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Suggestions for Using Labs and Imaging in Your Practice

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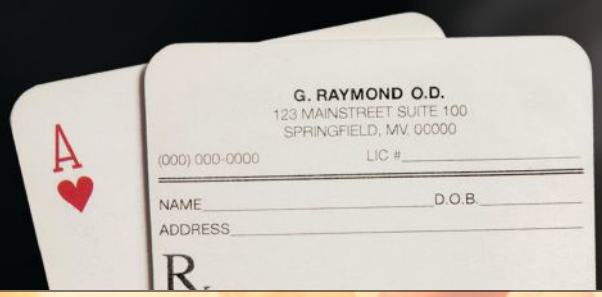
ANNUAL PHARMA ISSUE

Restrictive Drug Formularies: HOW TO BEAT



*Based on *in vitro* measurments of unworn lenses.
**Based on *in vitro* studies on unworn lenses.
†Based on lens movement, centration, and rotation at initial fitting.

References: 1. In a clinical trial to evaluate on-eye performance of TOTAL30® for Astigmatism lenses where n=69; Alcon data on file, 2021. **2.** Based on a clinical trial where n=18; Alcon data on file, 2021. **3**. In vitro analysis of lens oxygen permeability, water content, and surface imaging; Alcon data on file, 2021. **4.** In vitro analysis of lehfilcon A contact lenses outermost surface softness and correlation with water content; Alcon data on file, 2021. **5.** In vitro evaluation of bacterial adherence in commercial lenses: Alcon data on file, 2020. **6.** In vitro evaluation of bacterial biofilm in commercial lenses: Alcon data on file, 2020. **7.** Ishihara K, Fukazawa K, Sharma V, Liang S, et al. Antifouling silicone hydrogel contact lenses with a bioinspired 2-methacryloyloxyethyl phosphorylcholine polymer surface. *ACS Omega*. 2021;6:7058-7067. **8.** In vitro evaluation of lipid deposition for lehfilcon A
and commercial lenses using 3D confocal imaging; Alcon data on file, 2021.

See product instructions for complete wear, care, and safety information. Rx only

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ANNUAL PHARMA ISSUE

Restrictive Drug Formularies: HOW TO BEAT THE ODDS

When insurers stack the deck against you and your patients, you can still play a winning hand. ***PAGE 36***

ALSO INSIDE

Earn 2 Free CE Credits: Exploring the Impact of Lens Coatings on Emotional Connection, *PAGE 89*

When Selecting a Prescription Dry Eye Treatment

DON'T MAKE HER WAIT.

Not an actual patient.

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

xiidra® (lifitegrast ophthalmic solution)5%

CHOOSE XIIDRA

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

Access to Xiidra is better than ever[2]

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

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.

Please see Brief Summary of Important Product 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 Eye Dryness Score [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. DRF Fingertip Formulary® 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.

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ODs in South Dakota, Washington Push Laser Bills

If the proposed legislation passes, in addition to Nebraska's SLT bill, the number of states where optometrists have laser surgical authority would jump to 13.

Things are heating up in several scope expansion battles. On January 26th, Nebraska's scope expansion bill, LB 216, was heard by the Health and Human Services Committee and currently awaits the committee's vote. The bill would allow trained optometrists to perform selective laser trabeculoplasty (SLT) for the treatment of glaucoma. What's even more exciting is that Nebraska isn't the only state where legislative efforts for scope expansion are underway.

The prospect of expanded practice rights also draws nearer for ODs in South Dakota following the state Senate's 26-9 vote in favor of SB 87 last month. The bill, introduced by Senator Sydney Davis, proposes an update to optometry's practice scope in the state that would include various in-office procedures being taught in optometry schools today. This includes several forms of laser surgery (*e.g.*, capsulotomy, peripheral iridotomy, SLT) and corneal crosslinking. The legislation would also allow ODs in South Dakota to administer injections around the eye, remove chalazia and lid lesions, use a local anesthetic for lesion removal, remove superficial foreign bodies from the eye and prescribe pharmaceutical agents.

According to the bill text, if SB 87 is voted into law, optometrists in South Dakota will have to apply for authorization from the state's Board of Optometry before performing the procedures outlined. This authority will be granted by the Board if the optometrist fulfills one of two requirements:

(1) received a passing score on the laser and surgical procedures examination offered by the National Board of Examiners in Optometry or

(2) satisfactorily completed a training session approved by the board and proctored by an optometrist or an ophthalmologist authorized to perform the procedure in any state.

Now that SB 87 has passed the Senate, the bill has been referred to the South Dakota House Health and Human Services where it awaits review.

Another state where advocates are pushing scope expansion legislation is Washington, where such laws for optometry haven't been updated since 2003. The proposed bill, substitute SB 5389, would allow ODs with the proper training to remove lumps and bumps from the eyelids, prescribe oral steroids, administer injections around the eye and perform in-office laser procedures such as YAG capsulotomy and SLT. It would also give authority to the state's Board of Optometry to engage in rulemaking regarding the education and testing requirements that optometrists would have to meet to perform these procedures, as well as to determine whether new technologies designed to replace these procedures and treat the same conditions are allowed.

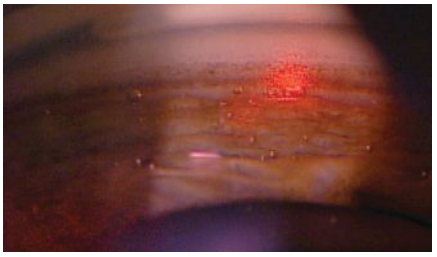

Photo: Nathan Lighthizer, OD

Scope expansion advocates in South Dakota, Nebraska and Washington are all currently fighting to pass bills that would allow ODs to perform certain advanced ocular procedures including SLT.

One organization actively advocating for the bill is the Optometric Physicians of Washington (OPW). "We worked hard to develop a solid proposal and build awareness among lawmakers," said OPW president Michael Sirott, OD, who practices in Omak, WA. "It's a disservice to my patients to have to refer them to other providers located hours away for care that I am trained to provide. Our message is very patient-centric, emphasizing the lower costs and improved access to timely care that will result from an expansion of our scope."

Given that inadequate training is a common argument from the opposition, it's important that advocates of scope expansion take the time to educate legislators—in addition to patients and the community—about the safety of optometrists performing these advanced procedures. Dr. Sirott said that in the months leading up to the January start of the legislative session, OPW did just that. During that time, "OPW members held approximately 20 local events with small groups of legislators at which they discussed the benefits of the proposed legislation and performed demonstrations of the proposed laser procedures."

The Washington State Department of Health recently reviewed the proposal and determined that today's

schools of optometry are teaching the procedures outlined in the bill. Additionally, Dr. Sirott added that the department "acknowledged that optometrists in other states are already safely performing these procedures with patient outcomes that align with those of ophthalmology."

If SB 5389 becomes law, it will help improve eyecare access for communities across the state. A study commissioned by OPW confirmed that patients in Washington who would benefit most from an increase in optometry's scope of practice are more likely to be low income, of color and rurally located, Dr. Sirott pointed out.

The legislation is being opposed by the Washington Academy of Eye Physicians and Surgeons, who argue the difference in education and training standards for ODs vs. ophthalmologists.

Washington's legislative session runs through late April. The bill received a hearing January 31 with the Senate Health & Long Term Care Committee and awaits a full vote of the committee. If approved, it would head to the House Rules Committee before reaching the Senate floor for a vote.

Several other states also have scope expansion bills currently in play or slated for introduction this year.

First Geographic Atrophy Drug Approved

Syfovre slows lesion progression in dry AMD patients but does not improve visual acuity. FDA trials showed the best results in those who maintained therapy at least 18 months.

Retina specialists will soon be able to treat patients with geographic atrophy (GA) in hopes of mitigating retinal cell loss and subsequent visual impairment that often develops in those with dry AMD. On February 17th, the FDA approved the use of pegcetacoplan, a C3 inhibitor, from Apellis Pharmaceuticals for this indication. It will be marketed under the brand name Syfovre and priced at $2,190 per vial, the company announced.

In an investor call last month, Chief Medical Officer Caroline Baumal estimated that patients will need six to eight vials of Syfovre per year. A program called ApellisAssist will provide insurance support, financial assistance and disease education for eligible patients, the company said in the release.

Syfovre is approved for GA patients with or without subfoveal involvement and should be administered every 25 to 60 days, a flexible dosing schedule that should help patients and doctors alike maintain therapy over the long haul, the company noted.

Photo: Apellis

GA patients experienced 36% reduction in lesion growth in the 18-24 month period of treatment.

Patients need to commit to an extended course of therapy to experience the drug's benefits. "This is not a drug that flips the switch on day one," Apellis CEO Cedric Francois, MD, PhD, told *Fierce Pharma* in a recent interview. "It's a drug where you make an investment over many years, and where the longer you stick to the therapy, the better this drug is going to work for you."

In its FDA clinical trials (named OAKS and DERBY), the drug "reduced the rate of GA lesion growth compared to sham and demonstrated increasing treatment effects over time, with the greatest benefit (up to 36% reduction in lesion growth with monthly treatment in DERBY) occurring between months 18-24," according to the press release. OAKS and DERBY subjects are currently participating in three-year extension trials to gauge the durability of treatment effect out to five years.

More than one million Americans have GA, Apellis says. The condition arises from the combined effects of genetic influencers, environmental stressors and the aging process. Central to the pathogenesis is the complement cascade, an immune response in which a protein compound called membrane attack complex is created, which then adheres to cells and causes lysis and cell death. Pegcetacoplan blocks the cleavage of complement protein C3 into C3a and C3b; the latter is an upstream precursor of membrane attack complex.

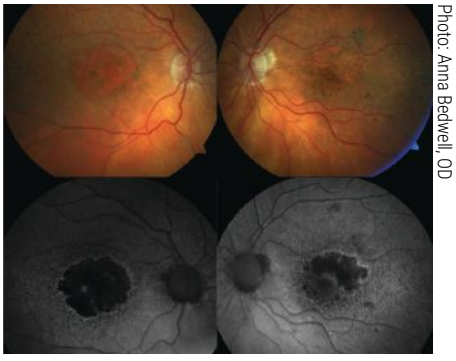

Photo: Anna Bedwell, OD

Bilateral GA in a 90-year-old (not part of the FDA trials).

Apellis says that Syfovre availability will begin this month. For more information, visit https://syfovreecp.com.

A second investigational drug for GA will soon follow. The developer, Iveric Bio, announced in a recent press release that the FDA accepted the New Drug Application for its complement C5 inhibitor, avacincaptad pegol, for the treatment of GA secondary to AMD. The application has been granted Priority Review with a Prescription Drug User Fee Act and will either be approved or denied by the FDA by August 19 of this year.

Nine of 10 of US Counties Have No Pediatric Ophthalmologists

A new study in *JAMA Ophthalmology* accessed information from the public databases of American Academy of Ophthalmology and American Association for Pediatric Ophthalmology and Strabismus to identify current pediatric ophthalmologist distribution in the US as of March 2022.

Researchers found a total of 1,056 practicing pediatric ophthalmologists, with the highest concentrations in the four most populous states of California (11%), New York (9.2%), Florida (6.5%) and Texas (5.9%). Concerningly, 90% of all US counties and four states (8%) had zero pediatric ophthalmologists. The range of practitioners to million persons has grown in disparity since last data was obtained in 2007, despite a moderate increase in number of practitioners (300) since that time.

Those counties with one or more pediatric ophthalmologists displayed higher median household income than counties without any. Even further, the percentage of families without internet access, persons younger than 19 years without health insurance and households without a vehicle were all higher in counties with no pediatric ophthalmologists when compared with counties that had at least one.

Based especially on the expanding discrepancy between practitioners to million persons, the authors of the study, in their paper on the work, endorse that "these results support the need to improve incentive structures to redistribute pediatric ophthalmologist resources to match the unequal health burden in underserved counties."[1] As a possible solution, they suggest introducing the field to individuals who are interested either before entering ophthalmology residency or even before going into the medical field, bringing attention to high school and college students. They cite that this could work because evidence has found that students introduced to niche specialties earlier are more invested in them long-term.

What the study authors can agree on is the importance of these findings. "The aforementioned factors all can have marked implications for patients' ability to seek and consistently access both virtual and in-person pediatric ophthalmological care, which may be exacerbated by the lack of available local practitioners evidenced here."[1]

With the study outlining well what shortcomings currently exist in the US population demographically, as related to pediatric ophthalmology, an invited commentary in the same issue of *JAMA Ophthalmology* further refines the information and takes a more nuanced approach to analyzing the study trends.

The authors of the commentary highlight the importance of economic viability concerns with the occupation. This includes lengthy and complex examinations for children, meaning pediatric ophthalmologists see less patients, thus resulting in lower reimbursement than ophthalmologists seeing only adults. They also point out the fact that it is a seller's market, with this profession able to select their location practice, since the number of professionals is small. As a result, physicians have been shown to choose areas that already see high patient volume, thus the underserved areas remain vulnerable to access.

The commentary authors do make sure to add, "However, while the authors suggest a notion of incentivizing the redistribution of the existing pool of pediatric ophthalmologists to more underserved areas, the more significant problem appears to be the astonishing scarcity of total pediatric ophthalmologists."[2] They further elaborate that two-thirds of American counties would remain unfilled if all pediatric ophthalmologists were evenly distributed, one by one, across all counties.

Despite this disagreement, the commentary echoes the same sentiment as the general findings of the study: "We should dedicate resources to the development of pediatric ophthalmology fellowship programs in geographically underserved areas and provide economic incentives for those willing to remain there after training." This, as well as potential legislative reform to allow for cross-state coverage, could be the first steps to reversing the issue.

1. Walsh HL, Parrish A, Hucko L, Sridhar J, Cavuoto KM. Access to pediatric ophthalmological care by geographic distribution and US population demographic characteristics in 2022. JAMA Ophthalmol. January 26, 2023. [Epub ahead of print].

2. Oatts JT, Indaram M, de Alba Campomanes AG. Where have all the pediatric ophthalmologists gone?—Pediatric eye care scarcity and the challenge of creating equitable health care access. JAMA Ophthalmol. January 26, 2023. [Epub ahead of print].

IN BRIEF

Check for Chorioretinal Thinning in Kidney Disease. Fundus examination can be a valuable tool for visualizing the chorioretinal microvasculature that may be affected in chronic kidney disease. Researchers in Egypt believe that noninvasive OCT for imaging the retina and choroid could also identify these changes. Their recent study determined that **chorioretinal thinning in chronic kidney disease was associated with a lower estimated glomerular filtration rate, a higher serum C-reactive protein concentration and greater proteinuria**. They believe that further studies with a larger scale could detect whether these eye changes reflect the natural history of chronic kidney disease.

A cross-sectional study was conducted on 144 eyes of 72 patients divided into three groups according to the stage of chronic kidney disease: stages one and two with glomerular filtration rate >60, stage three with filtration rates 30 to 59 and stages four and five with estimated rates <29.

The study found that a thinner retina and choroid were associated with chronic kidney disease stage three with even more thinning in stages four and five. Also, associations between C-reactive protein concentration and albuminuria were inversely correlated with choroidal thickness in chronic kidney disease and were independent predictors of thickness. The researchers believe these findings may be explained by the role of inflammation in the development of both vascular and renal disease.

Basiony AI, Atta SN, Dewidar NM, Zaky AG. Association of chorioretinal thickness with chronic kidney disease. BMC Ophthalmol. February 9, 2023. [Epub ahead of print].

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Anticholinergic Drugs Increase DED Risk Threefold

This relationship remained even after adjusting for age, gender and comorbidities.

If you have patients who routinely use any medication classified as anticholinergic—including some popular antidepressants and antihistamines—bear in mind that they are a key culprit in medication-induced dry eye. In a recent study, researchers examined the relationship between anticholinergic burden and dry eye disease (DED), and found that taking at least one such drug was associated with an approximately threefold increase in the risk of DED in adults.

A total of 120 participants (more than half women) who underwent ophthalmological examination between February 2021 and February 2022 were evaluated, and drugs used by the patients in the last two months were recorded. Anticholinergic burden was assessed using a scale called the Anticholinergic Cognitive Burden (ACB).

Patients with dry eye had significantly higher Charlson comorbidity index (CCI) scores—a measure of the relative one-year risk of mortality based on 17 possible comorbid conditions—lower Schirmer test values, higher Ocular Surface Disease Index scores and higher anticholinergic burden, even after adjustments were made for possible confounding factors such as age, gender and comorbidity.

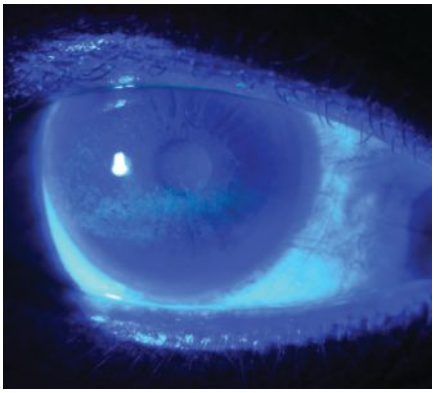

Photo: W.R. Buie, OD

This study revealed that the co-occurrence of DED and exposure to anticholinergic drugs is not uncommon among adults.

"As is known, there are many confounding factors in cases involving elderly patients, such as cognitive status, multiple drug use and comorbidities in particular, and this can be a problem, especially in studies conducted with this population," the authors wrote in their paper for the journal *Eye*. In one study, for example, "the peripheral side effects of anticholinergic burden were evaluated in a younger population (mean age of 56 years) using the ACB scale, and it was ascertained that an excess of anticholinergic load had a statistically significant effect on peripheral side effects such as fractures and falls. In light of the findings described here, we can say that our study is one of the rare studies evaluating anticholinergic burden, and especially in a younger population, while taking into account all comorbidities."

Anticholinergic burden was associated with an approximately threefold increase in the risk of DED in adults (11.9%). All of these findings were consistent with previous study results.

"We showed for the first time that every one-unit increase in CCI score more than doubled the risk of DED," the authors noted. "Therefore, systemic comorbidities such as drug use in people diagnosed with DED should not be ignored. These results also shed light on the importance of embracing a multidisciplinary approach toward affected patients."

Greater caution in prescribing anticholinergic drugs for adult patients is important to reduce rates of adverse outcomes, the authors suggested.

"In individuals at risk of DED, increased awareness of anticholinergic burden may allow for earlier targeted health interventions," they concluded. "There is a need for future longitudinal studies to recommend strategies such as treatment changes or drug reduction for preventing the risk of dry eye in adults with high anticholinergic burden."

Katipoglu Z, Abay RN. The relationship between dry eye disease and anticholinergic burden. Eye. February 9, 2023. [Epub ahead of print].

IN BRIEF

Pseudophakic CME in One Eye Increases Fellow-eye Risk. A common complication of cataract surgery, pseudophakic cystoid macular edema (CME) is often addressed prophylactically in high-risk patients using NSAIDs or periocular steroid injections. Recently, **researchers investigated the risk of developing CME in fellow-eye cataract surgery and reported that first-eye CME was a strong independent risk factor for the finding.**

The retrospective study included 54,209 patients (mean age: 74.6 years, 38.8% male). The researchers reported that 1% of patients developed CME in the fellow eye. **They found a 0.9% risk for fellow-eye CME in those without first-eye CME and a risk of 10.7% in those with first-eye CME.**

Risk factors for fellow-eye CME based on the researchers' fully adjusted model included **first-eye CME (risk ratio [RR]: 8.55), epiretinal membrane (RR: 4.1), history of retinal vein occlusion (RR: 2.94), diabetes without history of diabetic macular edema (RR: 2.08), advanced cataract (RR: 1.75), preoperative prostaglandin analogue use (RR: 1.49) and male sex (RR: 1.19).**

The researchers concluded in their paper for the *Ophthalmology* journal that **first-eye CME results in an independent eightfold increase in the risk for fellow-eye CME.** "While clinicians have been anecdotally aware of this increased risk, our findings add objective data and provide useful numbers when counseling patients undergoing fellow-eye cataract surgery," they wrote in their paper. They also noted that these findings may **"help in identifying high-risk patients who may benefit from prophylactic therapy."**

Shakarchi AF, Soliman MK, Yang YC, et al. Risk of pseudophakic cystoid macular edema in fellow-eye cataract studies: a multicenter database study. Ophthalmology. February 3, 2023. [Epub ahead of print].

0.05% Atropine Linked to Low Incidence of Myopia in Kids

This concentration of eye drops, but not 0.01%, resulted in a significantly lower occurrence of the condition at two years in those ages four to nine in a recent study.

Low-concentration (0.01% to 0.05%) atropine can reduce myopia progression, but studies of 0.01% atropine have produced inconsistent findings. The Low-Concentration Atropine for Myopia Prevention (LAMP2) trial was conducted to assess the efficacy of low-concentration atropine in delaying myopia onset among children. It found that, among children four to nine years old without myopia, nightly use of 0.05% atropine eye drops compared with placebo resulted in a significantly lower incidence of myopia and lower percentage of participants with fast myopic shift at two years.[1]

This randomized, placebo-controlled, double-masked trial conducted at the Chinese University of Hong Kong enrolled 474 nonmyopic children between the ages of four and nine (mean age: 6.8, 50% female) with cycloplegic spherical equivalent between +1.00D to 0.00D and astigmatism less than -1.00D. They were assigned at random to the 0.05% atropine (n=160), 0.01% atropine (n=159) and placebo (n=155) groups and had eye drops applied once nightly in both eyes over two years.

Of the 474 randomized patients, 353 (74.5%) completed the trial. The two-year cumulative incidences of myopia in the 0.05% atropine, 0.01% atropine and placebo groups were 28.4%, 45.9% and 53.0%, respectively, and the percentages of participants with fast myopic shift at two years were 25.0%, 45.1% and 53.9%, respectively. Compared with the placebo group, the 0.05% atropine group had a significantly lower two-year cumulative myopia incidence (difference: 24.6%) and percentage of patients with fast myopic shift (difference: 28.9%). Compared with the 0.01% atropine group, the 0.05% atropine group had a significantly lower two-year cumulative myopia incidence (difference: 17.5%) and percentage of patients with fast myopic shift (difference: 20.1%). The 0.01% atropine and placebo groups were not significantly different in two-year cumulative myopia incidence or percentage of patients with fast myopic shift.

Photo: Maria K. Walker, OD

Use of 0.05% atropine had significantly lower two-year cumulative myopia incidence and percentage of patients with fast myopic shift.

"In this study, 0.01% atropine did not achieve a statistically significant difference compared with placebo," the study authors wrote in their paper, published in *JAMA*. "This result suggests that the concentration of 0.01% atropine might not be strong enough to achieve sufficient treatment effects."

Photophobia was the most common adverse event and was reported by 12.9% of participants in the 0.05% atropine group, 18.9% in the 0.01% atropine group and 12.2% in the placebo group in the second year.

"Nevertheless, this study provides evidence for atropine as an additional strategy for delaying myopia onset beyond increasing time spent outdoors," the authors wrote. "Although increasing outdoor time offers an effective approach for general populations of children, the addition of low-concentration atropine could be considered for children at high risk of developing myopia."[1]

A commentary also published in *JAMA* noted, "It is not yet known whether delaying the onset of myopia will reduce the final degree of myopia as an adult or whether it simply postpones the typical myopia progression to later years and thus does not decrease the long-term risk associated with higher degrees of myopia."

"It is also unknown whether decreasing the myopic shift in refractive error and eye growth by initiating treatment prior to myopia onset amplifies the benefit or whether a similar reduction can be achieved by initiating treatment early after onset," the commentary authors also stated. "Answering these questions will require longer follow-up."[2]

"The original LAMP study looked at various concentrations of low-dose atropine including 0.01% and 0.05% in myopic children and found that 0.01% did not significantly slow eye growth," David A. Berntsen, OD, PhD, co-author of the commentary says. "Based on these findings, many have been recommending concentrations greater than 0.01% (up to 0.05%) for slowing myopia progression." The LAMP2 results, he says, add further support for that approach.

Another commentary, this one published in *JAMA Ophthamology*, highlighted that certain questions remain to be answered, such as:

- How early should atropine treatment be initiated? On the other hand, is there an age at which it is too late for atropine treatment to be beneficial?
- How long should treatment be continued to prevent myopia?
- Are these findings applicable to non-Asian populations?

(Continued on page 14)


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Blood Riboflavin Levels Lower in Keratoconus

However, this study found no differences in the amount of homocysteine, vitamin B12 or folic acid between patients and controls.

Research has yet to confirm the pathogenesis of keratoconus, a disease characterized by progressive thinning and corneal steepening. Ongoing studies are investigating the effects of various factors on its etiology, including genetic, biomechanical, proteomic, metabolic, endocrinological and environmental. Recently, researchers looked into whether metabolic substances like vitamin D, vitamin B12, riboflavin, homocysteine, folic acid and arginine might play into the development of keratoconus, confirming that every substance did either directly or indirectly.

Piggybacking off of this previous research, a team performed a study to evaluate the blood levels of homocysteine, vitamin B12, folic acid and riboflavin in patients with or without keratoconus. Among their findings, published recently in the *Journal of Cataract and Refractive Surgery*, was that low blood riboflavin levels in keratoconus patients are a possible risk factor in the pathogenesis of the disease.

One hundred patients with keratoconus and 200 healthy controls were included in the prospective study (age range: 18 to 35). All patients completed ophthalmologic exams and corneal tomography and gave blood samples at a single hospital eye clinic between 2019 and 2020.

The researchers found that there were no differences in levels of homocysteine, vitamin B12 or folic acid between keratoconus and non-keratoconus patients. However, riboflavin level was significantly different between the two groups (84.0µg/L in keratoconus patients and 183.6µg/L in controls). Additionally, riboflavin levels were below 180µg/L in 99% of keratoconus patients but only 53.5% of controls.

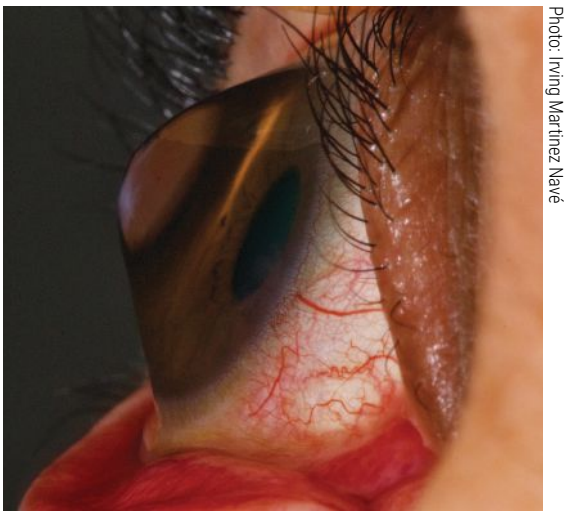

Photo: Irving Martinez Navé

This study found that riboflavin deficiency may play a role in the pathogenesis of keratoconus.

"The significant decrease in riboflavin levels detected in keratoconus subjects in our study indicates that riboflavin deficiency may have a potential role in the development of keratoconus," the researchers explained in their paper. "Riboflavin deficiency is frequently seen in the community in conjunction with other water-soluble vitamin deficiencies. The fact that vitamin B12 and folic acid levels were normal in our study makes determining the cause of isolated riboflavin deficiency difficult."

In light of these results, the study authors stress that future studies should investigate the causes of low-endogenously synthesized riboflavin in keratoconus patients. "A longitudinal study should also be conducted to determine whether progressive keratoconus is caused by an ongoing/worsening riboflavin deficiency," they concluded in their paper for *JCRS*.

Sozer O, Ozalp O, Atalay E, et al. Comparison of blood levels of vitamin b12, folic acid (b9), riboflavin (b2), and homocysteine in keratoconus and healthy subjects. J Cataract Refract Surg. February 2, 2023. [Epub ahead of print].

0.05% Atropine Shown to be Efficacious in Slowing Myopia Development

(Continued from page 11)

The authors say that if atropine does receive FDA approval for myopia, "Widespread administration of atropine to prevent myopia in children should not be recommended indiscriminately, since children with hyperopia may be harmed if atropine interferes with emmetropization."[3]

"There is one US-based large-scale clinical trial conducted by Vyluma (the CHAMP study) that reported recently in a press release that 0.01% did slow eye growth in myopic children," Dr. Berntsen notes. "The difference between the results in Asia and the US could potentially be due to differences in the study population or drug formulation."

According to him, there are other US-based trials in progress that will hopefully soon shed more light on the conflicting reports involving the effect of 0.01% atropine on eye growth in myopic children so that effective guidelines can be developed.

1. Yam JC, Zhang XJ, Zhang Y, et al. Effect of low-concentration atropine eyedrops vs. placebo on myopia incidence in children: the LAMP2 randomized clinical trial. JAMA Ophthalmol. 2023;329(6):472-81.

2. Berntsen DA, Walline JJ. Delaying the onset of nearsightedness. JAMA Ophthalmol. 2023;329(6):465-6.

3. Musch DC, Archer SM. Can we prevent or delay the onset of myopia? JAMA Ophthalmol. February 14, 2023. [Epub ahead of print].

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High Retinal Vessel Tortuosity Indicative of Several Cardiovascular Diseases

Including some common ones like hypertension, myocardial infarction and stroke, this was determined by the largest genome-wide association study of the condition yet conducted.

Recent research from the journal *Ophthalmology Science* has identified novel genetic loci that may help better understand the molecular mechanisms both causing and modulating tortuosity of the retinal vasculature. Even further, this new study revealed causal relationships with other diseases and their risk factors.

The work itself, conducted in Lausanne, Switzerland, was a genome-wide association study (GWAS) of vascular tortuosity of retinal arteries and veins, replicated through meta-analysis and Mendelian randomization. Included was a total of 116,639 fundus images primarily from the UK Biobank dataset.

The researchers determined vessel type with a deep learning algorithm and annotated vessels through use of a fully automated retina image processing pipeline. From there, the tortuosity of the median arterial, venous and combined vessels were computed and was measured by the distance factor, defined as the length of a vessel segment over its chord length. Six other measures were included that integrated over vessel curvature. Finally, the GWAS was performed of these measured traits and assessed through gene set enrichment.

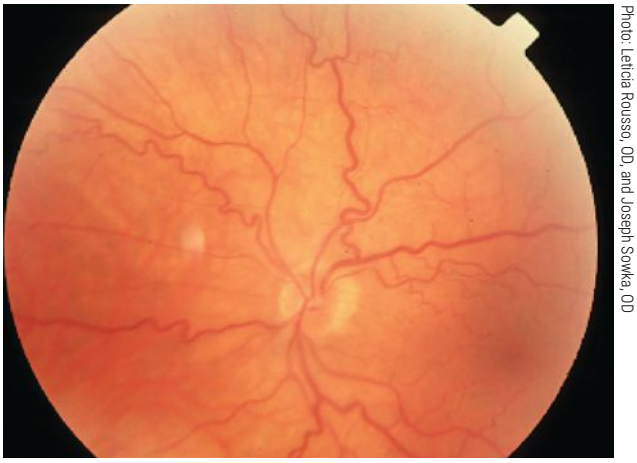

Photo: Leticia Rousso, OD, and Joseph Sowka, OD

Several alleles associated with retinal vessel tortuosity suggest a common genetic architecture of this trait with cardiovascular diseases and metabolic syndrome.

What they found was an association of higher retinal tortuosity levels to elevated instances of angina, myocardial infarction, stroke, deep vein thrombosis and hypertension. A total of 175 genetic loci were identified in the Biobank to be associated with findings in the subjects, with 173 novel ones and four being replicated in the smaller meta-cohort. The GWAS revealed 114 loci for vessel type specific arteries and 63 for veins.

Heritability was estimated to be about 25%. The genes that showed significant association signals were shown to be overexpressed in both arteries and heart muscle, while also showing linkage with vascular structural property-related pathways.

The loci related to retinal tortuosity were determined by the researchers of this study as pleiotropic functions as cardiometabolic disease variants and risk factors. The pleiotropic effects of the loci were independently associated with coronary artery disease, myocardial infarction, hypertension, diabetes, chronic lymphocytic leukemia, Alzheimer's, myopia and glaucoma. Related to this finding, the Mendelian randomization yielded causal effects of tortuosity with both BMI and LDL cholesterol levels. More specifically, elevated LDL levels causally were found to reduce arterial tortuosity. Conversely, a negative causal effect was seen of venous tortuosity on BMI, even though an established positive correlation already exists between BMI and retinal tortuosity. This might be due to other environmental factors influencing this relationship.

The researchers go on to report that their results are consistent with tortuosity-related genes being overexpressed in the aorta, tibial artery, coronary artery and heart tissues. The genes were specifically involved in development of blood vessels, vessel integrity maintenance and remodeling as a consequence of disease processes taking place.

By identifying specific loci associated with tortuosity, the study authors say in their paper, "our findings provide a significant process in understanding of molecular players and mechanisms modulating retinal vessel tortuosity, and their links to ocular and cardiometabolic diseases, which is fundamental for developing better tools for diagnosis and treatment."

Tomasoni M, Beyeler MJ, Vela SO, et al. Genome-Wide Association Studies of retinal vessel tortuosity identify numerous novel loci reveling genes and pathways associated with ocular and cardiometabolic diseases. Ophthalmol Sci. February 16, 2023. [Epub ahead of print].

CORRECTION

The January 2023 article "Bouncing Back" by Paul Karpecki, OD, included an incorrect detail about the concentration of Vyluma's investigational low-dose atropine therapy. The correct concentration is 0.01%. *Review* regrets the error.

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FEATURES

REVIEW OF OPTOMETRY • Vol. 160, No. 3 • March 15, 2023

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[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.*

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BY JACK PERSICO
EDITOR-IN-CHIEF
OUTLOOK

This Year's Model

New presbyopia drugs are on the way. It's reasonable to expect incremental, steady improvement as the category matures.

It's fashionable in some circles these days to write off the concept of pharmaceutical treatment of presbyopia in light of the rocky start the category has seen. Allergan's 2021 launch of Vuity was met with initial enthusiasm, but then its limitations became manifest. Now, a slate of new options are on their way, hoping to remedy the issues that have stalled the concept. Will they face similar stumbles?

Probably. But I'm reminded of how the established players in the smartphone market reacted to Apple's 2007 launch of the iPhone. The most infamous blown call came from the CEO of Palm, maker of (at the time) several popular smartphones back when they were still called personal digital assistants. "We've learned and struggled for a few years here figuring out how to make a decent phone. PC guys are not going to just figure this out. They're not going to just walk in," Palm CEO Ed Colligan said, condescendingly, about the prospect of competing with Apple's entry into the market.

Three years later, the iPhone was a phenomenon and Palm was out of business. Even Blackberry, the original behemoth in smartphones, failed to adapt to the threat and eventually went out of business in 2016.

None of this is to suggest presbyopia drops will follow the same course—corrective lenses ain't going anywhere. In fact, it would be overstating matters greatly to expect iPhone-like impact for *any* new product. But the lesson of the iPhone is: patience.

The first-generation iPhone was primitive by today's standards: its internet connectivity was painfully slow, third-party apps didn't exist yet, the camera was terrible, copy/paste for text hadn't been developed yet, and so on. But the device showed us an ideal for the future, and that vision guided the developers of successive products, both inside and outside of Apple. The company and others iterated on the smartphone year in and year out, device by device, with better technology and new features at each launch. Nowadays, smartphones are pretty much essential devices for billions of people worldwide.

Medical therapy for presbyopia feels very much like a first-gen iPhone right now, but the drug developers have a clear set of known shortcomings to chip away at with each next iteration on the concept. This month's annual pharmaceuticals issue includes an interesting article on the state of the presbyopia eye drop category and where it's headed. Rather than dwelling on today's deficiencies, it's helpful to think a few years out about where we'll be at the end of the decade. Even in a more advanced form, this isn't a product that will suit everyone, that's for sure. But it's usually a bad idea to bet against something that aims to satisfy the aesthetic anxieties of people in their mid-40s. The drops will find a suitable place in your practice.

Beyond that look at presbyopia drugs, this pharmaceutical-themed issue is packed with discussions of recent and upcoming progress in dry eye therapy, proper use of oral steroids, newly identified side effects of cancer drugs and a wide-ranging feature on how to fight insurance denials for new meds. Enjoy! ■

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BY PAUL M. KARPECKI, OD
CHIEF CLINICAL EDITOR

Game Changers

Get ready for new medications targeting common conditions.

It's an exciting time for optometrists prescribing therapeutics. A number of blockbuster topical ophthalmic drugs should become available within a year and can potentially make a big impact for you and your patients. We'll revisit a few significant recent approvals along with what's on the horizon.

Recent Advances

Three therapeutics come to mind that you should consider:

- ***Oxervate*** (Dompé) for neurotrophic keratitis has changed the usual progression of the disease from punctate keratitis to eventual corneal perforation. In clinical studies, 72% of patients went from persistent corneal epithelial defects or ulcers to complete corneal clearance after two months of therapy, with 80% remaining that way one year later.
- ***Upneeq*** (RVL Pharmaceuticals) has done wonders for patients with ptosis. Patients showed a lift in their eyelids that corresponds to a statistically significant increase in visual fields plus the aesthetic effects.
- ***Tyrvaya*** (Viatris Pharmaceuticals) has shown a significant improvement in basal tear production of all three contributing glands, including the lacrimal glands, meibomian glands and the mucin-producing goblet cells.

In the Pipeline

One of the first is a lipid layer enhancing topical agent called NOV03 (Bausch + Lomb) or perfluorohexaloctane, which remains in the meibomian glands for over 24 hours and on the ocular surface for four to six hours after a single drop. It appears to interdigitate with an existing dysfunctional lipid layer to stabilize and enhance it, preventing evaporation by more than that of our existing lipid layer. Since 86% of all dry eye disease (DED) involves meibomian gland dysfunction, this could be the first topical agent targeting that critical layer.

> **"Start preparing your practice and patients for these new therapeutics that target DED in novel ways, the first blepharitis indication and a new approach to presbyopia."**

Around the same time, its sister product, CyclASol, which contains 0.1% cyclosporine, may be approved. Up to 86.5% of patients considered CyclASol comfortable and 99.8% reported no or mild instillation site pain, leading to very low discontinuation rates. This drug may be ideal for patients with ocular surface staining and aqueous deficient dry eye.

A third dry eye drug, Reproxolap (Aldeyra Pharmaceuticals), works by inhibiting reactive aldehyde species, or RASP, which is found to be highly elevated in patients suffering from DED (and allergic conjunctivitis). Reproxolap showed almost immediate positive effects in tear production as well as long-term effects on DED patients with inflammation. It has a unique mechanism beyond inflammation control that could significantly help DED sufferers.

Demodex blepharitis will have its first prescription foe this fall. TP-03 (Tarsus Pharmaceuticals) achieved a clinically meaningful collarette cure rate of almost 90% and statistically improved lid erythema and mite eradication rates when used BID for six weeks. These impressive results were without any eyelid rubbing.

Although I see success with manuka honey extract, coconut oil and aloe (MyboClean, Danelli Ocular Creations), as well as intense pulsed light with low laser light treatment and blepharoexfoliation, we need a powerful prescription product like TP-03.

A New Shot at Presbyopia

CSF-1 (Orasis Pharmaceuticals) is a new, low-dose pilocarpine that has an optimized formulation at the lowest effective dose, 0.4%—which is one-third less than the currently available presbyopia drop—a near-neutral pH, is preservative-free and has two lubricating agents. In clinical studies, two thirds of patients gained three lines or more on day 15 (two hours post dose two) with over half maintaining a two-line gain eight hours after instillation.

Optometry is the number one prescribing profession of topical agents for everything from DED to presbyopia. Pharmaceuticals will be optometry's focus in 2023 as these exciting topical agents lead the way. Start preparing your practice and your patients for these new therapeutics that target DED in novel ways, battle blepharitis for the first time and offer a new approach to presbyopia. ■

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

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BY MONTGOMERY VICKERS, OD

CHAIRSIDE

Keep Your Friends Close and Your Elders Closer

The older, the wiser.

My parents, and by parents I mean my mother, were always concerned about who I hung out with. My mom carefully considered multiple important factors in determining which of my acquaintances would be most likely to get me in trouble. When I say "multiple factors," what I mean is things like hair length and church attendance, certainly critical areas to consider when one chooses their son's friends.

Although those were probably good enough reasons back in the day to blackball those little town ne'er-do-wells, I've spent the past 60-plus years developing my own idea of who to hang out with throughout my career.

Earlier on I decided to make it my mission to hang out with "the old guys" of optometry every chance I could get. I've told every young doctor I meet to look for the table at the OD dinner where most of the doctors have had more than one colonoscopy and sit there. The old guys have a little thing called experience under their belts.

Now, back in the day, most optometrists were indeed guys, but I certainly did not exclude the women of optometry. I adored Dr. Slaymaker in West Virginia. She was the straightest shooter I ever met. When the fellows all started posturing about who had the best ideas, it was always Dr. Slaymaker who brought them down to earth in her brilliant, salty ways.

At one of the first optometric society meetings I ever attended right after graduation, Dr. Slaymaker, after casually destroying a room full of male-induced pomposity, announced the only doctor in the room who made any sense was "Dr. Vickers." That's right, me. I barely knew her at the time, but I did know this: she only said that to see the shocked expressions on the faces of the establishment ODs. And it worked. This had nothing to do with my amazing insight and wisdom, as I truly had none of it then, but it still made me feel good and gave me confidence that I would at least be an okay OD if I hung in there.

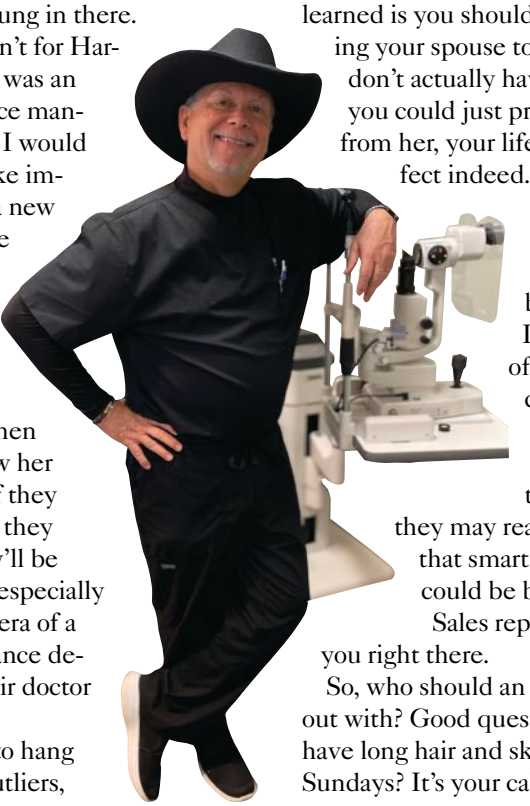
And if it wasn't for Harriet Stein, who was an amazing practice management guru, I would have gone broke immediately. As a new OD, I would've been heartbroken if a patient changed doctors. But I remembered then and still do now her wise words: "If they love you when they leave you, they'll be back." This is especially true in today's era of a patient's insurance deciding who their doctor has to be.

