] The resultant inflammation

About Dr. Sowka

Dr. Sowka is an attending optometric physician at Center for Sight in Sarasota, FL, where he focuses on glaucoma management and neuro-ophthalmic disease. He is a consultant and advisory board member for Carl Zeiss Meditec and Bausch Health.

clinical research • legislative updates • product launches • conference reports



Find out first from

REVIEW of OPTOMETRY

THE NEWS FEED

Updated every weekday

www.reviewofoptometry.com/news

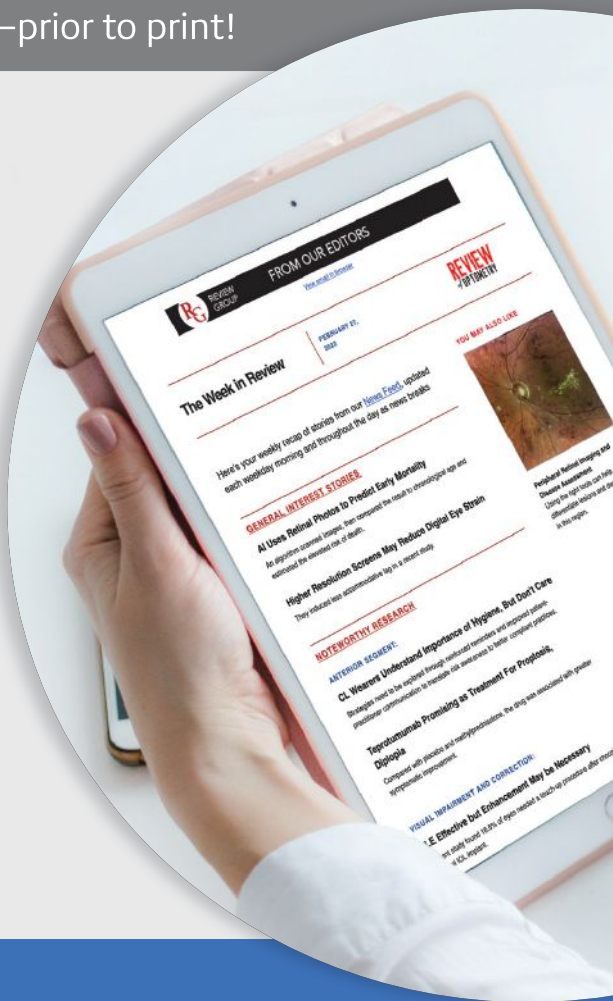
OVER **60** NEWS STORIES PUBLISHED EVERY MONTH

Read the latest news as it happens—prior to print!

Three ways to keep up with current events:

1 on the website 2 through social media
3 in your inbox

FACEBOOK: /revoptom
INSTAGRAM: @revoptom
TWITTER: @revoptom
LINKEDIN: review-of-optometry



fragments the vascular walls and leads to collapse of the vessel lumen with resultant ischemia. Conclusive diagnosis of GCA occurs through temporal artery biopsy. However, the procedure is invasive, and false-negative results can confound the diagnosis. More recently, temporal artery ultrasound has been increasingly used as an accurate, noninvasive method for assisting in disease diagnosis.[16]

Therapy Protocol

Treatment is high-dose systemic steroids, either oral or in-patient intravenous infusion.[17-19] Patients with vision loss or other ocular complications should receive four daily infusions of 250mg of methylprednisolone for three days, which is best done on an in-patient basis.[20] After the initial infusion regimen, the patient is released with instructions to continue the oral steroid until they can be seen by a rheumatologist.

For oral administration, the initial prednisolone dose is 60mg to 80mg/day. It should be reduced in weekly steps of 5mg to 10mg until 20mg/day, and by 2.5mg until 10mg/day. Dose reduction is then 1mg/month below 10mg/day, depending on symptoms, erythrocyte sedimentation rate and C-reactive protein. Suppression of the disease usually takes months to years, leaving patients and physicians to cope with complications of long-term steroid use such as ulcers and gastrointestinal bleeding, osteoporosis, increased risk of heart disease, diabetes, decreased bone density, increased risk of infections, thin skin, easier bruising and slower healing of wounds.

Actemra (tocilizumab, Genentech) is a biologic IL-6 receptor antagonist, used as a steroid-sparing therapy to maintain disease remission in patients with GCA.[21] It has been used in conjunction with oral steroids to better suppress the disease long term. Patients receiving tocilizumab had superior disease remission at one year compared with the steroid-only taper. Challenges to adjunctive use of tocilizumab include expense, formulary limitations and uncertainly when to finally stop use in disease suppression.

In each of the three patients presented here, I used local hospital emergency departments to get testing, evaluation and management initiated quickly.

> **“Use local hospital emergency departments to get testing, evaluation and management for GCA initiated quickly.”**

In each case, a typical trend was followed. Shortly after discharging the patient, I received a call from an emergency room physician who relayed positive test results and then asked what protocol for therapy should be followed. We discussed the patient and the disease entity, and I recommended that each patient be admitted for intravitreal (IV) steroid therapy. I recommended 250mg solumedrol every six hours for 12 doses in-patient with discharge with 80mg prednisone PO until consultation with a rheumatologist. I also helped them to arrange a temporal artery ultrasound with a local vascular surgeon skilled in the technique. In each case, several hours later I received telephone calls from the admitting hospitalists who also wanted to discuss the patients' cases and verify the orders for IV steroids and the proper dosing.

What I found in all cases is that the emergency physicians and hospitalists all had excellent knowledge of GCA but lacked confidence and experience and were extremely grateful that I could walk them through the steps, steroid dosing, route of administration, need for ancillary testing, and discharge plans. In each case, the patients maintained vision in their remaining fellow eye, and one had some visual improvement in the involved eye.

As optometrists, we are unlikely to be administering IV steroids and admitting patients for GCA treatment, but knowledge of treatment for this disease is critically important when we are working collaboratively with other physicians to obtain the best possible outcome for our patients. ■

1. Hayreh SS, Podhajsky PA, Zimmerman B. Ocular manifestations of giant cell arteritis. Am J Ophthalmol. 1998;125(4):509-20.

2. Wein FB, Miller NR. Unilateral central retinal artery occlusion followed by contralateral anterior ischemic optic neuropathy in giant cell arteritis. Retina. 2000;20(3):301-3.

3. Nordberg C, Johansson H, Petursdottir V, et al. The epidemiology of biopsy-proven giant cell arteritis: special reference to changes in the age of the population. Rheumatology (Oxford). 2003;42(4):549-52.

4. Salvarani C, Gabriel SE, O'Falon WM, et al. The incidence of giant cell arteritis in Olmstead County, Minnesota: apparent fluctuations in a cyclic pattern. Ann Intern Med 1995;123(3):192-4.

5. Rahman W, Rahman FZ. Giant cell (temporal) arteritis: an overview and update. Surv Ophthalmol. 2005;50(5):415-28.

6. Zachariades N, Skoura C, Spanou A, et al. Temporal arteritis: report of a case. Oral Surg Oral Med Oral Pathol Oral Radiol Endod. 2006;102(2):192-7.

7. Gurwood AS, Brilliant R, Malloy KA. The enigma of giant cell arteritis: multidisciplinary management of two cases. J Am Optom Assoc. 1998;69(8):501-9.

8. Liozon E, Ouattara B, Portal MF, et al. Head-and-neck swelling: an under-recognized feature of giant cell arteritis. A report of 37 patients. Clin Exp Rheumatol. 2006;24(2 Suppl 41):S20-5.

9. Gonzalez-Gay MA, Garcia-Porrua C, Llorca J, et al. Visual manifestations of giant cell arteritis. Trends and clinical spectrum in 161 patients. Medicine (Baltimore). 2000;79(5):283-92.

10. Nordborg E, Nordborg C. Giant cell arteritis: strategies in diagnosis and treatment. Curr Opin Rheumatol. 2004;16(1):25-30.

11. Liozon E, Loustaud V, Fauchais AL, et al. Concurrent temporal (giant cell) arteritis and malignancy: report of 20 patients with review of the literature. J Rheumatol. 2006;33(8):1606-14.

12. Manetas S, Moutzouris DA, Falagas ME. Scalp necrosis: a rare complication of temporal arteritis. Clin Rheumatol. 2007;26(7):1169.

13. Biebl MO, Hugl B, Posch L, et al. Subtotal tongue necrosis in delayed diagnosed giant-cell arteritis: a case report. Am J Otolaryngol. 2004;25(6):438-41.

14. Albert DM, Searl SS, Craft JL. Histologic and ultrastructural characteristics of temporal arteritis. The value of the temporal artery biopsy. Ophthalmology. 1982; 89(10):1111-26.

15. Ashton-Key M, Gallagher PJ. Surgical pathology of cranial arteritis and polymyalgia rheumatica. Baillieres Clin Rheumatol 1991; 5(3):387-404.

16. Scheurer RA, Harrison AR, Lee MS. Treatment of vision loss in giant cell arteritis. Curr Treat Options Neurol. 2012;14(1):84-92.

17. Serling-Boyd N, Stone JH. Recent advances in the diagnosis and management of giant cell arteritis. Curr Opin Rheumatol. 2020;32(3):201-7.

18. Gonzalez-Gay MA, Martinez-Dubois C, Agudo M, et al. Giant cell arteritis: epidemiology, diagnosis, and management. Curr Rheumatol Rep. 2010;12(6):436-42.

19. Schmidt J, Warrington KJ. Polymyalgia rheumatica and giant cell arteritis in older patients: diagnosis and pharmacological management. Drugs Aging. 2011;28(8):651-66.

20. Schmidt WA. Current diagnosis and treatment of temporal arteritis. Curr Treat Options Cardiovasc Med. 2006;8(2):145-51.

21. Unizony SH, Dasgupta B, Fisheleva E, et al. Design of the tocilizumab in giant cell arteritis trial. Int J Rheumatol. 2013;2013:912562.

Medscape LIVE!

LIVE COPE*

REGISTER NOW

IN-PERSON EVENTS

Join Review Education Group and MedscapeLIVE! this December for the West Coast Optometric Glaucoma Symposium (WCOGS) and Retina Update 2022. The conferences will be co-located at the Hilton La Jolla Torrey Pines in La Jolla, California. Attendees are encouraged to participate in both symposia to greatly enhance their learning experience.

Early bird special pricing: $149 single conference | $250 bundled

Deadline to register with special rate: October 21, 2022

WEST COAST OPTOMETRIC GLAUCOMA SYMPOSIUM

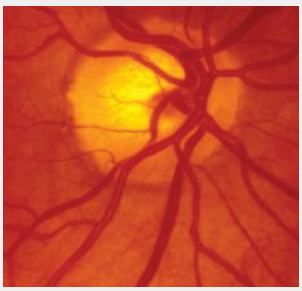
DECEMBER 9–10, 2022

LA JOLLA, CALIFORNIA

Program Co-chairs: Murray Fingeret, OD, FAAO; Robert N. Weinreb, MD

EARN UP TO 12 LIVE CE CREDITS*

WCOGS is a 2-day biannual symposium designed to provide optometrists with exposure to current thinking on evolving standards of care, state-of-the-art technology and breaking research that will guide current and future glaucoma care in the optometric setting. Incorporating cases, clinical pearls, and discussion sessions, the program will maximize the opportunity for participant/faculty engagement.



THE OPTOMETRIC RETINA SOCIETY AND REVIEW EDUCATION GROUP PRESENT

RETINA UPDATE 2022

DECEMBER 10–11, 2022

LA JOLLA, CALIFORNIA

Program Co-chairs: Mohammad Rafieetary, OD, FAAO; Steven Ferrucci, OD, FAAO

EARN UP TO 11 CE CREDITS*

Retina Update 2022 will help ensure that primary practitioners consider all relevant research so they can practice in an effective and appropriate manner. The program will offer specific direction and practical advice on how to detect and manage a broad range of retinal disease and promote improved retinal health.

Earn up to 23 LIVE COPE credits*

For more information and to register

www.reviewedu.com/winteroptometry

REGISTER

cope *Approval pending

PIM Postgraduate Institute for Medicine

REVIEW Education GROUP

BY MARC B. TAUB, OD, MS, AND PAMELA H. SCHNELL, OD

If At First You Don't Succeed

It's our job to use every possible tool at our disposal to improve patient vision and quality of life.

Over the eight-year lifespan of this column, we have covered many topics related to binocularity. We have presented ways to enhance it with lenses and prism, ways to help recover it with vision therapy and a combination of the two. Even though we strive toward clear, single binocular vision, that is not always the best approach, nor is it even always possible to achieve.

In the February 2017 column, titled, "Binocularity, How Sacred Art Thou?" a case of diplopia was presented following surgical tumor removal and chemotherapy. After prism and 11 sessions of vision therapy failed to move the patient toward fusion, a spot patch was employed with great visual success and patient satisfaction. Later that year, in October, "Discretion is the Better Part of Valor" introduced a patient who had undergone decompression surgery for thyroid eye disease and developed subsequent noncomitant diplopia. In that case, a different approach—monovision in glasses—was discussed. Again, the flexibility to disregard the ingrained goal of binocular vision led to positive outcomes.

The following case is yet another outside-the-box approach to double vision for when your regular tools don't make the cut.

Case

A 56-year-old female presented with complaints of double vision and shadowing for the past three years following an acute angle closure in the left eye. She saw 30 images but had cataract surgery in the left eye, which reduced the number to six to seven images. She reported closing her left eye when reading and turning her head to reduce reflections when looking at screens. The left eye was her dominant eye. She was taking both Combigan (brimonidine/timolol, Allergan) and dorzolamide as prescribed by her glaucoma specialist. Her medical history was unremarkable.

The patient's uncorrected acuity was 20/70 OD, 20/60 OS and 20/60+ OU. Corrected acuity was 20/20 OD and OU. No new glasses were prescribed post-cataract surgery, so no correction was present OS. Confrontation fields and ocular motility were normal. Cover test showed 3PD left hypertropia at distance and 6PD left hypertropia at near. The right pupil was normal to direct and indirect reaction, but the left was fixed at 4mm and was irregular in shape. Both pupils had a peripheral iridotomy, and the left had iris atrophy from three to six o'clock. The posterior capsule IOL was centered. The cornea showed stromal haze greater superior than inferior, which coalesced at three and nine o'clock. Pigment was scattered on the endothelium. The right cornea was unremarkable. The anterior chamber of the right eye was shallow, but the left was deep and quiet.

With a prescription of +4.00 -1.00x115 and -1.00 -0.50x055, her acuity was 20/20 and 20/30+2. Base-up prism of 1.5PD was shown in a trial frame, which reduced symptoms of doubling/shadowing but did not eliminate them altogether. The patient was prescribed two pairs of glasses, distance vision only and near vision only (+2.25 add) with prism in both, and was referred to the contact lens department for evaluation to assess whether her corneal issues might be causative of her symptoms. Corneal topography ruled out irregular astigmatism; it showed 45.8/4.7 @ 54.6 and 46.9/47.5 @ 87.8. The contact lens department chose to wait until the patient got her new glasses and showed adaptation to the prism as well as further reduction in symptoms before attempting a fit. She was scheduled for a follow-up a month after she began wearing her new glasses.