I also loved to hang out with the outliers, those doctors who were always trying radical things, ordering new technologies, etc. This is where I was pitched the revolutionary idea of having a surgeon implant a small magnet in everyone's glabellas so their glasses would not slide down their nose. Might have been one of my worst investments in hindsight.

Then this doctor told me he thought he could use some kind of high-tech laser to sculpt a patient's cornea to eliminate myopia. Seemed pretty dumb to me.

But we need these visionaries. Without visionaries, we would never have 4,000 antihistamine eye drops at our disposal. I like hanging out with these kinds of doctors. I seem less nerdy when I'm with them.

Once you've been married a hundred years, you also hang out with your wife's friends. The secret I've learned is you should keep encouraging your spouse to work so they don't actually have friends. Now if you could just pry the TV remote from her, your life would be perfect indeed.



What about staff? If you have read this column before, you know I am not in favor of hanging out with coworkers except at work. If you spend too much time with them, they may realize you are not that smart after all. That could be bad for business.

Sales reps? Uh, no. I'll stop you right there.

So, who should an optometrist hang out with? Good question. Do they have long hair and skip church on Sundays? It's your call. ■

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

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TECS Book Case

An expansion of basic eyecare services can especially benefit those far away from medical centers.

Q I have a patient who has been unable to get eye care at the nearest Veterans Affairs (VA) Medical Center in a timely manner. What are his options?

A 65-year-old male patient with a family history of glaucoma was "examined remotely" through the Technology-based Eye Care Services (TECS) program in the rural mountains of Georgia. His IOPs were measured at 28mm Hg OD and 29mm Hg OS. His optic nerve photographs revealed rim tissue thinning, with the OCT showing corresponding thinning of the nerve fiber layer. He was diagnosed with glaucoma by the remote optometrist reviewing the patient's findings and started on latanoprost OU qhs.

The patient was then referred for an in-person gonioscopy exam at the main VA medical center eye clinic but will come back to the TECS site near his home for further testing, including a VF test and monitoring in the teleglaucoma program. "This is one example of thousands that has already prevented blindness through telemedicine," says Trennda Rittenbach, OD, reader for the Atlanta VA TECS program. "This patient might not have sought out care because the closest VA Medical Center was over 2.5 hours away in Atlanta." Dr. Rittenbach and her team were able to get him started on medication immediately, all from the Seattle area.

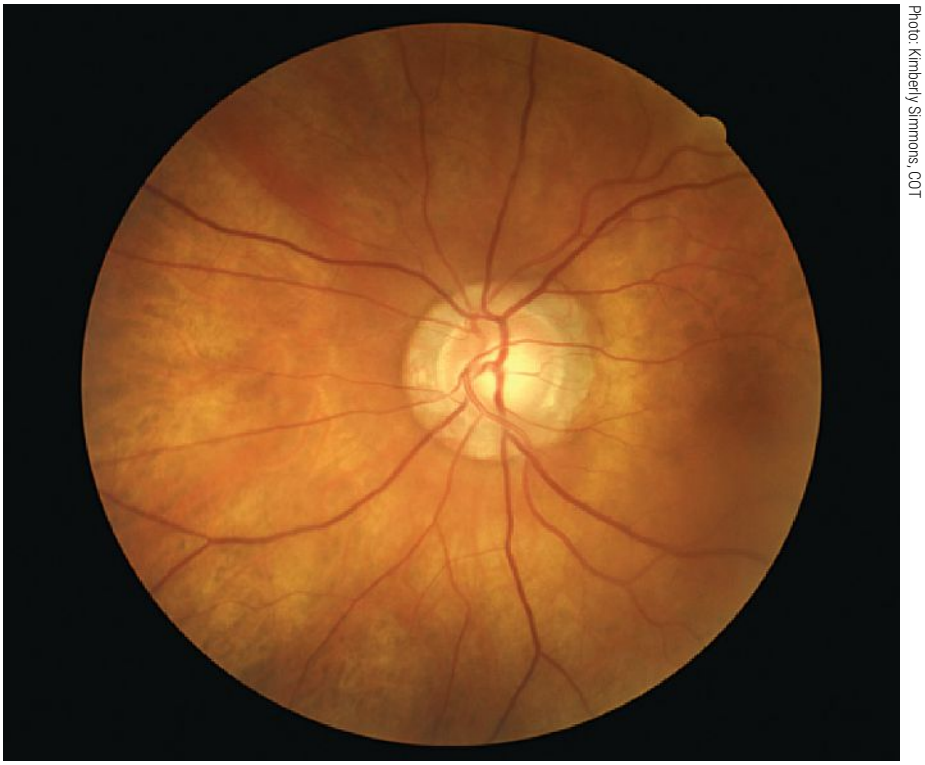

Photo: Kimberly Simmons, COT

Optic nerve with neuroretinal rim loss could be diagnosed in a VA telehealth setting.

A Growing Need

The US has a very large rural population that has difficulty accessing our healthcare system. The projected number of adults with a diagnosis of diabetes will increase from 22.3 million in 2014 to 39.7 million in 2030, and to 60.6 million in 2060.[1] By 2020, it is expected that approximately 76 million people will suffer from glaucoma, with that number estimated to reach 111.8 million by 2040.[2] The number of people with AMD was estimated to be 196 million in 2020 and predicted to be 288 million in 2040.[3]

"These are ocular diseases that can be diagnosed and often times managed and treated in the telemedicine setting," Dr. Rittenbach says.

In 2015, the VA launched the TECS program to bring specialty eye care to underserved veterans who have limited access to eye and vision exams. Quality care measures are in place that monitor the initiative, and so far those evaluations have proven that vision care and medical eye care can be more conveniently accessed, and that patients are very happy with the process.

The Way It Works

Trained technicians at community-based outpatient clinics gather information such as visual acuity, ancillary testing and fundus photography. Doctors such as Dr. Rittenbach then come up with an assessment and treatment plan for the patient. Veterans who need follow-up care can see an eye

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.

care provider at a VA medical center or a local provider in the community.[4] This newer tele-eye program goes beyond the diabetic eye screening to look for other common conditions.[5]

> **The private practitioner could model a similar telehealth clinic and be quite successful in improving access to either underserved populations or in urban areas where shortages of eyecare providers exist.**

"We see a lot of ocular disease each and every day in this program and can treat and manage much of this via telemedicine," says Dr. Rittenbach. "Some of the conditions regularly seen beside diabetic retinopathy include hypertensive retinopathy, retinal artery and vein occlusions, Hollenhorst plaques, AMD, glaucoma and cataracts."

Dr. Rittenbach recently detected an eyelid lesion based on an external photo, and she suspected basal cell carcinoma and was able to get the patient in quickly for a biopsy which confirmed the diagnosis. "This type of patient may not have been seen in a timely manner due to their rural location, and the lesion could have grown in size and become invasive," she says. "By using telemedicine, I was able to refer this patient promptly to a community specialist." Dry eye, pinguecula, pterygium and cataracts are conditions also frequently seen in the TECS protocol using anterior segment photography.

"The private practitioner could model a similar telehealth clinic after the TECS program and be quite successful in improving access to either underserved populations or in urban areas where shortages of eyecare providers exist," Dr. Rittenbach says. "Doctors in the private sector can use available exam lanes in their office—offices that don't have a doctor staffed on a particular day," she notes. "If we as a profession don't embrace teleoptometry, other groups will and we will be left behind," she warns.

Dr. Rittenbach and a panel of other experts recently discussed the new paradigm at the opening session at SECO's 100th anniversary meeting titled, "Remote Exams: Virtual Reality or Virtual Certainty?" ■

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BY JEROME SHERMAN, OD, AND SHERRY BASS, OD

YOU BE THE JUDGE

Return of the Cat's Eye

The vast majority of cataract extractions are successful, but there are some clinical signs not to be ignored.

When Bev, a 41-year-old white female at the time, walked into my (JS) exam room decades ago, it was a trip down memory lane. My memories of her dated back to the year I graduated from high school and when I escorted her to her senior prom.

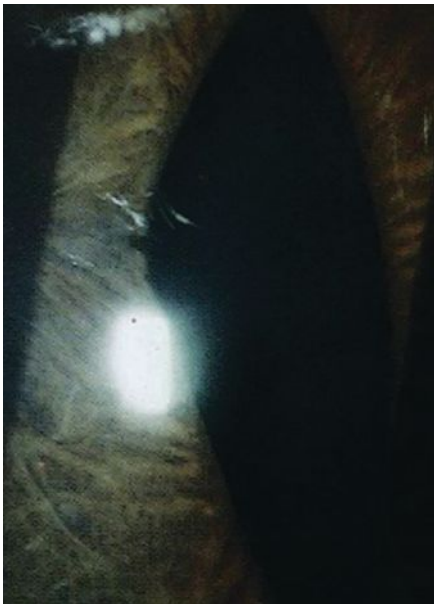
Bev wasn't visiting to rehash our past romance but to obtain a second opinion about her right eye and to test my memory. Bev began experiencing occasional blurred vision in her right eye, and when she looked in a mirror, she observed that her right eye looked different from her left. Bev was now quite concerned and decided to be examined by a local ophthalmologist. The MD detected both an unusual-shaped pupil and iris structure in her right eye only but a normal exam otherwise. He reassured Bev that she wasn't going blind, had 20/20 visual acuity in each eye and suggested that the findings may have been congenital and perhaps slowly progressive but less than obvious because of Bev's dark brown eyes.

As recommended by the ophthalmologist, Bev decided to obtain a second opinion from her old high school prom date. Bev asked me, "When you looked into my eyes the night of the senior prom, did I look like a cat?" I did not recall anything unusual about Bev's eyes the night of prom, but perhaps we both had too much scotch.

Testing

Bev was quite cooperative with numerous imaging procedures and, as requested, brought in several dozen pictures of her face over the years. I performed what we facetiously term a "FAT-scan"—or family album tomography—and could not detect any previous evidence of the cat's eye pupil in her right eye. Hence, the condition appeared to be acquired and unilateral.

Bev was in good health, had no history of trauma and had no family history of eye problems. Uncorrected VA was 20/20 in each eye, and IOPs were 16mm Hg OD and 17mm Hg OS. A slit lamp exam revealed a vertical pupil in the right eye only, and both pupils constricted normally. The iris stroma was observed to be thickened in some areas but atrophic in others. The Swiss-cheese appearance of her right iris appeared to be due to parts of her iris literally wasting away, and other areas were thickened, likely resulting in traction. The resulting regrouping of the iris tissue produced a rather remarkable vertical pupil. Gonioscopy revealed an unusual trabecular meshwork and mild peripheral anterior synechiae (PAS) in the right eye only. A dilated fundus exam was unremarkable, and both optic nerve heads appeared normal with cup-to-disc ratios judged as 0.4 OU.



ICE in this patient.

Threshold fields were obtained on the second visit and were normal OU. Imaging of the corneal endothelial cells with the Noncon Robo specular microscope by Konan revealed a remarkable difference between the two eyes. Of importance, the cell density in the right eye was 959mm^2 in contrast to 2,188mm^2 in the normal left eye.

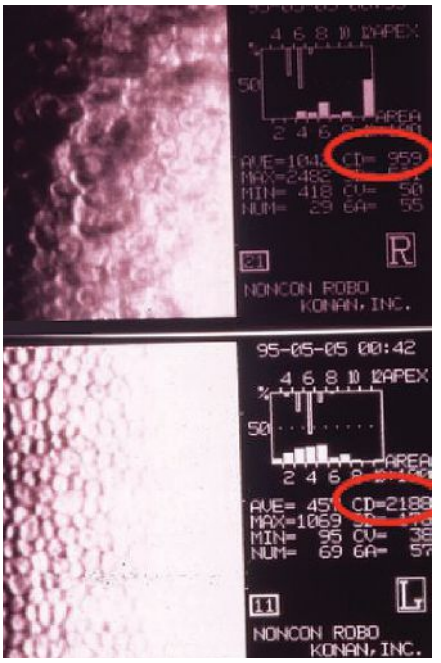
Ultrasound biomicroscopy was later performed and revealed the iris in contact with the corneal endothelium in several clock hours. The PAS appeared to be extending above the normal position of Schwalbe's line.

Diagnosis

Based on all of the above, the most probable diagnosis was iridocorneal endothelial (ICE) syndrome. This unique, most often unilateral ophthalmic disorder involves an irregular corneal endothelium that can lead to varying degrees of corneal edema, iris atrophy and secondary angle-closure glaucoma.[1] The etiology is unknown,

About Drs. Sherman and Bass

Dr. Sherman is a Distinguished Teaching Professor at the SUNY State College of Optometry and editor-in-chief of *Retina Revealed* at www.retinarevealed.com. During his 52 years at SUNY, Dr. Sherman has published about 750 various manuscripts. He has also served as an expert witness in 400 malpractice cases, approximately equally split between plaintiff and defendant. Dr. Sherman has received support for *Retina Revealed* from Carl Zeiss Meditec, MacuHealth and Konan. **Dr. Bass** also holds the position of Distinguished Teaching Professor at the SUNY State College of Optometry. She is a Diplomate of the American Board of Optometry. She is an attending in the Retina Clinic of the University Eye Center and currently serves as the residency supervisor for the Residency in Ocular Disease at SUNY. She has no financial disclosures.



Note the difference in endothelial cell density between the right eye (top circle) and left (bottom circle).

but herpes virus has been implicated in some cases.[2]

Follow-up

Over the next decade, Bev's ICE progressed slowly. IOP in her right eye was occasionally elevated, and I treated her with various drops to lower it. I told Bev that she would likely need surgery in the future since she was slowly developing a form of angle-closure glaucoma in her right eye.

Bev eventually decided to be followed by a local ophthalmologist rather than making frequent trips into the big city. Her vision eventually dropped to 20/40 OD, and a local cataract surgeon recommended that she have cataract surgery in the right eye. Bev told the ophthalmologist all about the ICE syndrome that was diagnosed and treated over the past decade by her prom date optometrist and all the imaging that was performed and available. The cataract surgeon responded that it did not matter.

As recommended by the ophthalmologist, Bev had the routine procedure—with disastrous results. Her vision after cataract extraction was dramatically reduced and has not improved to this day. Corneal decompensation resulted, and steroid drops increased her IOPs.

Bev has undergone three penetrating keratoplasties and two glaucoma surgeries and still can barely see the big E on the Snellen chart at high contrast. Of even greater concern to Bev, her right eye remains cosmetically unacceptable and still appears abnormal even when viewed from across the room.

Bev decided to initiate a lawsuit against the surgeon and, as recommended by her attorney, against two ODs who examined Bev along the way, since she was not warned about the significant risk of cataract surgery in a patient with ICE.

You Be the Judge

Questions to consider:

- If the patient has an irregular corneal endothelium and iris atrophy, what secondary conditions may result?
- If this patient develops a cataract in the affected eye, what are the risks of cataract surgery?
- If the patient develops a cataract, should you refer for cataract surgery or for a cataract surgery consult?
- Is referring this or a similar case for cataract surgery malpractice?
- Is performing cataract surgery without appropriate discussion of risks and benefits malpractice?

Our Opinion

We find the surgeon culpable of malpractice for not explaining the risks and benefits of cataract surgery to a patient with only a mild to moderate cataract and with ICE. However, for the case to go forward, an ophthalmologist, preferably a cataract surgeon, will need to render the same opinion.

The surgeon recommended and performed cataract extraction on an eye with a previous diagnosis of ICE. By definition, Bev had a condition affecting her iris and her corneal endothelium. The surgeon should have known and recognized that, with ICE, there is a reduced number of endothelial cells and that increases the risk of corneal decompensation because of the trauma of cataract surgery.

It is important to note that corneal endothelial cells function to maintain corneal clarity by regulating corneal hydration. Corneal endothelial cells do not regenerate. A dramatic reduction in the number of corneal endothelial cells as documented by the endothelial cell device predicts corneal decompensation and bullous keratopathy because of the trauma of cataract surgery. Changes to corneal endothelial density are often considered the canary in the coal mine for distress to the cornea.

We recommend never referring atypical patients for cataract surgery but for a cataract surgery consult. This distinction may be critical in impending lawsuits. We recommend endothelial cell counts in all patients who may have a reduced cell density because of conditions such as Fuchs' dystrophy and similar ones involving the endothelium.

Outcome of Malpractice Litigation

It is unclear how far the case went forward, but it is known that the case did not go to trial. I (JS) was not contacted for old records and was never deposed. However, we believe the case has substantial educational value. ■

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

BY BISANT A. LABIB, OD

A Gold Standard

With suspected tuberculosis, diagnosis can exclude other ocular conditions that exhibit similar symptoms.

Numerous systemic conditions can manifest in the eye. In addition to clinical presentation, laboratory testing is often used in an ophthalmic setting to determine any underlying disease process and employ appropriate treatment strategies. Often, timely and accurate management of said conditions are necessary to prevent permanent vision loss. As such, initiating and interpreting lab tests is essential to determine a diagnosis and subsequent plan.

Infectious disease processes are often difficult to distinguish because of overlapping clinical features. A prime example is tuberculosis (TB), which may cause a range of ocular findings and is necessary to distinguish from other types of infection, as it can exhibit similar signs.[1] There are a number of supporting ancillary tests to consider when making this diagnosis. Recognizing the mechanisms, indications and drawbacks of each test allows them to be used most effectively.

On the Rise

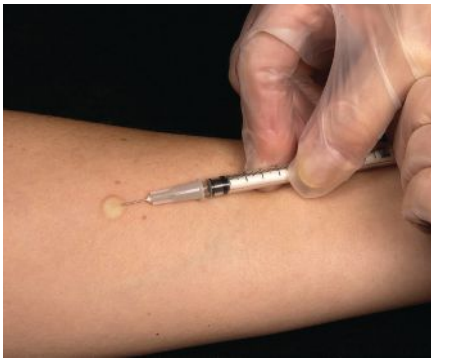
TB is one of the leading causes of death worldwide and affects nearly a third of the world's population.[2] While the overall incidence of TB has been declining, there has been a re-emergence of infection, particularly in the developing world, caused by increased multi-drug resistance, poor socioeconomic conditions and global migration.[2,3] Consequently, it remains a major public health concern and serious consideration to eyecare practitioners.[3]

TB arises from the infection of *Mycobacterium tuberculosis*, an obligate aerobic bacterium evident in tissues with high oxygenation. As such, the most common location of TB infection is in the lungs. The choroid, which is one of the most oxygenated tissues in the body, predisposes the eye to exhibit TB manifestations as well.[2] Ocular TB can be caused by either primary or secondary infection of *Mycobacterium*. Most commonly, ocular TB occurs as a secondary manifestation of the bacteria through seeding and hematogenous spread from a distant site.

What makes the eye susceptible is its highly vascular nature, particularly the uveal tract, consisting of the iris, ciliary body and choroid.[2,3] Another secondary form of ocular infection is through contamination of the patient's own sputum. Primary exogenous spread of ocular TB is rare and manifests more in external ocular tissues and the anterior segment. There is another form of ocular TB that is secondary to hypersensitivity reaction, such as phlyctenular and Eales' diseases.[3]

TABLE 1. SUMMARY OF AVAILABLE SUPPORTIVE LAB TESTING FOR TB

Lab Test	Method	Drawback
TST	Intradermal skin test measuring hypersensitivity and induration	Cross reactivity with BCG vaccine, reader reliability, false positives in skin hypersensitivity conditions, false negatives in immunocompromised, malnourished and elderly
IGRA	Blood test measuring interferon gamma release	Does not distinguish between active and latent disease



The TB skin test works by measuring a hypersensitivity reaction to the tuberculin protein, injected in the forearm.

TB or Not TB?

Ocular manifestations of TB affect all areas of the eye and often overlap with clinical findings common to other infectious or inflammatory conditions.

Adnexa. Externally, lid lesions can develop and appear as a soft, non-inflammatory mass in children. Another TB-specific lid lesion is lupus vulgaris, which is a reddish-brown mass that blanches upon pressure.

Conjunctiva. Involvement here can present with non-specific redness, mucopurulent discharge and lymphadenitis. Phlyctenular keratoconjunctivitis is a more specific finding, appearing as a small pink nodule at the limbus, which may later migrate onto the corneal surface, thereby leading to an epithelial defect. This form of keratoconjunctivitis indicates hypersensitivity to TB, which must be ruled out if present.

Cornea. In addition to phlyctenular keratoconjunctivitis, interstitial

About Dr. Labib

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

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TABLE 2. TB OCULAR SYMPTOM OVERLAP

Location	Ocular Manifestation
Eyelid	Lupus vulgaris; non-inflammatory soft nodule
Conjunctiva	Phlyctenular keratoconjunctivitis
Cornea	Interstitial keratitis
Sclera	Anterior, localized scleritis
Iris/ciliary body	Granulomatous or nongranulomatous uveitis
Choroid	Choroidal tubercles, tuberculomas, choroiditis
Retina	Retinitis

keratitis can also be a sign of ocular TB. It will appear as stromal corneal vascularization. Unlike phlyctenulosis, though, interstitial keratitis can occur from other types of infection. With TB, it is characteristically unilateral and confined to a sector of the corneal periphery.

Sclera. Refractory anterior scleritis cases should be evaluated for ocular TB infection. Typically, this form of scleritis manifests as a localized, dark red area with granulomatous inflammation and necrosis. Very rarely, the posterior sclera may also be inflamed.

Uvea. A well-known cause of granulomatous uveitis is TB. This includes clinical findings such as mutton fat keratic precipitates and Koeppe or Busacca nodules on the iris. Nongranulomatous presentations are also possible.

Choroid. The choroid, due to its high vascularization, is a common and unique site of ocular TB. The spectrum of choroidal involvement includes choroidal tubercles, tuberculomas and choroiditis. Choroidal tubercles are the most common ocular manifestation of ocular TB. These lesions are white, gray or yellow with indistinct borders measuring from 0.5mm to 3.0mm in diameter. They are located in the posterior pole and may lead to exudate formation, hemorrhages or edema. Due to the specificity of these lesions in association with TB, they should be very carefully looked for in patients who have a fever of unknown origin or other suspicious symptoms. Tuberculomas are similar in appearance but larger, measuring up to 7mm in diameter. They are usually a sole nodule with more distinct borders. Choroiditis in TB can be multifocal or serpiginous-like.

Retinitis. Tuberculous retinitis can appear as localized tubercles or diffuse inflammation. Associated features are vitreous opacification and retinal vasculitis. Neovascularization and peripheral capillary occlusion may also result. Retinitis of this nature can either be to the infection in the underlying choroid or hematogenous spread. Eales' disease has also been associated with TB.[1,2]

Diagnosing

When ocular TB is suspected, there is no definitive gold standard of testing. Diagnostic challenges arise from the impractical and invasive nature of culture biopsies from ocular fluids.[2] Besides the unique ocular features, supplemental testing can help confirm the diagnosis, which is imperative to initiate proper treatment and reverse findings. Patients with accompanying pulmonary symptoms may benefit from chest radiography to confirm diagnosis. In the absence of pulmonary manifestations or even for confirmation, laboratory tests are often acquired.[3]

TB skin testing (TST) has long been used as a screening test for TB. The way this test works is through measurement of the hypersensitivity reaction to the tuberculin protein. This protein is extracted from M. tuberculosis and is used as a purified protein derivative. It is then injected intradermally on the surface of the forearm, where the type IV hypersensitivity reaction is then measured 48 to 72 hours later. This reaction appears as erythema and induration. The induration, or palpable raised swelling, is measured. A positive test is a measurement of 10mm or larger.[2,3]

The drawback to this test is that it is time sensitive and requires accurate reading. Furthermore, false positive tests can occur in patients who have previously been vaccinated for Bacille Calmette–Guerin (BCG), which is a nontuberculous mycobacterium. Additional false positives can arise in patients who have excessive skin hypersensitivities, such as in Behçet's disease. False negatives are just as possible and occur more so in elderly, malnourished or immunocompromised patients.[4]

More recently, blood testing using interferon-gamma release assay (IGRA) such as QuantiFeron TB gold, has been used in the diagnosis of TB. Similar to the TST, this test also works through cell-mediated immunity secondary to TB exposure. As the name suggests, this blood test measures interferon gamma release by antigen specific T-cells in response to TB antigens. It is preferred over the TST because it does not have the same drawbacks of cross reactivity with the BCG vaccine and does not require the same timeliness and reliability of the reader. Both forms of testing, however, do not have the ability to distinguish between active and latent forms of TB.[4,5]

While TST has been the mainstay of TB testing for decades, the clinical utility of IGRA has substantially impacted the diagnosis of disease in recent years. Since ocular manifestations of TB are common and variable, the mechanism of infection, clinical manifestations and supporting laboratory tests must be widely understood in order to form an early diagnosis. Timely intervention with systemic TB treatment can reverse many of these ocular manifestations and preserve vision. ■

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ESTABLISHING THE NEXT LEVEL OF EYECARE

Bringing Together Technology to Better Monitor Pathology and Intraocular Pressures

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(Moderator)
Prism Eye Institute

Barbara M. Wirostko, MD, FARVO
John A. Moran Eye Center, University of Utah Health

Steven R. Sarkisian, Jr., MD
Oklahoma Eye Surgeons

Farrell C. Tyson, MD, FACS
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In today's busy eyecare practice, having the right tools to quickly and reliably assess ocular pressures and pathology is the first step to making the best clinical decisions for patients. Pairing innovative imaging devices, perimeters, and handheld rebound tonometers with clinical expertise can move providers from uncertainty to greater certainty on critical issues concerning patient ophthalmic disease status.

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DR. AHMED: Please discuss how the iCare tonometer has advanced your practice.

DR. WIROSTKO: We use the IC100 in the clinic and as an alternative to dye-based application for routine exams. It requires little training, as opposed to the advanced training required for GAT, is easy to use, and is accurate. We also have found the iCare tonometer is less subjective than GAT, with less of a user "influence." Acquiring IOP in children along with people who squint or have other issues at the slit lamp is challenging with GAT. These and other patients who have trouble fitting into a slit lamp may be better candidates for the iCare tonometer.

DR. SARKISIAN: When I was in a university setting, I advocated for introducing the iCare tonometer at all of the clinics because of its clear superiority over the Tono-Pen, which we used frequently for pre- and post-retina/glaucoma laser patients, postoperative patients, and pediatric patients. A single-use sterile probe was mandatory, and many of us were frustrated by the constant need to calibrate the instrument. The iCare tonometer enables less experienced technicians who are not as skilled at GAT to provide more accurate pressure readings. Since going into private practice four years ago, I now own two iCare tonometers. The ability to capture data to 1/10th of a mmHg has been particularly helpful, and the ability to use supine is beneficial for certain patients.

"We use the iCare tonometer as a screening tool. Our technicians measure pressures with the device when they first see patients, which helps us identify individuals with high IOP that need to be seen more urgently by the doctor."

—Ike Ahmed, MD

DR. TYSON: I was actually standoffish about adding the iCare tonometer. My optometrist came to me and asked me about it, and I put it off for about a year or so. Then I brought in a cornea specialist who wanted the device for his corneal transplant and DSAEK/DMEK patients, and for irregular corneas that weren't going to yield good Kaplan-Meiers analysis. After we bought our first iCare tonometer for our cornea department, I kept hearing back from my technicians how much they liked it and how it

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Research On iCare HOME Tonometer

By Ike Ahmed, MD

Our group published a paper discussing the benefits of the iCare HOME tonometer and cases for which it may be most clinically useful.[1]

We concluded the iCare HOME tonometer "demonstrated excellent potential to transform the traditional approach to glaucoma diagnosis and management" and that it "is reasonably similar to GAT measurements, easy to use, and well accepted by patients."[1]

We determined the device was most useful for patients presenting with reasonable in-office IOP but whose disease may not be controlled due to significant visual field progression, optic nerve head and retinal nerve fiber layer changes, or other issues raising suspicion.[1]

Certain types of glaucoma patients—particularly those with pigment dispersion glaucoma, and suspects of angle-closure glaucoma and normal-tension glaucoma—were found to be especially well-suited to the home tonometer.

We also reported the iCare HOME tonometer was useful in monitoring postoperative IOP control and progress of patients after surgical interventions.[1]

1. Liu J, De Francesco T, Schlenker M, Ahmed II. Icare Home tonometer: a review of characteristics and clinical utility. Clin Ophthalmol. 2020 Nov 23;14:4031-45.

was speeding up the patient workup. I talked to my cornea specialist, and he felt that it was more than accurate so we bought several devices and started using them throughout our practice with seven locations.

The iCare tonometer has been a nice little workhorse; it speeds up our workup and adds a reliability factor because it removes some of the technical training necessary with other devices to get good readings. Overall, its ease of use and patient acceptance have been enormously valuable.

DR. AHMED: We use the iCare tonometer as a screening tool. Our technicians measure pressures with the device when they first see patients, which helps us identify individuals with high IOP that need to be seen more urgently by the doctor. With uncooperative patients or children, it enables us to get good IOP estimates. The device is easy to use, and instructions on the display as well as clear error messages help the technicians perform measurements correctly.

DR. AHMED: The iCare HOME2 tonometer, FDA-cleared in January 2022, includes a number of upgrades from its predecessor [e.g., measurements in supine position, patient mobile app, private patient cloud account, etc.) How has home tonometry improved short- and long-term patient care?

DR. WIROSTKO: With the iCare HOME2 tonometer, patient care continues to excel. The device

A Modern Approach To Diurnal IOP Monitoring

With the iCare HOME2 tonometer, patients can take IOP measurements throughout the day, at night, and when lying down. Measurement results are uploaded to a cloud database where they are accessible to the doctor and patient for accurate real-world IOP data to support treatment decisions.

iCare HOME2 tonometer

directly and immediately enables the doctor to alter treatment decisions to help slow disease progression and preserve patients' sight. We have many examples of catching IOP spikes outside of clinic hours with real-time information from the device, and have published numerous case reports on how these insights have informed medical and surgical treatment.[1] The newest home tonometer, HOME2, also empowers our patients to better understand their IOPs and fluctuations, and become more involved as a partner in their care decisions.

DR. SARKISIAN: The iCare HOME2 tonometer has captured critical data for our patients. I believe many patients are misdiagnosed as having low- or normal-tension glaucoma when in fact they simply have broad diurnal curve fluctuations. With this home tonometer, we can capture morning and late-evening IOPs. Not only does this make diagnosis more precise, but it provides more data to reassure the patient that we are in fact improving IOP fluctuation by doing treatments such as SLT or adding medications. Previously, we had to wait for a patient's glaucoma to progress before acting. In my practice, the device has also been helpful in monitoring patients after SLT to determine when repeat treatment is appropriate.

DR. AHMED: We provide (rent and sell) the iCare HOME and HOME2 tonometers to our patients and actually use it frequently in our clinic. After individual training, patients rent the device for a number of days to perform measurements and take notes about their activity. We often use the device for normal-tension or angle-closure glaucoma patients with intermittent eye pressure spikes. We find the SD analysis and the plotted graph for our patients particularly useful.

RETINAL IMAGING

DR. AHMED: Following the merger of iCare and CenterVue in 2019, iCare added retinal imaging products, including TrueColor Confocal Imaging Systems (EIDON, EIDON AF, EIDON FA, EIDON Ultra-Widefield Module, DRSplus). Please discuss the benefits of confocal imaging technology.

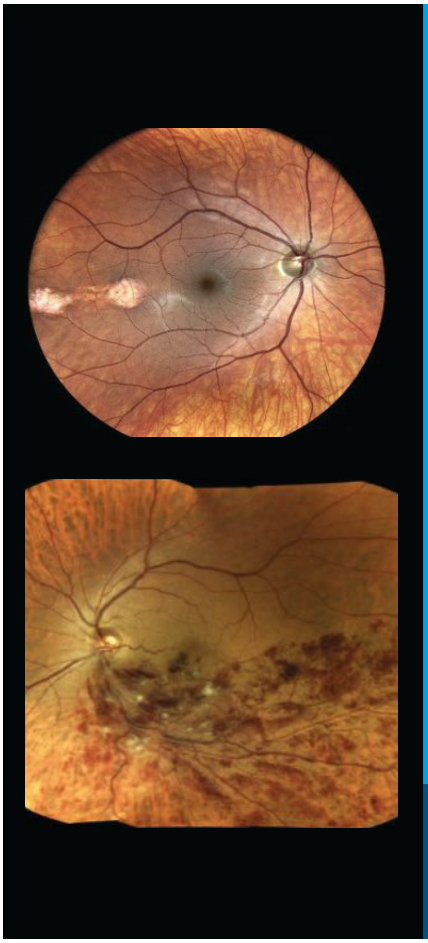
DR. WIROSTKO: Non-mydriatic confocal fundus imaging technology is almost always able to power through refractive errors, cataracts, or corneal issues and produce good images. EIDON's use of real light technology, and its ability to produce sharp, crisp, and real color images make it possible to easily detect abnormalities. I can have confidence that, if I'm not seeing serious issues such as choroidal nevi, etc., the findings likely aren't pathologic. Moreover, the "flicker" function, enabling side-by-side comparison of images taken at two different time points, helps me monitor subtle changes over time. What is particularly nice is the ability to share with the patient what I'm seeing, giving them a sense of involvement and empowerment in their management.

"Confocal imaging speeds up my workup because now I can get a very good view of the back of the eye at the beginning of the exam. Even if the patient is a poor dilator, I'm not held up waiting 30 or 40 minutes for the patient to dilate. "

—Farrell C. Tyson, MD, FACS

DR. SARKISIAN: I have found major benefits of the technology to be ease of use by my staff and the ability to capture high-quality images without dilation. In addition, the "flicker" function is uniquely beneficial for image comparison once a long series of images has been obtained. My EIDON fundus camera is an excellent value considering the amazing quality of images it produces and the growing need for fundus photography in a busy ophthalmic practice.

DR. TYSON: Our practice owned several CenterVue devices prior to iCare purchasing the company so we already had an EIDON and COMPASS. We really liked the fact that we were getting TrueColor im-



Harnessing The Power Of Confocal Imaging & TrueColor

Confocal imaging is considered superior to conventional fundus photography because it blocks the backscattered light of structures from the outside of the retina focal plane, increasing sharpness, optical resolution, and contrast.

Confocal imaging maintains strong image quality, even in the case of media opacities such as cataracts, and can work with pupils as small as 2.5mm without the need for dilation.

TrueColor imaging utilized in iCare devices employs white light LED for distortion-free, exceptional color fidelity. The retina appears as it does when directly observed due to the presence of the entire visible spectrum in the captured image.

iCare EIDON TrueColor technology can potentially improve the clinician's ability to diagnose and monitor retinal diseases. One study found iCare EIDON provided more balanced color images with a wider richness of color content than a conventional flash fundus camera.[1]

In addition, iCare EIDON's higher chromaticity offers the provider greater discriminative power and the opportunity for increased accuracy when diagnosing patients.

1. Sarao V, Veritti D, Borrelli E, Sadda SVR, Poletti E, Lanzetta P. A comparison between a white LED confocal imaging system and a conventional flash fundus camera using chromaticity analysis. BMC Ophthalmol. 2019 Nov 19;19(1):231.

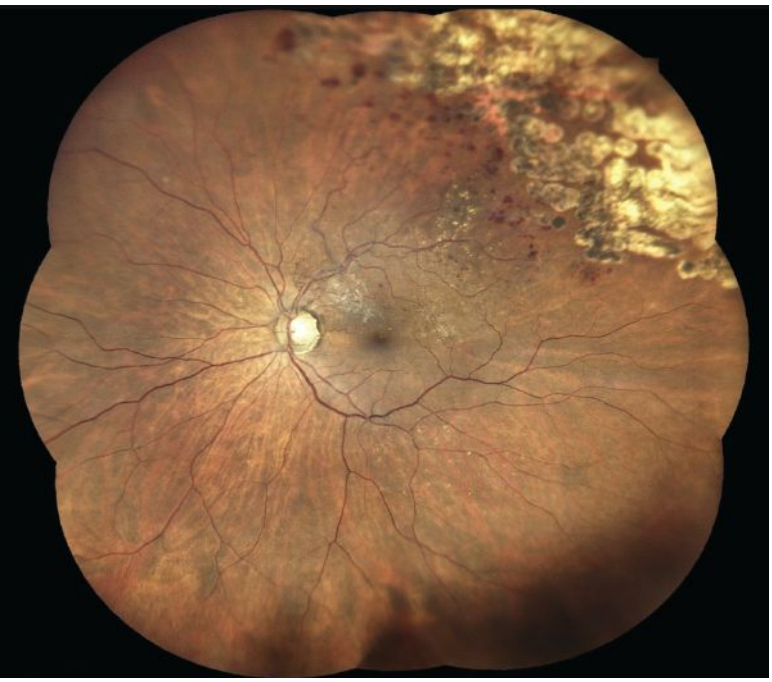
ages. The technology means you see what you normally see with the naked eye, but the confocal laser is able to go through a much smaller pupil, about a 2mm pupil, to produce a beautiful view of the back of the eye.

I'm primarily a cataract/refractive practice, and when I'm doing workups, the way the system takes the image makes epiretinal membranes practically glow at you so you really see them. With the 90-diopter slit lamp lens, you'd be much more challenged to pick them up. But when you're getting this comprehensive view and the epiretinal membrane is just shimmering on the image, it really makes you take notice and helps you to adjust your surgical plans.

Confocal imaging speeds up my workup because now I can get a very good view of the back of the eye at the beginning of the exam. Even if the patient is a poor dilator, I'm not held up waiting 30 or 40 minutes for the patient to dilate. I can go ahead and have a direct discussion with the patient about their eyes, their vision, and their pathology.

DR. AHMED: What is the importance of UWF's capability [up to 200˚ panoramic view] to illuminate early signs of ocular pathology in your patients, and how does this surpass standard field view?

DR. WIROSTKO: UWF's faster acquisition and wider field of view is vital for difficult imaging cases. Outlying areas are able to be imaged, giving the physician greater ability to more accurately diagnose and analyze normal vs. abnormal findings. UWF has far



iCare EIDON's ultra-widefield optics from 120° to 200° field of view allows imaging of the central retina as well as the periphery.

surpassed the original capture lens. Even if you are only able to get one picture of a patient, you can still acquire the most critical areas for diagnostic comparisons. This can be pivotal for catching diabetic retinopathies, BRVO, CRVO, etc., in the far periphery.

DR. TYSON: With UWF, you're not just getting from arcade to arcade, but you can see way out into the periphery. If you want to go even further, you can use Mosaic mode and see just about the whole back of the eye. This has helped us to confirm findings in the back of the eye and view certain pathologies more vividly.

DR. AHMED: iCare COMPASS combines visual field tests, fixation loss correction by a real-time retinal tracker, and ultra-high resolution confocal TrueColor fundus imaging for efficient assessment of function and structure, with reduction of motion artifacts. How does fundus-controlled perimetry aid you in assessing disease status?

"We have cases every day that are diagnosed, tracked, and followed more efficiently via the use of the EIDON. This is where normal fundus photography falls short or is cumbersome. "

—Barbara M. Wirostko, MD, FARVO

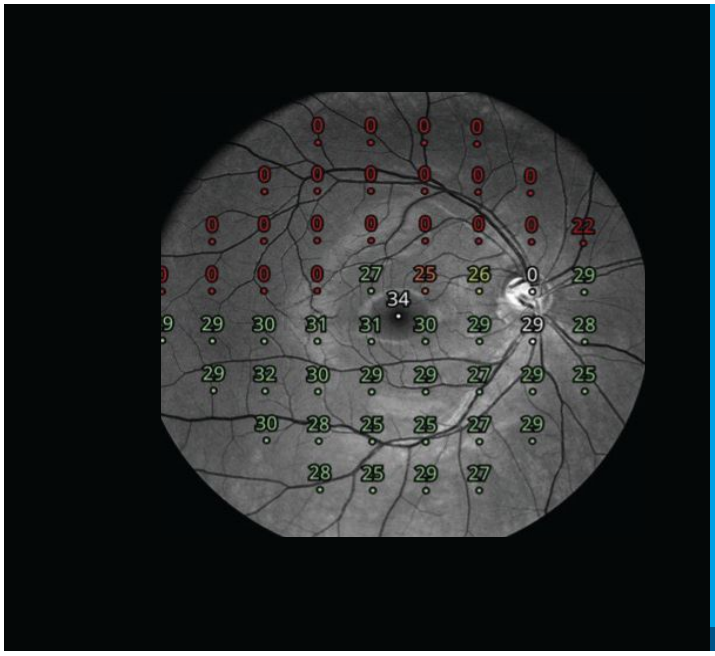
DR. TYSON: The beauty of the COMPASS is that the retina is being directly stimulated by the machine rather than indirectly off of a reflective perimetry bowl. The COMPASS knows where the nerve is, where the arcade is, which enables reproducibility. And the device can adjust for movement. With many machines, you have to do pupil tracking and see how well the patient is staying centered. We have found the COMPASS test is quicker, and more accurate and reproducible because the device knows where it is stimulating the retina and restimulates the same area from test to test.

DR. AHMED: We prefer the COMPASS visual fields over classic Humphrey fields for multiple reasons. The retinal tracker helps avoid errors caused by poor fixation and ensures accurate tracking of localized defects over multiple field tests. The high-resolution images of nerve and macula, as well as the retinal correspondence map aid us in deciding whether the field defects are glaucomatous in nature or potentially caused by retinal issues.

IMPROVING DISEASE MANAGEMENT AND PATIENT CARE

DR. AHMED: Do you have any cases to share that demonstrate how iCare technology helped you better identify or track disease, and care for patients?

DR. WIROSTKO: We have cases every day that are diagnosed, tracked, and followed more efficiently via the use of the EIDON. This is where normal fundus photography falls short or is cumbersome. The repeatable clear and sharp, colorful images that the EIDON can produce at the touch of a button are re-



Fundus-Controlled Perimetry Key Features

- Standard automated perimetry
- Active retinal tracking compensating for poor patient fixation in real-time
- Auto-focus—no trial lens needed
- Illustrative fixation analysis (fixation area and plot)
- High-resolution confocal TrueColor imaging of the retina
- The patient can blink freely and the test can be suspended at any time without data loss
- User friendly, requires minimal operator training

markable. The device makes physicians much more informed regarding treatment paths in a quick and effective manner. We use the iCare tonometer and EIDON on all of our patients with glaucomatous, retinal, and macular pathologies, and those who are pre- or post-surgery.

DR. TYSON: The COMPASS has given us the same quality as, if not better than, what we've been used to. It's not a compromise in the quality of the information we're receiving. We're getting better reproducibility and, therefore, can get fewer false positives and negatives. At the same time, we're gaining comfort from knowing the data is as accurate as what has been considered the Gold standard with Humphrey perimetry.

DR. AHMED: The iCare HOME tonometer has helped us discover high IOPs in dim lighting conditions in many of our angle-closure patients that would have otherwise been missed in the bright office. For our normal-tension glaucoma patients, minimal fluctuations are important and the iCare HOME results often lead to changes in medication (timing/frequency of drops, long- or short-lasting drugs) or indication for surgery.