The patient returned with complaints of constant "splotchy" vision OS at both distance and near. She initially reported double vision but later described it as the light "expanding" in side gazes rather than obvious doubling. She disliked switching between her glasses, as she previously had progressive addition lenses. Her visual acuity was 20/15-1 OD, 20/40+1 OS and 20/15 OU at distance and 20/20 OD, 20/40 OS and 20/20 OU at near. Further exploration with prism proved unsuccessful.

At this point in the exam, our options were dwindling. Prism was off the table. Occlusion was discussed but

About Drs. Taub and Schnell

Dr. Taub is a professor, chief of the Vision Therapy and Rehabilitation service and co-supervisor of the Vision Therapy and Pediatrics residency at Southern College of Optometry (SCO) in Memphis. He specializes in vision therapy, pediatrics and brain injury. **Dr. Schnell** is an associate professor at SCO and teaches courses on ocular motility and vision therapy. She works in the pediatric and vision therapy clinics and is co-supervisor of the Vision Therapy and Pediatrics residency. Her clinical interests include infant and toddler eye care, vision therapy, visual development and the treatment and management of special populations. They have no financial interests to disclose.

An approximation of the patient's vision based on her complaints.

rejected by the patient for cosmetic reasons. The dreaded black patch was not an option either. Bangerter foils, stick-on occlusion filters that blur the patient to specific acuity levels but are less cosmetically visible, were briefly considered. Still, given that her symptoms had been present for almost four years now, we needed something functional and cosmetically acceptable. How could we blur the left eye enough so that she might not notice the odd shadowing that she took issue with?

We pulled a +2.50 lens out of the lens kit and put it in front of her left eye while she was wearing her distance vision only glasses. The response was immediate and positive. The shadows were gone, and the patient's body relaxed noticeably. To make sure this worked, we brought her into our 60-foot-long hallway and showed her again. Success, no shadows. We then showed her the +2.50 over the near vision-only glasses. Double success! Due to her dislike for the two-pair option, we reluctantly agreed to go back to the progression addition lenses for daily use and changed the left lens of the near vision-only pair for when she was going to read for a longer period of time. She was scheduled to return for follow-up in six weeks.

Upon returning, she was quick to say that she loved the progression addition lenses and could tolerate the near vision-only glasses in the morning while reading in bed, but once she used the progression addition lenses at any point during the day, she had trouble going back to the near vision-only glasses. In addition, the left eye was "fighting" in the near vision-only glasses but not in the progression addition lenses. She no longer noticed the shadows in the progression addition lenses but still did with the near vision-only glasses.

With a little trial and error, an extra +2.00 in front of the left eye eliminated the shadows, and there was no fighting. We changed the left eye of the near vision-only glasses up another +2.00 and asked the patient to return in another month. She was excited at the opportunity to read for pleasure again and left with a spring in her step.

Takeaways

The extra plus in the left eye blurred the input just enough to block the patient from acknowledging the shadows. As to why exactly she needed more plus in the near vision-only glasses than the progression addition lenses, we surmise that the variable prescription through which she was looking might have been helpful, or perhaps she was not looking directly in the right part of the lens in the first place.

This case highlights the intersection of medical and refractive care in optometry. Once the angle closure was addressed, the patient was unhappy with her vision. Not attending to her complaints and using every tool possible to improve her quality of life was simply not an option. As the medical side of our profession continues to expand, we cannot lose touch with the basic tenets of refractive care, sight and vision. With our help, this patient is finally regaining part of what was lost four years ago. You can and should do the same for your patients when given the opportunity. ■

BY JAMES L. FANELLI, OD

Focusing on Fields

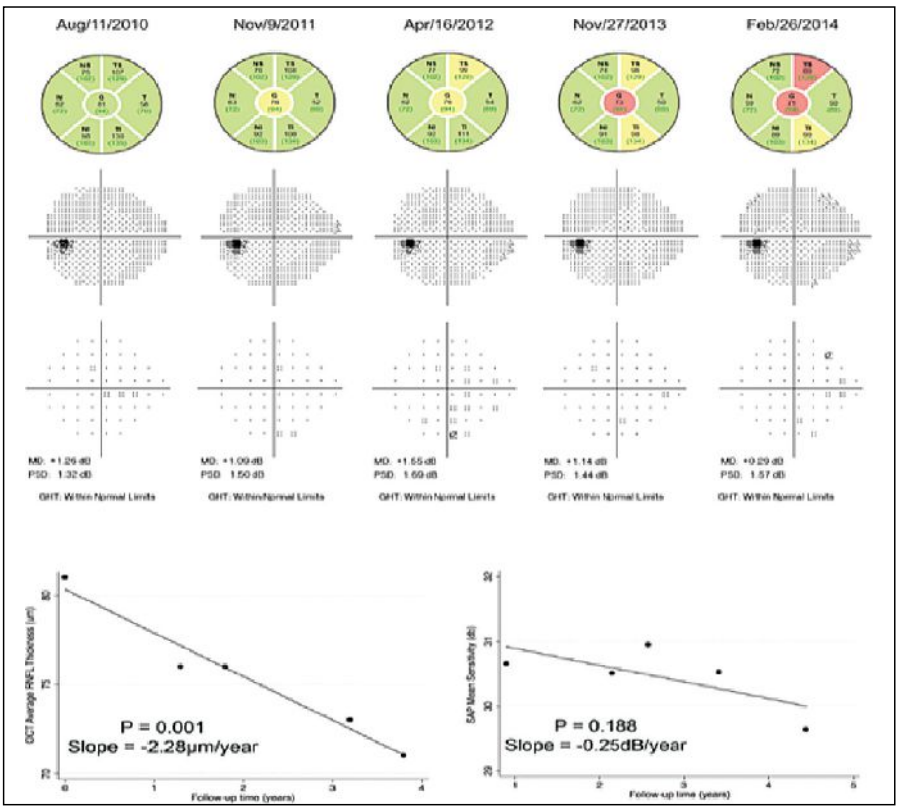
This test remains of clinical value to glaucoma care.

Whether you're relatively new to treating glaucoma or you're a well-seasoned clinician in this area of ophthalmic care, we've all seen a significant change in the technology used to evaluate and manage this ocular disease. Without a doubt, OCT has revolutionized glaucoma care, affording us the opportunity to visualize details of several structures—the optic nerve, retinal nerve fiber layer and ganglion cell layer—and detect change at the micron level.

Just as these significant advancements in technology have increased our ability to manage glaucoma, so has the expansion of optometric glaucoma care to include ODs in all 50 states. Adding to this is the aging population and the increasing incidence of glaucoma we expect to see throughout our careers.

With increased optometric scope of glaucoma care comes the responsibility of proper management, especially in more complex cases when the patient has advanced disease. In early to moderate glaucoma, since the disease progresses slowly in the majority of cases, there's time to evaluate progression before initiating treatment. That safety window diminishes significantly when the patient has more advanced disease and an increased risk of further vision loss.

It is estimated that about 80% of glaucoma patients fall in the mild to moderate category, 10% in the advanced category and another 10% in the refractory category. With clinical experience and comprehensive education, ODs should be able to care for that 10% with advanced glaucoma, in addition to the 80% in the mild to moderate category.



This figure shows the relative stability of serial visual field testing in a patient with mild to moderate glaucoma, whereas OCT shows structural change in the same time period.

Discussion

With advances in technologies, especially OCT, we've grown accustomed to determining change and progression in terms of microns, which has certainly led us to offer better care.