"With the iCare product line, you have a range of diagnostics that touches all aspects of ophthalmology—from retina, to glaucoma, to general ophthalmology."

—Steven R. Sarkisian, Jr., MD

DR. AHMED: How can a comprehensive family of products such as the one iCare offers benefit practices across the eyecare spectrum?

DR. WIROSTKO: The iCare devices, with their diagnostic advantages, far exceed expectations and elevate patient care to ever higher levels. The ease and speed with which these devices collect accurate and vital information provides the clinician with the most up-to-date information at the touch of a button to direct specific and urgent, possibly sight-preserving changes of medical management. The iCare family delivers essential insights—from the retina to the optic nerve and cornea, offering the provider and patient the opportunity for superlative preventative care.

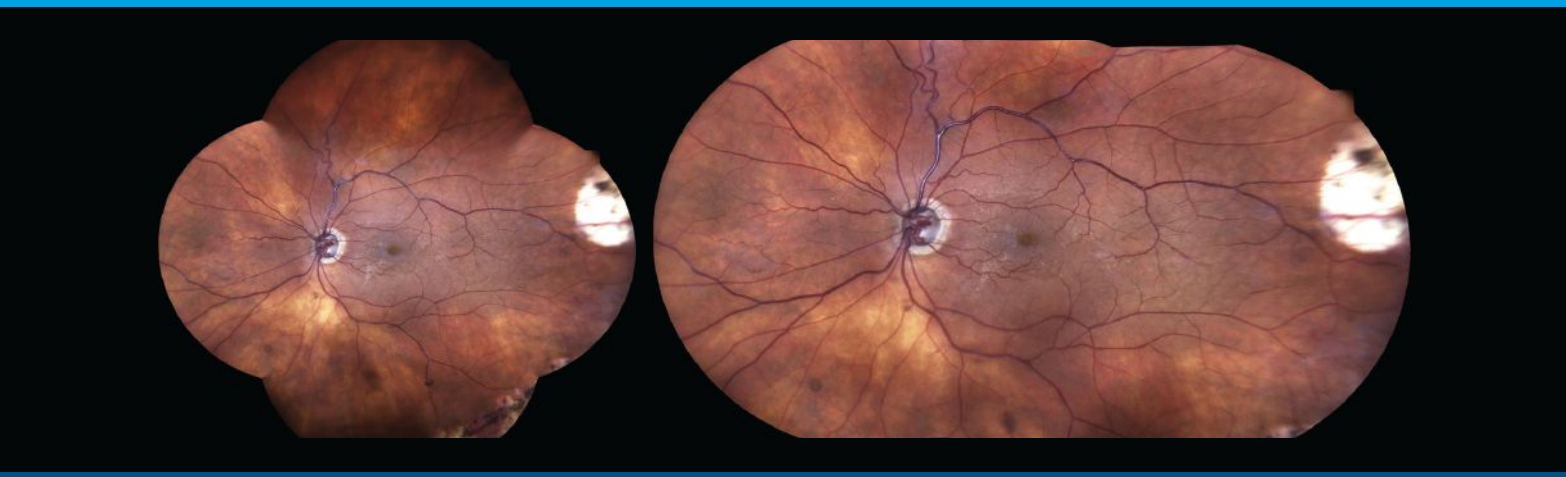
Case of Impending RVO

By Barbara M. Wirostko, MD

An 81-year-old male patient was followed for mild glaucoma damage for several years. His IOPs were well controlled, and he also had mild HTN, high cholesterol, and was a smoker.

On a routine dilated exam, he was discovered to have dilated and tortuous retinal venules in his left eye (OS) and was diagnosed as being at risk for an impending retinal vein occlusion on fluorescein angiography.

Carotids and systemic workup proved non-contributory. We made sure to control his HTN and IOP, and started him on a full aspirin a day.



EIDON widefield imaging helped illuminate a tortuous retinal venule in this patient's left eye (OS). Images: Barbara M. Wirostko, MD

DR. SARKISIAN: With the iCare product line, you have a range of diagnostics that touches all aspects of ophthalmology—from retina, to glaucoma, to general ophthalmology. As a glaucoma specialist, I would recommend all offices utilize the iCare tonometer for handheld tonometry due to its ease of use and accuracy.

DR. TYSON: iCare is giving you top-shelf technology at a very reasonable price point, enabling practices of all sizes access to the best technology in their office. And at the same time, this family of products—whether it's EIDON, COMPASS, EIDON FA, the tonometers—offers the same ease of use. Once you get the techs trained on one device, it's very simple for them to move to the next one. It's clear by all of our iCare devices that the team designing them really has the technician in mind. This isn't a technological masterpiece that nobody can operate. These devices are really straightforward and easy-to-use, but you're getting unbelievable images and testing out of them.

DR. AHMED: By providing a seamless user experience between its products, and ideally by combining all results into one single software, iCare continues to improve efficiency in today's eyecare practice. ■

1. Levin AM, McGlumphy EJ, Chaya CJ, Wirostko BM, Johnson TV. The utility of home tonometry for peri-interventional decision-making in glaucoma surgery: case series. Am J Ophthalmol Case Rep. 2022 Sep 7;28:101689.

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RESTRICTIVE DRUG FORMULARIES: HOW TO BEAT THE ODDS

When insurers stack the deck against you and your patients, you can still play a winning hand.

BY CATLIN NALLEY
CONTRIBUTING EDITOR

A top priority for any healthcare provider is ensuring optimal outcomes for their patients. However, restrictive drug formularies can make it difficult to execute the care plan of their choice. Prior authorization denials are a challenge seen across the continuum of care, and optometrists must be prepared to face the issue head-on. That's often easier said than done when dealing with a problem that places undue burden on the entire clinical practice, including providers, staff and patients.

A recent 2021 AMA survey revealed that 88% of physicians characterized the burden associated with prior authorizations as high or extremely high. The survey also found that physicians and their staff spend an average of almost two business days—13 hours—each week completing prior authorizations. Additionally, survey participants reported that prior authorization often delays care and results in negative clinical outcomes.[1]

"Prior authorizations remain a major burden for doctors and patients alike. There are many times when I will write for an ophthalmic drop/medication only to have it denied and substituted for a generic without my consent," notes Patrick Vollmer, OD, of Shelby, NC. "Insurance companies are making healthcare decisions for our patients—is the medication the doctor prescribes really medically necessary?"

Prior authorization denials frustrate both providers and patients and waste time, resources and money, emphasizes Dr. Vollmer. "Many doctors will quickly become exasperated with prior authorizations (and with good reason) and avoid them all together by writing for a generic drug from the beginning."

So, what can optometrists do to contend with prior authorization denials and ensure their patients receive the necessary care at an affordable cost? This article will explore into the ins and outs of navigating this issue, including appeals, when to fight and when to change course, creative solutions and patient education.

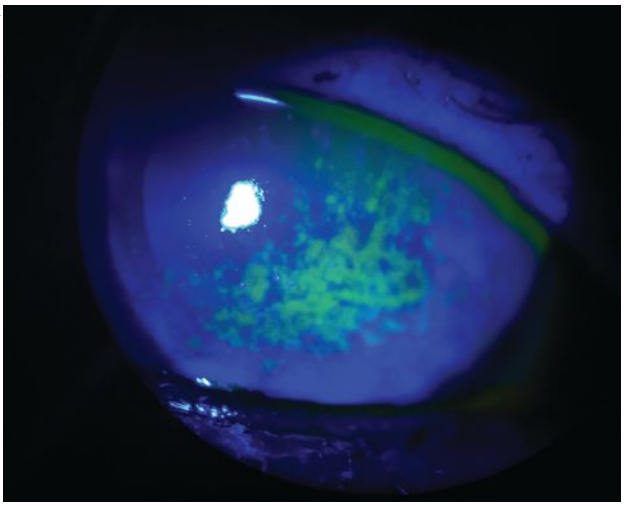


Photo: Vin Dang, OD

A shared-cost treatment model can end up being the best approach when treating conditions such as dry eye disease with the newest—and priciest—medications.

Navigating Insurance Hurdles

Taking a preemptive approach can help optometrists when working through the prior authorization process. In a busy clinical environment without a prior authorization specialist, Nova Southeastern's Jessica Steen, OD, and colleagues do their best to anticipate and minimize potential medication challenges that could delay or prevent a patient from receiving a prescribed medication for a reasonable cost.

"This starts," she notes, "by using the expertise of pharmaceutical sales representatives who have knowledge of the most current information of insurance carrier coverage in our area for specific products."

"Given the frequent changes to insurance coverage, another option for ODs is to check EHR platforms to estimate cost beforehand," suggests Joseph Shovlin, OD, of Scranton, PA.

Comprehensive documentation is critical to the prior authorization process. Dr. Steen emphasizes the need for clear and accurate records, including start and stop dates for each medication prescribed for a patient. If a medication was discontinued, optometrists should clearly describe and document the reason, such as failure to reach clinical effect, or include a description of the specific adverse event that led a patient to stop using the medication, she explains.

"For payers that have step-therapy policies, clearly organized information about previous medication failures and the specific reason for each failure supports your clinical decision-making and helps identify medical necessity of a prescribed medication," Dr. Steen says.

"Current successful use of a chronic care product, whether that was a previously filled prescription or use of a professional sample with documented clinical success and patient tolerability, also help to support medical necessity of continued use of the product," she adds.

Another challenge ODs may have to deal with is continued adherence to medical therapy due to pre-specified quantity limits. "For example, a 2.5mL bottle of a prostaglandin analog may be the quantity limit for a 30-day supply for bilateral use," says Dr. Steen.

"If the patient has difficulty successfully instilling the medication and requires the use of two drops to ensure that one makes it into the eye or they misplace a bottle, the patient may require more medication than the pre-specified quantity limit for continued use which may require additional communication with the payer," she explains further.

It is also important that optometrists recognize that only prescribing generic medications does not guarantee that they will be able to avoid prior authorization requests, advises Dr. Steen, whose practice has received a number of prior authorization requests from a specific pharmacy benefit manager prior to coverage determination of generic latanoprost 0.005%.

"While the prior authorizations in these cases have been straightforward—asking only whether the indication for medication use is reduction of intraocular pressure (IOP) or treatment of a cosmetic condition—there is still an additional step which needs to be taken that may delay the patient's ability to have access to a prescribed medication," she notes.

When to Appeal and Regroup

If a prior authorization is denied, prescribers have the opportunity to appeal the decision by submitting additional documentation. If the appeal doesn't work but the drug is medically necessary, Dr. Steen recommends requesting a peer-to-peer discussion.

"The physician with whom you speak may not always be familiar with management of ocular conditions, current clinical best practices and standard of care, but they will be familiar with the specific criteria for medication coverage," she explains, while noting that a peer-to-peer discussion gives optometrists the opportunity to communicate medical necessity.

This also gives the provider a chance to "describe the specific circumstances of the patient's need, including their treatment history and the next steps in their care if the denial stands," Dr. Steen says.

Optometrists must use their discretion and clinical experience to determine when an appeal is necessary and when a change in care plan is a better use of their practice's time and resources. A prime example is glaucoma management.

"There is a significant cost to the patient, society and eventually the insurance company when the patient's vision declines. There are increasing expenses for a patient who is declining in glaucoma vs. one who is stable and being managed at a simpler level of intervention," says James Thimons, OD, of Meriden, CT. "And yet, the majority of doctors are being pushed to use a preset generic drug or panel of drugs by the insurance company: latanoprost, bimatoprost and travoprost."

This makes it challenging to access newer agents in the space such as Rocklatan (netarsudil 0.02% and latanoprost 0.005%, Aerie) and Vyzulta (latanoprostene bunod 0.024%, Bausch + Lomb).

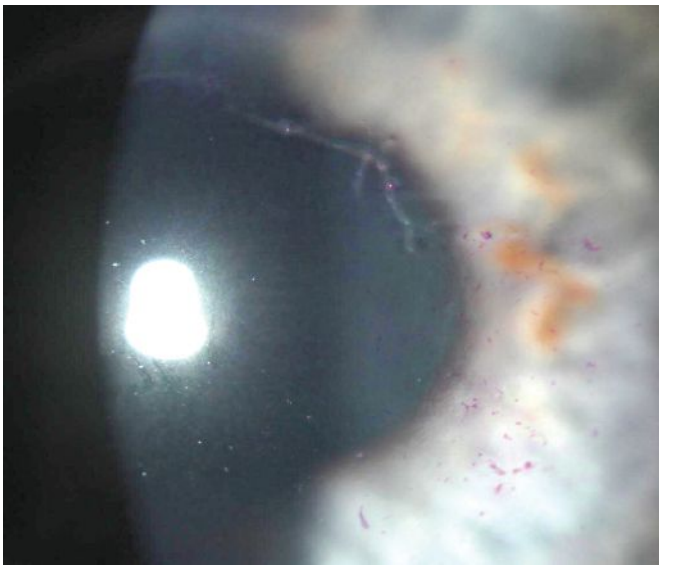
"The FDA trials clearly demonstrate that there's a heightened level of efficacy in achieving more IOP control at higher levels with those two drugs than there is with latanoprost," explains Dr. Thimons.

"And as we all know, every study and every doctor who speaks about glaucoma says every millimeter of IOP is important," he continues. "These are not small numbers. These are two, three and four millimeter differences. That's sight-saving and potentially life-changing for the patient if that drug works."

When deciding what approach to take, ODs must decide whether or not the drug works for their patient and, unfortunately, the insurance company will often force the use of the generic product to prove inferiority, explains Dr. Thimons. In some instances, he notes, it may be worth starting with the generic.

"As the provider, you set the goal pressure for the patient, and then if you don't meet that goal at four weeks, you move forward with a claim that the drug failed," he says.

Photo: Aaron Bronner, OD



Prior authorization denials and associated delays can impact vision and outcomes. Antivirals used early are important in patients with herpes zoster ophthalmicus.

"Detailed documentation is key and it must be entered into the medical record."

He acknowledges that this isn't a perfect system, but their practice has found success with this approach.

> **If a prior authorization is denied, appeal the decision by submitting additional documentation. If the appeal doesn't work, but the medication is medically necessary, request a peer-to-peer discussion.**

Before approving the branded agent, some companies may require ODs to add another agent to the generic drug. Another potential challenge is the issue of "soft steroids," which insurance carriers often refuse to cover due to the higher cost.

"They may even want you to add an additional drop to lower IOP along with a generic topical steroid—that might raise IOP—instead of going with a medication less likely to cause an increase in pressure," explains Dr. Shovlin.

Given the demands of the prior authorization process, some ODs and their patients may even opt to proceed with selective laser trabeculoplasty, which is just as likely to be successful and is always covered by insurance, notes Dr. Thimons.

"Optometrists also need to understand that there is a percentage of patients who were not going to get covered regardless of how many times we pound on the door," he advises. "In those cases, you will have to come up with alternatives. Cataract surgery is an outstanding system for lowering IOP, and in conjunction with a MIGS procedure can be incredibly effective."

An example where appealing a prior authorization denial may not be the best course of action is ocular surface treatment.

"Dry eye may be a scenario where a lengthy battle with the insurance company is not the right avenue for you or your patient," Dr. Thimons says. "While I am not arguing that we shouldn't use the best products, this is a situation where it may be worth exploring other options. There are a number of ways that doctors can maintain the level of care that's important for the patient without having to fight these battles all the time."

A shared cost treatment model can end up being the best approach when it comes to the treatment of conditions like dry eye, suggests Dr. Thimons.

"Five hundred dollars for Restasis (cyclosporine 0.05%, Allergan) is sinful, but it happens every day in my practice. I think that is where doctors have to draw the line and come up with creative alternatives that are clinically proven and don't have the associated costs of a variable pricing market from the manufacturers and pharmacies."

As previously mentioned, prior authorization denials and the associated delays can have a significant impact on vision and outcomes. For instance, this is of particular concern, according to Dr. Shovlin, "when we need a good fluoroquinolone (later generation) for a corneal ulcer and the generic (first generation) is offered.

"Also, antivirals used early are important in patients with herpetic disease," he adds. "We have one carrier who only covers Viroptic (trifluridine 1%, Monarch) for epithelial herpes simplex, which we can't even get because they don't cover Zirgan (topical ganciclovir ointment, Bausch + Lomb), a newer medication."

Fortunately, oral antiviral medications generally work as well as topical agents for epithelial herpes, Dr. Shovlin says.

Finding Creative Solutions

In cases where a prior authorization denial cannot be resolved—or fighting the decision is not the best use of resources—optometrists will have to find creative solutions to ensure the best possible outcomes for their patient.

Many pharmaceutical companies have discount or access cards that allow doctors to prescribe branded drugs, typically without a prior authorization, suggests Dr. Vollmer. For example, Bausch + Lomb's Access Program allows patients to pay a flat fee for a variety of branded drugs that includes steroids, antivirals, antibiotics and glaucoma medications.

"Programs like this one are very beneficial because many times they limit or eliminate the need for a patient to fail on a generic medication first," he says. "When I personally use this method, I find that pushback is greatly diminished. A piece of advice I can offer to all prescribers is this: get to know your independent pharmacists really well."

Dr. Vollmer made a connection with one such individual in his community who is willing to take these access programs on and get his patients the drugs they need.

"I simply tell the patient, 'This may not be the pharmacy you use, but this one will honor your access card.' I never receive any patient pushback over this because they realize they are going to save a lot of money for a superior drug," he notes. "The pharmacy is happy to do this because you are bringing them business. I have found that this 'triangle' is greatly beneficial for all parties."

If all of these options fail and Dr. Vollmer has to prescribe a generic drug that is approved from the patient's healthcare plan, such as generic prostaglandin instead of Vyzulta for a new glaucoma patient, he will make sure to see the patient back on regularly scheduled visits and check that the patient's pressures are where they need to be.

"I may be forced to place the patient on dual therapy with another drug to get the pressures to target," he says. "In some instances where I know the patient does especially well on a branded medication, I will save my samples for that patient to limit their financial burden. I have a 31-year-old in my clinic who I do this for, and he is very appreciative."

As discussed above, dry eye is an area of care that can benefit greatly from out-of-the-box thinking. For instance, Dr. Thimons has used the Mark Cuban Cost Plus Drug Company—which aims to address rising drug costs—to get Restasis for his patients at a fraction of the cost a traditional insurance company charges.

Other options include programs such as GoodRx, which gathers current prices and discounts to help patients find the lowest cost for their prescriptions. Dr. Shovlin notes that ordering from Canada can work for some, but he acknowledges that it can be confusing for the patient and may not be the right approach for everyone. When doing this, he also emphasizes the importance of making certain you are ordering the same medications.

"This is the first legitimate agency to battle against this ridiculous cost override on the part of the pharmaceutical and insurance companies," Dr. Thimons says. "We'll see whether that plays out long-term, but that's one of the alternatives that I use in the ocular surface space."

When contending with prior authorization denials, Dr. Thimons has found that empowering patients to take the lead can prove successful. In cases where there is an issue with commercial insurance coverage, he has advised patients to connect with their HR departments.

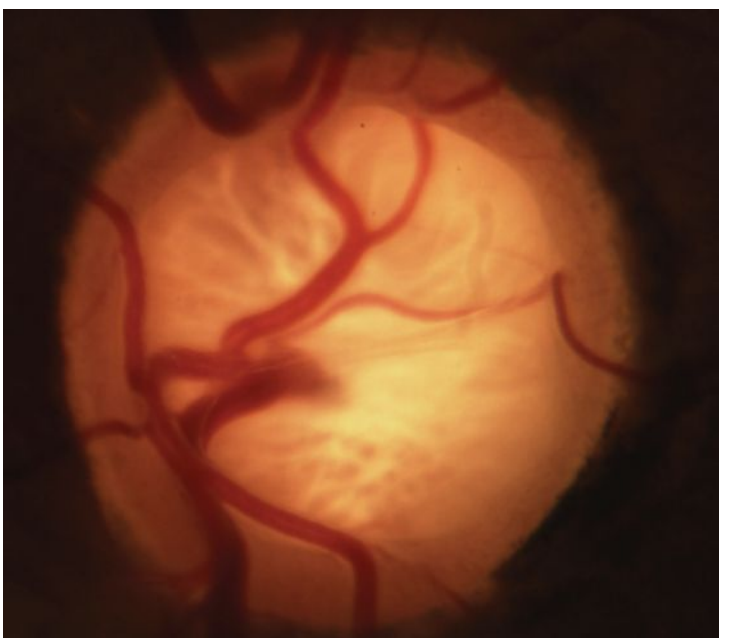


Photo: Michael Dorkowski, OD, Jim Williamson, OD, and Andrew Rixon, OD

In glaucoma, "every millimeter counts" and sometimes that means fighting for access to the latest and most effective meds. Otherwise, vision will continue to decline and expenses ultimately will rise.

Photo: Abagail Kirk, OD

The majority of doctors are being pushed to use a preset generic drug or panel of drugs by the insurance company, making it challenging to access newer agents in glaucoma therapy.

Dr. Thimons and colleagues will craft letters outlining the issue and their patients take it from there. When brought to their attention, HR departments can petition the insurance companies to expand coverage for specific medications or procedures.

Patient Education and Support

A key component of dealing with prior authorizations is educating patients and helping them understand the process. This goes a long way in building trust and avoiding upset patients who are blindsided by the cost of a prescription.

"Patient education is crucial, and especially important for patients with conditions like glaucoma who often are dealing with multiple medications," says Dr. Thimons. "I will have a conversation with these patients from the beginning explaining their options."

This includes a discussion about laser procedures and medication options as well as potential hurdles with insurance coverage.

"By doing this, I have prepared them for a potential preauthorization denial and discussed alternatives," Dr. Thimons explains. "This preliminary discussion is probably one of the most valuable steps I have integrated into my clinic in the last 10 years, for both my practice and patients."

> **By educating patients on potential insurance-related hurdles in advance, you are ensuring they are prepared while also making sure that they know you have their best interests in mind.**

Patient education for a condition like dry eye is different and sometimes more extensive because it is not as linear, according to Dr. Thimons. He begins these conversations by discussing the potential causes of their dry eye symptoms, and then advises the patient that there are a variety of pathways to treat this condition, but some may not be covered by their insurance.

"I emphasize the importance of tailoring an approach to meet their needs while making sure they understand that we may have to fight their insurance company, depending on coverage," Dr. Thimons says. "I want to avoid getting an angry phone call from a patient because they are shocked when a drug we prescribed is $500. That is why I shifted my approach and take control of the conversation from the beginning."

"I am going to be the one to deliver the bad news first," he adds. "For the most part, I am very blunt. I cannot control what an insurance company does and doesn't do, but I make it clear that I can work with my patients to still provide good care and here are our options. In the case of dry eye, that includes a discussion about shared cost options, omega-3 fatty acids, Regener-Eyes, autologous tears, interventional procedures and more. Dr. Thimons will also direct patients to educational resources.

Ultimately, you want to position yourself as not only an expert eyecare provider, but also as a patient advocate. By educating patients on potential insurance-related hurdles in advance, you are ensuring they are prepared while also making sure that they know you have their best interests in mind.

Prior authorizations can overwhelm clinical practices and have a significant impact on the entire care team as well as their patients. Having clear systems and plans in place can help mitigate some of the challenges associated with this issue.

"Avoiding burnout for your staff and yourself while also serving your patients is a very hard job these days," notes Dr. Thimons. "Doctors are the emissaries in the middle of this battle. We don't create the pricing, but we are responsible for our patients' well-being. We know what works best and yet sometimes we're denied. Navigating this challenge requires creative strategies, collaboration and support across the optometric profession." ■

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DRY EYE DRUGS: WHAT'S NEW AND WHAT'S NEXT

Let's dive into the substantial amount of meds that have come to market the last few years, along with a preview of others on the horizon.

BY PAM THERIOT, OD, AND LISA HORNICK, OD
SHREVEPORT, LA AND ROCKLIN, CA

Dry eye disease (DED) affects all pillars of our practices from simple refractions to systemic disease comanagement, and it of course dramatically affects our patients, disrupting their daily lives. Newer diagnostics and treatments, and the advanced technology and research behind them, are helping us better care for our patients, though.

Many new medications are making their way through the FDA approval process, and a few were added to our armamentarium over the last few years. By the end of 2023, we're hopeful to have two more drugs to add to the DED toolbox.

Let's dive into the newer drugs, how they work and where we fit them into our current clinic protocols.

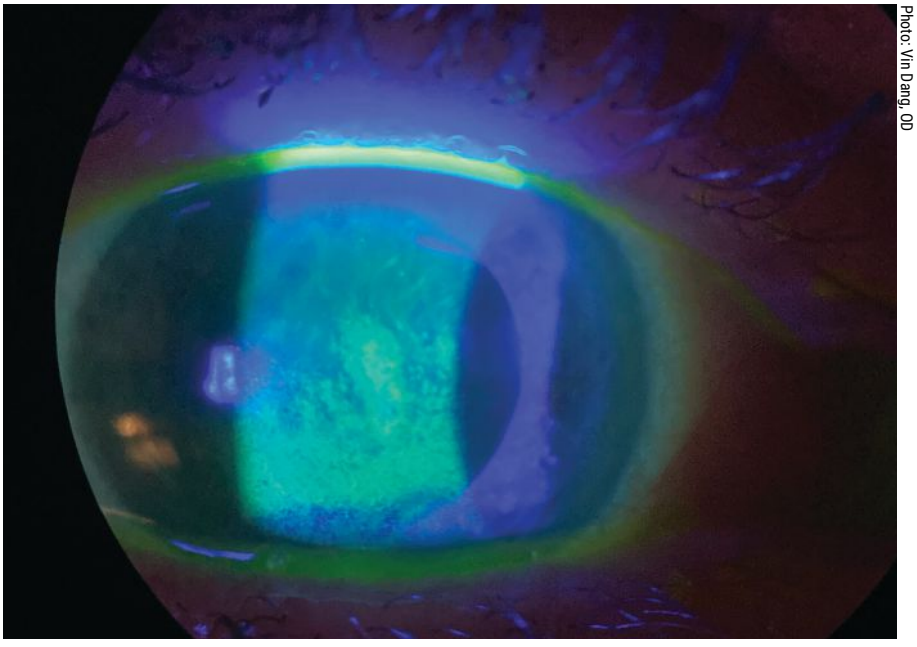

Photo: Vin Dang, OD

Sodium fluorescein staining shows this patient's corneal surface is compromised by dry eye disease.

Tyrvaya (varenicline tartrate solution 0.03mg, Viatris)

Approved by the FDA in October 2021, Tyrvaya is the first nasal spray to treat the signs and symptoms of DED. It is applied to the inside of the lower nasal area twice a day.

Mechanism of action: Although the exact mechanism is still unknown, it is believed to cause cholinergic neuro-activation via the trigeminal parasympathetic pathway, which is understood to play a role in tear film stability by stimulating the lacrimal functional unit.[1,2] Stimulation to the lacrimal functional unit increases

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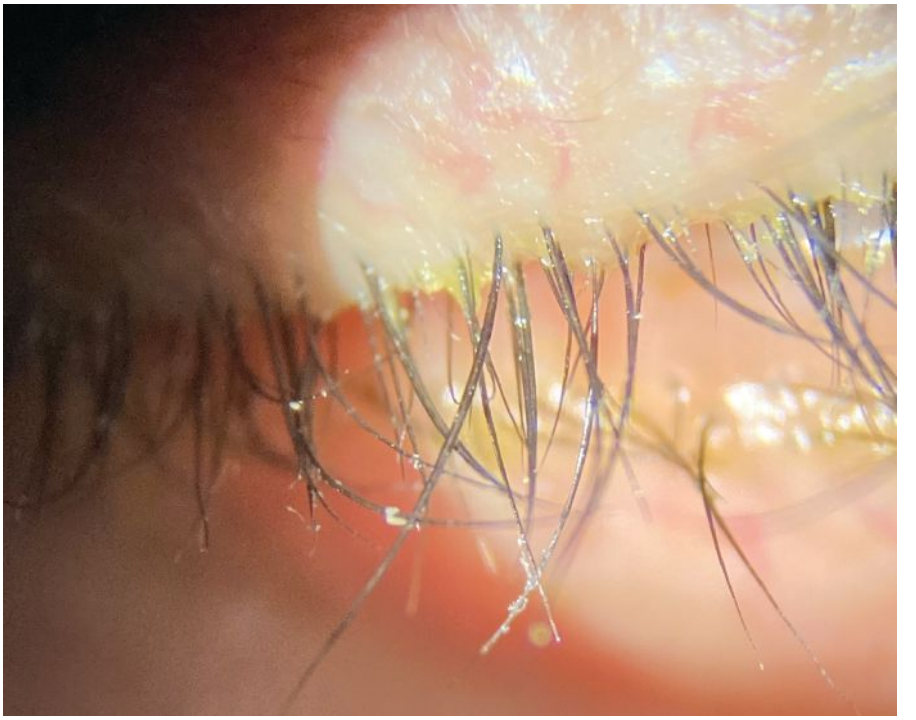
Dr. Theriot practices at a multi-specialty eye clinic in Shreveport, LA. Her clinical practice covers a broad spectrum of ocular care with a unique focus on ocular surface disease and dry eye. She received her doctorate in optometry from UC Berkeley School of Optometry and completed her residency at SUNY College of Optometry. She is a consultant for Novartis and key opinion leader for Sun Pharmaceuticals and Kala Pharmaceuticals**. Dr. Hornick** practices at Stanford Ranch Optometry in Rocklin, CA. She received her doctorate in optometry from the Southern California College of Optometry. She is a Fellow of the American Academy of Optometry and a board member for the Sacramento Valley Optometric Association. She has no financial disclosures.

basal tear film production, which makes up about 34% of the tear film and helps to relieve dry eyes.[3] Basal tears contain a complex mix of 2,000 molecules. Imbalance of the tear film leads to loss of tear film homeostasis, resulting in dessication and an inflammatory cascade that can cause DED.[4] Restoring the tear film was shown in clinical trials to improve both symptoms, using the Eye Dryness Score (EDS), and signs measured by Schirmer testing.[5]

Side effects: Tyrvaya is not reported to cause any significant adverse events to the ocular surface; however, it does have non-ocular side effects, including sneezing (82%), coughing (16%), throat irritation (13%) and instillation site irritation (8%).[5,6,7]

Why choose Tyrvaya: As a nasal spray, it's the first option that can spare the ocular surface from drug exposure. A review conducted in 2022 on the use of Tyrvaya reported that this agent is well-tolerated and advantageous over the available topical medications.[8]

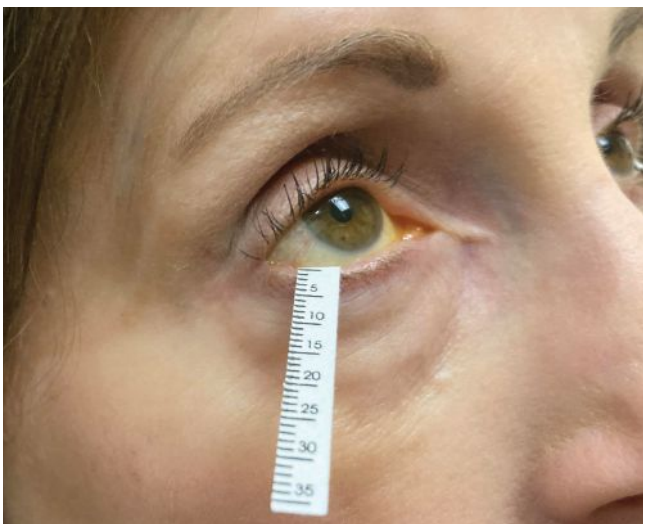
In clinical trials, study participants increased their Schirmer score after using Tyrvaya BID for four weeks.[5,6] In a prospective study where participants used cyclosporine 0.005% ophthalmic solution BID for six months, 35.1% achieved ≥5mm improvement and 18.9% achieved ≥10mm improvement in the average Schirmer scores.[9]



Collarettes are pathognomonic for *Demodex* blepharitis.

Cequa (cyclosporine 0.09%, Sun Ophthalmics)

Approved by the FDA in 2018, Cequa offers a 0.09% concentration formulation of the familiar drug cyclosporine in an aqueous nanomicellar formulation. It increases tear production in DED patients, and its use of nanomicelles—small, highly soluble colloids with a hydrophilic surface—for drug delivery aims to increase cyclosporine bioavailability while reducing adverse reactions.[10]



Schirmer's strip in use. Its scores are a mainstay of clinical trials of drug performance as well as clinical assessment by ODs.

Mechanism of action: Cequa is believed to work as an immunomodulator. Cyclosporine increases tear production in patients where it's presumed to be suppressed due to ocular inflammation associated with DED.[11] It inhibits the activation of transcription factors required for T-cell activation and inflammatory cytokine production, which decreases inflammation in the eye, leading to an increase in tear production.[12]

Cequa is unique due to its nanomicellar delivery system. The micelle formation has a hydrophobic core and an outer water-soluble or hydrophilic shell. These nanomicelles are thus more bioavailable in the precorneal tear film.[9]

Side effects: Ocular adverse events were mild and transient irritation, and no serious ocular adverse effects were reported in the Phase II and III studies.[11]

Why choose Cequa: The higher concentration and improved drug delivery method may be more effective and better tolerated than older forms of cyclosporine.[14,15]

After 14 days of BID dosing, cyclosporine 0.09% demonstrated a numerically greater treatment effect in conjunctival staining, corneal

TABLE 1. FDA-APPROVED DRUGS AVAILABLE FOR TREATMENT OF DRY EYE SINCE 2018

Drug	Therapeutic class	Mechanism of action	Side effects
Tyrvaya	Cholinergic agonist	Cholinergic neuro-activation, which increases the basal tear film.	Sneezing, cough, instillation site irritation
Cequa	Calcineurin inhibitor immunosuppressant	Partial immunomodulator. Inhibits the activation of transcription factors required for T-cell activation and reduces inflammation.	Temporary burning or discomfort
Xiidra	Anti-inflammatory	Blocks immunological synapse by binding to LFA-1.	Instillation site irritation, dysgeusia and reduced visual acuity
Eysuvis	Corticosteroid	Inhibits the inflammatory response by activating the glucocorticoid receptor and inhibiting prostaglandin production.	Instillation site irritation

staining and tear breakup time (TBUT), and at six months, after taking cyclosporine 0.005%, TBUT improved by more than 50% in both eyes.[9]

Eysuvis (loteprednol etabonate ophthalmic suspension 0.25%, Alcon)

This corticosteroid eye drop is used for the treatment of DED flares. In 2020, it became the first topical steroid to be approved by the FDA for the short-term treatment of dry eye. In one of its clinical trials, Eysuvis was found to be significantly effective for treatment of hyperemia and dry eye without elevating intraocular pressure (IOP).[16]

Mechanism of action: Corticosteroids work by suppressing cellular infiltration, capillary dilation, fibroblast proliferation and collagen deposition.[17] They also interfere with the synthesis of pro-inflammatory molecules and they inhibit scar formation.[18]

Eysuvis is an ophthalmic nanosuspension that delivers corticosteroid to the anterior eye using mucus-penetrating particles (MPPs). This delivery concept facilitates the drug penetration through the mucus barrier and enables the drug to spread more quickly and uniformly across the ocular surface than in conventional processes.[19] These are favorable properties for treatment of ocular surface disease.[16]

Side effects: Although corticosteroids are an effective treatment for DED, long-term use is associated with cataract development, increased IOP and opportunistic infections.[20] Eysuvis breaks down rapidly after administration to the ocular surface and reduces the risk of elevated IOP and cataract formation associated with other topical steroids.[16]

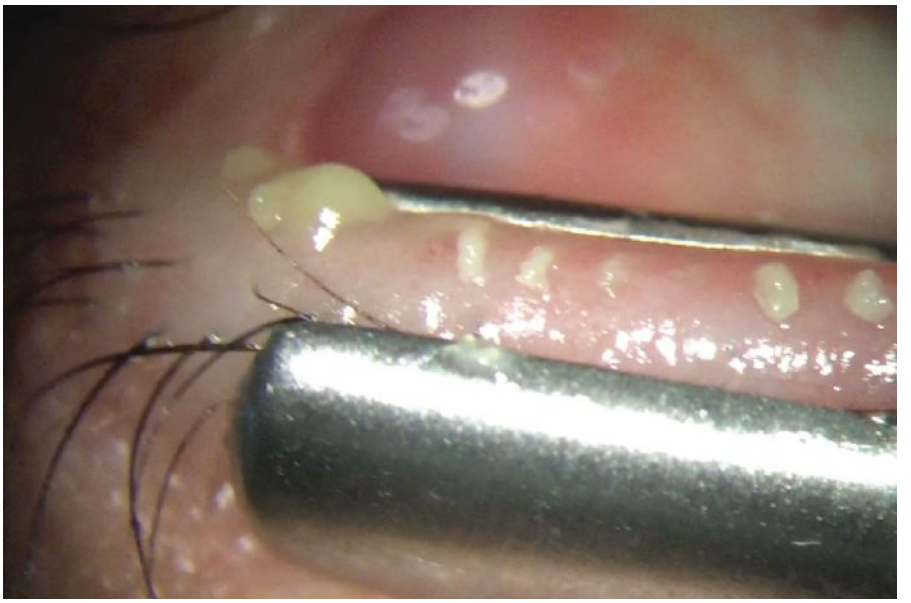
Why choose Eysuvis: In pre-clinical studies, 0.5% loteprednol vs. 0.4% loteprednol in MPP formulation was shown to have a 3.6-fold higher concentration in the corneal epithelium after just five minutes.[21] Eysuvis is used for short periods, so the side effects are minimal compared to traditional corticosteroids.[16] Eysuvis is the first FDA-approved ocular steroid indicated for DED, though off-label use of others, notably Lotemax (Bausch + Lomb), has long been recognized as effective.[20]

Regener-Eyes (Regener-Eyes)

This is a sterile, preservative-free option to relieve dryness of the eye that is nonsteroidal and derived from amniotic fluid.[23] According to the company, use of Regener-Eyes assists the tear film layer by increasing lubrication and hydration, which promotes homeostasis of the corneal surface and helps slow down the cycle of dry eye perpetuation. It is well-tolerated in patients, with the most common side effect being instillation site irritation. This drop does not have an FDA approved label and as such is an over-the-counter product.

TABLE 2. CLINICAL TRIALS FOR DRUGS PRIOR TO FDA APPROVALS

Drug	Phase I Clinical trial	Phase II Clinical trial	Phase III Clinical trial	NDA approval	FDA approval
Reproxalap	Data not available	Done, successful	First phase done, successful Second trial is ongoing	Submitted for NDA approval	PDUFA date 6/8/23
NOV03	Data not available	Done, successful	GOBI and MOJAVE done, successful	Submitted for NDA approval	PDUFA date 6/28/23
TP-03	Data not available	Saturn-1 study successful	Saturn-2 study successful	Submitted for NDA approval	PDUFA date 8/25/23



To minimize ocular surface drug exposure while also providing complementary therapy, many practices offer in-office procedures such as meibomian gland expression.

Inveltys (loteprednol etabonate ophthalmic suspension 1%, Alcon)

This drug was FDA-approved in August 2018 and is the only twice-daily ocular corticosteroid indicated for the treatment of inflammation and pain after ocular surgery.[39] It came to the market to meet the needs of surgeons who were looking for a drop that could control postoperative inflammation without elevating IOP.[39] Naturally, off-label use is widespread and that includes for appropriate dry eye patients.

Mechanism of action: As is the case with Eysuvis, the reliable efficacy of loteprednol etabonate gets a boost from MPP. According to the company, this allows more of the drug to penetrate through the mucins directly to the target ocular tissue. One study supports the premise that the MPP use can enhance ocular exposure of topically applied therapeutic agents.[21]

The mucins in the tear film have a protective effect, eliminating pathogens and other insults. In doing so, they also may limit the penetration of traditional suspension eye drops, as they can be rapidly cleared.[41]

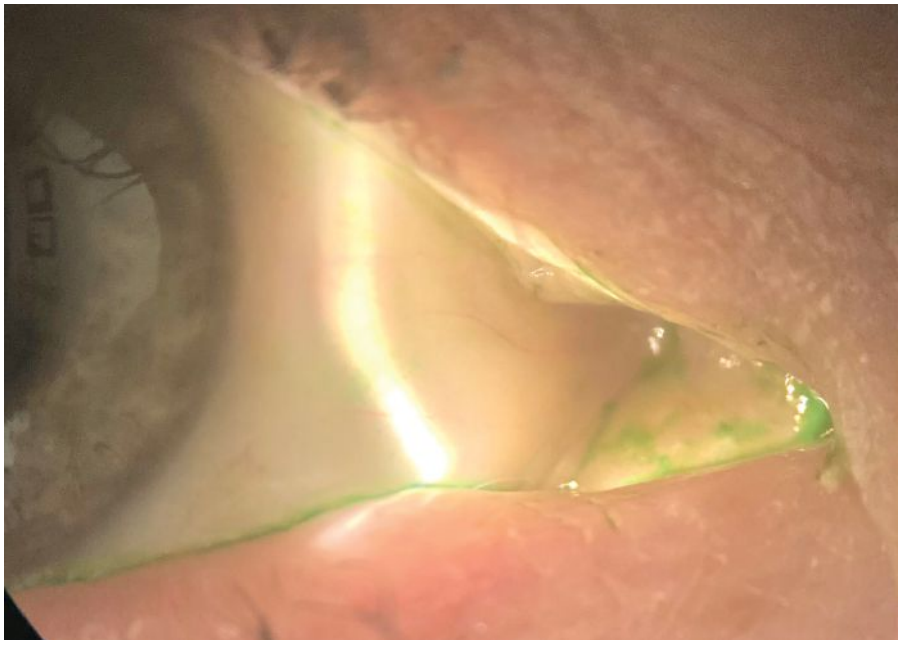
Why choose Inveltys: Loteprednol consistently demonstrates a low propensity to elevate IOP, regardless of formulation, dosage regimen or treatment duration, including in known steroid responders.[27]

Reproxalap (Aldeyra Therapeutics)

This agent is a reactive aldehyde species (RASP) inhibitor. RASP is elevated in ocular (allergic conjunctivitis and DED) and systemic inflammatory diseases. In the eyes, RASP can cause many symptoms including inflammation, redness, change lipid tear composition and decreased tear production.

Mechanism of action: Reproxalap may represent a new therapeutic approach for the treatment of DED. It works as a nonsteroidal anti-inflammatory by binding to RASP. In dry eye patients, reproxalap dosed QID results in reduction of inflammation and stabilization of the tear film by preventing RASP modification of tear lipids.

Clinical trials: Reproxalap 0.25% dosed QID over 12 weeks demonstrated rapid, broad and clinically relevant symptomatic control of DED as measured by OSDI and SANDE, and DED signs improved as demonstrated by fluorescein staining.



Here, the conjunctiva is stained with lissamine green. Cequa showed a reduction in conjunctival staining in its clinical trials.