I've spoken with many clinicians over the years, and I'm often asked if visual fields will eventually fall by the wayside in glaucoma management since OCT is so precise. Visual fields historically have been difficult tests for patients to undergo, especially the elderly or those with mobility problems. That, coupled with the fact that some patients find field testing to be burdensome and nearly impossible to perform accurately, has led many clinicians to rely less on visual fields and more on OCT imaging to drive the clinical decision-making process.

Fortunately, we've seen a new strategy and format for visual fields in glaucoma: virtual reality visual field headsets. I've been quite surprised at the level of patient acceptance of these devices. Patients don't dread the subsequent visit where a visual field is scheduled, nor do I dread telling them we'll be subjecting them to yet another

About Dr. Fanelli **Dr. Fanelli** is the founder and director of the Cape Fear Eye Institute in Wilmington, NC. He is chairman of the EyeSki Optometric Conference and the CE in Italy/Europe Conference. He is an adjunct faculty member of PCO, Western U. and UAB School of Optometry. He is on advisory boards for Heidelberg Engineering and Glaukos.

olleyes

olleyes.com

VisuALL VRP

VISION TESTING MADE EASY

Visual Field
+
Color Vision
+
Visual Acuity
+
Pupillometry
+
Extraocular Motility

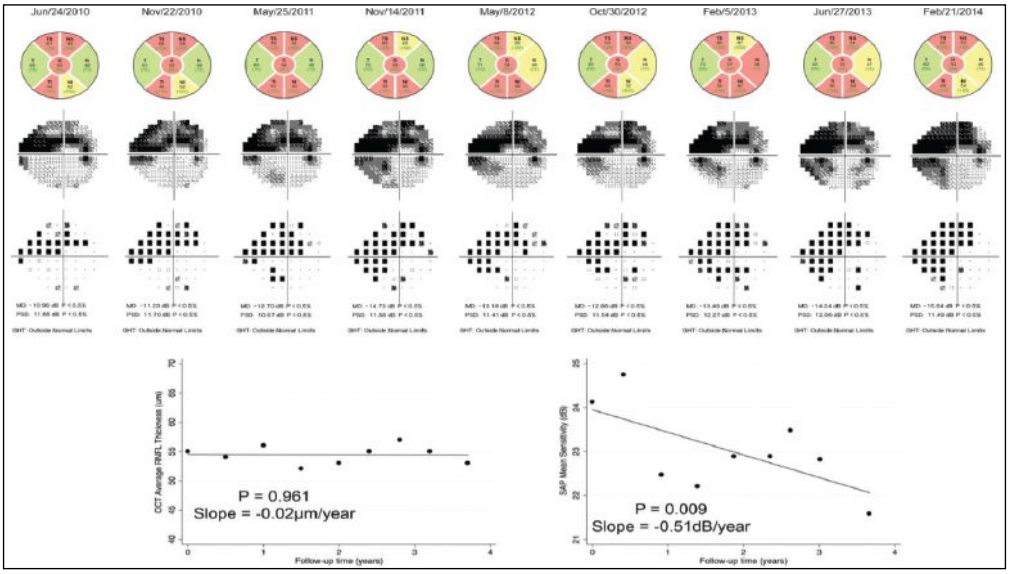
Join the Virtual Reality Revolution!

Increase patient flow
AND
satisfaction

Schedule a demo today!

MARCO

Visit us at Academy San Diego
Booth #508 and #300



This figure shows worsening visual field studies in a patient with more advanced glaucoma over time, whereas OCT does not show comparable change in the same time period.

visual field test. The comfort with which patients can now undergo visual field testing is much greater, but the real question is whether these new field units are valid and reliable. Fortunately, I've found them to be just that.

We began using the VisuAll (Olleyes) unit last January. With a large glaucoma practice, I was concerned that incorporating virtual reality technology would interrupt the reliability of information, but I've not found that to be the case. Studies have shown the tool's reliability and comparability to standard HFA visual field testing.[1]

Backing up, what is the role of visual field testing in managing glaucoma, and will we eventually be able to get rid of it entirely? Right now, I think the answer is clearly no for several reasons.

First and foremost, while OCT technology has resolution in the micron range, there is the undeniable reality that there is a floor effect especially in patients with advanced disease, exactly the ones we should be most concerned about when it comes to progression. As the name implies, as the specific metric being examined begins to erode, whether that is the thickness of the retinal nerve fiber layer or the ganglion cell layer or the minimum rim width of the neuroretinal rim, there is less and less viable tissue remaining. With little tissue remaining, you begin to reach the level of resolution of the OCT instrument itself, making determination of progression more difficult to ascertain.

Recent studies have looked at the relative odds of glaucomatous progression by structural and functional testing and have found that there is a significant difference depending on the stage of glaucoma.[2] In general, in early to moderate glaucoma, progression is more readily seen and identifiable by changes on OCT; whereas in more advanced glaucoma, progression is more readily identified by serial visual field testing. The floor effect may very well be contributing to these results, unsurprisingly. But the reality is that with more advanced disease, we need visual fields to help us determine progression.

What about the other end of the spectrum; namely, patients with early disease? Studies have shown that in early glaucoma, where OCT is employed to identify structural change, visual field testing is critical in identifying concomitant visual field defects. It's well documented that if we use a 24-2 standard SAP visual field test to determine the presence of field defects in early glaucoma, we will miss defects seen on 10-2 field testing, and those 10-2 defects coincide with the structural changes seen on OCT.[3] The 24-2C strategy may help, with its increased number of test points centrally, but 10-2 fields do in fact import valuable information in early glaucoma.

Taking this one step further, what about those patients with ocular hypertension who are at risk of developing glaucoma in the future? If we go back to the Ocular Hypertension Treatment Study (OHTS) study, the data initially showed that the majority of patients who converted from a glaucoma suspect to a glaucoma patient did so due to identifiable structural changes, whereas some showed conversion due to changes in the visual field status, with or without associated structural changes.[4] It's important to note that at the time of the OHTS study, current data pertaining to the advantages of 10-2 threshold field studies in early glaucoma was not well described. That prompts the question of how the prevalence of conversion to frank glaucoma in ocular hypertension would be different if 10-2 fields were employed more often.

Knowing all this, here is my advice to you: proceed as usual, with serial OCTs and visual fields. If you're not using 10-2 field studies in early glaucoma or patients without visual field defects on a 24-2 strategy, perhaps start doing so. If you're foregoing visual fields because you are worried that you are overburdening your patients, perhaps invest in a virtual reality field unit. Either way, keep running fields. ■

1. Razeghinejad R, Gonzalez-Garcia A, Myers JS, Katz LJ. Preliminary report of a novel virtual reality perimeter compared with standard automated perimetry. J Glaucoma. 2021;30(1):17-23.

2. Abe RY, Diniz-Filho A, Zangwill LM, et al. The relative odds of progressing by structural and functional tests in glaucoma. Invest Ophthalmol Vis Sci. 2016;57(9):421-8.

3. Grillo LM, Wang DL, Ramachandran R, Ehrlich AC, et al. The 24-2 visual field test misses central macular damage confirmed by the 10-2 visual field test and optical coherence tomography. Transl Vis Sci Technol. 2016;5(2):15.

4. Zangwill LM, Weinreb RN, Berry CC, et al. The confocal scanning laser ophthalmoscopy ancillary study to the ocular hypertension treatment study: study design and baseline factors. Am J Ophthalmol. 2004;137(2):219-27.