Adverse events: Although reproxalap is an anti-inflammatory, it has not been shown to cause elevated IOP in clinical trials. The drug has been well tolerated and symptoms have been reduced with QID dosing in as little as one week.

The NDA PDUFA date for reproxalap has been projected as June 8, 2023.

CyclASol (Novaliq)

This topical anti-inflammatory and immunomodulating ophthalmic drug solution contains 0.1% cyclosporine A in a unique water-free solution that the company calls EyeSol; it is believed to increase the tolerability of cyclosporine A on the eye, according to the company.

Mechanism of action: CyclASol's water-free formulation enables the cyclosporine to have a longer duration on the ocular surface. EyeSol is said to provide a small drop size of a nonaqueous and clear solution. The drug is designed for improved ocular tolerability and local bioavailability, which should allow for earlier onset of efficacy compared to other formulations of cyclosporine A.[28] The company says that CyclASol's clear solution quickly spreads across the ocular surface due to its low surface tension. This minimizes the usual decrease in visual acuity that is seen in lipid-based eye drops, ointments and emulsions.[28]

Clinical trials: CyclASol was studied in a 12-week, double-blind multicentered clinical trial that compared it to vehicle at a BID dosing regimen. In the Essence trial, statistically significant improvements in central corneal staining were reached after two weeks of therapy. Also, statistically significant improvement in EDS was met after four weeks of use. CyclASol was found to have an earlier onset of action compared to other cyclosporine formulations.

Essence-2 study showed that CyclASol was able to maintain its reduction in the signs and symptoms of DED over a 52-week period.

The drug also demonstrated favorable tolerability. Essence-2 showed visual disturbances of 7.8%, similar to that of Restasis. The other adverse events reported (present in <2% of subjects) were blurred vision, instillation site pain and conjunctivitis.

The FDA has assigned a PDUFA date of June 8, 2023.

NOV03 (Bausch + Lomb)

This investigational therapy is a preservative-free, water-free, nonsteroidal drop intended for treatment of DED with associated MGD.[29]

The active ingredient is perfluorohexyloctane. The product also contains the EyeSol formulation developed by Novaliq.

Mechanism of action: Its developers say that EyeSol allows the drop to stay on the eye up to 240 minutes, as opposed to traditional water-based topical agents, which last on the eye for three to five minutes. EyeSol consequently allows NOV03 to be up to four times more bioavailable than water-based drops. The use of EyeSol also allows NOV03 to penetrate the meibomian glands, the company says.

A Phase II trial successfully evaluated the efficacy, safety and tolerability of NOV03 in patients with DED associated with MGD. There was improvement in signs (corneal staining) and symptoms (by EDS).[30] NOV03 spreads rapidly across the ocular surface because of its low surface tension.[31] It does not cause blurred vision as ophthalmic gels or ointments do because its refractive index is similar to water.[32]

Both the signs and symptoms were statistically significantly reduced with QID dosing at two weeks.

Adverse events: The drop is said to be very comfortable and the only adverse event that occurred in more than 1% of study subjects was mild blepharitis. Even though the agent remains on the eye for several hours, patients did not report blurred vision.

NOV03 may offer an appealing new approach to care for the 86% of dry eye sufferers with some form of evaporative DED.[33] Altered tear film lipid layer in MGD leads to tear film instability and evaporative aqueous loss. Treatments thus far have relied on interventional approaches treating the eyelids. Having a pharmaceutical adjust would be welcome by many practitioners.

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TP-03 (lotilaner ophthalmic solution, Tarsus Pharmaceuticals)

This drug is currently undergoing its NDA phase of FDA approvals. It is a topical ophthalmic eye drop intended for use twice daily for six weeks to help paralyze, eradicate and exterminate *Demodex* mites.[35]

Although *Demodex* blepharitis is not a form of DED per se, long-term *Demodex* infestations will clog the meibomian glands, decrease meibum production and lead to or exacerbate MGD.[36,37] In such patients, eliminating *Demodex* could improve MGD, a root cause of evaporative DED.

Mechanism of action: Lotilaner, the active ingredient, uses parasite-specific GABA inhibition to paralyze the mites' nervous system, which leads to death. Clinical trials show more than 80% of participants reached a clinically meaningful cure to their *Demodex* blepharitis.[35]

The PDUFA target date for TP-03 is August 25, 2023.

Takeaways

It's an exciting time in our profession when contemplating treatment of our old foe dry eye, as many noteworthy new meds will certainly make a difference for you and your patients now and in the near future. ■

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Glossary of Terms for Investigational Drugs

FDA: Food and Drug Administration is the entity in the United States tasked with the responsibility to protect the health of our nation's people by ensuring the safety, efficacy and security of human and veterinary drugs, biological products and medical devices.

Phase I: used to determine the safety and dosage of the drug. Usually, this study takes several months and enrolls 20 to 100 healthy participants.

Phase II: used to determine the efficacy and side effects of the drug. It usually requires several months to two years of study and enrolls several hundred patients.

Phase III: used to determine the efficacy and monitor any adverse reactions. The study enrolls 300 to 3,000 participants and can take one to four years.

NDA: New Drug Application can be filed when the drug has passed all three phases of the clinical trial process.

PDUFA date: the name to the date to which the FDA must respond to an NDA with its approval or denial. It gives a more predictable timetable for new drug approvals.

Objective Functional Testing Needs in Diabetes and Glaucoma

Frances Bynum, OD
Northwest Tennessee Eye Clinic

Jeffry Gerson, OD, FAAO
Grin Eye Care

Justin Schweitzer, OD, FAAO
Vance Thompson Vision

Why is it necessary to complement structural testing with functional testing?

Dr. Schweitzer: Structural testing gives us a behind-the-scenes look at what's happening that a patient couldn't possibly tell us about. Structural tests are important because they show us what's happening anatomically and we are then able to increase our confidence in a diagnosis if we can match the anatomical changes to the functional changes a patient might be experiencing.

Functional testing is an important complement to structural tests. The RET*eval*™ in particular is a powerful, objective aid in the diagnosis and management of retina and optic nerve diseases, such as diabetic retinopathy and glaucoma.

Are visual fields and visual acuity sufficient functional complements to structural testing?

Dr. Bynum: Visual fields and visual acuity are subjective tests that rely on patient feedback. Results are often difficult to obtain and the tests can be very stressful for patients. There are times when, after several minutes of testing, we can't even use these results. This is why an objective measure of function is so valuable. An ERG test, in particular, provides objective information on the function of the visual system. It gives reliable guidance for medical professionals to manage functional changes that may impact a patient's vision, typically in advance of structural changes. This is an important feature of ERG testing—it allows us to detect functional stress so that we can anticipate structural damage. Since function is what's most important to patients and it's a big red flag for what we are likely to soon see on a structural test, its importance in eye care practices should not be minimized. On the contrary, functional tools like ERG can provide clear answers and allow us to confidently make clinical decisions, particularly when we're treating common conditions such as diabetic retinopathy and glaucoma.

How does the RET*eval* change the way you manage diabetic retinopathy in your practice?

Dr. Gerson: Optometrists rely on the RET*eval* to diagnose and manage a multitude of ocular conditions, but in my practice, the greatest value is in assessing diabetic retinopathy progression risk. The test is non-invasive and entirely objective, providing a simple score that indicates whether my patient may be in trouble. This is achieved by measuring both retina cell stress and pupil light response. This powerful combination provides a reliable progression risk assessment. It's also so easy to perform. Many of my colleagues delegate ERG testing to their staff and have a protocol to determine who to pretest before the doctor enters the exam room. It is so simple and quick to perform, that, when I have a patient that I need tested, I usually will just go and grab the hand-held unit and do the test myself. We're done within a matter of minutes without ever having to move my patient to do it. And, I get immediate results. A score of 23.5 or higher indicates an 11-fold risk of requiring intervention within 3 years,[1] which obviously plays a significant role in my clinical decision-making, especially with regard to setting follow-up intervals and appropriately timing referrals.

There are so many tests for managing glaucoma. Why should we add ERG?

Dr. Bynum: In short, ERG is one more tool in our arsenal as we try to make sense of a very complicated condition. Despite the availability of modern tools, 50% of true glaucoma patients remain undiagnosed and 50% of glaucoma patients are over-treated.[2] Tests such as perimetry and OCT imaging are standard of care, but are all too often hampered by media opacities (imaging for cup-to-disc-ratio), unspecific testing methods (IOP), or are subjective and bothersome to complete (visual field test). For glaucoma diagnosis and management using ERG, several parameters are given as the disease itself is complex and the condition is often challenging to diagnose and manage.

How does the RET*eval* change the way you manage glaucoma in your practice?

Dr. Schweitzer: Since early diagnosis is essential to preserve vision loss from further degeneration of ganglion cells, the RET*eval* PhNR test is useful during some glaucoma checks. PhNR stands for photopic negative response and is an electroretinographic test for analyzing how the ganglion cells function. During the PhNR test with full-field flash ERG, the retina is illuminated with a red flash on blue background under light-adapted conditions. The PhNR response from ERG is described by a time (implicit time) and amplitude. A delayed time generally indicates cell stress, while a lower amplitude indicates cell death. The RET*eval* PhNR test objectively measures the ganglion cells function by evaluating the electrical activity of the cells to a light stimulus. Knowing about the function of the ganglion cell assists in helping me make a more confident assessment of risk, detection, and management of glaucoma.

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KNOW THE INS AND OUTS OF ORAL STEROIDS

A review of the broad clinical applications, contraindications and potential side effects of these inflammation-fighting powerhouses.

BY JACKIE L. BURRESS, OD, AND MELISSA TURNER, OD
MUSKOGEE, OK

With the expanded scopes of practice in optometry across the country, optometrists currently have the legal authority to prescribe oral steroids in 43 of 50 states (*Figure 1*).[1] Prescribing oral steroids for ocular pathologies can be intimidating due to the possibility of adverse systemic effects. However, the anti-inflammatory properties of corticosteroids can not only improve a patient's severe anterior or posterior segment inflammatory event but can also be some of the most important vision-saving medications in neurological ocular events.

Here, we'll review the mechanism of action, most common uses in eye care, side effects and management of oral steroids.

Mechanism of Action

To gain confidence in prescribing oral corticosteroids, it is imperative to have a clear understanding of how these medications work to control the body's inflammatory response. Steroids function to inhibit the inflammatory cascade and prevent the damaging effects that severe ocular inflammation can cause, including scarring and neovascularization. These important medications work best in treating acute inflammatory processes, as opposed to chronic inflammation, which is better controlled with immunomodulators.[2]

Corticosteroids can be divided into two categories: glucocorticoids and mineralocorticoids. While both are 21-carbon structures synthesized in the adrenal cortex in response to ACTH (adrenocorticotropic hormone), each has distinct functions. Glucocorticoids function in the inflammatory pathway by binding to steroid receptors helping control the effects of stress on the body. Naturally occurring glucocorticoids include cortisol and cortisone. Synthetic glucocorticoids include prednisone, methylprednisolone, dexamethasone, fluorometholone and others. Mineralocorticoids bind to similar types of receptors and work to regulate water and electrolyte balance in the body. An example of a mineralocorticoid is aldosterone.[3] Steroids are metabolized in the liver via the cytochrome P450 pathway.[3]

Corticosteroids affect the immune and inflammatory responses at many points along their pathways. Steroids have been shown to function at both molecular and cellular levels to suppress inflammation and its effects. First, corticosteroids easily penetrate cell membranes and bind to specific steroid-binding protein receptors in the cytoplasm, creating a steroid-receptor complex. This complex travels to the nucleus, where it binds to chromatin and initiates the production of mRNA that codes for the proteins and enzymes that need to be synthesized in response to the steroid.[3] This is important because these cellular and molecular changes lead to the steroid's control over the cardinal signs of inflammation, including pain, erythema, edema and heat.[3]

There are numerous mechanisms of action that allow steroids to successfully control an inflammatory event. Edema is reduced by the

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constriction of blood vessels, limiting their permeability. This lessens the amount of fluid, protein and inflammatory cells that can leak into the extracellular space.[3] Steroids also help decrease cytokine activity. Cytokines are the inflammatory cells that signal to the body that an immune response is needed, flooding the site with inflammatory cells.[2] Steroids work to prevent these cytokines, such as polymorphonuclear cells, from clinging to vascular endothelium.[3] Steroids also inhibit phospholipase A2, which prevents the breakdown of arachidonic acid into prostaglandins and leukotrienes. These medications also prevent inflammatory cells such as neutrophils and macrophages from entering the affected tissues. Together, these mechanisms help to reduce pain, erythema and heat in the affected area. Lastly, and importantly, steroids quell fibroplasia or scarring.[3]

Oral Steroid Use in Eye Care

Since their introduction into ocular treatment in 1951 to manage both anterior and posterior chamber inflammatory pathologies, oral steroids have since been used to treat a wide range of eye conditions.[2] The two oral steroids that are typically prescribed are prednisone and methylprednisolone. All steroids have a basic structure of 21 carbons in four rings. Prednisone and prednisolone have an additional double bond in ring A. Methylprednisolone is created by the methylation of carbon 6 in ring B. It also has a slightly greater anti-inflammatory effect.[3] Prednisone is an oral medication only, while methylprednisolone can be given intravenously or orally.

Below are some of the most common etiologies optometrists will encounter that may require oral corticosteroid therapy.

Periocular dermatitis. For patients with inflammation of the eyelids and adnexa secondary to allergic dermatitis, methylprednisolone, commonly ordered as a 4mg Medrol Dosepak, is beneficial and convenient for ocular inflammation that is superficial

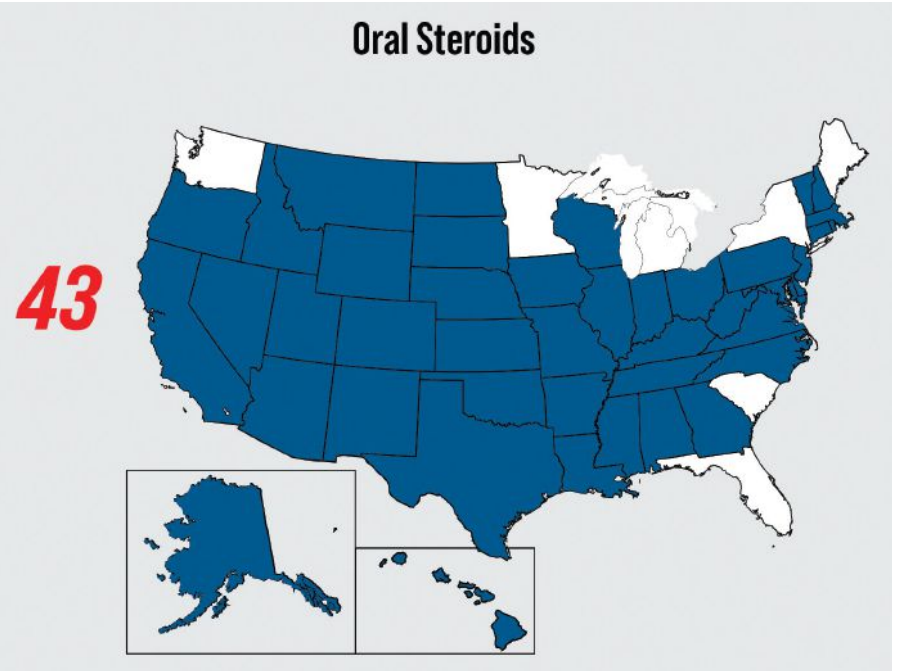

Fig. 1. This map displays the 43 US states where optometrists are currently authorized to prescribe oral steroids.[1]

(*Figure 2*).[2] A Medrol Dosepak is a pre-packaged dose of methylprednisolone that has the patient take six 4mg tablets on day one, tapering one tablet per day until all are taken. During the summer months, superficial ocular inflammation is most commonly seen with dermatitis secondary to allergy to poison ivy. Prescribing oral steroids in a Medrol Dosepak is one of the more convenient and economical options for patients. It delivers a higher dose of steroids on day one with a built-in tapering schedule that is easy to follow.

Bell's palsy. When patients present with new-onset Bell's Palsy, a short-term course of oral steroids can calm the inflammation of the seventh cranial nerve. The treatment outcome will be best if treatment is initiated within three days of the start of the facial nerve palsy. The recommended dose is prednisone 60mg to 80mg/day for one week. Treatment with a steroid at this dosage in short duration is likely to be easily endured without many side effects.[4] Antiviral agents may also be considered in addition to prednisone, but the benefit has not been well proven in literature.[6]

Thyroid eye disease (TED). In the treatment of this condition, previously known as Graves' ophthalmopathy, steroids are used to decrease inflammation or overcrowding by reducing soft tissue edema within the orbit. They are prescribed to decrease the intraorbital pressure and are only effective during new or quickly progressing ophthalmopathy, not with chronic disease.[2] Oral prednisone should be prescribed at 60mg to 100mg/day. Once improvement occurs, attempt to taper the daily dose to the least daily amount of prednisone that maintains the positive results.[5] Tapering the dosage by 5mg to 10mg/week is the recommended rate, but you may need to stop the taper and increase the steroid dosage if symptoms worsen again.[2] If there is no improvement within four to six weeks of oral prednisone, alternative treatments should be explored, including referral to oculoplastics for consideration of Tepezza (teprotumumab-trbw).

Non-infectious uveitis. If a non-infectious undifferentiated uveitis is not responding to topical steroids or sub-Tenon steroid injections, systemic steroids may be required. If the uve-

itis is bilateral, systemic steroids are often the preferred second line of therapy to topical instead of injections. In non-infectious undifferentiated intermediate uveitis that does not respond to topical or sub-Tenon steroid injections, oral steroids should be considered. Oral steroids are often needed for posterior uveitis. Oral prednisone dosed at 40mg to 60mg daily for four to six weeks, followed by a slow taper, is the recommended treatment course.[6]

Photo: Jessica Steen, OD

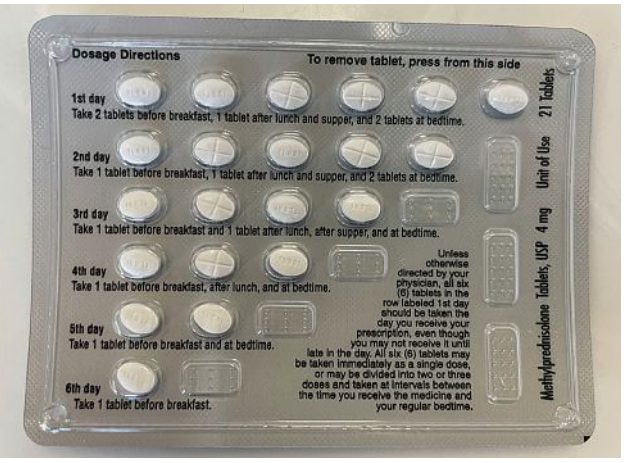

Fig. 2. Medrol Dosepak (4mg) showing easy-to-follow instructions for patients with a built-in taper.

Scleritis. For scleritis, topical steroids are not effective. In cases of diffuse, nodular and necrotizing scleritis, systemic steroids may be required. The recommended way to prescribe oral prednisone is for one week at 60mg to 100mg daily, then begin a taper to 20mg daily for two to six weeks, followed by a continued slow taper.[6] Scleritis that is recurrent in nature or due to underlying autoimmune disease should be referred to rheumatology for consideration of other immunosuppressive therapies.

Giant cell arteritis. In patients suspected to have giant cell arteritis, emergent testing of erythrocyte sedimentation rate (ESR), C-reactive protein and platelets should be performed. If giant cell arteritis is diagnosed, systemic steroids should be initiated as soon as possible. The initial treatment is methylprednisolone 250mg intravenously every six hours for 12 doses followed by oral prednisone 80mg to 100mg daily while awaiting the results of a temporal artery biopsy, which is the most sensitive and specific test for giant cell arteritis.[2,6]

The initiation of treatment should not be withheld while awaiting the temporal artery biopsy. It is recommended that temporal artery biopsy should be done within one week of the initiation of treatment with systemic steroids. Once the results of the temporal artery biopsy have come back with positive findings, the patient needs to remain on the prednisone 1mg/kg/day.[6] The original dosage of the steroid is continued until the ESR returns to normal and symptoms improve. This is followed by a slow taper with monitoring of the ESR and symptoms with each dosage reduction or at least monthly. If the ESR begins to rise or symptoms recur, prescribers should revert patients to the previous increased prednisone dosage.

When treating giant cell arteritis with oral steroids, consider comanagement with a neurologist or neuro-ophthalmologist due to the dosage and length of treatment and the host of potential side effects. Treatment should continue for at least six months to a year.[6]

Idiopathic orbital inflammatory syndrome. Also known as orbital inflammatory pseudotumor, the suggested treatment for diagnosed cases is oral prednisone 1mg to 1.2mg/kg/day as the initial dose. Patients who respond to the oral steroids should remain at the original dosage for several days. Then, a slow taper to 40mg/day for two weeks is recommended, followed by a continued unhurried taper below 20mg/day completed through several weeks.[6]

Optic neuritis. Another neuro-ophthalmic disorder that can require steroid therapy is optic neuritis. A pulsed dose of IV methylprednisolone should be given at 1g/day for a total of three days. The patient can then be converted to oral prednisone dosed at 1mg/kg/day for 11 days, after which the medication can be tapered over four days, with 20mg the first day and 10mg on days two to four.[6] This should be initiated within 14 days of the onset of vision loss. The Optic Neuritis Treatment Trial found that oral prednisone should never be used as the first-line treatment due to the potential for an increased chance of recurrence. The trial also found that steroids only shortened the amount of time until vision is fully recovered. Another treatment choice is simply observation, as visual acuity will return to the same level as if it was treated by steroids.[6]

Managing Side Effects

Nearly every tissue in the human body has steroid receptors, which may lead to adverse effects in many different organ systems. These adverse effects are also dependent upon the strength of the dose and the length of the treatment. Patients taking higher dose steroid treatment for chronic conditions like giant cell arteritis are more likely to have systemic side effects than patients taking a short course of lower-dose steroids for an etiology such as contact dermatitis secondary to poison ivy.

Let's review the most common side effects of oral steroids and how to best approach them.

Gastrointestinal. Various GI side effects can arise from oral steroid use, including gastritis, peptic ulcers and bleeding in the GI pathway. If steroids are combined with NSAIDs, the risk of gastrointestinal effects increases two-fold.[7] To protect the stomach, it is highly recommended for the patient to be placed on an anti-ulcer medication such as a proton pump inhibitor (available as OTC Prilosec or Prevacid) or a histamine type 2 (H2)

receptor blocker (available as OTC Pepcid).[1,6] In addition, be sure to educate patients to not take NSAIDs such as ibuprofen or naproxen while on oral corticosteroid therapy.

Adrenal insufficiency. When oral steroids are taken for a prolonged period, the adrenal system ceases making the natural cortisol used in the daily functioning of the body. The hypothalamic-pituitary-adrenal (HPA) axis is the pathway that controls endogenous cortisol production and becomes inactivated when a patient takes steroids over time. The amount of endogenous corticosteroids created by the HPA-axis is equivalent to 7.5mg of prednisolone daily (or about 8mg of prednisone daily).[8] When high-dose steroids are discontinued abruptly, acute adrenal insufficiency may occur.[12] Acute adrenal insufficiency can be life-threatening with symptoms including hypotension, severe weakness, acute abdominal pain with nausea and vomiting, fatigue and lethargy.[9]

To prevent acute adrenal insufficiency, tapering of steroids is imperative. HPA-axis suppression is not likely to occur in patients who have received glucocorticoids for less than three weeks in duration.[10] In patients treated longer than three weeks, HPA-axis suppression has likely occurred, meaning the body is no longer synthesizing its own cortisol. Tapering the patient slowly will allow the HPA-axis to regain function and prevent the recurrence of any inflammation from withdrawal of the corticosteroid.[10] Due to this, it is recommended that patients on therapy courses longer than two weeks should be tapered. This is slightly less than the three-week mark to ensure all patients who have HPA-axis suppression are treated safely. See Table 1 for recommended tapering schedules.

Endocrine. Oral systemic steroids can cause hyperglycemia by stimulating the liver to create glucose and by reducing the rate at which glucose is used.[11] The higher the steroid dosage, the higher the risk for increased blood glucose. Patients with diabetes may experience elevation of blood glucose levels and will need comanagement with their primary care provider to help control blood glucose levels.[7]

Long-term use of corticosteroids may also lead to Cushing syndrome, which is the redistribution of body fat that occurs in response to hypercortisolism. The three primary sites of increased body fat are the face (moon face), neck (buffalo hump) and the trunk (truncal obesity). These effects tend to be dose-dependent and can occur within the first two months of steroid therapy.[7,10] Cushing syndrome can be treated by the slow taper of the corticosteroid treatment. Weight gain without Cushing syndrome may occur as well due to steroids causing increased appetite.[7]

Central nervous system. Oral glucocorticoid treatment can lead to numerous side effects of the central nervous system. In short-term therapy, the most reported effect is mood elevation. Though this effect doesn't sound all that threatening, it can be more severe in some patients who report mania, insomnia and restlessness.[11,12] One of the only circumstances when a patient should abruptly have steroids either discontinued or the dose significantly reduced is in the case of steroid-induced psychosis that does not respond to antipsychotic medications.[10] Depression may also occur with patients on a longer course of steroid therapy.[11,12] Most of the time, these symptoms are minor and will resolve after oral steroid discontinuation.[7]

Cardiovascular. Hypertension can be seen in patients on oral steroid treatment, especially in patients who have underlying heart or kidney disease. This is due to corticosteroids promoting the retention of fluid due to changes in electrolyte and water balance.[7,11] Steroid-induced hypertension has been observed in up to 20% of Cushing syndrome patients and is largely dose-dependent.[7] Comanaging the patient with their primary care provider, internist or cardiologist is recommended to ensure blood pressure remains in therapeutic range while on long-term steroid therapy.

Ophthalmological. Ocular side effects of oral steroids include cataracts, elevated intraocular pressure (IOP) increasing the risk of glaucoma and in rare cases, exophthalmos.[7] The most common form of cataract seen with systemic steroid treatment is posterior subcapsular. The incidence of cataracts is heavily dependent on dose and duration.[2,3]

It is common for optometrists to monitor IOP closely when topical steroids are used in the eye, but it's also important when patients are undergoing systemic therapy. Systemic therapy has been shown to elevate IOP that can potentially lead to optic nerve damage and visual field loss.[3] IOP-lowering medications can be initiated to prevent this damage while a patient is undergoing long-term steroid therapy. It's wise to ask all autoimmune disease patients about any steroid therapy, past or present.

Steroid IOP response is much more common in patients with an existing diagnosis of glaucoma. For these patients especially, IOP should be closely monitored throughout treatment with oral steroids.

TABLE 1. RECOMMENDED TAPERING SCHEDULE FOR ORAL STEROIDS[10]

Dose	Appropriate Taper
>40mg prednisone/day	5mg-10mg/day every 1-2 weeks
20mg-40mg prednisone/day	5mg/day every 1-2 weeks
10mg-20mg prednisone/day	2.5mg/day every 2-3 weeks
5mg-10mg prednisone/day	1mg/day every 2-4 weeks
<5mg prednisone/day	0.5mg/day every 2-4 weeks

Lastly, another instance when steroids should abruptly be discontinued, or dose quickly reduced, is a patient with a herpesviral corneal ulcer. Oral steroid treatment could lead this to perforate causing irreparable damage.[10]

> **Steroids decrease calcium absorption in the GI tract while increasing osteoclast activity to break down bone. This is another reason the dosage and length of steroid treatment should be kept to as little and short as possible.**

Skin, skeletal and muscle. Skin thinning and bruising can occur with steroid treatments. Glucocorticoid induced myopathy can also occur, leading to muscle weakness and fatigue.[7] Osteoporosis is a common side effect of systemic steroids that also increases a patient's risk for bone breakage. Steroids decrease calcium absorption in the GI tract while increasing osteoclast activity to break down bone.[12] This is another reason the dosage and length of steroid treatment should be kept to as little and short as possible.

Patients at higher risk of these effects due to fragility or elderly status should be monitored more closely for osteoporosis or treated prophylactically. OTC calcium and vitamin D supplementation should be recommended to anyone at risk or anyone who will likely require steroid treatment lasting three months or longer. For these patients, calcium intake should be 1000mg to 1200mg/day and vitamin D intake should be 600 IU to 800 IU per day.[13]

Immune system. While a patient is undergoing oral steroid treatment, their immune system activity is reduced. Hence, any new infection or injury may result in serious consequences. Quick antimicrobial therapy is important during this time to prevent any opportunistic infection from causing further issues with the patient's health.[11] Wound healing is also impaired, so close monitoring is especially required for patients with diabetes, cancer, those who are elderly or those on other immunosuppressive medications.[7]

Contraindications to Steroid Use

Peptic ulcer disease, tuberculosis, active infections and psychosis are all contraindications to the prescribing of oral corticosteroids.[6] Patients need to be screened for symptoms of psychosis, which may include a history of depression, delirium, hallucination, confusion or distress.[7] Steroids are also contraindicated during pregnancy.[6] Children should be prescribed steroids with caution due to inhibition of growth with steroid medications.[12]

Corticosteroids may also cause interactions with other medications the patient may be taking, and it will be important to review their current medications prior to prescribing. Caution is advised with nonsteroidal anti-inflammatory agents or anticoagulants, which may need prophylaxis to avoid gastroduodenal toxicity.[7]

While not a contraindication, patients with comorbidities—including diabetes mellitus, poorly controlled hypertension, significant cardiovascular issues (*i.e.*, atherosclerotic disease and arrythmias), cataracts, glaucoma, peptic ulcer disease and osteoporosis should be prescribed steroids judiciously.[7] It is wise to consult with the patient's primary care provider or internist when considering oral steroid therapy for these individuals.

Conclusion

Oral steroids offer patients multiple advantages, such as the ease of administration and potential ability of the drug to calm whole-eye inflammation.[2] Yet, the potential for systemic side effects can make prescribing oral steroids daunting. To help reduce incidence of these adverse events, the dosage for systemic oral steroids should be tailored to each individual patient, prescribing the lowest dosage that delivers control of the inflammatory event.

Always remember to recommend preventive ulcer medications and calcium supplements for long-term steroid use. Understanding the mechanism of action of oral steroids, the most common uses in eye care and the side effects/contraindications to oral steroids makes prescribing them when indicated much less intimidating. ■

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PRESBYOPIA DRUGS: A DROP IN THE BUCKET?

With one med available and others coming soon, patients have more options than ever for near vision correction. Do they offer enough to make a difference in a well-established market?

BY RACHEL RITA
ASSOCIATE EDITOR

A broader range of product choices is becoming available to consumers across all facets of life, and optometry is certainly no exception. New technologies and treatments in eye care are developed every year, and 2023 may be the annus mirabilis for developments in presbyopia management.

Current presbyopia correction strategies already have a whole gamut of options for patients and eyecare providers to choose from, as corrective lenses in one form or another have always done the job well enough.[1] We're still in the very early days of pharmaceutical options for near vision correction but the category is set to blossom soon, with newer options offering different active ingredients and mechanisms of action. Let's review several agents in the pipeline that may work their way to the public in the near future.

The Trailblazer

Vuity, approved in late 2021, has made its mark as the sole pharmaceutical agent available to the public as a form to treat presbyopia.[2] How has the drop worked for patients since its approval and how does it fare in terms of efficacy?

Produced by Allergan (now a part of AbbVie), Vuity's active ingredient is a pilocarpine hydrochloride ophthalmic solution at 1.25% concentration.[3] While pilocarpine has decades of familiarity to eye doctors as a now-outdated therapy for glaucoma, what makes Vuity different is Allergan's use of a pH buffer (Allergan calls it pHast) that rapidly adjusts to the ocular surface pH and increases the drug's bioavailability.[4]

Bisant Labib, OD, a professor and associate dean of optometric special programs at The Eye Institute at Salus University, reminds us how pilocarpine works on the eye in order to contextualize Vuity. "The action would stimulate parasympathomimetic effects, acting on those receptors of the ciliary body and iris sphincter, causing some degree of miosis to increase clarity up close." This type of parasympathomimetic action on the eye creates a pinhole effect, allowing the decreased size of the pupil to achieve greater depth of focus and subsequently improving a patient's near visual acuity.

As with any product to be the first of its kind, it's not without shortcomings. The most notable include the duration of effect, potential side effects and cost. Allergan states that its drops are to be administered once daily in the morning. But with only about a six-hour duration—many anecdotal reports describe briefer periods—the effect can wear off and become inconvenient for users who are doing more throughout the day.[3]

Mile Brujic, OD, a partner of Premier Vision Group in Northwest Ohio, notes that, in his practice, he's seen anywhere from four to 10 hours of effectivity, depending on the

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Dr. Milton Hom: Allergan/AbbVie, Bausch Health, Novartis, Sun Pharma, Kala Pharma, Tarsus Pharma, Hovione Scientia, Silk-Tech, Sydnexis, Topcon, Eyenovia Bio, Laboratories Thea, Aurinia Pharma, Eyevance Pharma, Surface Pharma, Nevakar, Visus Therapeutics, Aperta Biosciences, Astareal, Azura Ophthalmics, Aldeyra Therapeutics, FAMY Group, Bruder Health, Kowa, Ocuphire.

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patient. Milton Hom, OD, of Azusa, CA echoes that sentiment, advising that you have to pick the right patients for this type of drop. He emphasizes that patients should have distance vision corrected to make the drops work more effectively. Dr. Brujic cites success not only with emmetropic presbyopes, but also with contact lens wearers who became presbyopic, multifocal users, uncorrected low myopes and uncorrected low astigmatism patients.

Another detriment to success is the potential side effects. While the most commonly occurring ones (>5%) are headache and eye redness, more troubling ones can occur. Dr. Hom highlights that because pilocarpine causes the ciliary muscles to contract, patients also complain of brow ache, as this mechanism can cause the brow to contract, too. Ciliary contraction is the same mechanism that can contribute to the rarer but much more serious side effect of vitreoretinal problems such as retinal detachment. A few such cases have been reported in patients using Vuity.

While inadequate duration of effect and potential side effects may not negatively affect every patient, price is a more pervasive stumbling block. At $79 for a one-month supply, the therapy is an investment, especially since it's an out-of-pocket expense to patients.[5]

Dr. Brujic believes the impact of price is relative. "I think it totally depends on the patient, what the expectations are and what they're interested in paying for it," he says. "At the current dosing, you're really looking at Vuity being essentially $2.50 per use. That's what it really boils down to. Some people would say, 'No, that's not worth it to me.' Other people say, 'Yeah, it's more than worth it.'"

Chris Wroten, OD, a partner at the Bond-Wroten Eye Clinics in Louisiana, has seen some patients embrace Vuity at launch, but didn't see a significant increase in prescription fill rate even when the manufacturer temporarily cut the price per bottle in half. As he puts it, "Those who like it have filled it, but for others, it would appear that cost may not have been the only barrier to adoption. We all know there's a certain percentage of patients who don't like taking eye drops in general, so perhaps that is another barrier."

Photo: Getty Images

Dr. Hom notes that use of an eye drop for presbyopia may be worth the out-of-pocket cost for some if they don't use it regularly but rather only in certain social or recreational occasions.

A slew of next-generation products are hoping to leap these hurdles. Let's review what's being proposed.

Dynamic Duo

Some investigational presbyopia therapies use two active ingredients in hopes of overcoming the limitations of pilocarpine alone. Brimochol, currently in development by Visus Therapeutics, doesn't use pilocarpine at all. Instead, its active ingredients are carbachol, a cholinergic agent, and brimonidine tartrate, an alpha-2 agonist. The two active agents are supposed to complement each other in their effects.

"They're making the pupil constrict as well as blocking the pupil dilator," explains Dr. Hom. Dr. Brujic goes into more detail, outlining how brimonidine reduces pupils dilation by reducing the effect of the dilator muscle while carbachol acts on the sphincter muscles. As a result, "they seem to be having this long-lasting effect with a single dose."

Like Vuity, Brimochol is supposed to be administered once daily, and Visus claims its product will work for a minimum of eight hours.[6] The drug is currently in Phase III clinical trials with two underway: BRIO-I and BRIO-II.[7]

The company's Phase II VIVID study documented a minimum of 83% of subjects achieving the three-line endpoint of improvement in binocular near visual acuity under mesopic conditions, while one line of distance vision was not lost after one hour. The same endpoint was met in a minimum of 82%, 52% and 35% of subjects after three, seven and nine hours, respectively.[8]

The most common side effects or adverse events (>5%) were similar to those of Vuity. These included headache and brow ache, as well as temporary burning or stinging upon drop instillation.[8]

TABLE 1. MIOTIC AGENTS FOR PRESBYOPIA DROP TREATMENT

Manufacturer	Product (brand name)	Active Ingredient(s)	How Often Used	Duration of Effect	Side Effects
Allergan	Vuity	Pilocarpine hydrochloride 1.25%	Once daily	Up to 6 hours	Headache (mostly mild), eye redness, retinal detachment (rare)
Visus Therapeutics	Brimochol	Carbachol and brimonidine tartrate	Once daily	Minimum of 8 hours	Headache, brow ache, burning/stinging upon instillation
Orasis Pharmaceuticals	CSF-1	Pilocarpine hydrochloride 0.4%	Twice daily	Up to 8 hours post-dose 1	Headache, instillation site pain
Eyenovia	MicroLine	Pilocarpine hydrochloride 2%; administered with Optojet microdose dispenser		3 to 4 hours	Mild or transient
Ocuphire	Nyxol	0.75% phentolamine OR Nyxol (phentolamine) with low-dose (0.4%) pilocarpine	Once daily	NA	Eye redness
Lenz Therapeutics	PRX-100	Aceclidine OR aceclidine with brimonidine tartrate	Once daily	Up to 10 hours	Mild

Also like Vuity, carbachol likely acts in a way similar to pilocarpine through causing a degree of miosis, increasing near clarity, Dr. Labib notes.

Less is More

Other companies are taking a different approach to improve efficacy, opting for a lower strength pilo but more frequent instillation rather than doubling down on active ingredients. That's the plan for CSF-1, a low-dose pilocarpine drop being developed by Orasis Pharmaceuticals. Unlike Vuity's once-daily dosing, this version of pilocarpine was administered twice daily in its Phase III clinical trials, NEAR-1 and NEAR-2.

At only 0.4% concentration (about one-third that of Vuity), the drops displayed good efficacy in the trials. Across both studies, 40% and 50% of participants demonstrated a three-line or more gain with no loss of one line or more in distance visual acuity one hour after the first dose and one hour after the second dose.[9] At day 15, this improvement occurred as early as 20 minutes and up to eight hours after the first dose.[9]

Adverse events included headache in 6.8% of participants and instillation site pain in 5.8%. Moderate adverse events were present in 2.6%.[9]

Understandably, the lesser adverse events are likely due to the decreased concentration of active ingredient used to achieve the same effect. As Dr. Hom explains, "When you reduce the concentration down, what you're doing is reducing the risk of adverse events. What you want to do is achieve efficacy. But on the flip side of that, you want to use the lowest dose possible, because the higher dose will give you higher efficacy, but will also introduce more adverse events. So, you want to get the minimum dose you possibly can get and achieve efficacy."

This thought process seems to be working for Orasis, as the company announced in February that the FDA accepted its New Drug Application for review. The agency has assigned a Prescription Drug User Fee Act goal date of October 22 of this year.[10]

Presbyopia Spray

Much different from any of the other options, at least in terms of drug delivery method, Eyenovia's MicroLine solution is meant to be dispensed through an aerosol dispenser it calls Optojet.[11] Essentially making the liquid spray into the eye, this delivery method of pilocarpine offers better efficacy because of the administration type, its developers claim.

"It sprays into the eye, and it does it through a screen, so it has very small particles, making it like a mist," Dr. Hom elucidates. "A regular drop will deliver so many milliliters or microliters of the drug, but this spray will imprint the cornea with a much smaller amount, so you get better penetration. That's the reason why they can administer a lower concentration. He also mentions that the lower dosage additionally should lead to fewer adverse events.

Dr. Brujic brings up the point that this delivery system offers a solution for those who might have problems administering regular eye drops, making it more usable for some.

Eyenovia has released results from its Phase III clinical trial, VISION-2, about MicroLine's efficacy. A 2% pilocarpine "micro-array print formulation," as it's called, was used and met its primary endpoint, the company says. The micro-array is a tool allowing for cells, proteins, DNA or polymers to be printed in complex patterns at high speeds.[12] This approach allowed patients to achieve a 15-letter or more improvement of near visual acuity with less than a five-letter loss in distance acuity in low light conditions two hours post-administration.[13]

Adverse events were reportedly low, with fewer than 3% of patients experiencing mild or transient symptoms, possibly because the way the device works.[13]

Something Old, Something New

Combining pilocarpine with a novel agent is a further treatment possibility. Ocuphire's Nyxol is another product with a unique active ingredient: 0.75% phentolamine ophthalmic solution. The company's Phase II VEGA-1 trial tested both options of Nyxol with low-dose pilocarpine (0.4%) and Nyxol alone.[14]

For the group that was administered both phentolamine and low-dose pilo, 61% improved greater than three lines in near vision after one hour, compared to the placebo at 28%. This group also met the standard of less than five letters of distance vision loss.[15]

Since phentolamine is an alpha-adrenergic antagonist, it prevents or reverses pupil dilation, explains Dr. Brujic. He further explains that "it doesn't necessarily work directly on the sphincter." In addition to using the phentolamine, the additional low-dose pilocarpine allows the lower dose of pilocarpine to act with the alpha-adrenergic antagonist, resulting in complementary effects.

The Nyxol plus pilocarpine solution displayed full efficacy by 30 minutes and extended near vision improvement for at least six hours in the VEGA I trial. Some subjects even experienced a sustained reduction in pupil diameter over at least 18 hours.[15]

Unlike with many other presbyopia drops, no instances of headache, brow ache or blurry vision were reported in the VEGA-1 trial. However, there was mild and transient eye redness observed in less than 5% of participants.[15]

In a recent developmental milestone, Ocuphire announced in January that a first patient has been enrolled for the Phase III trial, VEGA-2.[16]

Photo: Getty images

The availability of presbyopia eyedrops allows even patients who rely on progressive lenses to occassionally get a boost in near vision if desired.

Killer Combo

There's no shortage of new agents being tested as alternatives to pilocarpine. One final presbyopia drug in the near-term pipeline that fits this description is PRX-100. Currently being developed by Lenz Therapeutics, this drop's active ingredient is aceclidine, a cholinergic agonist. This agent acts similarly to other agents that are cholinergic agonists but, interestingly, aceclidine seems to be more specific to just activating just the sphincter muscle with less activation of the ciliary muscle, Dr. Brujic points out.

He continues that there "apparently isn't a lot of activity in the area of the ciliary muscle, making it so the muscles aren't active. As such, it doesn't have that level or that layer of cross-reactivity that we would expect to see with the other cholinergic agonists." He does make sure to point out that there is a question surrounding this mechanism. That is: is there an additional level of safety conferred when ciliary muscles are left inactivated?

With this type of agent, Lenz was able to advance PRX-100 past Phase II. A clinical trial named INSIGHT included two formulations; LNZ100 (aceclidine) and LNZ101 (aceclidine + brimonidine). Both test formulas of the drug achieved a three-line or greater improvement of near visual acuity without loss of one or more distance visual acuity lines at one hour. LNZ100 experienced this result in 71% of patients and LNZ101 in 56%.[17]

Both groups maintained this result at the 10-hour mark, displayed at a rate of 37% in the LNZ100 group and 48% in LNZ101. Related to this result was the observed average pupil size staying within the range of 1.5mm to 2mm for the extent of the 10 hours.[17]

Lenz reported only low rates of mostly mild adverse events. With all these data, Phase III trials are to begin soon.

Where They Stand

After getting a sense of how each drop differs from the others, as well

Photo: Getty Images

With near vision tasks more prominent these days, given the ubiquity of digital device use, more patients will be amenable to hearing about new options that can improve their lives.

as their similarities, let's consider how they might stack up outside of clinical trials and hard data points. With only one approved agent thus far, much of the sentiment is necessarily speculative at this point. But one good indication is how likely doctors are to prescribe or recommend these drops in their own practice, and why.

Dr. Labib believes presbyopia drops in general are better suited for people who are not doing near work all the time. "I don't think that drop use is going to be the same as throwing on a pair of glasses that's tailor made for you and lasts longer than six to eight hours. But if you're just trying to get by and have some clarity at near, as well as distance, like if you're a basketball coach or hairdresser who isn't looking up close all the time, it's going to be very different." Ultimately, though, she believes the decision is going to come from the patient's desire, lifestyle, amount of near work and how much extra near focus they'll need.

She also considers age a factor to bear in mind if she were to prescribe any presbyopia drops, advising it may help more for younger presbyopes. The well-known and largely inevitable process of lens thickening with age makes the structure less prone to change shape and subsequently raises the bar for the drops to provide the same effectivity in more advanced presbyopia. As such, medical therapies may be a more useful treatment option only in emerging presbyopes.

Dr. Wroten comments on what patient personality might find drops appealing, as well as who might have the ideal ocular status. "Certainly, it's got to be someone who doesn't mind putting a drop in their eye every day. At least with pilocarpine-based drops, patients need to be aware of the potential for a slight headache, at least initially, as well as possibly a slight darkening of their vision. If they are aware of those side effects, which may be temporary, and can get past those, it seems to be most readily adopted in our patient base by those who reach presbyopia without requiring much correction for distance vision. That has been the sweet spot so far in our practice, but I look forward to trying the other presbyopia drops in the pipeline."

He warns that some patients should be excluded from using presbyopia therapies, such as high myopes, because of the potential impact the active ingredients may have on the retina.

Dr. Brujic similarly points out that patient selection is "so dependent upon the individual's wants, what they're looking for and also what their current prescription is, because sometimes people just aren't candidates for drops based on their prescription." But for those who are a better fit, he sees no problem in prescribing the drops.

Dr. Hom believes the pharmaceutical therapies for presbyopia can be used in combination with other treatments, making it a flexible option for patients rather than a rigid all-or-nothing choice. "There's no reason why you have to use it all the time. You can use it part time with whatever else you're using. If you want to use them before putting on contact lenses or use them to do computer work, then they definitely work as an option."

Worth the Cost?

If the going rate is $79 a bottle per month and supposing the newer therapies are priced comparably (actual prices have not been disclosed yet), this is a significant price to pay for the average person looking to manage presbyopia, potentially for several years, depending on the viability of the option for their eyes. All doctors have different, unique takes on whether the somewhat steep price is worth it to customers, but they agree on one point: as more presbyopia drops become approved and available to the public, competition should drive prices down.

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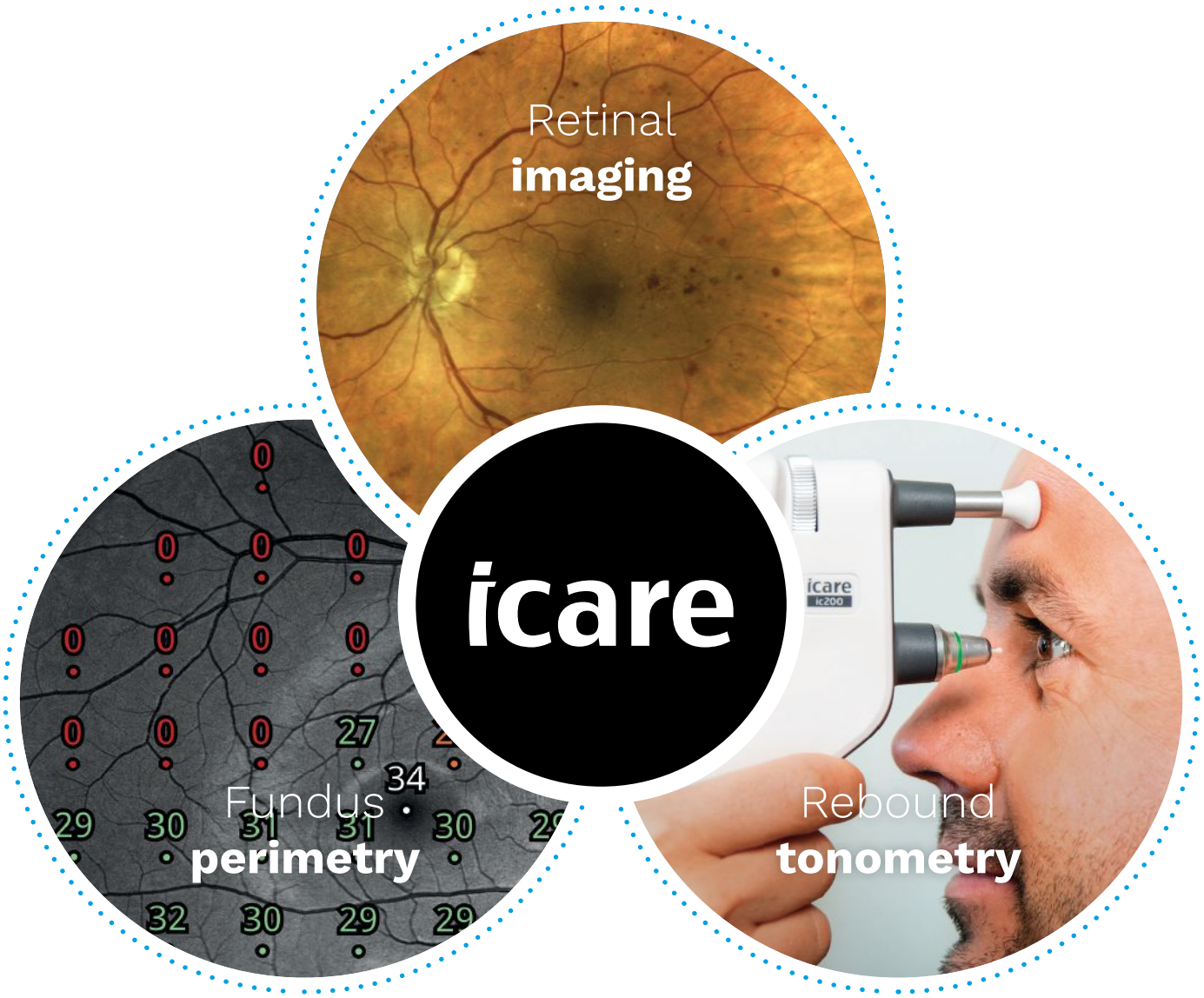

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"I think it's still finding its place in the market and will be adopted by a subset of eligible presbyopes desiring independence from contact lenses and glasses, but for our colleagues concerned with losing a significant percentage of optical sales, I don't foresee that happening," Dr. Wroten says. "I think this gives our patients additional options, which is always a good thing, and can be additive with existing options."

> **I hope we start getting to the root cause: lens inelasticity. The current drops are increasing depth of focus through reduced blur circles, but it's not functionally making the lens do anything differently.**

Dr. Labib has a different perspective, thinking that the drops target exactly who they're supposed to: a regular contact lens wearer who doesn't want to wear glasses at all. "I feel like they're targeting the right people—the people who don't want to wear glasses are the ones who are shelling out the money for multifocal lenses, so they would probably be the same people who would be amenable to spending money on an eye drop."

Dr. Hom points out it may be worth the cost for some if they don't use it regularly, but instead opt for using the drops in certain social or recreational occasions.

The general consensus from all doctors was that the cost will be worth it to some patients and others not. It really depends on the patient's expectations and what they value in a treatment.

On the Horizon

What does the future of presbyopia drops look like? These doctors offer insight that establishes where drops started and where they might go.

Dr. Wroten looks ahead to the future of drops, hopeful to see potential alternative drug delivery options, like an extended-release option that could be incorporated into a drug-eluting contact lens, extending efficacy and eliminating the need to instill eye drops. If the patient did require distance correcting contacts, this could allow them to stay in a monofocal design. "Getting the effect of the medication without having to put a drop in could certainly be very attractive to patients," he posits. Another extended-release option could be a punctal plug delivery system that also bypasses the need for drop instillation.

Dr. Brujic takes a similar approach to looking at alternative technologies, but not specifically for how to improve presbyopia drop administration. Instead, he hopes "we get to a place where we're exploring alternative mechanisms other than reducing pupil size. I hope we start getting to the root cause, which is lens inelasticity. The current drops are increasing depth of focus through reduced blur circles, but it's not functionally making the lens do anything differently. The lens is still inactive. We're just strategically providing a different way to provide more functionality to presbyopes."

This may be the case as presbyopia drops become more and more mainstream. Dr. Hom mentions that he was recently reading Walter Isaacson's biography of Steve Jobs and a quote stuck out to him that he thinks applies to the state of presbyopia drops. Originally said by hockey legend Wayne Gretzky and often quoted by Steve Jobs during his life, a forward-thinking person should "skate to where the puck is going, not where it's been." Dr. Hom believes optometry must heed that advice, too. ■

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OCULAR SIDE EFFECTS OF NEW CANCER AGENTS

Understanding how molecularly targeted chemotherapeutic agents can impact patients is key for primary eyecare providers.

BY JULIA CANESTRARO, OD
NEW YORK CITY

The Centers for Disease Control and Prevention reported approximately 1.7 million new invasive cancer cases in the United States in 2019.[1] As primary eyecare providers, we will encounter patients undergoing cancer treatment who may have ocular sequelae as a result.

Traditional chemotherapeutic agents can cause a variety of side effects that may affect all ocular tissue ranging from dry eye to optic neuropathy. However, the face of cancer treatment is shifting toward specialized treatment, targeting specific pathways for certain types of cancers, and with this shift comes a range of different ocular toxicities. And so, primary eyecare providers need to be familiar with newer cancer drugs and the possible ocular sequelae of these agents.

In this article, we will discuss molecularly targeted agents and the ones most likely to cause ocular toxicity. This is not an exhaustive list but offers optometrists insight into some of the most common agents they may see in their clinical practice and how to provide comprehensive care to their patients.

Introduction to Grading Ocular Toxicity

Ocular toxicity is graded using the Common Terminology in Cancer Adverse Events (CTCAE v5.0) grading scale.[2] The grading scale was created to allow for common labelling and grading of drug toxicity in various parts of the body. Specifically for the eye, it provides guidelines for grading various eye disorders such as blurred vision, dry eye, keratitis, uveitis and retinopathy, to name a few, and allows for accurate reporting of side effects. This grading scale should be used as a reference when grading ocular toxicity and can be easily found online (*Table 1*). It is worth mentioning that some drug companies manufacturing antibody drug conjugates (*i.e.*, Elahere) have created their own keratopathy grading scale, and this can be used as a guideline instead.

Antibody Drug Conjugates (ADCs)

This increasingly used targeted cancer therapy is comprised of a tumor-specific monoclonal antibody with a potent anti-cancer agent through a chemical linker.[3] Targeted malignancies include ovarian cancer, cervical cancer, B-cell lymphoma, multiple myeloma, breast cancer, urothelial cancer and leukemia.[3] There are currently 11 FDA-approved ADCs including Kadcyla (ado-trastuzumab emtansine), Enhertu (fam-trastuzumab deruxtecan-nxki), Tivdak (tisotumab vedotin-tftv) and Elahere (mirvetuximab soravtansine-gynx). The other FDA-approved ADCs (which will not be discussed in this

About the author

Dr. Canestraro is an assistant attending optometrist at Memorial Sloan Kettering Cancer Center, Ophthalmic Oncology Service. She has experience in the diagnosis and non-surgical management of ocular disease, including ocular tumors. She also specializes in treating the ocular consequences of cancer and its treatments. She has no relevant financial interests to disclose.

TABLE 1. AN EXAMPLE OF HOW TO GRADE KERATITIS/KERATOPATHY USING THE CTCAE GRADING SCALE[2]

Eye Disorder Grading – Keratitis					
CTCAE Term	**Grade 1**	**Grade 2**	**Grade 3**	**Grade 4**	**Grade 5**
Keratitis	Asymptomatic; clinical or diagnostic observations only; intervention not indicated	Symptomatic; moderate decrease in visual acuity (best-corrected visual acuity 20/40 and better or 3 lines or less decreased vision from known baselline)	Symptomatic with marked decrease in visual acuity (best-corrected visual acuity worse than 20/40 or more than 3 lines of decreased vision form known baseline, up to 20/200); corneal ulcer; limiting self-care ADL	Perforation; best-corrected visual acuity of 20/200 or worse in the affected eye	–

Definition: A disorder characterized by inflammation of the cornea.

Navigational Note: Also consider corneal ulclers as an eye disorder.

article) are Mylotarg (gemtuzumab ozogamicin), Adcetris (brentuximab vedotin), Besponsa (inotuzumab ozogamicin), Poliyv (polatuzumab vedotin-piiq), Padcev (enfortuamb vedotin-ejfv), Trodelvy (sacituzumab govitecan-hziy) and Zynlonta (locastuximab tesirine-lpyl).

Toxicity. The incidence of corneal toxicity (often referred to as keratopathy) ranges from 11% to 37% in clinical trials, depending on the ADC.[4,5] In clinical trials, 3.2% of patients on Tivdak developed severe ulcerative keratitis and 40% experienced conjunctival adverse reactions, including conjunctivitis, conjunctival abrasion and conjunctival hyperemia.[6] Elahere caused uveitis in 1% of patients.[5]

Microcyst-like epithelial changes (MECs) develop in the epithelial layer of the cornea. These spherical "cysts" do not stain with fluorescein dye and are best visualized with a parallelopiped slit lamp beam or indirect illumination (*Figure 1*). Ocular dryness with resulting corneal staining and refractive error changes can occur. Hyperopic shifts are seen in early treatment while myopic changes are more common in later treatment.[3] The resulting decreased vision from corneal staining and refractive shifts generally reverses with cessation of the drug. The mechanism for what causes corneal MECs is still not fully understood, but the most recent literature suggests that the ADC enters the corneal epithelial cells, the cells become apoptotic (observed as MECs) and these cells are eventually shed and replaced by new epithelial cells.[7]

Treatment and management. There is no treatment for MECs, and they are often observed if there is no change in vision. If and when the cancer treatment is discontinued, the MECs will resolve within weeks to months. Treatment of concomitant dry eye includes preservative-free artificial tears at least three times a day and cyclosporine ophthalmic solution

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- Recognize the potential ocular side effects of targeted cancer therapies.
- Monitor patients on these drugs for potential ocular adverse events.
- Comanage these patients with specialists when needed.
- Educate their patients on how these medications may impact their eye health.

Target Audience: This activity is intended for optometrists engaged in cancer patient management.

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Credit Statement: This course is COPE-approved for two hours of CE credit. Activity #125569 and course ID 83324-PH. Check with your local state licensing board to see if this counts toward your CE requirement for relicensure.

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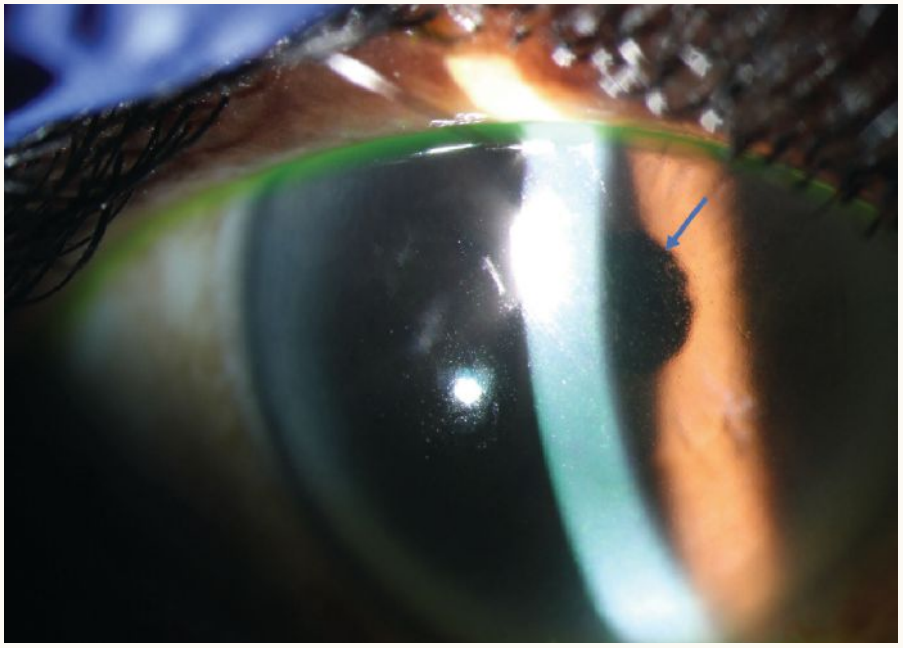

Fig. 1. Corneal MECs (blue arrow) in a patient with ADC-related keratopathy.

or emulsion, or lifitegrast ophthalmic solution, if needed. Treating concomitant blepharitis with lid hygiene and/or warm compresses is also recommended. Treatment of uveitis or conjunctivitis includes corticosteroid drops. The use of contact lenses is restricted in these patients, as there is a concern for the drug sitting in the tear film and therefore absorbing into the contact lens and exacerbating keratopathy, although this has not been formally studied to date. If vision is severely impacted with/without moderate to severe keratopathy, the drug may be held or given at a lower dose, as deemed by the oncologist.

A baseline eye exam is critical to ensure the cornea is healthy and to make note of any other ocular pathology. Patients should be educated thoroughly on possible ocular side effects, including blurred vision and dry eye, prior to starting treatment so they can expect the changes that may come. It is worth mentioning that these changes to the cornea are generally reversible and rarely cause permanent changes in vision.

Both Tivdak and Elahere have an FDA black box warning and therefore require ocular toxicity monitoring at baseline and prior to each dose for Tivdak and every other cycle for the first eight cycles for Elahere. Patients on Tivdak are required to instill vasoconstricting eye drops the day of infusion and corticosteroid drops on days zero through four of each treatment cycle.[6] Patients on Elahere are required to use corticosteroid drops before day one and through day eight of each treatment cycle.[5] Results of the eye examination, including ocular toxicity grading, must be reported to the oncologist each visit (particularly for Elahere and Tivdak), as they determine whether the patient should proceed with treatment and may also impact dosing. Comanagement with ophthalmology may be needed for cases of severe keratopathy or corneal ulceration.

BRAF Inhibitors

These agents are approved for the treatment of BRAF v600E mutant melanoma.[8] The mitogen-activated protein kinase (MAPK) signaling pathway regulates the proliferation of melanoma cells, and these drugs target BRAF kinase, which interferes with this MAPK pathway.[8] BRAF inhibitors are now often prescribed in combination with MEK inhibitors, thereby increasing the probability of ocular toxicity. Examples of FDA-approved BRAF inhibitors include Zelboraf (vemurafenib), Tafinlar and Rafinlar (dabrafenib) and Braftovi (encorafenib).

Toxicity. The most common ocular toxicities are dry eye/conjunctivitis, which occurred in approximately 2% of patients, and uveitis (ranging from anterior to posterior), which was observed in 4% to 9% of patients receiving Zelboraf.[9,10] This agent may also cause cutaneous squamous cell carcinoma, verruca vulgaris lesions and keratoacanthoma, which can be found on the eyelid (*Figure 2*).

Treatment and management. Dry eye symptoms from BRAF inhibitors are generally mild and often do not require intervention or can be managed with artificial tears. Depending on the location of the uveitis, it can be treated with topical, periocular or intraocular corticosteroids, in addition to cessation, paused or continued drug therapy (at the same or a lower dose). Braftovi's label specifies it should be withheld for a grade 1 or 2 uveitis that does not respond to ocular treatment, or for any grade 3 uveitis.

Squamoproliferative lesions (particularly squamous cell carcinoma) should be referred for surgical excision, and patients are often able to continue drug therapy. Braftovi's label specifies that ophthalmologic evaluation should be performed at regular intervals and for any new or worsening disturbances. Clinically or visually significant findings, including ocular toxicity grading, must be reported to the oncologist as they may impact dosing and treatment, and comanagement with ophthalmology may be needed.

EGFR Inhibitors

Epidermal growth factor receptor (EGFR) is a glycoprotein that is abnormally activated in a variety of can-

cers, leading to cellular proliferation, differentiation and survival.[12] EGFR inhibitors are used to target EGFR and treat metastatic colorectal cancer, head and neck cancer, non-small cell lung cancer, pancreatic cancer and some types of breast cancer. Current FDA-approved EGFR inhibitors include Erbitux (cetuximab), Vectibix (panitumumab) and Rybrevant (amivantamab). Examples of small molecule EGFR inhibitors are Tarceva (erlotinib), Iressa (gefitinib) and Exkivity (mobocertinib).

Toxicity. Dry eye is a common side effect of these drugs, due to poor healing of the corneal epithelium, and can lead to persistent epithelial defects.[13] Other anterior segment findings include conjunctivitis, blepharitis and, very rarely, corneal thinning/melt.[13] There are rare cases of anterior uveitis reported with Tarceva. All drugs in this class have been associated with hypertrichosis and trichomegaly, which in some case have caused corneal ulceration due to eyelashes misdirected at the cornea.[14] *Figure 3* demonstrates both blepharitis and trichomegaly in a patient treated with an EGFR inhibitor.

Treatment and management. Dry eye can be managed with lubricating drops and cyclosporine ophthalmic solution or emulsion, or lifitegrast ophthalmic solution, if needed. Blepharitis can be managed with lid hygiene, warm compresses and steroid/antibiotic ointments.[13] These patients should be monitored routinely, particularly if symptoms develop. There is no set interval as indicated by the pharmaceutical companies for ocular toxicity monitoring of these drugs. Clinically or visually significant findings, including ocular toxicity grading, must be reported to the oncologist as they may impact dosing and treatment.

FGFR Inhibitors

Fibroblast growth factor receptor (FGFR) inhibition interferes with the MAPK signaling pathway, and the retina expresses targets of this pathway, thereby causing retinal toxicity.[15] These drugs treat cancers such as FGFR-mutated urothelial cancer and cholangiocarcinoma. FDA-approved agents include Balversa (erdafitinib), Pemazyre (pemigatinib) and Truseltiq (infigratinib).

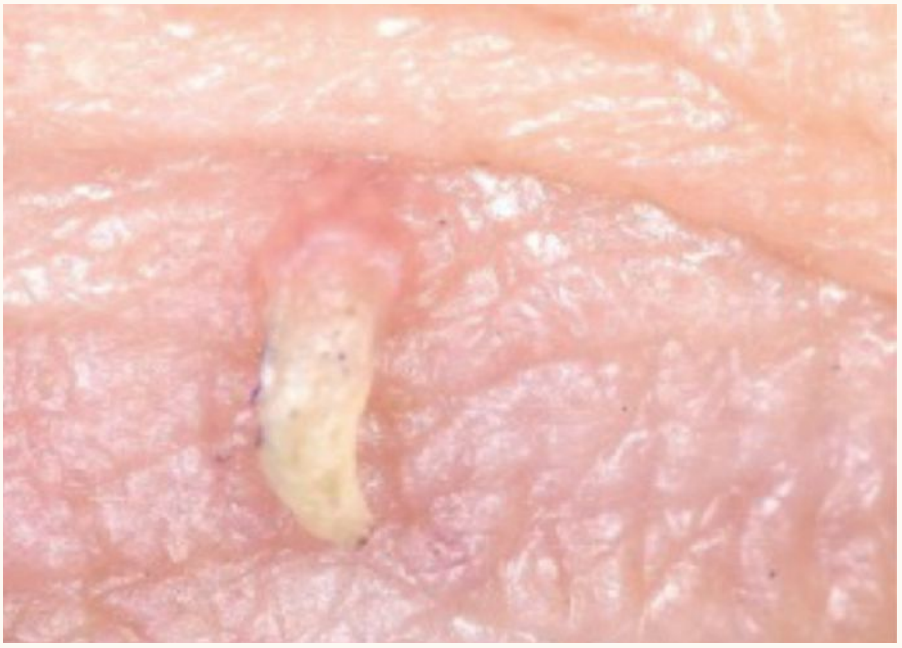

Fig. 2. Eyelid verruca in a patient treated with a BRAF Inhibitor.[10]

Toxicity. Patients may develop serous retinopathy and have similar characteristics to MEK inhibitor-associated retinopathy. OCT reveals fluid between the interdigitation zone and retinal pigment epithelium in varying configurations. Dry eye and trichomegaly are also reported side effects of these drugs.[14]

Treatment and management. Patients taking Balversa should stop treatment if serous retinopathy occurs. It may be restarted if the fluid resolves within four weeks; otherwise the drug should be discontinued. It should also be discontinued in the scenario of grade 4 ocular toxicity.

Patients taking Pemazyre can be monitored on the drug if they are asymptomatic and if retinopathy is stable. If they are symptomatic or their retinopathy worsens, the agent should be held and re-examined. The patient may only resume the drug if symptoms and retinopathy improve.

Patients taking Truseltiq may continue at the same dose if retinopathy occurs; however, if it does not resolve within two weeks, the drug should be held until resolution of fluid. It can then be restarted at the same or a lower dose.

Patients on Balversa should be examined monthly during the first four months of treatment, then every three months thereafter. Patients taking Pemazyre should be examined at baseline, every two months for the first six months of treatment and then every three months thereafter. Patients taking Truseltiq should be monitored at baseline and then one month, three months and every three months thereafter during treatment.

All patients should be seen urgently for any visual symptoms, and examination should include visual acuity testing, slit lamp evaluation and OCT imaging. Clinically or visually significant findings, including ocular toxicity grading, must be reported to the oncologist as they may impact dosing and treatment, and comanagement with ophthalmology may be needed.

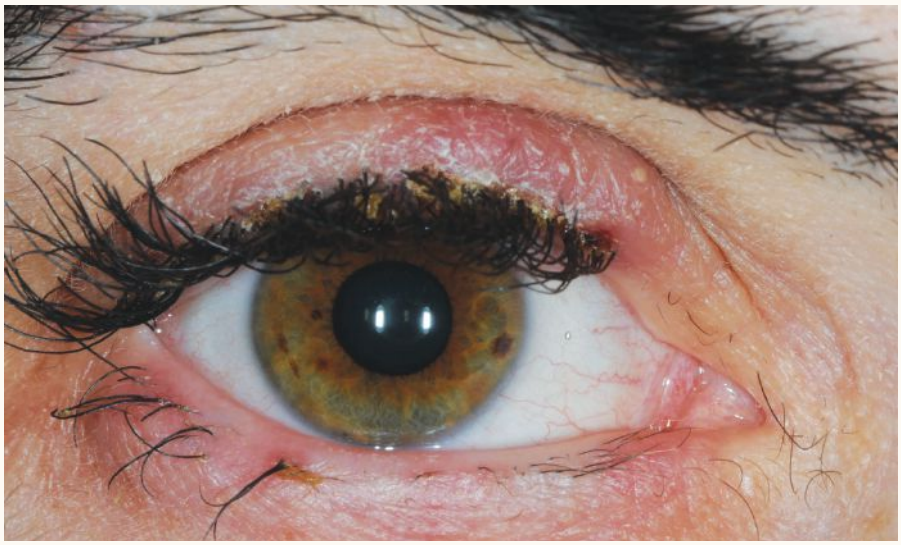

Fig. 3. Blepharitis and trichomegaly in a patient treated with an EGFR inhibitor.

Immune Checkpoint Inhibitors (ICI)

This anti-cancer therapy is now widely used to treat advanced cancers. There are three main classes of checkpoint inhibitors, which act by potentiating the immune system to attack cancer cells. The classes include cytotoxic T-lymphocyte-associated antigen-4 (CTLA-4), programmed cell death (PD-1) and programmed cell death protein 1 (PD-L1) inhibitors. They have been approved by the FDA to treat various types of cancers such as melanoma, non-small cell lung cancer, renal-cell carcinoma, urothelial carcinoma and Hodgkin's lymphoma.

By unleashing the immune system to attack cancer cells, ICIs can also cause an inflammatory reaction in healthy cells, thereby resulting in immune-related adverse events.[16] There are a number of FDA-approved ICIs, including Yervoy (ipilimumab), Imjudo (tremelimumab), Keytruda (pembrolizumab), Opdivo (nivolumab), Libtayo (cemiplimab), Tecentriq (atezolizumab), Bavencio (avelumab) and Imfinzi (durvalumab).

Toxicity. Ocular immune-related adverse events occur in about 1% of patients. Inflammation of any part of the eye is possible with ICI treatment. Potential adverse events include blepharitis, conjunctivitis, keratitis, uveitis (anterior or posterior), vitritis, retinitis, orbital myositis (Graves'-like ophthalmopathy), cranial neuritis and optic neuritis.[16]

Treatment and management. Treatment of anterior segment inflammation includes topical corticosteroid drops (*i.e.*, prednisolone acetate ophthalmic suspension four times per day in both eyes). Treatment of posterior segment inflammation (including optic neuritis) involves systemic steroid treatment with a slow taper (*i.e.*, treatment of a 60kg patient for optic neuritis may begin with 60mg prednisone PO for two weeks, then 40mg for two weeks, then decrease by 10mg for two weeks, then keep at 5mg or 2.5mg for two or four weeks, respectively). Taper is dependent on response to treatment and should be comanaged with the oncologist. If there is no improvement in ocular conditions, the drug should be discontinued. Before attributing the ocular condition to drug toxicity, other inflammatory/infectious etiologies should be ruled out with bloodwork, such as ESR, CRP, HSV1/2 titer, RF, QuantiFERON-TB, RPR, ANCA and Lyme, if applicable. Any case of orbital or optic nerve involvement should also have MRI imaging of the brain/orbits.

Patients who develop blurred vision, pain or redness should be seen promptly, including dilated fundus examination. Special attention to the anterior chamber and vitreous will help detect subtle inflammation. Clinically or visually significant findings, including ocular toxicity grading, must be reported to the oncologist as they may impact dosing and treatment, and comanagement with ophthalmology may be needed.

Mitogen-Activated Protein Kinase (MEK) Inhibitors

MEK inhibitors work by blocking the MAPK pathway, which is often

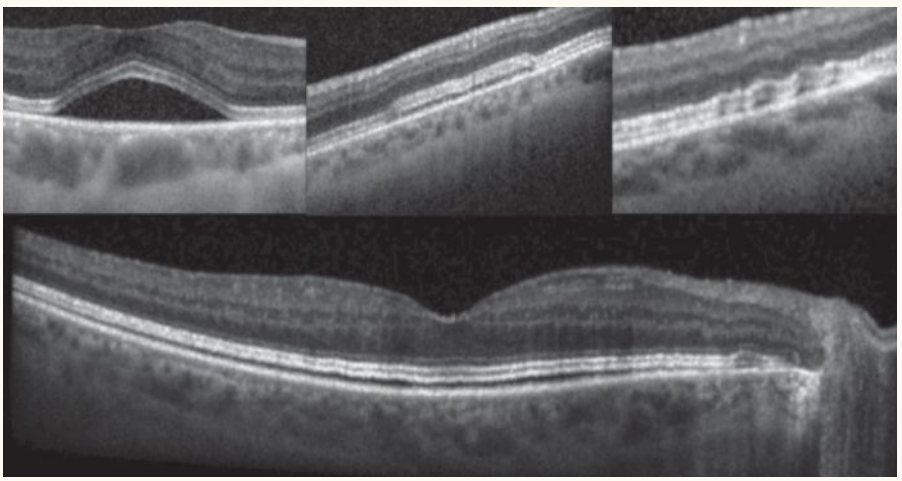

Fig. 4. OCT reveals fluid between the interdigitation zone and retinal pigment epithelium in varying configurations in patients with MEKAR.[16]

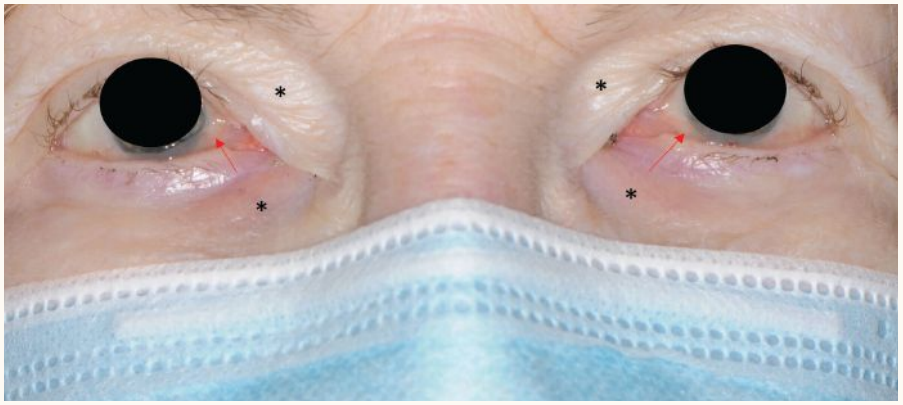

Fig. 5. Periorbital edema (black asterisks) and conjunctival chalasis (red arrows) in a patient on Gleevec.

dysregulated in human cancers. These drugs are used to treat BRAF v600E mutant melanoma, histiocytic neoplasms and neurofibromatosis type 1, and many MEK inhibitors are now used in combination with BRAF inhibitors for the treatment of certain cancers, increasing the probability of ocular toxicity. Examples of FDA-approved MEK inhibitors include Mekinist (trametinib), Cotellic (cobimetinib), Koselugo (selumetinib) and Mektovi (binimetinib).

Toxicity. MEK inhibitor-associated retinopathy (MEKAR) may occur within the first week of the first dose of MEK inhibitor therapy. This entity is characterized by bilateral, yellow-grey elevations of the retina, circular in configuration without inferior tracking.[17] OCT reveals fluid between the interdigitation zone and retinal pigment epithelium in varying configurations (*Figure 4*). Forty-eight percent of patients with MEKAR will complain of blurred vision and/or metamorphopsia or see a "bubble" in their vision.[17] Another potential ocular complication is retinal vein occlusion with an incidence of 0.2%, and predisposing risk factors include glaucoma, uncontrolled hypertension and diabetes mellitus.[14]

Treatment and management. In patients who present with MEKAR, it is our clinical experience that the fluid tends to resolve on its own without the need for intervention. However, the drug label instructions should be followed for ocular toxicity: withhold Mekinist and Cotellic in a patient with MEKAR, but the patient may resume the drug if fluid resolves within three to four weeks.[17] Patients taking Mektovi only need to pause the drug if they develop MEKAR and experience visual symptoms. In those patients who develop retinal vein occlusion, treatment may involve intravitreal anti-VEGF injection, and they will need to discontinue the drug.

Patients should be monitored regularly and be seen immediately if there is a change in vision. As with other types of agents, it is critical that clinically or visually significant findings, including ocular toxicity grading, must be reported to the oncologist as they may impact dosing and treatment, and comanagement with ophthalmology may be needed.

Selective Estrogen Receptor Modulators (SERMs)

This class of drugs blocks estrogen action by binding to estrogen receptors (ER), thereby treating cancers such as ER+ breast cancer or

TABLE 2. SUMMARY OF EACH DRUG CLASS AND THE LOCATION OF POTENTIAL OCULAR TOXICITY

Drug Class	Ocular Toxicity
Antibody Drug Conjugates	- Keratopathy - Dry eye - Conjunctival adverse reactions - Uveitis (only reported in Elahere)
BRAF Inhibitors	- Dry eye - Conjunctivitis - Uveitis - Squamoproliferative lesions
EGFR Inhibitors	- Dry eye - Conjunctivitis/blepharitis - Trichomegaly
FGFR Inhibitors	- Serous retinopathy - Dry eye - Trichomegaly
ICIs	- Inflammation of any part of the eye (and surrounding structures)
MEK Inhibitors	- Serous retinopathy - Retinal vein occlusion
SERMs	- Corneal deposits - Retinal deposits/macular edema
TKIs	- Periorbital edema - Conjunctivochalasis - Retinal hemorrhages (rare) - Cystoid macular edema (rare) - Optic nerve edema (rare)

metastatic breast cancer. Nolvadex or Soltamox (tamoxifen) and Fareston (toremifene) are examples of current FDA-approved SERMs.

Toxicity. Asymptomatic corneal deposits may occur in these patients, although the incidence is less than 0.7%.[18] This drug class may also cause irreversible refractile retinal deposits, more commonly as total cumulative doses reach 100g.[14] These retinal deposits may cause macular edema and affect vision.

Treatment and management. If corneal deposits are found, continuation of the drug is likely the safest option. However, there is no proven treatment for macular edema associated with tamoxifen, besides discontinuation of the drug. These patients should be monitored regularly and immediately if the patient experiences changes in vision. Clinically or visually significant findings, including ocular toxicity grading, must be reported to the oncologist as they may impact dosing and treatment.

Tyrosine Kinase Inhibitors (TKIs)

Tyrosine kinases phosphorylate amino acids on substrate enzymes, which go on to alter signal transduction pathways. Dysregulation of these pathways is found in many human cancers, and TKIs work by blocking these signals. While there are many TKIs currently on the market, the one most likely to cause ocular toxicity is Gleevec (imatinib). This agent is used to treat leukemia, myelodysplastic disease, hypereosinophilic syndrome, dermatofibrosarcoma protuberans and gastrointestinal stromal tumors.

Toxicity. Mild to moderate periorbital edema occurs in 47% of patients on Gleevec, in addition to conjunctivochalasis as seen in Figure 5.[14] This causes poor lid apposition, leading to epiphora. These patients also may experience spontaneous subconjunctival hemorrhages and, in rare cases, retinal hemorrhages, cystoid macular edema and optic nerve edema.

Treatment and management. Treatment of periorbital edema includes topical corticosteroid drops and, in some cases, oral diuretics.[19] Epiphora will improve with cessation of therapy. There is no known treatment for optic neuritis in these patients, and the drug will likely need to be discontinued. Patients should be monitored regularly and at the onset of visual symptoms. Clinically or visually significant findings, including ocular toxicity grading, must be reported to the oncologist, and comanagement with ophthalmology may be needed.

Summary

Our patients are on a variety of medications that we have been trained to learn about due to their potential impact on the eye. But as medicine changes, so too should optometry, as we are often the gatekeepers of the visual system.

Here are some helpful tips to ensure you are providing complete care for your patients:

1. Ask for a complete medical history, and if this includes a history of cancer, you should ask the name of the medication(s) the patient might be taking.

2. Google is your friend. It can be hard to remember the names and mechanisms of every new drug. Look up the drug name and class. For example, "Elahere drug class" search results will remind you that this is an antibody drug conjugate and therefore the place you need to check for ocular toxicity is the cornea.

3. If you forget to ask these questions upfront and see something new in the eye—for example, retinal vein occlusion, subretinal fluid, inflammation, etc.—be sure to ask about medications as you formulate your list of differentials because this may help you hone in on a cause for an ocular disorder.

4. *Table 2* is a good reference to help remember which parts of the eye may be affected in each drug class. ■

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OPTOMETRIC STUDY CENTER QUIZ

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1. Which ocular side effects can occur in patients taking ADCs?
a. Keratopathy/MECs.
b. Conjunctivitis.
c. Ulcerative keratitis.
d. All of the above.

2. MECs are found in which layer of the cornea?
a. Endothelium.
b. Stroma.
c. Descemet's membrane.
d. Epithelium.

3. The treatment for MECs that are not affecting vision is which of the following?
a. Discontinuation of drug.
b. Preservative-free artificial tears and observation.
c. Bandage contact lens.
d. Corneal debridement.

4. Ocular toxicity monitoring is required by the drug company for which of the following ADCs?
a. Kadcyla.
b. Enhertu.
c. Elahere and Tivdak.
d. None of the above.

5. Which is the most common ocular toxicity in patients taking BRAF inhibitors?
a. Uveitis.
b. Corneal deposits.
c. Refractive shifts.
d. Both b and c.

6. Patients taking BRAF inhibitors may develop which of the following eyelid lesions?
a. Verruca vulgaris.
b. Keratoacanthoma.
c. Squamous cell carcinoma.
d. All of the above.

7. Treatment of uveitis in patients taking BRAF inhibitors may include which of the following?
a. Corticosteroids.
b. Artificial tears.
c. Dose holds.
d. Both a and c.

8. EGFR inhibitors are associated with which of the following ocular toxicity?
a. Trichomegaly.
b. Blepharitis.
c. Uveitis.
d. Both a and b.

9. FGFR inhibitors can cause ocular toxicities similar to which other drug category?
a. EGFR inhibitors.
b. Immunotherapy.
c. MEK inhibitors.
d. ADCs.

10. Serous retinopathy in FGFR inhibitors is characterized by which of the following?
a. Pigment epithelial detachments.
b. Retinal hemorrhages.
c. Exudates.
d. Subretinal fluid.

11. Ophthalmic examination of patients on FGFR inhibitors should include which of the following?
a. Corneal topography.
b. OCT.
c. Gonioscopy.
d. Ultrasound.

12. Which ocular adverse events may occur in a patient on immunotherapy?
a. Uveitis.
b. Optic neuritis.
c. Choroiditis.
d. All of the above.

13. Treatment of intraocular inflammation related to uveitis may involve which?
a. Topical corticosteroids.
b. Topical cyclosporine.
c. Oral corticosteroids.
d. Both a and c.

14. MEK inhibitors may cause ocular toxicity characterized by which of the following?
a. Bilateral, yellow-grey elevations of the retina.
b. Circular elevations without inferior tracking.
c. Exudation.
d. Both a and b.

15. Aside from MEKAR, MEK inhibitors may also cause which of the following ocular toxicities?
a. Uveitis.
b. Subconjunctival hemorrhage.
c. Retinal vein occlusion.
d. Conjunctivitis.

16. Which are possible treatment options for MEKAR, depending on the specific drug?
a. Withhold drug and resume if fluid resolves within three to four weeks.
b. Intravitreal anti-VEGF injections.
c. Continue with drug unless visual symptoms occur.
d. Both a and c.