Centennial Celebration
ACADEMY 2022
san diego
OCTOBER 26–29, 2022
Presented by AMERICAN ACADEMY of OPTOMETRY
Registration now open!
Visit aaopt.org for details.

BY DEREK N. CUNNINGHAM, OD, AND
WALTER O. WHITLEY, OD, MBA

SURGICAL MINUTE

Sweep for RCE

Newer diagnostic techniques can identify patients as well as guide appropriate medical and surgical treatments.

Patients with recurrent corneal erosions (RCE) typically experience sudden onset of eye pain on first awakening. Associated symptoms include redness, photophobia, blurred vision and tearing. Pain may last from minutes to several hours, and, in the most severe cases with persistent epithelial defects, patients can experience pain for several days.[1]

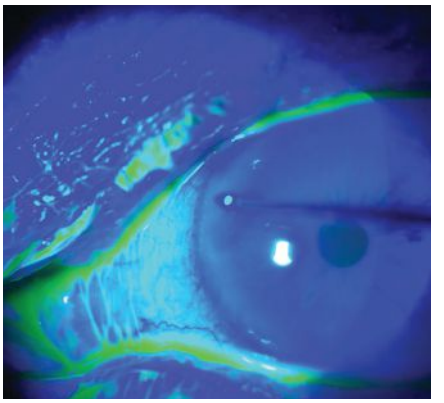
Many patients with RCE have a history of corneal trauma, corneal dystrophies and degenerations or previous surgery that may predispose them to the condition. Other times, the RCE can occur spontaneously due to preexisting dystrophies or diabetes. In all cases, RCE is characterized by a disturbance at the corneal epithelial basement membrane, resulting in defective adhesions and recurrent breakdowns of the epithelium.

By asking the right questions and performing a thorough examination, we can successfully diagnose our patients and treat them accordingly the majority of the time. Ocular signs found on slit lamp include punctate epitheliopathy, corneal abrasions, loose and/or irregular epithelium and cystic and map-like changes associated with EBMD.[1]

Although we can identify the signs and symptoms, patients may have corneal erosions in the absence of visible corneal findings. The cornea sweep test is a new and effective technique to help diagnose corneal erosions. Using this test could lead to a paradigm shift in the way clinicians approach RCEs and patients with a persistent ocular pain syndrome. A handheld instrument with a straight handle and rounded tip with smooth and tapered edges sweeps the entire corneal surface to identify the areas of loose epithelium.[2] Topical proparacaine eye drops and fluorescein dye are instilled and gentle pressure is applied to the corneal surface tangentially with the instrument.[2]

For a video of the procedure, read this article online at www.reviewofoptometry.com.

Photo: Brian Kim, MD



The cornea sweep test can help identify this acute and chronic condition.

The cornea sweep test was necessary on 49 of 58 eyes in one study to help confirm a corneal erosion diagnosis. In 34 eyes that had an occult corneal erosion, they were initially defined with a normal-appearing cornea on slit lamp examination but found to have loose corneal epithelium with the test.[2]

Choice of Therapy

No matter the cause, various medical, conservative and surgical treatments are available. Medical options include lubrication using preservative-free artificial tears, pressure patching and cycloplegia to help promote surface healing, topical antibiotics to prevent bacterial infection with existing epithelial topical corticosteroids and oral doxycycline.[1,3-5] Bandage contact lenses, punctal occlusion, autologous serum and amniotic membranes are additional measures.[1]

For patients who suffer from repeated episodes of RCE, our threshold for referral for corneal surgeries is low, and we frequently make one after the first repeat, depending on initial appearance. These procedures are reserved after failed medical therapy.

Anterior stromal puncture (ASP), phototherapeutic keratectomy (PTK), Nd:YAG laser or epithelial debridement with diamond burr polishing can help address the underlying cause of poor basement membrane adhesion. Surgical success rates for RCE vary from ASP at 80%. PTK varies from 60% to 100% depending on the study, and epithelial debridement with diamond burr polishing decreases the recurrence rate to 6% when compared with debridement alone (18%).[1,3,6]

Proper identification is key to address RCE. Many symptoms and signs may overlap between it and a variety of ocular surface diseases. Using novel diagnostic techniques, we can help identify this acute and chronic condition to treat and minimize patient suffering. ■

1. Miller DD, Hasan SA, Simmons NL, Stewart MW. Recurrent corneal erosion: a comprehensive review. Clin Ophthalmol. 2019;13:325-35.

2. Kim ME, Kim DB. Implementation of the corneal sweep test in the diagnosis of recurrent corneal erosion: a two-year retrospective study. Cornea. 2022;41(10):1248-54.

3. Lin SR, Aldave AJ, Chodosh J. Recurrent corneal erosion syndrome. Br J Ophthalmol. 2019;103:1204-8.

4. Sobrin L, Liu Z, Monroy DC, et al. Regulation of MMP-9 activity in human tear fluid and corneal epithelial culture supernatant. Invest Ophthalmol Vis Sci. 2000;4:1-7.

5. Dursun D, Kim M, Solomon A, Pflugfelder S. Treatment of recalcitrant recurrent corneal erosions with inhibitors of matrix metalloproteinase-9, doxycycline and corticosteroids. Am J Ophthalmol. 2001;132:8-13.

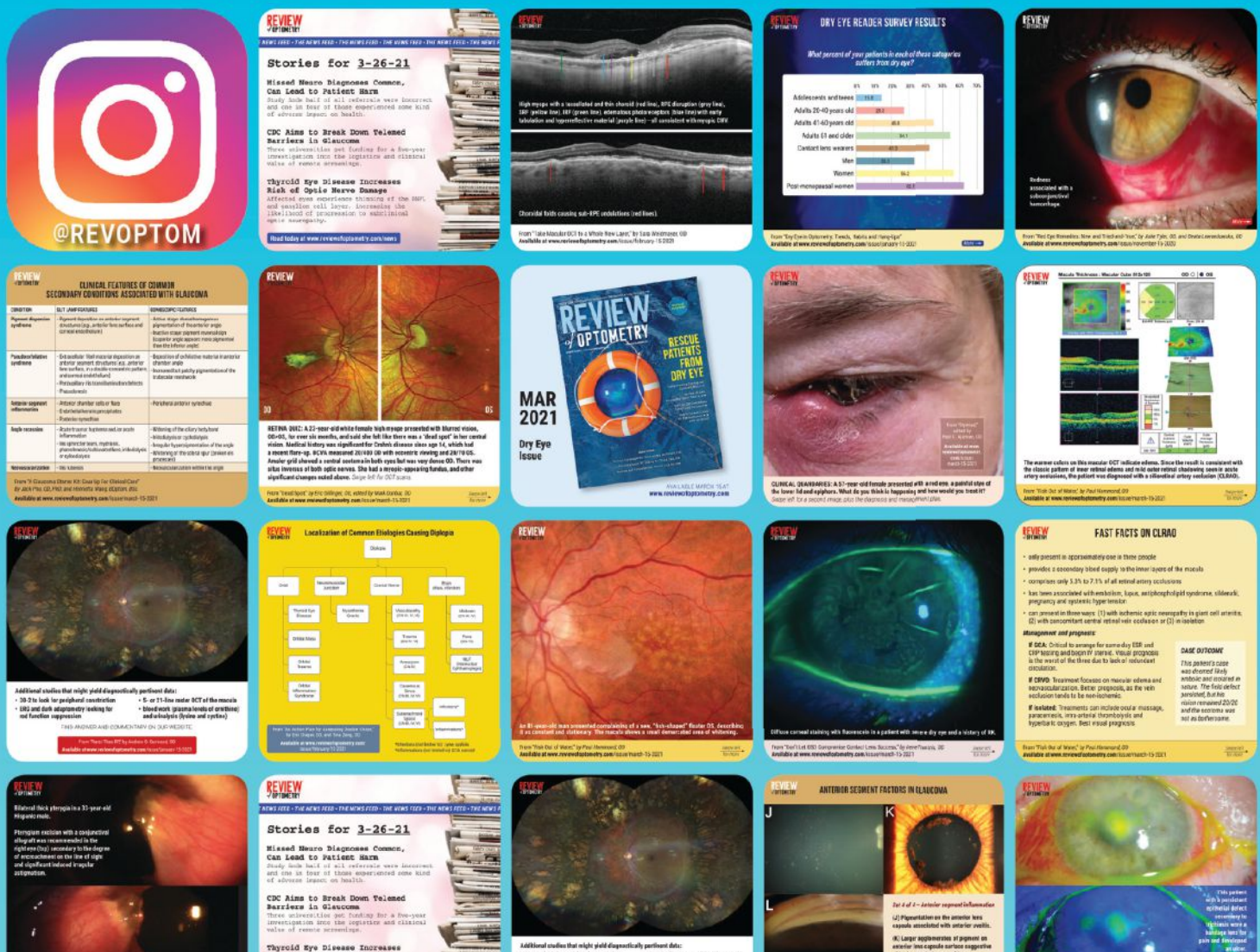
6. Wong VW, Chi SC, Lam DS. Diamond burr polishing for recurrent corneal erosions: results from a prospective randomized controlled trial. Cornea. 2009;28(2):152-6.