17. Which is the treatment for corneal deposits in an asymptomatic patient taking tamoxifen?
a. Observation.
b. Discontinue drug.
c. Corticosteroids.
d. Ocular hypotensives.

18. Which is the treatment for macular edema/retinal deposits in patients taking tamoxifen?
a. Intravitreal anti-VEGF injections.
b. Observation.
c. Topical corticosteroid drops.
d. Cessation of drug.

19. Which is the mechanism for epiphora in patients on TKIs?
a. Canalicular stenosis.
b. Poor lid apposition.
c. Subconjunctival hemorrhages.
d. Corneal abrasions.

20. Which is the treatment for periorbital edema and conjunctivochalasis in patients on TKIs?
a. Topical corticosteroid drops.
b. Oral diuretics.
c. Topical antihistamine drops.
d. Both a and b.

Examination Answer Sheet

Ocular Side Effects of New Cancer Agents

Valid for credit through March 15, 2026

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

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

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

Jointly provided by PIM and the Review Education Group.
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Answers to CE exam:

1. Ⓐ Ⓑ Ⓒ Ⓓ
2. Ⓐ Ⓑ Ⓒ Ⓓ
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Post-activity evaluation questions:

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

21. Recognize the potential ocular side effects of targeted cancer therapies. ① ② ③ ④ ⑤
22. Monitor patients on these drugs for potential ocular adverse events. ① ② ③ ④ ⑤
23. Comanage these patients with specialists when needed. ① ② ③ ④ ⑤
24. Educate their patients on how these medications may impact their eye health. 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.

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Last Name
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Rate the quality of the material provided:

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

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 123676 RO-OSC-0323

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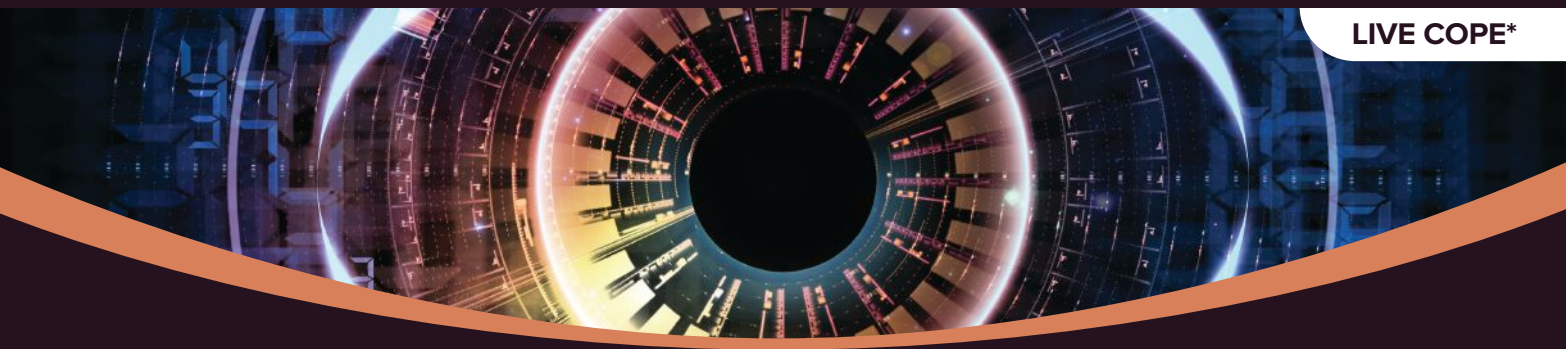

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Single Vision just got upgraded.

ZEISS ClearView Lenses

Single Vision that is anything but standard:

- On average **3× larger** area of excellent vision clarity[1]
- **Very thin** and **very flat** without optical compromise
- **Freeform technology** in standard single vision lenses

[1] ZEISS ClearView FSV Lenses vs. to ZEISS SPH FSV Lenses -5D, -3D, -1D, +1D, +3D, +5D with and without Cyl -2D in 1.60.

www.zeiss.com/pro-clearview

NEW AND NOTEWORTHY SPECTACLE LENSES AND COATINGS

Get to know how some of the latest options on the market improve the visual experience for patients.

BY JOHNNA DUKES
SPIRIT LAKE, IOWA

The only certainty in spectacle lens design is that the minute you think you've got a great selection of lens options, a new slate of products hits the market. The oldest product category in eye care—by a margin of centuries—still manages to continually reinvent itself with new products and refinements to existing ones.

Fashion frames get a lot of attention, and rightfully so, as these are huge drivers of a patient's buying habits and overall satisfaction with their experience at an eyecare practice or optical shop. But the key reason people come to our establishments is to see better. New ophthalmic lens technologies are changing the product landscape and broadening the options to provide the best possible visual experience in all settings. Here, I will discuss several recent launches and trends that might be worth adding to your lineup. Some are newer than others, but all are unique and noteworthy.

Photos: Hoya

Attention to detail of the lens edge designs in the Hoya MySV lens not only reduces thickness in high prescriptions but also improves clarity of the wearer's peripheral vision.

Hoya Vision Care's MySV

A notable new lens is the MySV from Hoya Vision Care. This lens uses aspheric and atoric curves in order to improve the aesthetic of the finished lens edge and enhance the visual experience for the wearer by widening their perceived field of vision, especially when compared to traditional spherical lens designs. It incorporates freeform technology and design compensation to correct oblique, or off-gaze, aberrations that can be found in traditional spherical lens designs. The lens design also considers Listing's law when calculating and compensating for how the position of wear, as well as the eye's axis of rotation, will affect the perception of prescription in areas of the lens outside of the optical center. Wearers of these lenses often report a noticeable improvement in the way of visual comfort, increased clarity in their peripheral vision and increased satisfaction with their single vision spectacles overall.

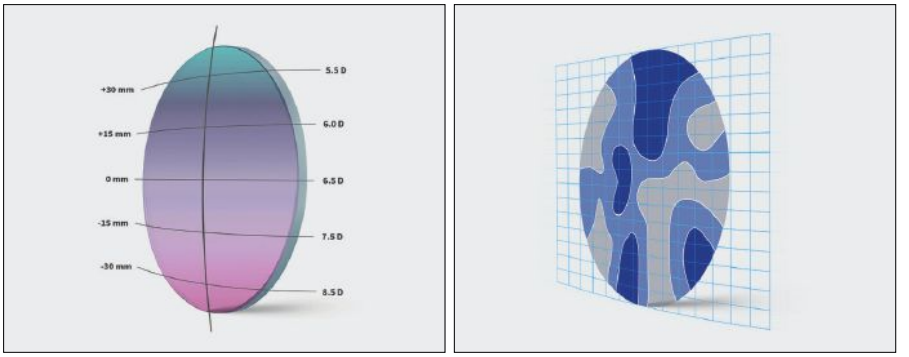
IOT's Camber Steady Plus Progressive

This lens from IOT turns convention on its head, as every ounce of the design challenges the status quo. The

About the Author

Johnna Dukes is a board-certified optician who owns her own optical boutique in Spirit Lake, Iowa. She is past-president of the Opticians Association of Iowa and the current president of the Opticians Association of America. Johnna has over 20 years in the optical industry, as well as both private practice and retail setting experience. She is an American Board of Opticianry-certified speaker and was named one of *Vision Monday*'s most influential women in optical in 2021.

Photos: IOT



Using a variable front surface base curve (left), the IOT Camber lens blank creates a continuously increasing curve that is better suited for progressive prescriptions, the company says. A design approach that compensates for peripheral aberrations (right) and accounts for the wearer's accommodation reduces aberrations across the field of vision. IOT also says the designs incorporate strict control of mean power to reduce spherical error laterally, resulting in improved lateral vision and superior image stability.

Camber Steady Plus progressive addition lens (PAL) uses a lens blank that has variable base curves on the front surface to compensate for the need for a steeper curve as the add power increases at the bottom of the lens. Then, when the back side compensations are taken into account, the end result is the feeling of width in both the near zone as well as the distance zone, which can be perceived by the wearer as increased peripheral vision.

This lens also uses something called "Digital Ray-Path 2 technology," which takes into account the accommodative power of the eye when considering the compensations necessary within the lens design, and an approach called "Steady Plus" that maximizes the intermediate vision zone and creates an easy transition between the midrange and near vision zones. This combination can serve to reduce the peripheral "swim" effect that PAL users often experience. By contrast, wearers of this lens report easier adaptation to PAL wear and are more pleased with the aesthetic of the finished lens, as the variable base curve design yields a flatter, thinner lens than a traditionally designed PAL.

Zeiss's DriveSafe Progressive

This lens from Zeiss meets a need that few others on the market are geared toward: DriveSafe seeks to create solutions for the complex visual tasks and lighting situations that occur while driving, especially at night. Low-lighting conditions allow the driver's pupil to dilate slightly in mesopic lighting conditions, which would be fine until you consider the quick lighting change that occurs when oncoming bright headlamps cause a quick change to photopic lighting conditions.

The DriveSafe lens is designed to perform especially well in mesopic vision (low-lighting conditions, which result in a wearer with a slightly dilated pupil) to minimize the increased peripheral aberrations that would happen with a traditionally designed PAL. This is recommended to be used in combination with Zeiss's DuraVision DriveSafe antireflective (AR) coating, which is designed to create more contrast and to decrease glare when encountering new high-intensity discharge and LED headlamps.

The overall design maximizes the distance vision portion of the lens, as the rigorous R&D testing for the development indicated that drivers tend to focus straight ahead and on distant and moving objects about 97% of the time while driving (vs. spending that amount of time in the intermediate or near vision zones). So, maximizing the distance portion of this PAL design makes the wearer less bothered by the unwanted peripheral distortion that typically occurs in more traditionally designed general use progressive lenses.

The DriveSafe lens incorporates a long and soft intermediate corridor in order to keep the width of the distance portion of the design intact. In short, if you're one who drives often at night and experiences discomfort associated with lighting conditions and complex visual tasks of driving, this lens might be one for you to try.

Photos: Carl Zeiss Vision

Patients who have concerns about clarity of vision while driving at night can get a better experience with Zeiss DriveSafe progressives. The design prioritizes distance vision (essential while driving) and minimize the adverse effects of glare from oncoming headlights.

Essilor's Varilux X Series Progressive

These lens options are designed to neutralize wavefront aberrations, typically in the form of high-order aberrations, which usually present to the wearer in the way of visual distortion within the lenses. Using this compensatory feature in the X Series lenses can leave the patient with a perception of increased clarity within the lens.

The design also takes into account each eye's refractive correction with modifications to encourage the eyes to work together better and create a set of lenses truly designed for binocularity (Essilor calls this "SynchronEyes technology"). These lenses can be especially effective in patients with asymmetric prescriptions and are designed to create a balanced viewing experience.

However, what really differentiates the Varilux X design is a feature that allows the wearer multiple near viewing distances through one point in the lens (called "Xtend technology" by the company). Wearers often report more forgiveness, as the design allows a dramatic reduction in the need to move one's head in order to find the right spot in the lens particularly when looking at items within arm's reach.

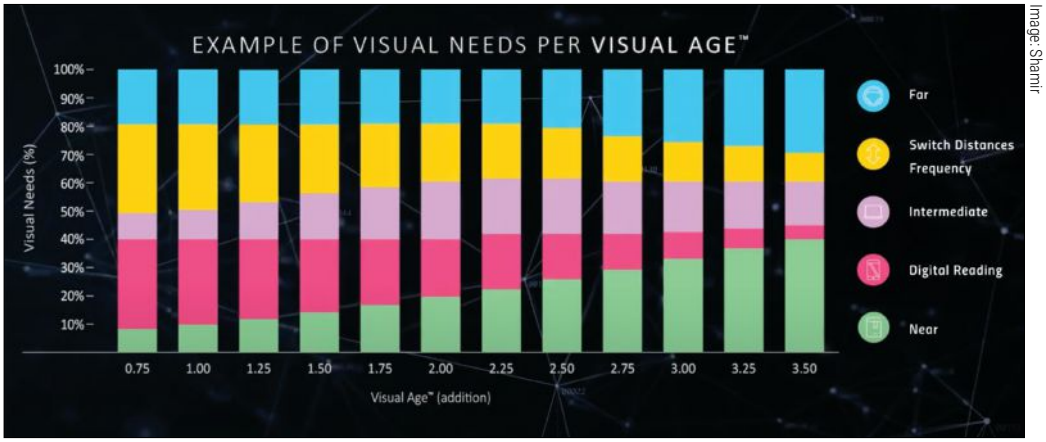


Image: Shamir

Shamir has devised the concept of "visual age" and incorporated it into the power profile of its Autograph Intelligence progressive lenses for better adaptation, the company says.

The amount of craft and knowledge involved in the development of these lenses has truly created a game changer.

Shamir's Autograph Intelligence and Glacier Expression

For easier adaptation to progressive wear, Shamir created a unique lens design that takes into account the person's likely near vision needs based on their "visual age." Called Autograph Intelligence, the lens's intermediate vision zone has been enhanced by creating a soft transition between intermediate and near, and the power distribution in each lens is modified based on the visual age of the wearer. The company says this approach better reflects real-world visual needs, particularly during computer use.

The company has also identified that the obscuration of a wearer's eyes by lens glare not only reduces visual clarity but also can change the way we perceive ourselves and the way others perceive us. The use of an antireflective coating can help, however. Shamir says its Glacier Expression AR coating has been designed to increase light transmittance, reduce visual noise and improve contrast sensitivity for the wearer. The company states that their clinical research shows use of Glacier Expression AR coating allows one to gain significantly accelerated reaction times, especially when driving at night, compared with standard AR coatings.

IOT's Endless Office Occupational

Lenses designed expressly for use at work—particularly work involving lots of computer time—have certainly had a moment as of late, considering the fact that many consumers found their habits changed drastically during the COVID-19 pandemic. The Endless Office Occupational lens from IOT is a great choice for occupational

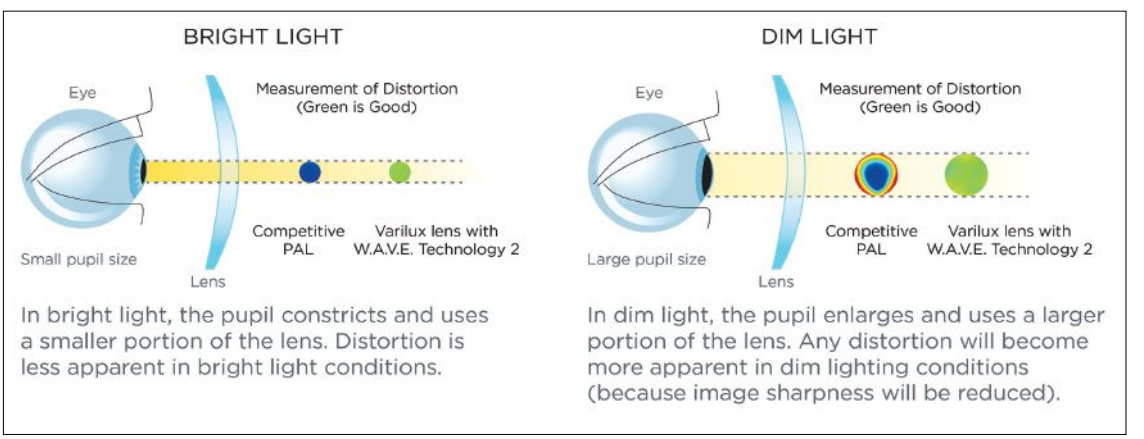


Image: Essilor

Variation in pupil size as lighting conditions change is a common source of PAL dissatisfaction. Essilor says its custom wavefront designs account for this (as well as correcting higer-order aberrations).

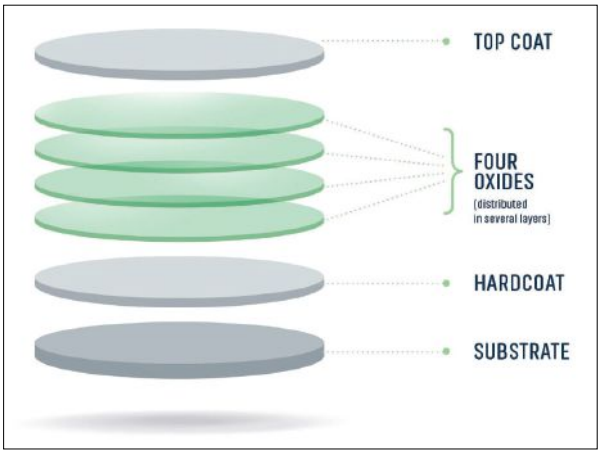
lenses, as it offers the ability to tailor the wearer's experience to their focal range needs. It is available in three focal range options: 1.3m (4.2ft), 2m (6.5ft) and 4m (13.1ft). These selections allow for you to distinguish the needs of a patient who needs only to see their computer screen and near-vision vs. a patient who needs to see across a board room or wants to wear their occupational lenses as they move around their workspace, as well as experiencing a wide near-vision zone.

Endless Office lenses are designed to maximize the near and intermediate zones in order to allow the wearer to maintain a comfortable posture by eliminating the need for them to tilt their head up in order to reach their intermediate zone. IOT's freeform manufacturing technology (Digital Ray-Path 2) and compensated design reduces the oblique aberrations that are commonly referred to as peripheral blur, giving the wearer a feeling of width in their near and intermediate viewing tasks, and a comfortable computer viewing experience.

Essilor's Crizal Rock AR Coating

If you're looking for an extra level of durability in AR coating performance, you might consider the Crizal Rock coating from Essilor. A study found that, on average, 77% of eyeglass wearers wipe their lenses with t-shirts, tissues or towels at least once per week.[2] Crizal Rock uses a "high-resistance" oxide that is described as a combination of specific oxides chosen to resist scratches and dust, as well as a "high surface density super hydrophobic layer" that is intended to repeal smudges and improve ease of cleaning. Essilor's testing shows these lenses to be three times more scratch resistant than entry-level Crizal coatings.

Image: Essilor



Essilor's Crizal Rock AR coating uses four layers of oxide to resist scratches and dust, as well as a hydrophobic layer intended to repel smudges and improve ease of cleaning.

Zeiss ClearView

Stock single vision lenses get too little attention these days. This segment of the market could use a bit of an upgrade when you consider that, visually, standard single vision lenses are great when the optical center is taken into account but can underperform at areas outside of the optical center. Zeiss had these goals in mind when designing its ClearView lenses, which are up to 16% thinner than their other spherical lenses and up to 8% thinner than aspherics. By use of freeform technology, Zeiss has created a single-vision lens with three times larger central viewing zone vs. a standard aspherical lens.

The company also has identified that the eye's center of rotation varies by prescription and has taken this into account with the ClearView. The use of these center of rotation compensations creates wider viewing zones, especially noticeable in the peripheral meridians. Excitingly, Zeiss has been able to formulate its freeform design into stock lenses, allowing for a distinct difference from the stock lenses most practices use today. This lens could radically change the single vision lens space.

Takeaways

As you can see, many companies are taking a different approach when creating the next best lens. The options are endless and it's a lot to take in, but it's an exciting time for you and your patients when making the best decision to help them see and feel better. ■

Coming Soon: Myopia Management Spectacle Lenses

These options are already available in Canada and Europe; however, they are awaiting FDA approval in the US. There is no current information on release dates, although these are hotly anticipated products, especially when considering the advances in the field of myopia management with regard to the contact lens space.

Hoya's MiyoSmart Lens incorporates a concept called *defocus incorporated multiple segments* (DIMS). According to Hoya, this design uses a 9mm central optical zone with the patient's prescribed distance correction and a 33mm annular zone comprised of multiple segments that are approximately 1mm round in size and each segment would have approximately +3.50D within each segment—the premise being that round segment areas of more plus power would cause retinal defocus and hopefully signal the peripheral retina to stop adding axial length to the eye.[1,3]

Essilor's Stellest Lens uses a design element called *highly aspherical lenslets* to create retinal defocus. It has a 9mm central optical zone that would contain the prescribed distance correction and 11 concentric rings of aspheric lenslets that are approximately 1.1mm each in diameter.[1,3] The Stellest lens was recently designated by the FDA as a "breakthrough device."

SightGlass Vision Lens incorporates something called *diffusion optics*, which produces an unaffected central area surrounded by many light-scattering elements. The working premise is that these lenses aim to reduce the contrast detected by the peripheral retina, which may be helpful in preventing axial elongation.[1,3]

1. Bullimore M. The latest science on myopia control spectacles. Review of Myopia Management. www.reviewofmm.com/the-latest-science-on-myopia-control-spectacles. November 1, 2021. Accessed February 20, 2023.

2. Crizal Rock sales aid. Essilor. info.icarelabs.com/hubfs/Crizal%20Rock%20One-Page%20Sales%20Aid.pdf. Accessed February 20, 2023.

3. Philip K, PhD. What's new in spectacle lenses for myopia management? Brien Holden Vision Institute. January 1, 2021. bhvi.org/news/whats-new-in-spectacle-lenses-for-myopia-management. Accessed February 20, 2023.

SUGGESTIONS FOR USING LABS AND IMAGING IN YOUR PRACTICE

Various symptoms at the office require further investigation. *Part 2 of 2.*

BY JAMES L. FANELLI, OD
WILMINGTON, NC

Often, what's found at clinical presentation results in needing additional laboratory testing and/or imaging studies. In Part 1 of this series last month, we explored how to implement these procedures in your practice, who should be ordering the testing, along with the challenges of doing so. Here, in the second part of our two-part series on laboratory and imaging studies, a few scenarios are explored where these tests can be used in the optometrist's office. Several cases are presented where these studies played a crucial role in diagnosis, with all of the following scenarios presenting regularly to the optometrist. Understanding the role these tests play in patient management is imperative for the practicing clinician.

Anterior Segment: Inflammation

From an anterior segment perspective, some of the more common instances where lab studies are needed are in situations when the patient presents to the office with anterior segment inflammation, either with or without a previously diagnosed systemic etiology. Particularly challenging are the situations where no underlying diagnosis exists.

The patient who presents with inflammation of the anterior segment unfolds regularly in many clinics. As usual, the examination begins with a thorough clinical history. In many cases, the history is positive for some type of extraneous source that is contributing to the inflammation, such as contact lens overwear or ocular surface disease. Naturally, reducing inflammation in these cases occurs by treating the source of the problem, such as with inflammatory dry eye.

But where do you go when there are no clinically evident sources of inflammation from the history or physical exam and the spectre of autoimmune diseases is raised? This is often when lab studies become warranted. Often, these patients will present to the clinic with cases of episcleritis or anterior uveitis.

Episcleritis is often induced by external sources, as mentioned, and eliminating the underlying etiology can result in resolution of the episcleritis. However, it is estimated that upwards of 25% to 35% of patients with episcleritis have an underlying systemic disorder, which can be infectious or inflammatory in nature.[1] Diffuse episcleritis is more common than nodular episcleritis. A variety of systemic diseases are associated with episcleritis, including the autoimmune disorders lupus, rheumatoid arthritis, ulcerative colitis and Crohn's disease. Infections are also a possible cause, such as Lyme disease and herpes zoster virus.[2,3]

Given the relatively common incidence of episcleritis, not all cases need a systemic work-up. A good rule to follow is to consider work-ups when the condition is chronic, recalcitrant or bilateral, without obvious exogenous sources or if a systemic condition is suspected based upon review of symptoms. In many situations, we treat these patients empirically with topical steroids and/or oral NSAIDs.

About the author

Dr. Fanelli is in private practice in North Carolina and 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.

Anterior uveitis follows the same line of action, with initial empirical topical therapy with steroids and cycloplegics in many cases. In general, though, recurrent, recalcitrant, bilateral and/or granulomatous anterior uveitis increases the likelihood of systemic comorbidities as outlined above.

A word of caution here: When treating uveitis empirically, it is imperative to treat the condition aggressively with topical cycloplegics and steroids. Undertreatment can result in rebound uveitis, which may ultimately be misdiagnosed as a recurrent case, as opposed to simply undertreated inflammation. Aggressive treatment often includes atropine and a strong topical steroid with good penetration into the anterior chamber, such as Pred Forte (prednisolone acetate, Allergan) or Durezol (difluprednate, Novartis). Occasionally, subconjunctival steroid injections or oral steroid treatment (in addition to the aforementioned topical agents) are needed to wrest control of the inflammation. If, after aggressive treatment, the uveitis flares periodically or is recalcitrant, then an underlying systemic disease should be considered, especially if the initial presentation was bilateral and granulomatous.

Also keep in mind that autoimmune diseases usually take years to manifest in their full form, and can often create signs and symptoms in individuals in the 20- to 50-year-old range. As such, it is not uncommon for early lab studies to come back negative or initially be inconclusive. For this reason, exercise caution in ordering lab studies on all patients who initially present with anterior segment inflammation; the presentation and history are critical in initially determining when and when not studies should be ordered, as outlined above.

Sarcoidosis is a systemwide inflammatory condition characterized by pulmonary infiltration and granuloma formation. It is associated with elevated angiotensin converting enzyme (ACE) and a Westergren erythrocyte sedimentation rate (ESR) level. ACE is elevated in about 60% to 90% of active sarcoidosis, but consider that it may also be elevated in cases of histoplasmosis, toxoplasmosis and tuberculosis.[4,5] Pulmonary infiltration with granulomatous tissue is seen on plain film X-rays and computed tomography (CT) imaging of the chest, which are part and parcel of the work-up of a patient suspected to have sarcoidosis. Both ACE and ESR results are nonspecific markers of inflammation. In other words, they may be elevated in a variety of inflammatory conditions, not just sarcoidosis.

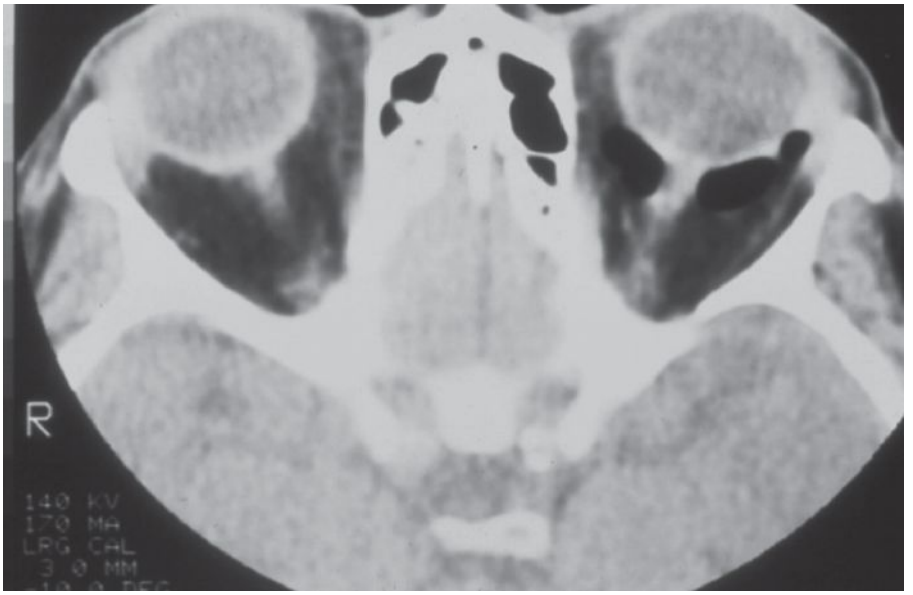


Fig. 1. A CT image of the orbits in a patient with a left orbital floor fracture. Note the image void behind the left eye; this is air, and the retrobulbar orbit is contiguous with the maxillary sinus beneath due to the fracture.

Rheumatoid arthritis and lupus are autoimmune disorders with elevated ESR and C-reactive protein levels (CRP). Note that these two indices are also simply a measure of current inflammatory activity and are not specific to these autoimmune disorders. Rheumatoid factors include various antibodies that are elevated in about 70% to 90% of patients with rheumatoid disease. Anti-nuclear antibodies (ANA) are antibodies that ultimately attack self cell nuclei. Interestingly, low or negligible levels of ANA typically rule out lupus, whereas elevated levels can indicate the presence of lupus, rheumatoid, scleroderma and Sjögren's. Anti-citrullinated protein (peptide) antibodies (ACPA) are also elevated in the majority of patients with rheumatoid arthritis.[6]

HLA-B27 is a specific type of protein found on white cells and is elevated in certain autoimmune diseases, such as ankylosing spondylitis, reactive arthritis and psoriatic arthritis. Most human leukocytic antigens are protective, but HLA –B27 can cause the opposite effect. Because the immune system uses proteins encoded by HLA to essentially determine which proteins are self and which are foreign, the HLA complex plays a protective role. However, certain HLA typing is associated with autoimmune disorders. In particular, HLA-B27 presents self and non self-antigenic proteins to T-cells, resulting in an autoimmune reaction.[7]

While the patient demographics are different between autoimmune diseases, there are many similarities that exist amongst them. However, as the name implies, juvenile

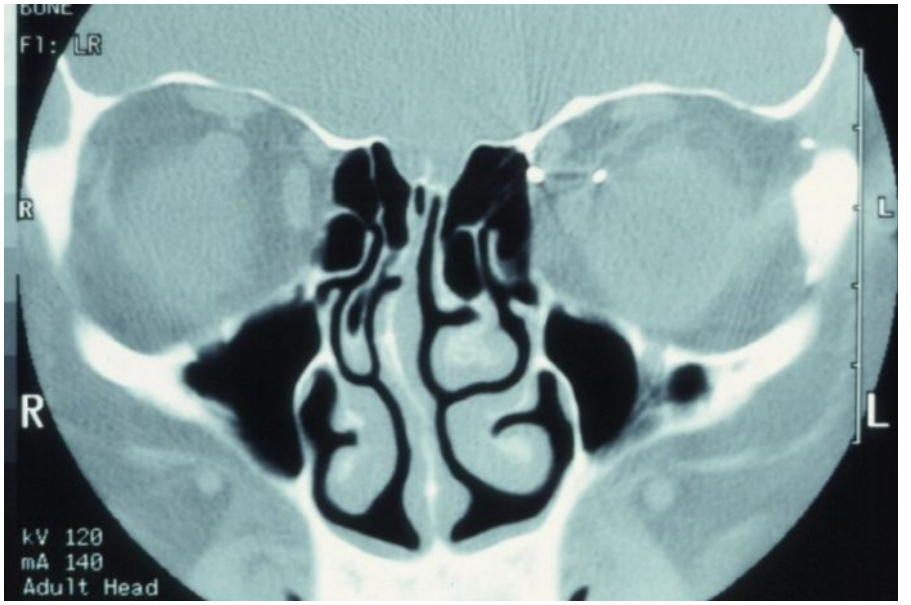


Fig. 2. Pictured here is a metallic foreign body in the left orbit. Consider that MRI physics employs a powerful magnet to obtain images. In cases where a metallic foreign body is suspected in the orbit or globe, CT imaging is warranted so as to not violently dislodge the foreign body.

rheumatoid arthritis (JRA) affects individuals younger than those with non-JRA rheumatoid. Also, ankylosing spondylitis patients have certain physical characteristics (lumbar spine abnormalities seen on plain film) that for example, a patient with systemic lupus erythematosus would not have. Delving deep into the history of these patients is critical in offering a target lab approach to facilitate a diagnosis.

Typically, I'll consider ordering an initial panel of labs for patients presenting with inflammation that is bilateral, granulomatous, recurrent or recalcitrant despite proper therapy. Which labs are ordered are generally tied to patient history with a suspected autoimmune disorder. Patients without a diagnosis of autoimmune disease are a challenge, as their systemic symptoms may simply be due to physical activity rather than an underlying condition. Typically, these initial labs include a complete blood count (CBC) with differential (indicative of infectious vs. inflammatory, etiology), ESR, CRP, rheumatoid factors ACPA and ANA. I also include a fluorescent treponemal antibody absorption test and venereal disease research lab test or rapid plasma regain test, as syphilis being the great masquerader, it can induce many of the ocular signs of inflammation that we see. In addition to these tests, I will add ACE levels and plain chest films (or CT imaging) if sarcoid or tuberculosis is suspected through the presence of persistent cough or malaise. Conversely, if the patient is younger, and I suspect ankylosing spondylitis or Reiter's, as characterized by anterior uveitis and urethritis, I'll add HLA-B27 and lumbar plain films or CTs.

Ultimately, the underlying systemic condition will be managed by the primary care physician, internal medicine or rheumatologist, but the OD is sometimes the first provider to initiate the work-up of a patient with undiagnosed systemic conditions manifesting as anterior segment inflammation. Coordinating with the PCP and/or rheumatologist can ultimately lead to the systemic diagnosis and consequently ensure appropriate treatment of these underlying conditions.

Posterior Segment Findings: Retina

Following are some conditions that ODs should feel comfortable ordering lab studies for, especially in emergent situations, such as with arteritic ischemic optic neuropathy.

One of the most common indications I see in clinic for ordering lab studies are retinal hemorrhages. As we know, the retina has a dual blood supply: one from the choroid and the other, more anterior circulation from the central retinal arteries.

Hemorrhages due to abnormalities of the anterior retinal circulation can result from arterial hemorrhages, venular hemorrhages or hemorrhages of the retinal capillary bed. Many instances present multiple hemorrhaging sources. Typically, retinal arterial hemorrhages result in 'flame-shaped' hemorrhages due to their anterior location in the nerve fiber layer. These are often the result of hypertension, Valsalva maneuvers and other diseases that affect the arterial tree, such as red blood cell anemias.

Conversely, diabetes mellitus typically induces hemorrhages in its early stages, based either in the retinal capillary bed or early venous segments. These tend to be dot and blot hemorrhages, owing to their deeper location in the retina.

Retinal venular hemorrhages typically appear as larger blot hemorrhages, sometimes associated with venular dilation. Though retinal hemorrhages can be caused by numerous systemic etiologies, the heart of lab studies associated with retinal hemorrhaging in non-diabetic patients is the CBC test. It's estimated that about 70% of hematologic conditions can be diagnosed with a CBC.[8]

Retinal arterial plaques are usually embolic in nature and can originate from degenerating atheromas, the heart or the carotid artery system. Patients with acute retinal emboli, either in the form of a branch retinal artery occlusion or a central retinal artery occlusion require urgent neuroimaging to assess stroke risk and

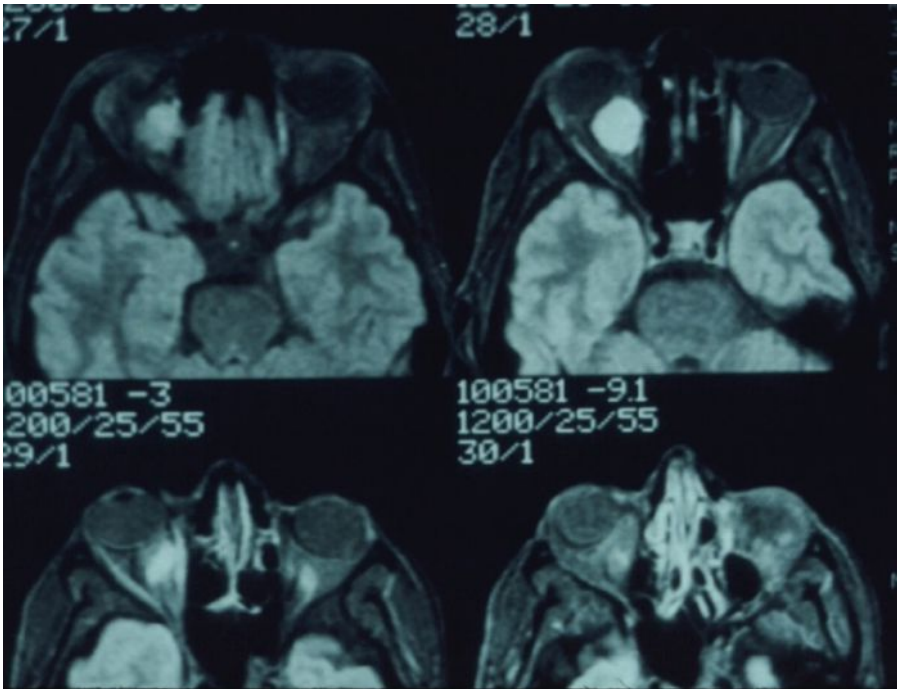


Fig. 3. Note the mass in the retrobulbar space of the right orbit.

cerebral ischemia but may also need further lab studies for dyslipidemia, aberrant glucose levels and red and white cell abnormalities.

The important point here is that retinal hemorrhaging can be caused by numerous conditions and the associated lab studies are directly tied to what the suspected underlying condition is. The overlap of atherosclerotic cardiovascular disease and many other vascular disease presentations in the retinal arterial, capillary and venular systems is the basis for evaluations of those entities that are associated with the development of this disease. Namely, these include diabetes, hypertension, hyperlipidemia, smoking and obesity.

Accordingly, lipid panels are an integral part of the work-up of many patients with retinal vasculopathies that imply atherosclerotic cardiovascular disease origins. These panels will include total cholesterol, triglycerides, HDL and LDL levels. New research suggests that stratified lipid panels provide a better picture of the systemic risk of dyslipidemia, with subtyping of HDL and LDL particles in particular.[9]

Of course, diabetes plays a large role in retinopathy in developed countries, and in lab studies, glycosylated hemoglobin is a strong indicator of glucose control and future risk of diabetic retinopathy development.

Posterior Segment Findings: Optic Nerve

Optic neuropathies originate from several different etiologies, but the non-glaucomatous optic neuropathies, specifically anterior ischemic optic neuropathy (AION) and non-arteritic anterior ischemic optic neuropathy (NAION), present frequently in patient populations over the age of 50.

Arteritic ischemic optic neuropathy (giant cell arteritis) is a medical emergency. This typically affects patients over the age of 65 and is characterized by sudden loss of vision, disc edema, dyschromatopsia and visual field loss, temporal head pain, jaw claudication and malaise. It is associated with inflammation of medium-sized arteries, including those in the distribution of the external carotid artery. The signs and symptoms of arteritic AION still remain an important criteria in impetus to begin the initial work-up of a patient suspected of having arteritic ischemic optic neuropathy.[10]

From a lab perspective, patients suspected of having arteritic AION need immediate laboratory investigations, including (primarily) an ESR and CRP. Elevated ESR and CRP levels, with a CRP greater than 2.45, are diagnostic of arteritic AION along with the aforementioned clinical findings. Treatment with intravenous or oral steroids is indicated to prevent similar ischemia in the fellow eye and the diagnosis is confirmed with temporal artery biopsy. Temporal artery ultrasonography is becoming more of a diagnostic tool in lieu of biopsy, especially in light of its easy accessibility and noninvasive methodology.[11]

NAION is also characterized by unilateral visual field loss, more often

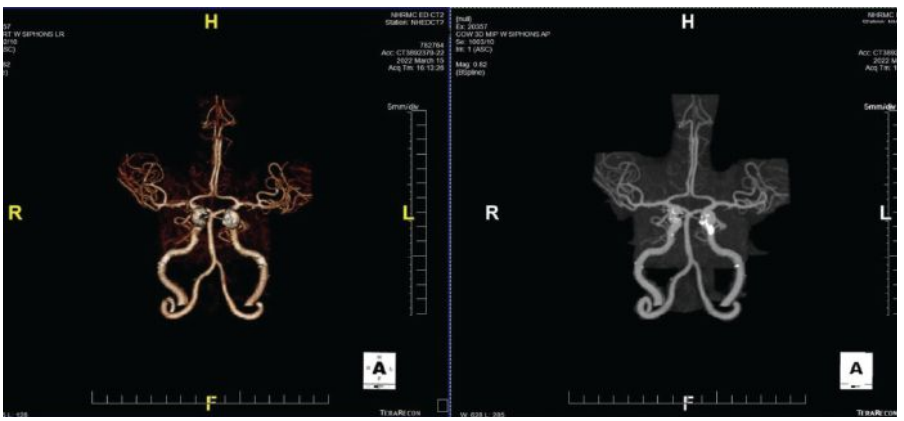


Fig. 4. A CTA demonstrating significant plaque formation in a patient with transient visual obscurations. Note the calcification of the L>R internal carotid arteries.

CASE 1. Here is one example showing the practical use in ordering a CTA. An 87-year-old female patient presented with painful and acute CNIII palsy *(Figure 5)*. The pupil was involved. She had a complex medical history, including hypertension and hypercholesterolemia of many years' duration. Patients with these conditions are considered medical emergencies, as rupture of cerebral aneurysms at the junction of the internal carotid artery and the posterior communicating artery can prove fatal, or at best, debilitating.

Fig. 5. These CTA images of the patient described show two different rotational views of the carotid, vertebral and basilar arteries, along with distributions of the anterior and middle cerebral arteries. The yellow arrows are directing to the aneurysm at the junction of the internal carotid artery and posterior communicating artery, which is the source of the third nerve palsy.

Given the urgency of the situation and the reality that, in our area, obtaining MRI imaging can prove more delayed than CTA, this patient was sent to the emergency department (ED), accompanied by a call from myself to the attending ED physician, outlining the findings and requesting a CTA. Without the relevant information presented to the ED physician, there is a higher likelihood that neuroimaging without angiography (CTA or magnetic resonance angiography (MRA)) would have been obtained instead, thus delaying the vascular diagnosis even further. This was discussed at length in Part 1 of this series.

Given the findings, the patient was then sent to neurosurgery and ultimately underwent coiling of the aneurysm. Included is the radiology report of the patient in Case 1 for reference *(Figure 6)*.

CONCLUSION:

RIGHT ICA ANEURYSM NEAR THE POSTERIOR COMMUNICATING ARTERY ORIGIN AS NOTED ABOVE. FURTHER EVALUATION WITH CATHETER ANGIOGRAPHY IS RECOMMENDED GIVEN THE CLINICAL HISTORY.

NO OTHER EVIDENCE OF INTRACRANIAL ANEURYSM, AVM, OR FOCAL STENOSIS

****CRITICAL RESULT****

Fig. 6. This is a portion of the radiologist's report in the Case 1. Most of these reports discuss the findings seen in the imaging ordered. Toward the end of the report, a conclusion is made of the radiologic findings, often accompanied by suggestions for further evaluation. Note that, for the radiologist to make further suggestions, an integral part of their interpretation and plan involves the information you initially conveyed to them.

noted upon awakening, and typically affects somewhat younger patients than AION. This too is an ischemic infarct of the optic nerve, but not associated with inflammation of the branches of the external carotid artery. This is an infarct involving the small vessels of the optic nerve head and it is related ultimately to the same risk factors that are associated with the development of atherosclerotic cardiovascular disease. Prominent risk factors include diabetes, hypertension, hyperlipidemia, smoking, obesity and a sedentary lifestyle. Another risk factor is the use of PDE5 inhibitors, such as Cialis (tadalafil, Eli Lilly) and Viagra (sildenafil, Pfizer), more so in patients with a small, crowded disc, which in and of itself can be a risk factor—the so-called "disc at risk."

Management of NAION is an internal medicine driven intervention, aimed at tightly controlling the aforementioned risk factors. Thus, lab studies for lipids and glucose are an integral part of managing these patients long-term.

Computed Tomography (CT)

This imaging uses electromagnetic radiation to generate images; this is the same type of energy used in plain film X-rays and therefore has limits to the amount of exposure a patient should have to this type of radiation.

CT imaging from an ophthalmic perspective is mainly useful to identify problems involving bone, the interface of bone and air and fresh hemorrhaging. Its soft tissue resolution is not nearly as high as with MRI.

The technology, however, is quite useful in orbital fracture evaluations, as the interface of bone (hyperintense on CT imaging) and air (dark) in the paranasal sinuses is quite indicative of bony abnormalities (*Figure 1*). Likewise, evaluation of the paranasal air sinuses can best be done by CT imaging. CT imaging additionally has value in cases where intraorbital or intraocular foreign bodies are suspected (*Figure 2*).

As previously outlined in Part 1 of this article in the February 2023 issue, CT imaging in the emergency

department is routinely performed on admitted unconscious patients for the evaluation of intracerebral hemorrhaging, due to fresh blood showing up readily on CT imaging. This imaging modality is also generally more accessible than MRI on short notice, but does have its own limitations, especially when looking at soft tissue detail.

Occasionally, we will use CT imaging to evaluate intracranial contents when there is suspected a mass or a mass effect. While subtle detail may not be present, gross structural changes can readily be seen, thereby offering an alternative to MRI in the initial evaluation of certain patients. The same holds true for orbital disease, especially cases of recent onset proptosis. While extraocular muscles are generally better visualized on MRI, a quick CT scan of the orbits can shed light onto the possibility of Graves' disease or orbital myositis or space occupying lesion (*Figure 3*).

With the increased usage of CT angiography (CTA), CT imaging has seen a resurgence in the number of cases being ordered from our office in the context of neuroimaging, especially if a vascular problem is suspected. CTA does a fantastic job of highlighting vasculature throughout the body (*Figure 4*). It is routinely performed in evaluation of patients with chest pain and coronary artery disease, as its images are outstanding in identifying vascular disease.

From an ophthalmic perspective, CTA is useful in patients who present with transient visual obscurations due to suspected carotid, vertebral or cerebral vascular disease. While the brain parenchyma is not visualized in CTA in detail, the presence or absence of significant vascular abnormalities is evident. These patients may still need MR imaging or intravascular catheter angiography, but in cases where the patient needs to be imaged quickly, this is a suitable alternative to MRI and MRA imaging.

Do note that when neuroimaging is ordered by any physician, including an optometrist, the radiology report accompanies the scan results, wherein the neuroradiologist makes a diagnosis based on the structural details seen on the imaging. While the OD is not necessarily interpreting the scans themselves, it is still good practice to read or examine them anyway to become more familiar with these images. The radiologist, however, is making the diagnosis. It then becomes incumbent upon the OD to act on that information in the appropriate fashion, which often involves referring the patient to the appropriate subspecialist.

Magnetic Resonance Imaging (MRI)

This imaging from an ophthalmic perspective is very useful in evaluating neuro-ophthalmic problems, orbital problems and soft tissue subtleties. MRI uses the basic principle of the polarity of water molecules being

CASE 2. Here is an example demonstrating why an OD may request MRI. A 69-year-old Caucasian female presented to the office with complaints of severe headache followed by a short episode (about one minute) of dysphasia which occurred five days earlier. She had a history of diagnosed chronic migraine, but this particular episode was more severe than typical presentation, thus prompting her visit to the office. In-office evaluation did not demonstrate clinical findings associated with acute stroke at the time of visit. However, her history warranted neuroimaging.

An urgent MRI/MRA was ordered (*Figure 7*). Based upon the radiologist's interpretation of the scan, the patient was found to have no evidence of stroke or any significant issue requiring hospitalization. The only findings on MRI were areas consistent with chronic small vessel disease, consistent with her age and is atherosclerotic in nature. The patient was ultimately sent to internal medicine in order to manage the underlying atherosclerosis (*Figure 8*). The MRA report was normal, as was, essentially, the MRI. Further investigation for carotid and coronary disease is underway.

MRA can be obtained at the same appointment as MRI and highlights cervical and cerebral arteries. This is useful in visualizing the carotid arteries, vertebral arteries, the circle of Willis and the major cerebral arteries. MRA is often obtained at the same time as MR imaging in the evaluation of patients with impending embolic stroke or suspected ischemic stroke.

[redacted]

Encounter Date: 02/04/2023

Ordering Provider: James Fanelli
Auth Prov: James Fanelli
[redacted]
WILMINGTON NC 28412

Department of Radiology
Novant Health
Wilmington, NC 28401
Imaging Results

Name: [redacted]
Accession Number: [redacted]
DOB: [redacted]
Account #: [redacted]
Patient Class: Outpatient Diagnostic
MRN: 776267
Procedure(s) Performed: **MRI Angio Head W and WO Contrast 02/04/2023**
Exam Date:
Reason for Exam: **None Specified**

Order Diagnosis:
**Acute loss of vision
Basilar artery migraine, intractable
Paresthesia**

Performing Location:
Novant Health Scotts Hill Medical Complex
Order Date
2/4/2023 7:06 PM
Exam performed
02/04/2023 8:20 PM

MRI BRAIN W AND WO CONTRAST - , MRI ANGIO HEAD W AND WO CONTRAST - :

HISTORY: Acute loss of vision
Basilar artery migraine, intractable
Paresthesia

COMPARISON: No comparison.

PROCEDURE: Routine T1 and T2-weighted routine MRI sequences of the brain with and without IV contrast.

MRA of the head with and without contrast. 3-D reconstructions were performed.

CONTRAST: Patient injected with 6 mL of ordered gadobutrol (GADAVIST) injection 6 mL, no reaction.

FINDINGS:

There are no extra-axial fluid collections, mass-effect, midline shift or cranial hemorrhage. Ventricles and cisterns are within normal limits. There are scattered and confluent foci of T2/FLAIR hyperintensity in the periventricular and deep white matter, nonspecific but commonly associated with chronic small vessel ischemic disease. Appropriate flow voids are identified and diffuse weighted images are normal.

Fig. 7. This is the typical radiology report you will see when ordering neuroimaging. In this case, both and MRI and an MRA were ordered. This first page is the report pertaining to the MRI. The MRA was entirely normal. Note here that as the findings are clearly laid out, it is incumbent upon the ordering provider to understand what these findings mean and ultimately to develop a plan related to these findings. Given these are consistent with small vessel ischemic disease, referral to internal medicine is warranted to mitigate the risks of continued atherosclerosis. While the initial symptoms initiated the MRI and MRA ordering, fortunately the patient did not require emergent or urgent treatment.

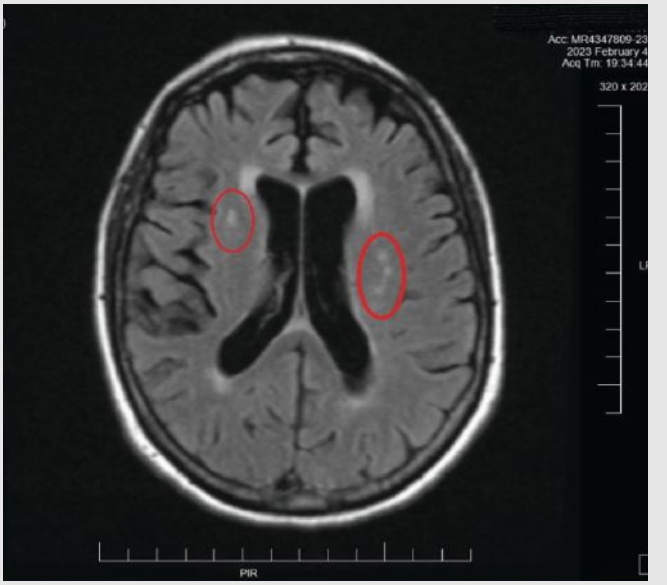


Fig. 8. This MRI image is from the patient described in Case 2. Note the hyperreflective areas in the periventricular white matter. These are consistent with age-related small vessel occlusive disease. Also note the fine brain parenchymal images obtained with MRI. This imaging method is preferred over CT imaging of the brain in many cases for this reason: resolution of fine detail of soft tissues.

placed in a strong magnetic field; each tissue in the body has varying amounts of water and the tissue density differences seen on MRI is related to the amount of water in the tissue. Paramagnetic contrast media is often employed to highlight adjacent tissues.

MRI is very much software-driven and various imaging techniques are obtained through software manipulation such as fluid-attenuated inversion recovery (FLAIR), apparent diffusion coefficient (ADC) and diffusion weighting. For example, FLAIR is very useful in identifying demyelinating disease in the white matter adjacent to the ventricles, whereas ADC mapping and diffusion weighting are important in determining the chronicity of cerebral ischemia. These imaging techniques do not need to be specified when you order an MRI; rather, their use is determined by the radiologist, driven to a significant degree by the clinical findings you relay to them. Each imaging technique is geared to highlighting certain structures, and the radiologist uses those techniques to facilitate their diagnosis, similar to our use of various OCT image techniques.

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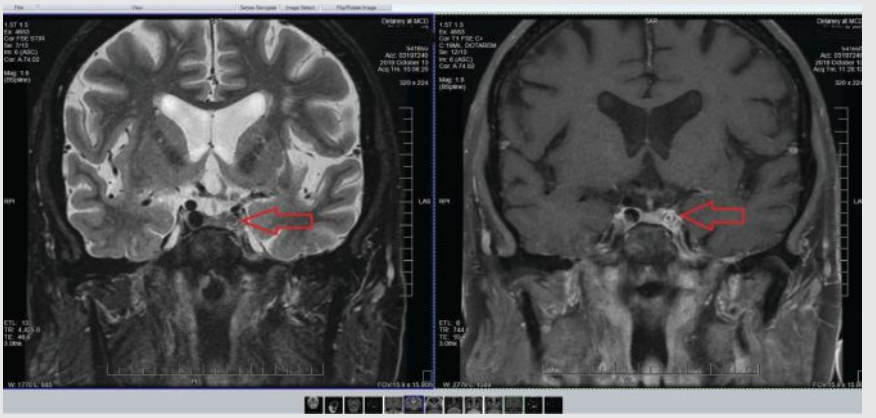

Fig. 9. Note in these images the marked stenosis of the internal carotid artery in the left cavernous sinus. Not surprisingly, other adjacent angiographic images demonstrated sclerosis of the middle and posterior cerebral arteries on the ipsilateral side and focal cerebral ischemia consistent with his chief complaint.

CASE 3. Here is another case involving MRI. A 76-year-old Caucasian male presented with transient visual obscurations. There was a distinct lack of symptoms related to acute stroke (*e.g.*, hemiplegia, hemiparesis), but the patient's age, presenting and medical history increased the likelihood that he was in fact demonstrating symptoms of cerebral ischemia.

Accordingly, an MRI/MRA was ordered and findings included atherosclerosis (*Figure 9*). The presence of atherosclerosis of cerebral arteries in a patient with transient visual obscurations and without embolic plaque presence is managed by medical or surgical intervention, depending on the age and health of the patient and location of the atherosclerosis. Ultimately, this patient was deemed not fit to be a surgical candidate. Accordingly, internal medicine management of the atherosclerosis was undertaken to mitigate the risks of acute stroke.

The number of indications for MRI in eye care is quite large and they generally center around orbital and neuro-ophthalmic diseases. These include, but are not limited to, evaluation of patients with retinal emboli of acute nature, specifically looking for cerebral ischemia and the consequent risk of debilitating stroke, incidences of suspected papilledema due to elevated intracranial pressure, afferent visual system field defects (either acute or chronic), acute efferent cranial neuropathies involving CN III, IV and VI, Chiari malformations, a variety of orbital disease and numerous other conditions. Its major advantage is its capability to differentiate soft tissue and visualization of the brain parenchyma. Entire textbooks are available that demonstrate the various indications of MRI in eye care if you are interested in delving further into the topic.

Magnetic resonance venography (MRV), along with MRI, is an integral part of the work-up of patients with clinical evidence suggestive of elevated intracranial pressure without gross CT or MR findings of abnormalities in cases when we suspect idiopathic intracranial hypertension (IIH). Upwards of 90% of patients with IIH have stenosis of the transverse sinuses (*Figure 10*)[12]. When IIH is suspected, it is imperative to include an MRV at the same sitting as the MRI, as the dural venous sinuses will not be visible on MRI nor on MRA imaging.

Takeaways

From anterior to posterior segment, there is no shortage of instances that warrant an OD's ability to call for further labs or imaging. While there are only three cases presented here, there exist many more than could be outlined. Though not all scenarios where neuroimaging is needed can be specified in one column, this piece should give ODs the essentials they need to carry with them when evaluating patients with underlying systemic conditions with ocular side effects. ■

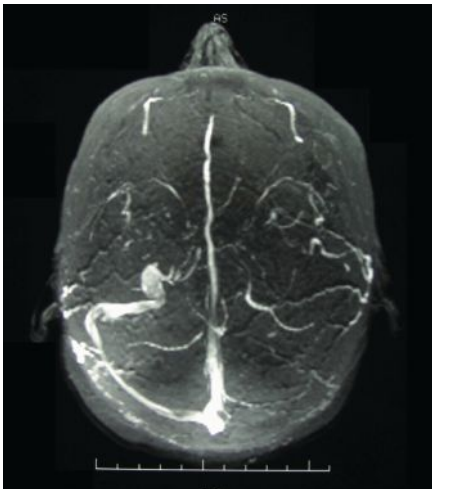

Fig. 10. An MRV image of transverse dural venous sinus stenosis in a patient with elevated intracranial pressure. The dural venous sinuses in MRV imaging are hyperintense; note the asymmetry of the transverse sinuses right vs. left.

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EXPLORING THE IMPACT OF LENS COATINGS ON EMOTIONAL CONNECTION

BY RAMIN RABBANI, OD, AND CARISSA DUNPHY, ABOC

Two top priorities that patients have when they select eyewear is how they see and how they look. This, in turn, affects how patients function and feel. However, there is a natural tendency to attribute looks and feelings exclusively to frames, when in fact lens properties play a significant role in the total wearer experience. Similarly, we don't often appreciate the multidimensional benefits of high-quality lenses. For example, improved eyesight can reduce eyestrain, improve comfort, and increase productivity. Consider too how vision can help patients feel more relaxed, secure and confident navigating the world around them.

Another consideration is that lenses don't only impact how patients see—they also affect how they are seen. Reflections have always been considered aversive, but now they're much more obvious because we can see them on Zoom and on images of ourselves on social media. Early research that emerged as our dependence on digital devices increased has expanded dramatically. Our initial focus was on eye strain and light wavelengths and how all of this impacts our overall physical wellbeing. But the immediate shift to digital face-to-face interaction has brought new concerns to light. As we are now recognizing, lens selection can also play a role in emotional wellbeing. In the pages that follow, we'll review the evolution of this emerging research and discuss the implications when making a lens recommendation.

HUMAN CONNECTION 101

For better or worse, we worry a lot about the impressions we make on others. Although these evolve over time, first impressions are formed very quicky. In fact, research shows that first impressions begin to form within

Exploring the Impact of Lens Coatings on Emotional Connection

This activity is supported by unrestricted educational grant from Shamir

Faculty: Ramin Rabbani, OD and Carissa Dunphy, ABOC

Release Date: March 15, 2023

Expiration Date: March 15, 2024

Estimated time to complete activity: 2 hours

Goal Statement: This course will explore the impact of lens coatings on emotional connection.

Educational Objectives:

- Explore the impact of lens coatings and its effects on patients
- Examine the connection between eye strain and light wavelengths and their connection to mental health
- Review various studies that look at ophthalmic lenses, mental health, and lens coatings

Target Audience: This activity is intended for optometrists who provide primary care optometry services, including but not limited to medical optometric services.

Faculty/Editorial Board: Ramin Rabbani, OD and Carissa Dunphy, ABOC

Continuing Education Credit: This activity, COPE Activity Number(s) 82320-GO is accredited by COPE for continuing education for optometrists.

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OPHTHALMIC LENSES AND MENTAL HEALTH

Depression and loneliness hit Americans hard in the early days of COVID. In fact, one-third of participants in a national study (32%) reported depressive symptoms, predominantly among women ages 20-29.[1] Notably, individuals who maintained very frequent in-person, but not remote, social connections had better mental health outcomes.[1] These findings have important implications for this new way of living and working that's evolved and continued even after stay-at-home orders were lifted. With so much of our personal and professional time being spent on-screen, connecting with others remotely in virtual environments, how can we, as eye care providers, minimize potential negative impacts with reduced in-person connection and heavy online interaction? In addition to what we already know about digital eye strain, new research shows that lens wear can also affect human connection and our perceptions of others when we communicate virtually.

one-tenth of a second, [2] and quite a lot happens in the span of seven seconds. That might sound rather immediate but the subconscious mind operates quickly. For example, our brains are rapidly judging trustworthiness and other traits that, from an evolutionary standpoint, were once relevant to human survival. Indeed, first impressions are yet another example of how survival of the fittest has played out since the dawn of time. Although our needs may be different now than they once were, our ability to assess other humans is no less important today than it was thousands of years ago.

We assess people all the time. What was once a way to ensure personal safety is now a mechanism to excel socially, build stronger support networks, and succeed in business. All of this circles back to our ability to form first impressions. Of course, first impressions aren't everything, but they exert a strong influence. In fact, in a series of experiments conducted by Princeton psychologists, scientists determined that looking at a stranger's face for longer than 100 milliseconds merely boosts one's confidence in their judgements rather than significantly altering those first impressions.[2]

First impressions are based largely on facial expressions. More than 100 years ago, Charles Darwin justified the theory of evolution by natural selection with the controversial argument that human facial expression is a sort of universal language.[3] Since then, hundreds of follow-up studies have been generated on this same topic, with recent investigations demonstrating universality despite cultural and demographic diversity, even in online contexts. [3]

When you think back to a more primitive era, it seems logical that showing one's teeth might be used to establish dominance whereas a smile can have a very different effect. In either case, these are messages that transcend time and place. But many facial expressions are more subtle than a scowl or a frown. Humans have 43 muscles in the face and they work together to create thousands of expressions, often using the muscles around the eyes to convey messages. Consider how smiles differ depending on whether they involve the eye area. Impressions about whether a smile is genuine are often based on whether you notice crow's feet around the eyes. We may assume that a smile is forced or lacks feeling when we don't see it in someone's eyes. We make these

VISION AND CONNECTION

Reflections don't only affect lens wearers, they are also experienced by the people with whom they connect. Like mirrors, due to a well-polished surface, ophthalmic lenses reflect light. If you stood in front of a mirror and took a picture of your reflection with the flash, how would the photo turn out? Chances are, your face would be obliterated by the light. A similar phenomenon often occurs when others view us when we are wearing ophthalmic lenses. Under certain lighting conditions, the lens wearer's face is obscured. As a result, the connection between two individuals who are trying to communicate is compromised. Viewing is disturbed on both sides. Anti-reflective coatings reduce the intensity of these reflections. [4]

judgements automatically, and without formal training, in a tenth of a second because, as Darwin would assert, that is how we're programmed.

Researchers at UC Berkeley and Google used machine learning technology to analyze facial expressions in 6 million YouTube video clips from people in 144 different countries. [3] Remarkably, this research showed that across these many different countries and cultures, at least 70% of the same facial expressions are shared and used in response to particular social and emotional situations. [3] These findings imply a universality of human expression that transcends geographic and cultural boundaries even in an online context. [3]

STUDYING MODERN CONNECTION

Although digital interaction has been on the rise for many years, when COVID hit there was a seismic shift in how we routinely connect with others and it's persisted despite businesses opening back up. Audio-only conference calls are out and video communication is here to stay. Indeed, many Americans have largely transitioned from in-person interactions to meeting, working, and socializing over digital platforms. As such, it has become more important than ever to find ways to trust and connect with people in this new on-screen environment. However, digital environments are such that we have other variables to contend with including pixel density, screen dimensions, Wi-Fi strength, lighting, reflection, and audio or video lags. Also, consider that we can only see about 15% of an interactant's body on screen — sometimes even less or at smaller dimensions depending on how screens are being shared. Understandably, connections are harder to establish and maintain on digital mediums.

A recent pair of studies sought to determine whether different lens coatings affect how people see others when they're meeting strangers in creating first impressions. Two experiments were designed to determine whether, for example, people respond differently or perceive others differently based on lens clarity.

FAST FACTS

THE SCIENCE AND EVOLUTION OF LENS COATINGS

Lens coatings date back to the 19th century, when they helped make lenses stronger and easier to clean. But today, they're expected to do much more. Today's anti-reflective (AR) coated lenses improve vision by reducing glare and reflection from the lens surface, while increasing light transmittance.

Lowering surface reflectance is accomplished by way of the principle of interference. This technique utilizes the fact that light travels as a wave and is based on the coating's ability to have the wavelengths from the front and back surfaces of the lens cancel each other out, resulting in no visible reflection. This is achieved by forcing the light-wave from the back of the coating (i.e. the reflection) to travel half a wavelength further than the light-wave from the front of the coating. This occurs when the coating is precisely a quarter of a wavelength thick (*see Figure 1*). Any light that would have been lost through reflection, is actually added to the energy transmitted by the lens.[4]

Since natural light is made up of a range of different wavelengths, a single-layer coating that is the right thickness for a particular color of light, will not be correct for other colors and wavelengths, hence the development of multi-layer coatings.[5]

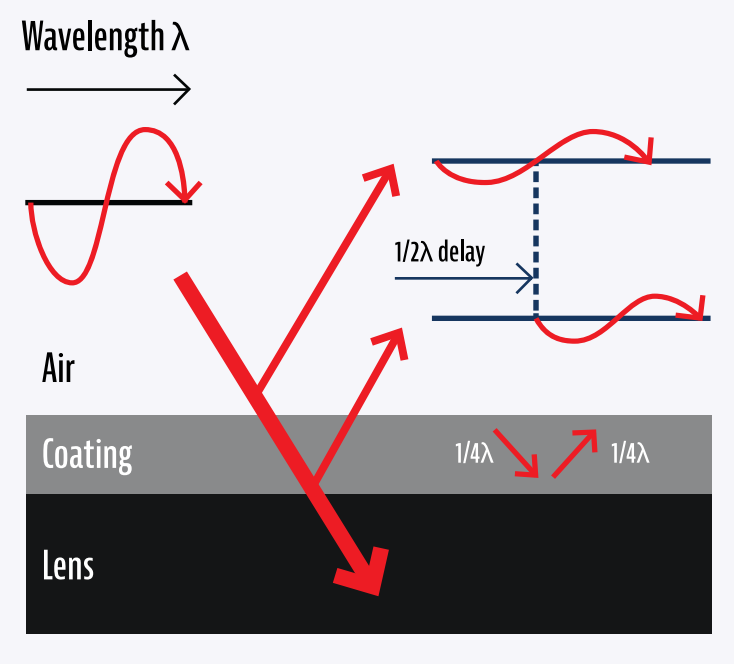


Figure 1

STUDY 1 FINDINGS:

- Visible lens clarity results in more positive first impressions across all three dimensions of likability, connection, and trust.
- Out of all respondents, 63% of subjects felt more connected to one of the subjects who wore lenses coated with Glacier Expression, compared to only 47% who said the same for the same person wearing lenses without anti-reflection coating in a different scenario. This means Glacier Expression increased sense of connection by 16%.
- 70-80% of all 1288 respondents stated they liked and would show empathic behavior towards subjects wearing lenses coated with Glacier Expression, which is statistically significant when compared to only 28-34% of those respondents who felt similarly for subjects wearing lenses without an anti-reflection coating. This means Glacier Expression lenses created ~2.5x more empathy.

STUDY 1

In the first experiment, researchers hypothesized that the better you can see someone's eyes when meeting them for the first time, the better you'll be able to read their emotions and gauge their intent, which in turn will positively impact the first impression. Positive first impressions are characterized by how connected you feel, how you perceive the stranger's trustworthiness and likability, and whether your connection elicits empathy. The following research questions were posed:

CONNECTION - Do anti-glare coatings impact a viewer's sense of connection?
TRUST - Do anti-glare coatings impact a viewer's perception of trustworthiness?
LIKABILITY - Do anti-glare coatings impact a viewer's perception of likability?
EMPATHY - Do anti-glare coatings impact a viewer's sense of empathy?
CONFOUNDING - Do any confounding variables potentially affect participant responses and synthesized findings?

The study was conducted online using video recordings of actors wearing lenses with Glacier PLUS coating, Glacier Expression coating, or lenses without any anti-glare coating. In all three scenarios, actors wore understated frames. Participants included 1288 men and women between the ages of 18 and 99. The sample was geographically balanced with incomes skewed to reflect US census data.

Results of the study 1 experiment reveal that clearer lens clarity results in more positive first impressions across all three dimensions (likability, connection, and trust). Out of all respondents, 63% of subjects felt more connected to one of the subjects wearing lenses with Glacier Expression coating, compared to only 47% who said the same for the same person wearing lenses without anti-reflection coating in a different scenario. In other words, Glacier Expression increased a sense of connection by 16%. In addition, 70-80% of all respondents stated they liked and would show empathic behavior towards subjects wearing Glacier Expression, which is statistically significant when compared to only 28-34% of those respondents who felt similarly for subjects wearing lenses without an anti-reflection coating. This means the anti-glare coated lenses created ~2.5x more empathy. Participants were also given the option to select from 20 positive and negative adjectives to describe subjects wearing lenses with an anti-glare coating. In this

FAST FACTS

SPECTRAL SENSITIVITY

The human eye is not equally sensitive to every color component of light. It's more sensitive to some wavelengths than to others. This is known as spectral sensitivity, and refers to the relative efficiency of detection of light or other signals, as a function of frequency or wavelength of the signal.

Spectral sensitivity, also known as spectral luminous efficiency, reflects F response sensitivity of the human eye in relation to various wavelengths of light. In a brighter environment, human vision is most sensitive to green light that has a wavelength of around 555 nm. In bright environments, human visual perception time is shorter, and the time it takes to develop visual fatigue is relatively longer.[5]

FAST FACTS

GHOSTING

Ghost images are another negative effect of reflections that represent a visual disturbance.[4,6] They occur because the lens surface divides incoming light. Part of this light doesn't pass through the lens. Instead, it bounces off the lens. When this reflected light is directed back again and reaches the focal plane, it forms a ghost image.

arm of the experiment, respondents consistently associated positive adjectives with those who wore lenses treated with an anti-glare coating. Furthermore, the adjective "trustworthy" consistently topped the list of adjectives. (*See Study 1 Findings*).

STUDY 2

Although impacts of lens coatings were evident in the study 1 research findings, researchers wanted to see if there was a significant difference between the current high-end lens coatings and Glacier Expression lenses. Furthermore, they wanted to determine whether clarity would be amplified if people were meeting in person versus online. Their research questions included:

ENVIRONMENT - Are impacts of lens clarity on impression more significant in person compared to digitally over video?

CONNECTION - Is lens clarity directly correlated with connection? Do clearer lenses make viewers feel more connected to the person wearing the glasses?

TRUST - Is lens clarity directly correlated with trustworthiness? Do people trust people wearing clearer lenses more than those who don't?

CONFOUNDING - Do any confounding variables potentially affect participant responses and synthesized findings?

VISIBILITY - Do the different lens coatings impact how the wearers feel and see?

In sum, 40 participants were recruited from coffee shops in Pittsburgh, Pennsylvania. As in the previous study, the sample was gender balanced. Study 2 was unique in that participants engaged in a hands-on activity. They were asked to try on a pair of glasses with lenses coated with Glacier Expression and a pair of glasses coated with Glacier Plus. Researchers then formally gathered feedback on how people feel and see the world when they wear glasses of varying lens coating qualities.

One of the key takeaways is that researchers found a direct correlation between clarity and positive impressions. Specifically, participants perceived more trustworthiness and a higher sense of connection to the people who were wearing lenses coated with Glacier Expression compared to those wearing lenses with Glacier Plus—and this was true regardless of whether the person wearing those glasses was male, female, had dark eyes, light eyes, or was the first or the second person that they met in the research session (*See Study 2 Findings*).

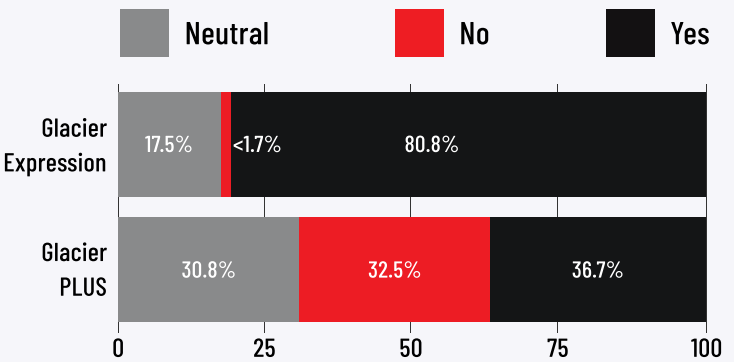
In short, consistent with evolutionary psychology theories, data shows that the better someone can see our eyes and determine our genuine emotion, the more trustworthy we appear, the more likeable we become, and the easier it is for people to connect with us.

There is a lot of data from this and other research experiments that suggest what characteristics or behaviors can contribute to increased connection and positive first impressions. There are things that we can and some things that we cannot control that contribute to those sentiments and judgements. Lens clarity is one of the easiest and most affordable ways, proven with both rounds of this research, to positively impact the sense of connection between people and positive first impressions.

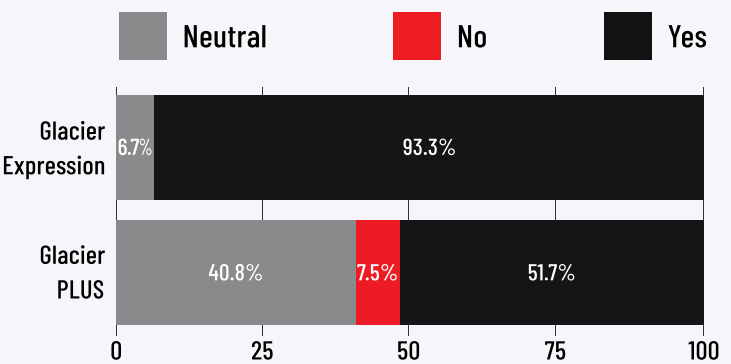
STUDY 2 FINDINGS:

- 72.5% of all 40 participants indicated that people wearing lenses coated with Glacier Expression appeared very trustworthy, which is more than 3 times the number of people who rated people wearing lenses coated with Glacier Plus as very trustworthy.
- 80% of all 40 participants indicated that they felt very connected to the people they met wearing lenses coated with Glacier Expression. That is almost 2.5 times more than the number of people who indicated feeling very connected to the subjects wearing lenses coated with Glacier Plus.

TRUSTWORTHINESS QUESTION



CONNECTION QUESTION



IMPLICATIONS

We take for granted that we feel more connected to people when we can see their eyes, but we don't always consider how online interaction inteferes with this fundamental component of interpersonal communication. Many of our patients spend 6, 8, or even 10 hours per day in front of the computer screen, which is visually demanding and very different from office working conditions. Working from home is very different. For example, often, most home environments are not optimized for heavy screen time, with light coming in from all directions. Glare is a barrier to connection.

We also usually view others on a smaller scale on-screen. In some cases, we can barely see the eye of the person we're talking with, much less read the eyes' expressions the way we can in person. In short, there's a lot of visual noise and a lack of clarity inherent in most digital environments, presenting a unique new challenge that ophthalmic lens manufacturers must aspire to overcome. In turn, as eye care providers, we need to be sensitive to these new visual and emotional demands so we can help alleviate our patients' struggles.

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CE QUESTIONS

1. Today's anti-reflective (AR) coated lenses improve vision by:

a) Reducing glare from the lens surface, while increasing reflection and light transmittance
b) Reducing glare and reflection from the lens surface, while increasing light transmittance
c) Reducing reflection from the lens surface, while increasing glare and light transmittance
d) Reducing light transmittance from the len surface, while increasing glare and reflection

2. A national study conducted in the early days of COVID found all of the following EXCEPT:

a) One-third of participants experienced depressive symptoms
b) Women were more likely than men to experience depressive symptoms
c) Depressive symptoms were most common in those aged 30-39
d) Those who maintained very frequent in-person social connections had better mental health outcomes

3. First impressions begin to form within:

a) 1/100 of a second
b) 1/10 of a second
c) 1 second
d) 10 seconds

4. Which of the following statements is TRUE?

a) From an evolutionary standpoint, first impressions form slowly
b) The subconscious mind operates slowly
c) First impressions can be tied to human survival
d) First impressions impeded survival of the fittest

5. Which of the following statements is FALSE?

a) The human eye is equally sensitive to every color component of light
b) The human eye is more sensitive to some wavelengths than to others
c) Spectral sensitivity refers to the relative efficiency of detection of light
d) The detection of light is a function of the frequency or wavelength of the signal

6. Looking at a stranger's face for longer than _____ merely boosts one's confidence in first impressions, without significantly altering initial judgements.

a) 1 second
b) 1 millisecond
c) 10 milliseconds
d) 100 milliseconds

7. Which of the following is FALSE?

a) First impressions are based largely on facial expressions
b) Charles Darwin argued that human facial expression is a universal language
c) Darwin's theory does not hold up across cultures
d) Darwin's theory does not hold up in online contexts

8. Humans have ___ muscles in the face that they use to create expressions.

a) 23
b) 33
c) 43
d) 53

9. We may assume that a smile is forced or lacks feeling when we don't see it in the:

a) Teeth
b) Eyes
c) Nose
d) Head Tilt

10. When researchers at UC Berkeley and Google analyzed facial expressions, results showed that:

a) At least 70% of facial expressions are shared across countries and cultures
b) Most facial expressions are used in response to different social and emotional situations that vary primarily by country and culture
c) Human expression does not transcend geographic and cultural boundaries
d) Human expression transcends geographic and cultural boundaries, EXCEPT in online contexts

11. Which of the following statements is TRUE?

a) Ophthalmic lens reflections only affect lens wearers
b) Ophthalmic lenses can compromise the connection between individuals who are trying to communicate
c) Anti-reflective coatings increase the intensity of reflections
d) Ophthalmic lenses do NOT reflect light

12. In digital environments pixel density, screen dimensions, Wi-Fi strength, reflection, and audio or video lags ...

a) Have not been studied
b) Have been found to have little to no effect on our ability to establish connections
c) Make connections easier to establish
d) Make connections harder to establish

13. Positive first impressions are characterized by all of the following EXCEPT:

a) How connected you feel
b) How you perceive the stranger's trustworthiness and likability
c) The similarities you recognize between yourself and the stranger
d) Whether your connection elicits empathy

14. Clearer lens clarity results in increases in all of the following EXCEPT

a) Likability
b) Connection
c) Trust
d) Sympathy

15. Research shows a direct correlation between lens clarity and:

a) Positive impressions
b) Environment
c) Gender
d) Frame Style

16. Which of the following statements is accurate, based on the research shared in this report?

a) Lens clarity studies contradict earlier evolutionary psychology theories
b) Lens clarity studies demonstrate that lens clarity does not aid in determining emotion
c) Lens clarity is connected to impressions of trustworthiness, but not to likeability
d) Lens clarity makes it easier for people to connect

17. According to the two studies shared in this report, increasing _____ is one of the easiest and most affordable ways to positively impact connections between people and positive first impressions.

a) Screen time
b) Face-to-face meetings
c) Lens clarity
d) Time spent off-screen

18. Which of the following statements is TRUE?

a) We feel less connected to people when we can see their eyes online
b) Online interaction improves our ability to see people's eyes when we're talking to them
c) The ability to see people's eyes is a fundamental component of interpersonal communication
d) The more light you add to an online viewing experience, the better

19. What adds to the challenges of online interpersonal communication?

a) Visual noise
b) Large screens
c) Reading eye expressions
d) All of the above

20. Lens coatings date back to the ___ century.

a) 17th
b) 18th
c) 19th
d) 20th

Examination Answer Sheet

Exploring the Impact of Lens Coatings on Emotional Connection

Valid for credit through March 15, 2024

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

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

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Credit: This course is COPE-approved for two hours of CE credit. Course ID 82320-GO

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

Jointly provided by PIM and the Review Education Group.

Answers to CE exam:

1. Ⓐ Ⓑ Ⓒ Ⓓ
2. Ⓐ Ⓑ Ⓒ Ⓓ
3. Ⓐ Ⓑ Ⓒ Ⓓ
4. Ⓐ Ⓑ Ⓒ Ⓓ
5. Ⓐ Ⓑ Ⓒ Ⓓ
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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. Explore the impact of lens coatings and its effects on patients ① ② ③ ④ ⑤
22. Examine the connection between eye strain and light wavelengths and their connection to mental health ① ② ③ ④ ⑤
23. Review various studies that look at ophthalmic lenses, mental health, and lens coatings ① ② ③ ④ ⑤

24. 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.

25. 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): ☐

26. If you plan to change your practice behavior, what type of changes do you plan to implement? _____

_____

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

Ⓐ Very confident Ⓑ Somewhat confident Ⓒ Unsure Ⓓ Not confident

28. What do you anticipate will be the primary barrier to implementing these changes in the future? _____

_____

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

29. The content was evidence-based. ① ② ③ ④ ⑤
30. The content was balanced and free of bias. ① ② ③ ④ ⑤
31. 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 123662 RO-PIM-0323

Turning Inward

Proper use of Quickert sutures is the lid-everting procedure all medical optometrists need to know.

BY BRADLEY A. DANIEL, OD
EDMOND, OK

Eliminating the anxiety of having to go "under the knife" goes a long way for most patients. Lid-everting sutures, also referred to as Quickert sutures, are simple to use, low cost and can drastically help. Being able to provide a functional change that greatly impacts your patient's quality of life is enough of an incentive to add this to your office-based procedure arsenal.

Background

Characterized as the inward turning of the eyelid margin, entropion occurs in up to 2.4% of people over 60 years of age.[1] The inward turning of the eyelid margin causes the eyelashes to come into contact with the corneal and conjunctival surfaces, resulting in irritation (*Figure 1*). This resulting secondary trichiasis, if left untreated, can lead to chronic ocular surface disease and subsequent keratinization of the cornea.

Entropion pathogenesis is multifactorial and consists of overriding of the preseptal orbicularis muscle, disinsertion of the lower eyelid retractors, increased horizontal laxity of the tarsus and canthal tendons, scarring from prior surgeries, radiation and trauma.[1]

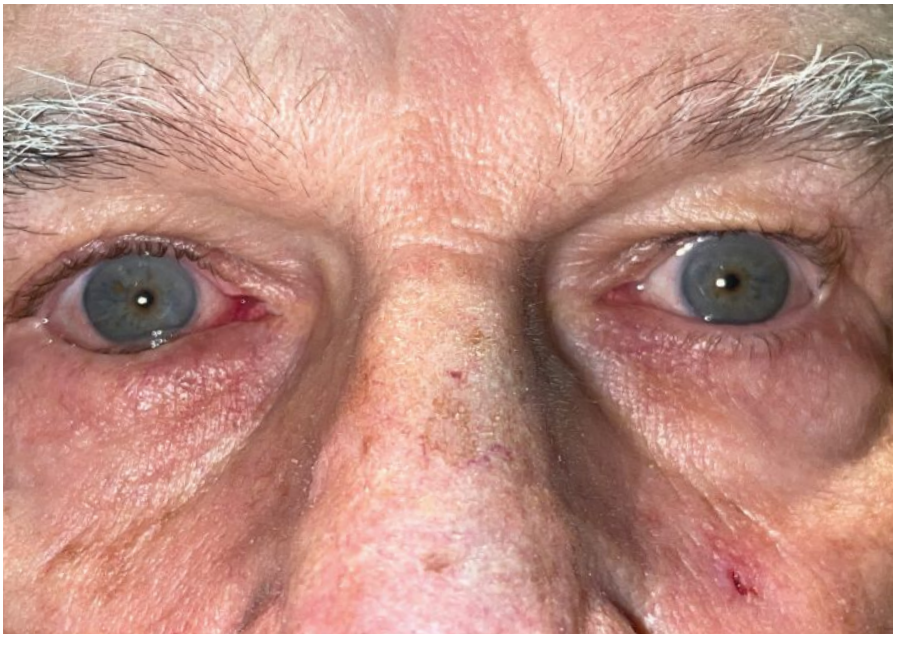

Fig. 1. Involution entropion in the right eye.

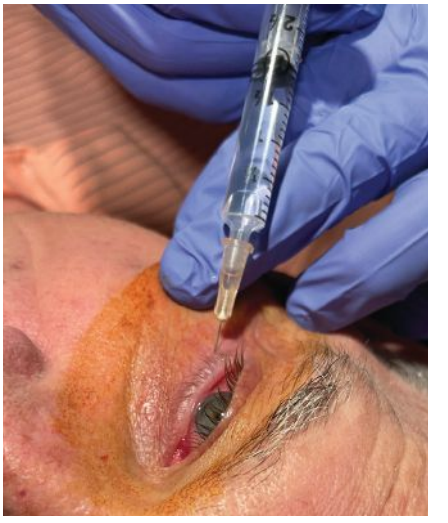

Fig. 2. Subcutaneous injection of Lidocaine 2% with epinephrine done to provide proper local anesthesia.

Entropion can be classified as involutional, spastic, congenital or cicatricial. Of these, only involutional and spastic apply to this article. Conservative treatment consists of lid taping, bandage contact lenses and artificial tears. However, these treatments do not address the underlying cause of the condition. Thus, the majority of cases will require some sort of corrective surgical measure, and therefore having the capability to offer one in-office is very advantageous.

First described in 1971, double-armed Vicryl absorbable sutures are safe, minimally invasive, effective, low cost and can be used in the office to address involutional and spastic entropions.[2] By inducing scar formation between the tarsal plate and low lid retractor, lid eversion is achieved to a more neutral/natural position. Additionally, this scarring between the orbicularis oculi and the lower lid retractors prevents the overriding of the preseptal orbicularis oculi muscle.[3]

About Dr. Lighthizer

Dr. Lighthizer is the associate dean, director of continuing education and chief of specialty care clinics at the NSU Oklahoma College of Optometry. He is a founding member and currently serves as president of the Intrepid Eye Society. Dr. Lighthizer's full disclosure list can be found in the online version of this article at www.reviewofoptometry.com.

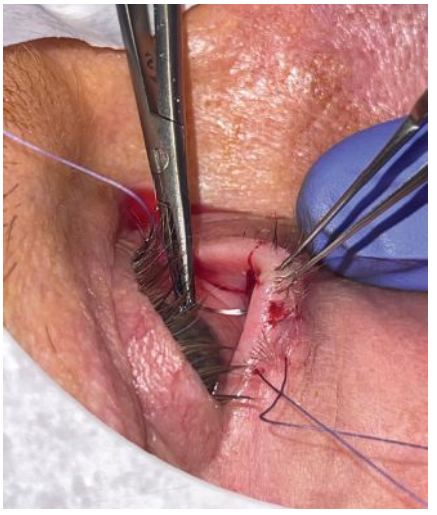

Fig. 3. The first arm of the second suture being thrown in the central third of the eyelid.