About Drs. Cunningham and Whitley

Dr. Cunningham is the director of optometry at Dell Laser Consultants in Austin, TX. He has no financial interests to disclose. **Dr. Whitley** is the director of professional relations and residency program supervisor at Virginia Eye Consultants in Norfolk, VA. He is a consultant for Alcon.

A NEW WAY TO EXPERIENCE *REVIEW OF OPTOMETRY*

Follow us on Instagram at @revoptom for striking clinical images, daily news headlines, issue previews and great content from the magazine—all formatted for mobile



PRODUCT REVIEW

New items to improve clinical care and strengthen your practice.

ONLINE FIRST:
GET THE LATEST
PRODUCT NEWS AT
www.reviewofoptometry.com

▸ DIAGNOSTICS

New Portable Osmometer Debuts

The number of people suffering from dry eye continues to climb each year, given the inexorable aging of the population and our increasing reliance on digital technology. It's more important now than ever that clinicians perform objective tests on patients experiencing signs or symptoms to help them receive timely and proper treatment.

One metric to help diagnose and determine severity of the condition is tear osmolarity. Several osmometers exist in the US market, but a recent addition called the ScoutPro from Trukera Medical (TearLab's new company name) distinguishes itself as the first handheld version of such a device, according to the company. A press release notes that the ScoutPro enables both nanoliter volume sample collection and analysis to be performed from anywhere in the practice and offers quick test results "in the palm of your hand."

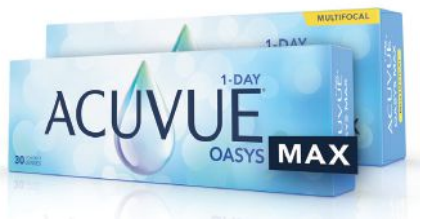
The device is rechargeable, with a battery life of eight hours. The charging base takes up less shelf space than some others and comes with an optional wall mount, Trukera says. The top of the ScoutPro uses what the company calls "VeriLyte technology" for specimen collection and analysis. The small screen on the device displays results shortly after each test is performed and can store the recent scores, the company explains. Trukera's website also notes that the test cards are interchangeable with those in the first-generation TearLab osmolarity system.

▸ CONTACT LENSES

Acuvue Oasys Max 1-Day Now Available

Extended periods of screen time disrupt the tear film, exacerbating feelings of dry eye, and contribute to symptoms of asthenopia—two effects that particularly impinge on contact lens wear. Recognizing these circumstances as a part of modern life, Johnson & Johnson Vision designed its newest Acuvue lens to work within those constraints and minimize the adverse effects, the company says.

The lens, called Acuvue Oasys Max 1-Day, was announced in June and is now available for purchase, according to J&J. It shares with the existing Oasys 1-Day lens a 38% water content silicone hydrogel material (senofilcon A). But this one also includes two design elements intended by the company to combat digital eyestrain. The first is a new polymerization process that J&J says optimizes wetting agent distribution throughout the lens and at the surface to maximize tear film stability, reduce evaporation and lock in moisture; the company calls this "TearStable technology." The second differentiator between the Oasys Max and other Oasys lenses is a blue light filter (coined "OptiBlue") that J&J says blocks 60% of blue-violet wavelengths to reduce light scatter, improving visual clarity. Like other lenses, Oasys Max also blocks UVA and UVB rays.



The following power ranges and base curves are available for Oasys Max 1-Day:

- *Single vision:* -12.00D to +8.00D in 0.25D steps (0.50D steps above ±6.00D); base curves: 8.5mm and 9.0mm.
- *Multifocal:* -9.00D to +6.00D in 0.25D steps with adds of low (+0.75D to +1.25D), mid (+1.50D to +1.75D) and high (+2.00D to +2.50D); base curve: 8.4mm.

ACUVUE® abiliti™

In a second recent press release from J&J Vision, the company announced that it will be expanding the power range for another contact lens in its line, Abiliti Overnight orthokeratology lenses for myopia management, from -4.00D to -6.00D of correction.

▸ PHARMACEUTICALS

New PGA Glaucoma Drop Hits US Market

Topical eye drops—predominantly prostaglandins—have long been the go-to treatment for reducing IOP and attempting to slow or prevent vision loss in patients with glaucoma. The newest prostaglandin to join the line-up, called Omlonti (omidenepag isopropyl 0.002%), features a unique mechanism of action that makes it the first relatively selective prostaglandin EP2 receptor agonist

"I was only seeing light flashes early on, but light FLASHES when you've not seen anything for so many years—it was wonderful"

—Keith H, retinal prosthesis recipient

WE'RE SEEING AMAZING RESULTS. AND SO ARE THEY.

At the Foundation Fighting Blindness our mission is everybody's vision. Our work shines a light on the darkness of inherited retinal diseases (IRDs).

We're the world's leading organization searching for treatments and cures. We need your help to fuel the discovery of innovations that will illuminate the future for so many. We have robust disease information, a national network of local chapters and support groups, local educational events, and our My Retina Tracker® Registry to help keep your patients connected with clinical and research advancements.

Help accelerate our mission by donating at **ECPs4Cures.org**.

FOUNDATION FIGHTING BLINDNESS

FightingBlindness.org

marketed in the US, according to manufacturer Santen and its partner UBE Corp. The drug has been sold in several regions of Asia since 2018. Omlonti works by increasing aqueous humor drainage through both the trabecular and uveoscleral outflow pathways, according to its developers. Recommended dosing is once daily at bedtime.

The safety and efficacy of Omlonti were evaluated in three randomized controlled clinical trials involving patients with open-angle glaucoma or elevated IOP with an average baseline IOP of 24mm Hg to 26mm Hg. Over three months, IOP lowered on average by 5mm Hg to 7mm Hg for those taking Omlonti (for study participants on timolol or latanoprost, the average IOP reduction was 5mm Hg to 7mm Hg and 6mm Hg to 8mm Hg, respectively).

With glaucoma being among the most common causes of vision loss worldwide, it's encouraging to both patients and providers to see the continual development of novel approaches to control IOP and reduce the impact of the disease.

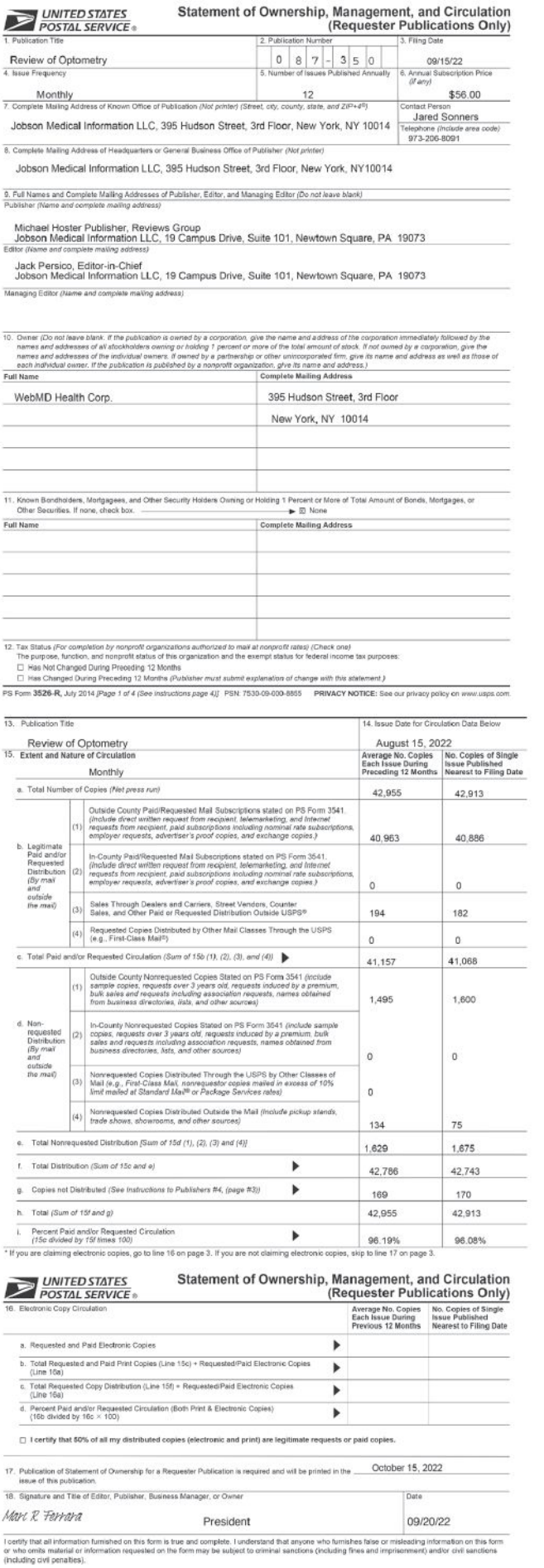
ImprimisRx Launches Compounded Antibiotic and Product Replacement Program

In eye care, treatment outcomes often rely on how soon a drug is accessed and administered, and that's definitely the case with eye infections. Although keeping medications on hand at your clinic would be ideal, these can be costly to maintain, especially given the frequent expiration of products. A new compounded antibiotic from ImprimisRx called Fortisite—which combines tobramycin 1.5% and vancomycin 5%—presents a solution, the company says. As part of the company's Patient Access Program, ImprimisRx says that it will offer a 100% replacement guarantee for any expired 503B Fortisite product. The formulation can last for up to 180 days when kept refrigerated at a temperature of 5°C, according to a company press release.

The antibiotic is now available for order by patients through the ImprimisRx 503A pharmacy, the company says. Physicians will be able to stock Fortisite in their clinics once it's available through the ImprimisRx 503B outsourcing facility, which is expected to happen in the first half of 2023. ■

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.



UNITED STATES POSTAL SERVICE®

Statement of Ownership, Management, and Circulation (Requester Publications Only)

1. Publication Title	2. Publication Number	3. Filing Date
Review of Optometry	0 8 7 - 3 5 0	09/15/22
4. Issue Frequency	5. Number of Issues Published Annually	6. Annual Subscription Price (If any)
Monthly	12	$56.00

7. Complete Mailing Address of Known Office of Publication (Not printer) (Street, city, county, state, and ZIP+4®): Jobson Medical Information LLC, 395 Hudson Street, 3rd Floor, New York, NY 10014 — Contact Person: Jared Sonners; Telephone (Include area code): 973-206-8091

8. Complete Mailing Address of Headquarters or General Business Office of Publisher (Not printer): Jobson Medical Information LLC, 395 Hudson Street, 3rd Floor, New York, NY10014

9. Full Names and Complete Mailing Addresses of Publisher, Editor, and Managing Editor (Do not leave blank)

Publisher (Name and complete mailing address): Michael Hoster Publisher, Reviews Group, Jobson Medical Information LLC, 19 Campus Drive, Suite 101, Newtown Square, PA 19073

Editor (Name and complete mailing address): Jack Persico, Editor-in-Chief, Jobson Medical Information LLC, 19 Campus Drive, Suite 101, Newtown Square, PA 19073

Managing Editor (Name and complete mailing address)

10. Owner (Do not leave blank. If the publication is owned by a corporation, give the name and address of the corporation immediately followed by the names and addresses of all stockholders owning or holding 1 percent or more of the total amount of stock. If not owned by a corporation, give the names and addresses of the individual owners. If owned by a partnership or other unincorporated firm, give its name and address as well as those of each individual owner. If the publication is published by a nonprofit organization, give its name and address.)

Full Name	Complete Mailing Address
WebMD Health Corp.	395 Hudson Street, 3rd Floor New York, NY 10014

11. Known Bondholders, Mortgagees, and Other Security Holders Owning or Holding 1 Percent or More of Total Amount of Bonds, Mortgages, or Other Securities. If none, check box. ☒ None

Full Name	Complete Mailing Address

12. Tax Status (For completion by nonprofit organizations authorized to mail at nonprofit rates) (Check one)
The purpose, function, and nonprofit status of this organization and the exempt status for federal income tax purposes:
☐ Has Not Changed During Preceding 12 Months
☐ Has Changed During Preceding 12 Months (Publisher must submit explanation of change with this statement)

PS Form **3526-R**, July 2014 (Page 1 of 4 (See Instructions page 4)) PSN: 7530-09-000-8855 **PRIVACY NOTICE:** See our privacy policy on www.usps.com

13. Publication Title	14. Issue Date for Circulation Data Below
Review of Optometry	August 15, 2022

15. Extent and Nature of Circulation (Monthly)			Average No. Copies Each Issue During Preceding 12 Months	No. Copies of Single Issue Published Nearest to Filing Date
a. Total Number of Copies (Net press run)			42,955	42,913
b. Legitimate Paid and/or Requested Distribution (By mail and outside the mail)	(1)	Outside County Paid/Requested Mail Subscriptions stated on PS Form 3541. (Include direct written request from recipient, telemarketing, and Internet requests from recipient, paid subscriptions including nominal rate subscriptions, employer requests, advertiser's proof copies, and exchange copies.)	40,963	40,886
	(2)	In-County Paid/Requested Mail Subscriptions stated on PS Form 3541. (Include direct written request from recipient, telemarketing, and Internet requests from recipient, paid subscriptions including nominal rate subscriptions, employer requests, advertiser's proof copies, and exchange copies.)	0	0
	(3)	Sales Through Dealers and Carriers, Street Vendors, Counter Sales, and Other Paid or Requested Distribution Outside USPS®	194	182
	(4)	Requested Copies Distributed by Other Mail Classes Through the USPS (e.g., First-Class Mail®)	0	0
c. Total Paid and/or Requested Circulation (Sum of 15b (1), (2), (3), and (4)) ▶			41,157	41,068
d. Non-requested Distribution (By mail and outside the mail)	(1)	Outside County Nonrequested Copies Stated on PS Form 3541 (include sample copies, requests over 3 years old, requests induced by a premium, bulk sales and requests including association requests, names obtained from business directories, lists, and other sources)	1,495	1,600
	(2)	In-County Nonrequested Copies Stated on PS Form 3541 (include sample copies, requests over 3 years old, requests induced by a premium, bulk sales and requests including association requests, names obtained from business directories, lists, and other sources)	0	0
	(3)	Nonrequested Copies Distributed Through the USPS by Other Classes of Mail (e.g., First-Class Mail, nonrequestor copies mailed in excess of 10% limit mailed at Standard Mail® or Package Services rates)	0	
	(4)	Nonrequested Copies Distributed Outside the Mail (Include pickup stands, trade shows, showrooms, and other sources)	134	75
e. Total Nonrequested Distribution (Sum of 15d (1), (2), (3) and (4))			1,629	1,675
f. Total Distribution (Sum of 15c and e) ▶			42,786	42,743
g. Copies not Distributed (See Instructions to Publishers #4, (page #3)) ▶			169	170
h. Total (Sum of 15f and g)			42,955	42,913
i. Percent Paid and/or Requested Circulation (15c divided by 15f times 100) ▶			96.19%	96.08%

* If you are claiming electronic copies, go to line 16 on page 3. If you are not claiming electronic copies, skip to line 17 on page 3.

UNITED STATES POSTAL SERVICE®

Statement of Ownership, Management, and Circulation (Requester Publications Only)

16. Electronic Copy Circulation	Average No. Copies Each Issue During Previous 12 Months	No. Copies of Single Issue Published Nearest to Filing Date
a. Requested and Paid Electronic Copies ▶		
b. Total Requested and Paid Print Copies (Line 15c) + Requested/Paid Electronic Copies (Line 16a) ▶		
c. Total Requested Copy Distribution (Line 15f) + Requested/Paid Electronic Copies (Line 16a) ▶		
d. Percent Paid and/or Requested Circulation (Both Print & Electronic Copies) (16b divided by 16c × 100) ▶		

☐ I certify that 50% of all my distributed copies (electronic and print) are legitimate requests or paid copies.

17. Publication of Statement of Ownership for a Requester Publication is required and will be printed in the October 15, 2022 issue of this publication.

18. Signature and Title of Editor, Publisher, Business Manager, or Owner	Date
Mark R. Ferrara — President	09/20/22

I certify that all information furnished on this form is true and complete. I understand that anyone who furnishes false or misleading information on this form or who omits material or information requested on the form may be subject to criminal sanctions (including fines and imprisonment) and/or civil sanctions (including civil penalties).

Practice For Sale

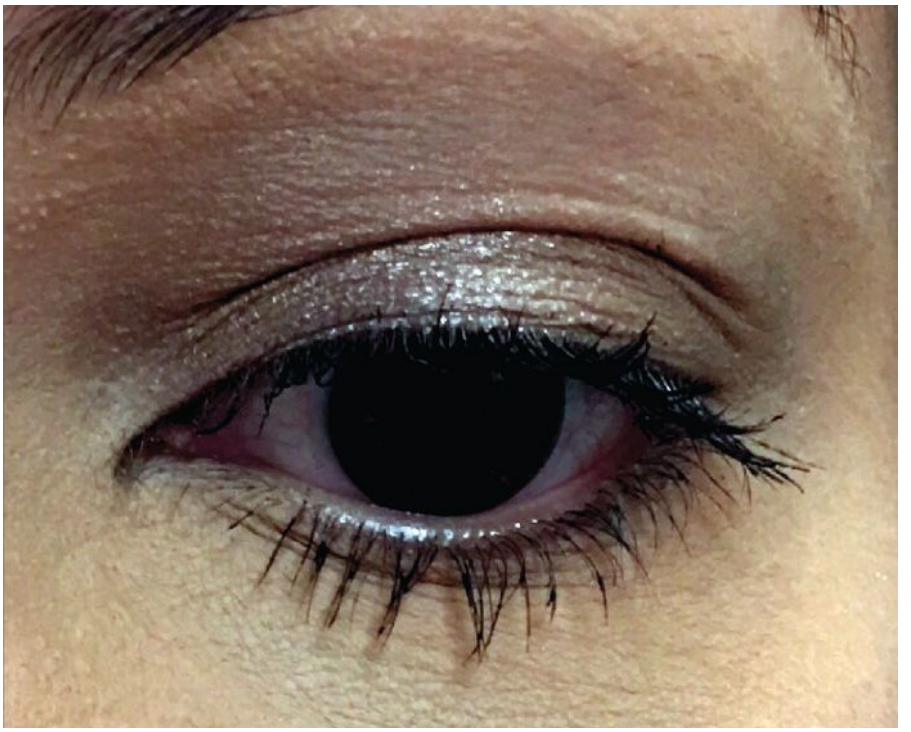
BY ANDREW S. GURWOOD, OD

DIAGNOSTIC QUIZ

Blink and You'll Miss It

When there's little to no clinical evidence to evaluate, we must rely on careful questioning to uncover the cause.

A 44-year-old woman presented to the office with a chief complaint of "a quivering left upper eyelid," of two weeks' duration. She said the issue has gradually become worse, making her self-conscious. She did not report any pain. She denied trauma, systemic disease and allergies of any kind.



This patient presented with no visible signs of pathology. What would be your approach?

Clinical Findings

This patient's best-corrected entering visual acuities were 20/20 OD and 20/20 OS at distance and near. Her external examination was unremarkable, with no evidence of afferent pupillary defect.

A normal appearing left lid is demonstrated in the photograph; however, in an exam setting it can be observed to episodically and randomly quiver. Her anterior segment findings were normal and Goldmann applanation tonometry measured 17mm Hg OU.

For More Information

Additional studies in this case included simple observation of her normal eyelid opening and eyelid closing. Health history questions were also asked to rule out connections to the facial nerve and issues of hearing (a place the facial nerve and auditory nerves have in common is along an anatomical pathway known as the cerebello-pontine angle).

Your Diagnosis

What would be your diagnosis in this case? What is the patient's likely prognosis? To find out, please read the online version of this article at www.reviewofoptometry.com. ■

Dr. Gurwood thanks Dr. Alan Kabat for his contributions to this case.

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.

NEXT MONTH IN THE MAG

In November, we present an issue devoted to diseases of the ocular surface. Articles will include:

- *Demodex* Infection: Meds and Methods to Eradicate
- Dry Eye: Know These Systemic Meds That Cause Symptoms
- The Conjunctivitis Differential—Simplified
- Diagnostic Tools and Medical Therapies for Epidemic Keratoconjunctivitis: Lessons from the Latest Research

Also in this issue:

- Assessing Visual Quality in AMD: Diagnostic Tools and Tips for Better Work-ups
- Neuromyelitis Optica and MS Assessment

MYDAY® TORIC'S UNPARALLELED RANGE[1] IS ABOUT TO GET EVEN

GREATER

For MyDay® toric, the pursuit of greatness doesn't stop. Even more parameters arriving November 2022.

CooperVision®

1. CVI data on file, 2021. Based on number of prescription options available in the USA across all soft 1-day toric lenses as reported by the 4 main manufacturers.

SYFOVRE™
(pegcetacoplan) injection

Coming Soon

Get Ready

Something new is on the way

Scan to sign up for updates or visit www.SyfovreECP.com today

Apellis