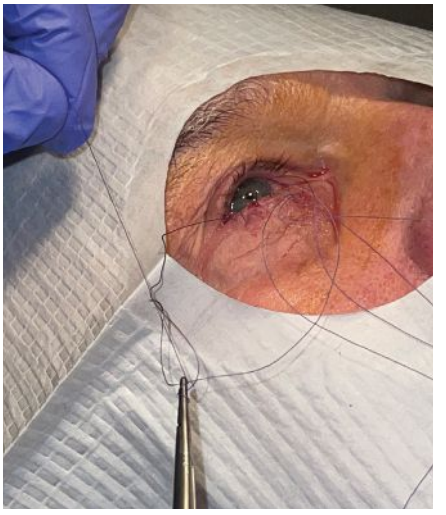

Fig. 4. Tying of the knots.

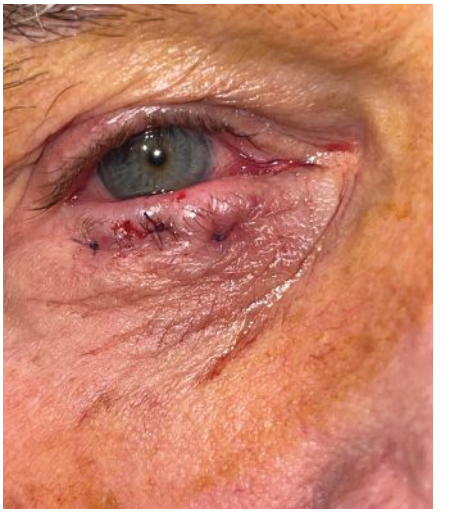

Fig. 5. Immediate post-op appearance. Notice the slight ectropion immediately following the procedure, which is the clinical endpoint to shoot for.

Patient selection and expectation is an important aspect to consider. For this procedure, only involutional and spastic entropion cases, where horizontal lid laxity is not the main contributor, are candidates. This is due to the fact that its method of action is tightening of the lower lid retractors, and therefore it does not address any horizontal lid laxity. Evaluating dehiscence of the lower lid retractors can be achieved by having the patient look downward and measuring the descent of the lower lid. The lower lid should descend 3mm to 4mm; if this is diminished, it is an indicator of dehiscence or disinsertion of the retractors.[4] Horizontal lid laxity can be evaluated by pulling the lower lid laterally while the patient is looking straight ahead and measuring the displacement from the medial canthus or puncta, then repeated medially measuring lateral canthus displacement. Normal displacement is from 0mm to 2mm.[5] Moreover, patients who do not wish to pursue or who do not qualify for traditional lid surgery are good candidates. Additionally, blood thinners do not have to be stopped prior to the procedure.

TABLE 1. RECOMMENDED INSTRUMENTS AND SUPPLIES

Double-armed 5.0 Vicryl sutures on S-14 needle
Lidocaine HCl 2% + epinephrine 1:100,000
30-gauge needle with syringe
Surgical drape, gauze and cotton tipped applicators
Needle driver
Surgical forceps with teeth
Topical proparacaine 0.5% or equivalent
Erythromycin ointment or equivalent

Procedural Technique

The procedure consists of three horizontal mattress sutures placed medially, centrally and laterally in the entropic lid. All sutures enter from the inferior conjunctival fornix and exit on the external side of the lid just inferiorly to the lash line. The everting sutures transfer the pull of the attenuated lid retractors to the anterior surface of the tarsal plate. Moreover, a horizontal barrier above the preseptal orbicularis is created to prevent further upward migration.[6] The main prognostic factor for permanence of the procedure depends on the extent of the fibrosis created.[7] The fibrotic response has been reportedly demonstrated as early as two weeks.[6]

The equipment required for the procedure is shown in *Table 1*. Sterilize the operative lid with a betadine or iodine swab, making sure to sterilize both the upper and lower lids extending downward to the cheek. Divide the lower lid into thirds, paying close attention to the puncta to ensure it does not get everted. The use of a surgical marker is highly suggested for the first few cases.

Anesthetize the palpebral conjunctiva by use of a topical anesthetic, for example proparacaine 0.5%. This is followed by the lower lid being injected with 1mL to 2mL of 2% lidocaine HCl with 1:100,000 epinephrine into the subciliary skin and palpebral conjunctiva (*Figure 2*). It is advised to test the anesthesia by palpating the target tissue with sterile forceps. Once proper anesthesia is achieved, decide on which side of the lid to begin.

For simplicity's sake, this article will begin with the lateral third of the lower lid first. A 5.0 double-armed polyglactin absorbable Vicryl suture on an S-14 needle is recommended and is held using a

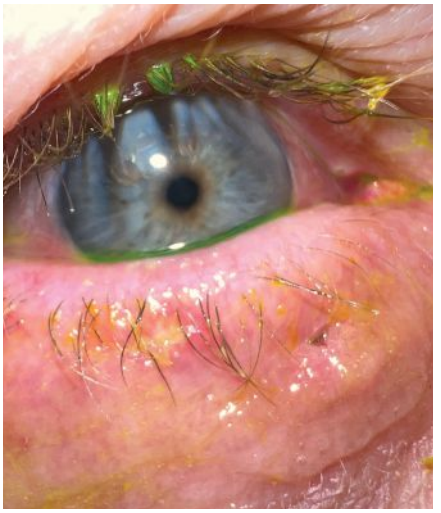

Fig. 6. The 10-day post-op visit. Note the perfect position of the eyelid margin.

needle driver in the dominant hand. The first arm of the suture is placed deep in the inferior fornix through the lower palpebral conjunctiva. To ensure it pierces through and engages the lower lid retractors, roll the wrist upward as you pass the needle through the capsulopalpebral fascia. This will also allow for the proper passing of the needle to exit the external side of the lid.

Holding the forceps in the non-dominant hand, pull the protruding needle through. It should be exiting the external side of the lid 2mm below the lash line. A greater everting effect is achieved by having the sutures deeper in the fornix and closer to the lash line.[8] Once the needle and suture have been pulled through and sufficient slack is left, the second arm of the suture is then ready to be placed. The second arm is placed 2mm to 3mm medial to and at the same level of the first arm.

Using the same technique described previously, the second arm should be exiting 2mm below the lash line. Again, being adjacent to and at the same level of the first arm. Once the second arm exits externally, use forceps to pull the slack evenly on both sides. The second suture is placed at the central third of the lower lid in the exact same manner as the first (*Figure 3*). Again, ensuring both arms are exiting at the same level, 2mm below the lash line. The third and final suture is placed at the medial third of the lower eyelid. It is imperative to stay lateral to the lower puncta. Doing so will avoid punctal eversion, which occurs when the sutures are placed too proximal to the puncta.

Tying the sutures can be done immediately after passing both arms of the needle through the lower lid or after all three sutures have been placed (*Figure 4*). To mitigate tangling, cutting off the needles on the sutures is recommended prior to tying them. When tying the suture, it is recommended to use at least a three-throw technique to ensure proper eversion. When pulling taut, ensure that no tissue strangulation occurs from over-tightening. The clinical endpoint immediately after the procedure should result in a slight ectropion (*Figure 5*). Once all three sutures have been successfully tied, a topical antibiotic ointment, such as erythromycin, is placed over the sutures and along the palpebral side of the lid.

It is advised to prescribe a topical antibiotic ointment with good gram-positive coverage for a course of at least two weeks. It is recommended to follow-up with the patient in 10 to 14 days.

Follow-up

The patient is instructed to apply the topical antibiotic ointment bid to the sutures for one week then Qhs for one week. Furthermore, the patient should be instructed not to get the sutures wet, as well as no prolonged bending or heavy lifting for the two weeks following surgery. By the two-week point, lower lid retractor fibrosis is achieved.[6] The sutures can be left to absorb on their own, and the knots can be trimmed at the follow-up (*Figure 6*). A final follow-up can be set at the six-week point to ensure proper healing.

The recurrence rate is variable according to multiple sources. At the two-year mark, it has been reported to be as low as 15% and as high as 42.9%.[6,9] The key factor to mitigating recurrence lies in patient selection. As stated earlier, this procedure does not address entropions with significant horizontal lid laxity. Another appealing feature of the procedure is that it is repeatable, with even lower rates of recurrence.[10] This quick in-office procedure is cost-effective with good medical reimbursement for those medical optometrists practicing in states with broadened scope. ■

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ABOUT THE AUTHOR

Dr Daniel specializes in ocular disease and refractive surgery at Edmond Regional Eye Associates in Edmond, Oklahoma, having received advanced clinical training in the diagnosis and management of ocular disease and is certified in laser vision correction, anterior segment laser procedures and other minor surgical procedures . Dr. Daniel is a fellow of the American Academy of Optometry, as well as a diplomate of the American Board of Optometry He has no financial disclosures.

BY ALISON BOZUNG, OD

URGENT CARE

Cloudy With a Chance of… Cataract?

This patient presented with pain and decreased vision in one eye.

A 72-year-old male presented to the ophthalmic emergency department with significantly decreased vision, pain and redness of his right eye for five days. He denied any ocular trauma. His ophthalmic surgical history was significant for cataract surgery in the left eye a number of years prior. His medical history revealed well-managed hypercholesterolemia. He was otherwise in good health and noted to be afebrile.

His visual acuity on presentation was light perception in the right eye and 20/25 in the left. His intraocular pressures (IOPs) measured at 23mm Hg OD and 12mm Hg OS. There was no view to the pupil in the right eye; the left eye's pupil was unremarkable. The right eye had moderate diffuse conjunctival injection with turbid and opaque fluid in the anterior chamber, but the cornea was notably compact and devoid of keratic precipitates (*Figures 1 and 2*). There was no view posteriorly. The left eye's exam revealed a quiet anterior chamber with a well-centered intraocular lens (IOL) and a normal-appearing posterior segment.

Due to the poor visualization inside the right eye, ultrasonography was conducted to view the ocular structures. First, a posterior segment ultrasound was completed, confirming there was no retinal detachment or mass lesion (*Figure 3*). Next, anterior segment ultrasonography was done, revealing a deep anterior chamber filled with dense, pin-like hyperechoic opacities. The angle was noted to be open circumferentially, and there was a thick and distended lens capsule with hyperechoic, dense lenticular material inside (*Figure 4*).

The patient was diagnosed with suspected phacolytic glaucoma and started on topical prednisolone acetate drops six times daily, timolol-dorzolamide drops twice daily and cyclopentolate drops twice daily in the right eye. He was asked to return the next day for surgical evaluation.

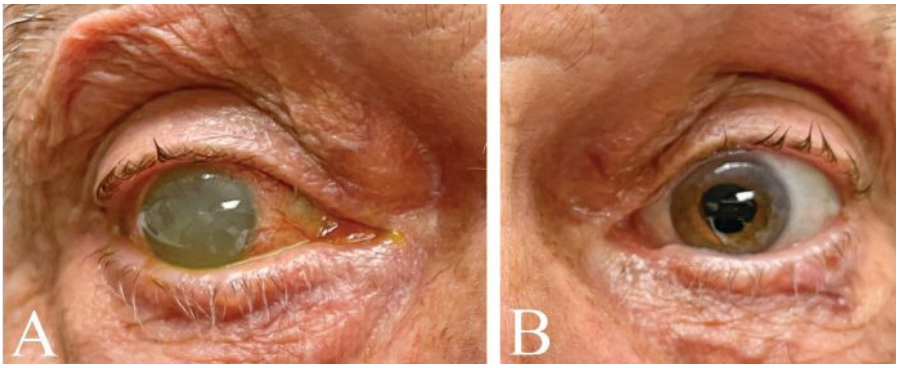

Fig. 1. The right (A) and left (B) eyes of this patient on presentation. Note the cloudiness apparent in the right eye's anterior chamber. The left eye had previously undergone cataract extraction.

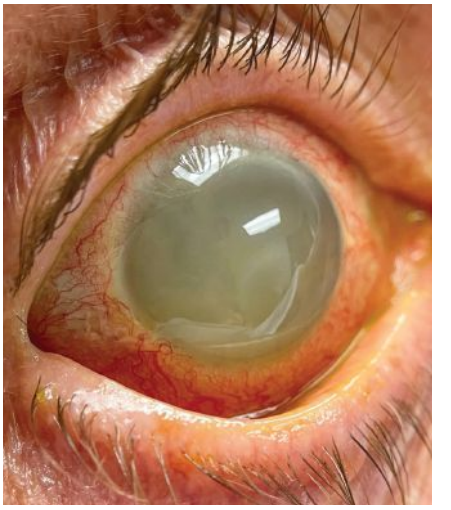

Fig. 2. A magnified view of the right eye's anterior segment.

Discussion

Somewhat of a rarity in first-world modern societies, severely advanced cataracts and their complications are not often seen. Once a cataract advances well into maturity, certain findings become more commonplace. A "white" cataract is seen clinically as a totally opaque, white lens that often precludes a view of even the retinal red reflex. A Morgagnian cataract occurs when the dense, yellowed lens nucleus drops to the bottom of the lens capsule due to liquified cortex.

Two mature lens–induced conditions that occur with an intact lens capsule include phacomorphic and phacolytic glaucoma. Although similar in nomenclature, complications and treatment, phacomorphic- and phacolytic-induced glaucoma

About Dr. Bozung

Dr. Bozung works in the Ophthalmic Emergency Department of the Bascom Palmer Eye Institute (BPEI) in Miami and serves as the clinical site director of the Optometric Student Externship Program as well as the associate director of the Optometric Residence Program at BPEI. She has no financial interests to disclose.

To treat ocular inflammation and pain following ophthalmic surgery or ocular itching associated with allergic conjunctivitis.

DEXTENZA KEEPS PATIENTS COMPLIANT AND SATISFIED[1-3*]

A hands-free advancement in ophthalmic steroid treatment.[1,4]
Easy-to-insert† and preservative-free intracanalicular DEXTENZA offers patients a satisfying post-op experience—providing up to 30 days of sustained steroid coverage.[1-5]

INDICATIONS

DEXTENZA is a corticosteroid indicated for:

- The treatment of ocular inflammation and pain following ophthalmic surgery.
- The treatment of ocular itching associated with allergic conjunctivitis.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DEXTENZA is contraindicated in patients with active corneal, conjunctival or canalicular infections, including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella; mycobacterial infections; fungal diseases of the eye, and dacryocystitis.

WARNINGS AND PRECAUTIONS

Intraocular Pressure Increase - Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. Intraocular pressure should be monitored during treatment.

Bacterial Infections - Corticosteroids may suppress the host response and thus increase the hazard for secondary ocular infections. In acute purulent conditions, steroids may mask infection and enhance existing infection.

Viral Infections - Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

Fungal Infections - Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

Delayed Healing - Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation.

Other Potential Corticosteroid Complications - The initial prescription and renewal of the medication order of DEXTENZA should be made by a physician only after examination of the patient with the aid of magnification, such as slit lamp biomicroscopy, and, where appropriate, fluorescein staining. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.

ADVERSE REACTIONS

Ocular Inflammation and Pain Following Ophthalmic Surgery

The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: anterior chamber inflammation including iritis and iridocyclitis (10%), intraocular pressure increased (6%), visual acuity reduced (2%), cystoid macular edema (1%), corneal edema (1%), eye pain (1%), and conjunctival hyperemia (1%). The most common non-ocular adverse reaction was headache (1%).

Itching Associated with Allergic Conjunctivitis

The most common ocular adverse reactions that occurred in patients treated with DEXTENZA were: intraocular pressure increased (3%), lacrimation increased (1%), eye discharge (1%), and visual acuity reduced (1%). The most common non-ocular adverse reaction was headache (1%).

Please see adjacent Brief Summary of full Prescribing Information.

*93% (187/201) DEXTENZA patients were satisfied with the insert in the Phase 3 Study for the treatment of ocular inflammation and pain following ophthalmic surgery.[3]

†73.6% of physicians in Study 1, 76.4% in Study 2, and 79.6% in Study 3, for the treatment of ocular inflammation and pain following ophthalmic surgery, rated DEXTENZA as easy to insert.[2,5]

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Dextenza®
(dexamethasone ophthalmic insert) 0.4 mg
for intracanalicular use

are different entities. Both often present with severely elevated IOPs, secondary corneal edema, ocular pain and conjunctival injection. Additionally, the treatment for both is emergent management of any elevated IOP to reduce the likelihood of glaucomatous damage and urgent cataract extraction.

Phacomorphic glaucoma is characterized by a dense and thick lens pushing the iris forward and angle structures closed. The suffix *-morphic* refers to form or structure, and this aptly defines phacomorphic glaucoma, as the lens's form is the primary cause for glaucomatous complications.

Phacolytic glaucoma, on the other hand, typically has a deep chamber filled with proteinaceous lens material and macrophages. The suffix *-lytic* refers to lysis or decomposition of a material, and in phacolytic cases, lenticular material leaks through spontaneous microperforations in an otherwise intact lens capsule.

There is some thought that there may be two subtly different subtypes of phacolytic glaucoma.[1] In some cases, there is a very acute onset of symptoms and IOP elevation. This is thought to likely be due to primarily liquefied lens proteins rapidly egressing through the lens capsule and into the anterior chamber, directly obstructing the angle's trabecular meshwork. In these cases, no macrophages are seen in the anterior chamber specimen.

The other subset of cases has a slower, more gradual onset of symptoms, including the presence of macrophages with nuclear debris (ingested lens material). The outcome is the same in both cases, but the patient with hyperacute onset of symptoms will likely present earlier due to the drastic, quick rise in IOP.

Interestingly, most patients who present with phacolytic glaucoma are pseudophakic in the other eye.[2,3] This is likely due to the fact that they have good, functional vision in one eye and are less symptomatic for visual decline with just one advancing cataract. Therefore, doctors should educate patients and reinforce the importance of considering cataract extraction in the fellow eye before the cataract becomes hypermature.

Additionally, it is important to understand that although cataract extraction is considered curative in most cases of phacolytic glaucoma, there is still a small subset of patients who have persistent elevated IOP after surgery and require continued glaucoma management.[2]

Two other lens-related glaucomas that occur with lens capsule violation are lens-particle glaucoma and phacoantigenic (or phacoanaphylactic) glaucoma.

Lens-particle glaucoma occurs after macroscopic (often visible) damage to the lens capsule from trauma or iatrogenically during intraocular surgery. Once lens material is liberated into the anterior chamber, the disease mechanism leads to elevated IOP primarily due to direct particle deposit into and blockage of the trabecular meshwork.[4,5]

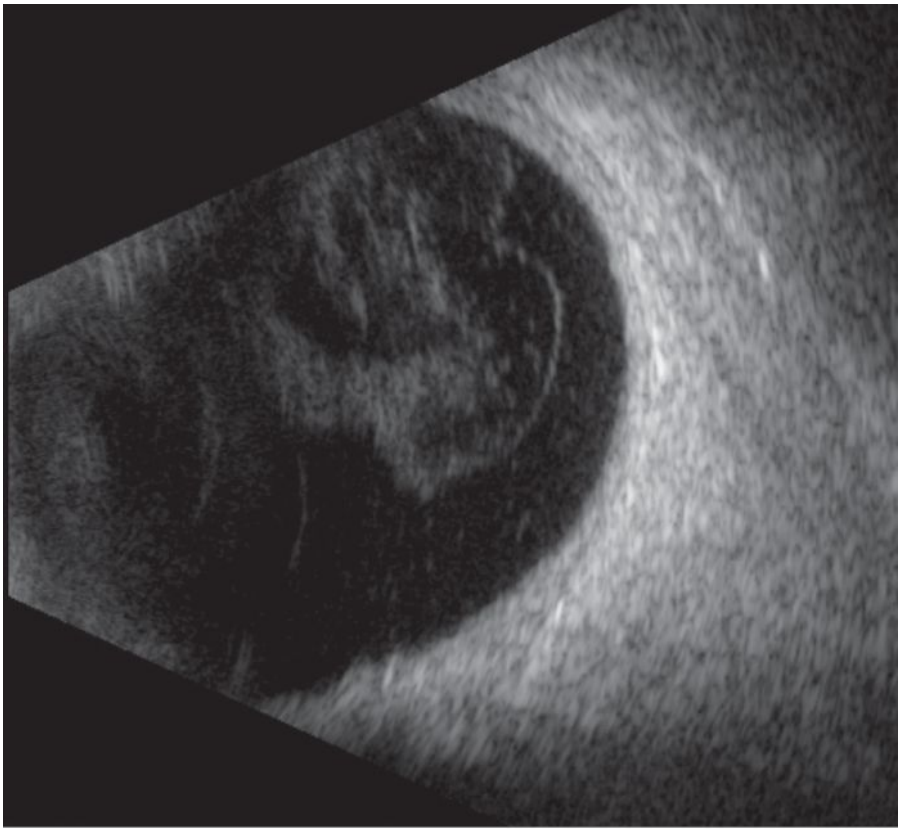

Fig. 3. A normal posterior segment exam with mild vitreous opacities but no retinal detachment or lesion.

Similarly, phacoantigenic glaucoma is typically caused by surgery or trauma with capsule violation and exhibits a sensitization period of one to 14 days, during which there is a Type III hypersensitivity reaction against the lens particles.[5] Often, there is significant inflammation visible, and granulomatous keratic precipitates may also be seen.

For both of these conditions, treatment is directed at managing any inflammation with topical corticosteroids, lowering IOP with topical aqueous suppressants and considering surgery if lens material remains exposed and/or does not absorb on its own.

Outcome

Our patient underwent cataract surgery within a few days of presentation and was noted intraoperatively to have significant zonular loss. This zonular dehiscence allowed for vitreous to prolapse anteriorly, so a pars plana vitrectomy was completed at the same time. The decision was made to remove the cataractous lens and use a sulcus-placed IOL due to poor zonular support. Mild optic atrophy was appreciable intraoperatively when the view allowed, which would likely limit the patient's ultimate visual acuity in this eye to some extent. The pathology report of anterior chamber fluid revealed histiocytes (macrophages) with granular material within them, consistent with a subacute phacolytic process. This could be why IOP was still relatively normal on presentation compared with the high spike that is typically seen.

At the three-week follow-up, the patient's visual acuity had improved significantly to 20/70. His IOP remained moderately elevated at 28mm Hg off IOP-lowering medication, so timolol-dorzolamide was reintroduced into his treatment plan. The patient will continue to follow-up for clinical care and glaucoma monitoring. ■

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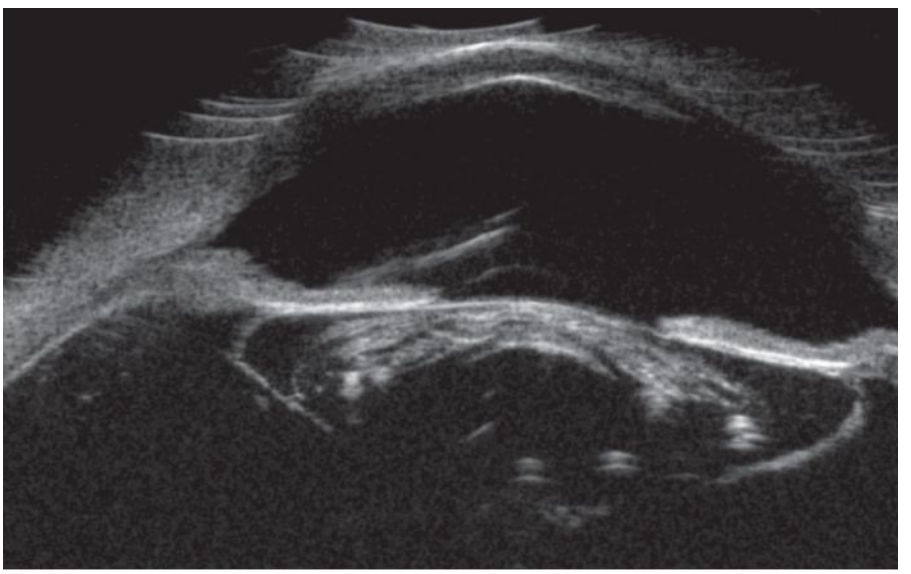


Fig. 4. A thickened mature lens with a very dense cortex causing posterior shadowing. Note the anterior chamber depth is preserved.

Cataract Qualms

Diabetic patients, more at risk for surgery complications, can benefit from these considerations.

Q Are these individuals at higher risk for corneal endothelial damage from cataract surgery? What precautions should I heed when referring them? How can I best protect them pre- and postoperatively?

A Corneal microstructural changes in endothelial cell measurements in people with diabetes compared with those without the condition is well documented. Here's the rub, though—do these morphometric changes lead to poorer post-op recovery and impaired function following cataract surgery in clinical practice? "The evidence for this is still confounding and predominantly theoretical, likely because surgical techniques have become advanced and adverse outcomes minimized with contemporary best practices and technology," says Bhawan Minhas, OD, of The Eye Institute at Salus University. That being said, effective comanagement requires careful awareness of differences for our diabetic patients—you can't look out for what you don't know, she adds.

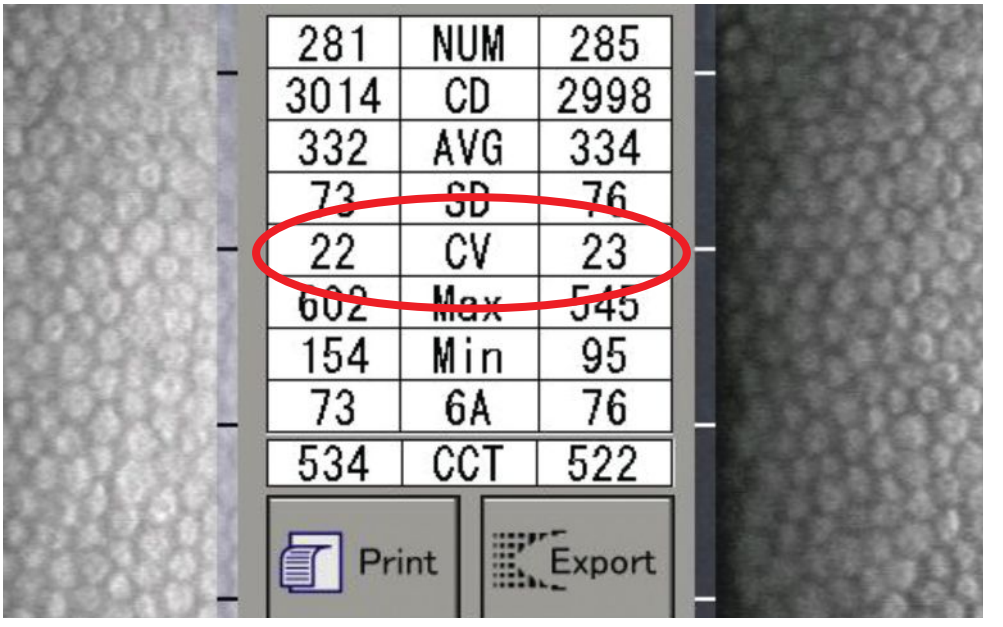
Diabetes and Cataract Surgery

Here's an overview of what we know about undergoing cataract surgery via phacoemulsification for patients with diabetes. This population has a higher percentage coefficient of variation (CV), as measured by specular microscopy, at a three month post-op mark compared to pre-op. This metric represents how much variation there is or degree in which endothelial cells' size differ (*i.e.*, polymegethism). The system can measure how much cell loss occurs through the size variation between those endothelial cells, with a CV of 40 or less being normal. However, this change is also significantly less than non-diabetic patients, indicating that these individuals start with a higher CV and don't change much after surgery.[1]

A higher CV suggests slower and weaker recovery of endothelial cells, according to Dr. Minhas. In a similar trend, endothelial cell density loss is also higher in these individuals compared to non-diabetic patients at one month and three months post-op.[1] Thus, endothelial cell count remains important to measure and compare in the pre- and post-op period. Central corneal thickness is noted to be significantly higher at one month for these patients compared with non-diabetic patients. However, the difference stabilizes by three months post-op, warranting careful measurements for the pre- and post-op period.[1]

Both these suggestions would be out of an abundance of caution for diabetic patients. Decrease in the percent of hexagonality has been noted in those with and without diabetes at one month and three months post-op, too.[1] However, different studies conflict on if this difference is statistically significant, she cautions.[2]

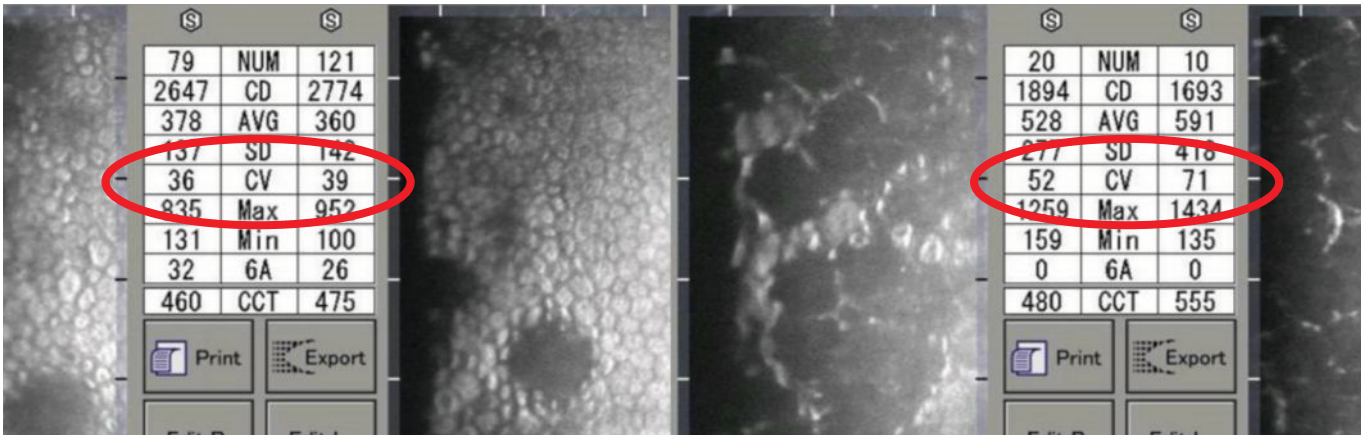
The minor increase between average ultrasonic energy used for phacoemulsification in diabetic individuals



A CV less than 40 is normal. Note that CV here is of typical condition.

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.



As CV value increases, the greater the variation seen in the size of endothelial cells. Both left and right photos show less uniform cells and greater CV values, accordingly.

compared with those without is not significant in cataracts graded III or below on the Lens Opacities Classification System III scale.[1]

"It can be postulated that very hard nuclei would require higher energy, thus potentially showing a more significant difference, given that those with diabetes have a lower functional reserve and their corneas are theoretically more vulnerable to injury," notes Dr. Minhas.

As for other considerations, CV is significantly higher and percentage of hexagonality significantly lower in patients who wear contact lenses compared with those who do not and non-diabetic patients.[3] "As a precaution, those who wear contact lenses should be even more closely monitored in the pre- and post-op setting. There is no difference in endothelial cell density among the various degrees of diabetic retinopathy, nor with a history of photocoagulation, so the modifiable risk factor remains glycemic control," Dr. Minhas explains.[4]

Comanagement

Given this data, what best practices should comanaging optometrists employ? It is proven that endothelial cell density is inversely correlated with duration of disease and HbA1c, so a modifiable risk factor for post-op complication is good glycemic control as measured by HbA1c.

"Comprehensive and ongoing patient education and comanagement with endocrinology is strongly suggestive of improved outcomes," Dr. Minhas advises. "Furthermore, comanagement with nutritionists and dieticians can help empower patients to make better choices in the early stages of the disease."

> **"Comprehensive and ongoing patient education and comanagement with endocrinology is strongly suggestive of improved outcomes."**

Given the relationship to duration, timely and even early referral for cataract extraction may be considered. Remember that a harder nucleus would require more ultrasonic energy during phaco and cause further damage to the endothelium, she adds.

Considerations for discontinuation of all contact lens use prior to cataract surgery evaluation in these patients may prime the cornea for scheduled injury with known handicaps. This 'washout' period theoretically may allow for the known difference of CV and percent hexagonality to stabilize in diabetic patients prior to going under the knife. This would be done out of caution and would likely be reserved for the most uncontrolled cases. Finally, comanaging optometrists could consider performing endothelial cell count and use reliable means to measure central corneal thickness in high-risk individuals undergoing cataract extraction during pre-op and at multiple stages in the post-op period (consider one week, one month, three months, and six months). That being said, ophthalmologists have easy access to these measurement tools, and all that may be needed is to alert the surgeon upon referral if they have a higher-risk case on their hands—those include patients with higher HbA1c, concurrent retinopathy or proliferative disease and previous use of contact lenses.

A majority of research demonstrates that although microstructural changes can be seen, they return to pre-op values—albeit more slowly in this patient population. Dr. Minhas advises other practitioners to keep in mind that "watchful monitoring and timely intervention in the pre- and post-op period should these negative outcomes present themselves, are the only precautions we can take as comanaging providers." ■

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BY PAUL M. KARPECKI, OD
CHIEF CLINICAL EDITOR

Toxic Work Environment

Be aware of certain glaucoma therapy options that could harm the ocular surface.

It's becoming clear that glaucoma patients are not compliant with topical medications if there is irritation upon instillation or the integrity of the ocular surface and vision is compromised. Here, I'll discuss a number of possible solutions to combat these issues.

Medications

Studies have revealed that as many as 59% of patients with glaucoma or ocular hypertension suffer from dry eye disease and that 96% of patients on prostaglandin analog (PGA) medications have meibomian gland dysfunction, as well as a significantly worse ocular surface disease index compared with patients not on PGAs.[1,2] Even non-PGA topical medications can disrupt the ocular surface due to preservatives such as benzalkonium chloride (BAK), which is a quaternary ammonium compound that acts as a detergent and can disrupt cell membranes, reduce cell proliferation and decrease corneal epithelial tight junctions.[3,4] This detergent disrupts the lipid layer, resulting in a rapid tear film breakup time and the potential for evaporative dry eye.[5] Ultimately, patients with ocular surface disease, blurred vision or pain may not remain adherent to the cause—the glaucoma medications.

Surgeries

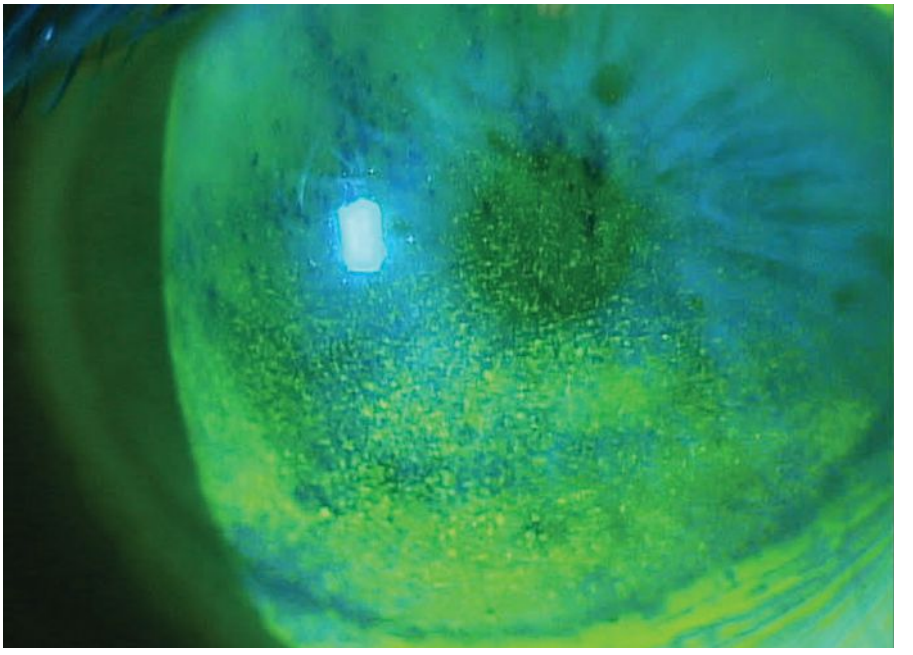
Many of the first-line surgeries for primary open- angle glaucoma can be performed by optometrists if they have the credentials, practice and are licensed in any of the 10 states that allow for this. These procedures, including selective laser trabeculoplasty (SLT), can lower intraocular pressure (IOP) by 25% to 30%. SLT is highly effective, relatively noninvasive, quick, easy to perform, repeatable and cost-effective.

Laser peripheral iridotomy is another surgery that can be administered for narrow-angle glaucoma patients.

There is also the bimatroprost sustained-release implant known as Durysta (Allergan), which can often be performed at the slit lamp. To implant the device, prep the ocular surface, place the inserter at the limbus, move toward the center, aiming down, and press the release button. The time-released pellet floats to the lower anterior chamber, where the drug is provided over the next three to four months, although studies show that 28% to 40% of patients have sustained IOP lowering one to two years after implantation.[6]

MIGS

If your glaucoma patient has significant cataracts, consider minimally invasive glaucoma surgery, or MIGS. Currently, it can only be performed at the time of cataract surgery, so you don't want to miss the opportunity to lower IOP without drops. Studies have shown as many as 78% of MIGS patients were glaucoma medication-free two years after the procedure, which was 30% more patients than the non-MIGS study group.



Corneal superficial punctate keratitis in a patient on multiple topical glaucoma medications.

About Dr. Karpecki

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

Compounded Drops

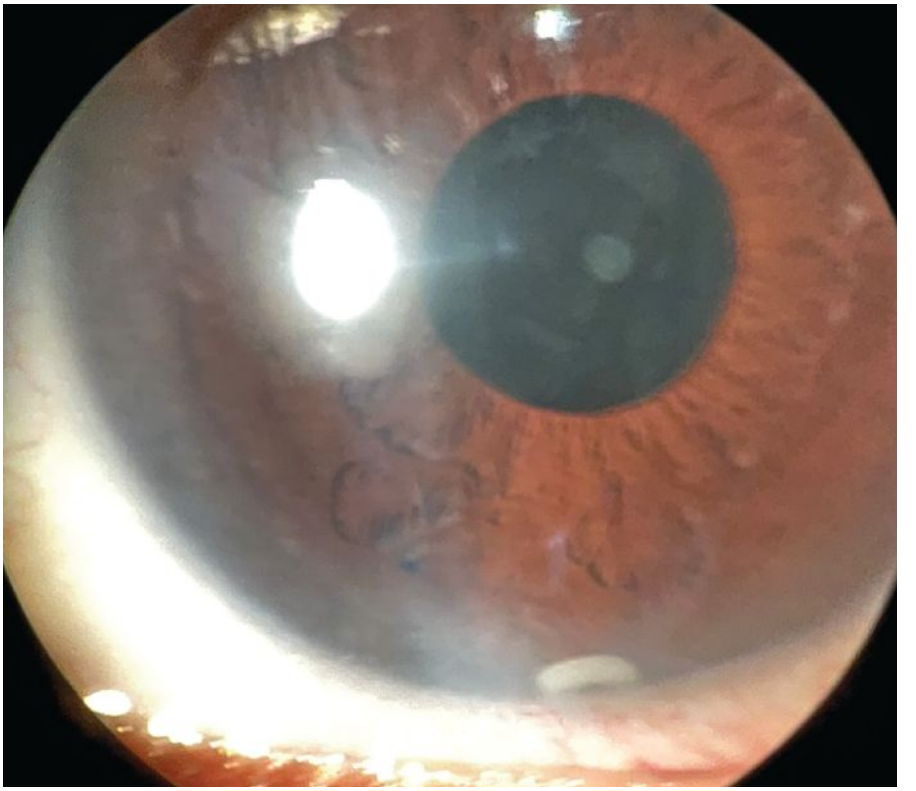
Using multiple glaucoma drops (including a PGA) with preservatives takes an even greater toll on the ocular surface. An innovative way to resolve this is compounding combination glaucoma drops through ImprimisRx. They are preservative-free and combine various meds in one bottle. This aids the ocular surface by producing less toxicity; it is also simpler for patients to only apply one drop rather than two to four, enhancing patient adherence. Any number of combinations are available depending on what you require for your patient.

Recently, I observed an advanced glaucoma patient I treated with the quad drop QHS (timolol 0.5%, brimonidine 0.15%, dorzolamide 2%, latanoprost 0.005%) and the triple drop in the morning (timolol 0.5%, brimonidine 0.15%, dorzolamide 2%, 10ml bottle). His IOP has remained stable for over three years at 11mm Hg OD and OS, and ocular surface staining has cleared.

> **Ultimately, patients with ocular surface disease, blurred vision or pain may not remain adherent to the cause—the glaucoma medications.**

Fewer Drops and Preservatives

If one can get fewer drops in the eye, patients would be exposed to less BAK and perhaps experience less toxicity from the PGAs. Our eye only holds about 20µm of fluid and most drop sizes are 30µm to 50µm. One way to reduce the drop volume is through the use of Nanodropper, a novel tip that patients place on their glaucoma medication bottles and reduces the drop size by over 60%. Studies show equal efficacy but less volume means less toxicity and better adherence, not to mention cost savings of extending the bottle life by more than 60%.



Anterior segment slit lamp photo of Durysta implant still visible at six-month follow-up.

The Near Future

TearClear recently announced that it met the primary and all secondary endpoints for its latanoprost 0.005% drop and is on track for a New Drug Application filing with the FDA the first quarter of this year, and numerous other glaucoma drops are to follow. What's unique about this formulation is that it has BAK in the bottle, but none of it gets to the eye. BAK is a terrific preservative as it maintains sterility, increases stability and aids in solubility—it's just bad for the ocular surface.

This unique platform allows for the use of a normal bottle (not preservative-free vials or multi-dose bottles that don't seem to work like normal ones), but the neck of the bottle contains polymers that remove 100% of the BAK as the drop leaves the bottle. So, only the preservative-free medication reaches the eye.

Be Alert

It's critical for us to observe the ocular surface and meibomian glands closely in all our patients taking chronic glaucoma medications so that we can spot early potential issues involving drug toxicity before adherence is affected. With a plethora of options available, you can help your glaucoma patients maintain a target IOP without compromising their vision, tear film, meibomian glands or ocular surface health. ■

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Not the Brightest Idea

A photoshoot gone wrong led to this patient's condition.

BY RAMI ABOUMOURAD, OD
MIAMI

A 40-year-old Caucasian female presented with three days of paracentral visual disturbance in both eyes (OU). She denied flashes, floaters, pain or photophobia. Her medical and ocular histories were unremarkable; she denied any prescription, over-the-counter or illicit drug use. She also denied any similar previous episodes and had no known environmental or drug allergies.

Her entrance visual acuities with pinhole were 20/25 OD and 20/20 OS. Her pupils were equally round and reactive without a relative afferent pupillary defect. Confrontation visual field and extraocular motility testing were both normal, and intraocular pressure was 14mm Hg OD and 12mm Hg OS by applanation. Anterior segment examination revealed 3+ diffuse punctate epithelial erosions (PEE) OD and 2+ PEE OS. Posterior segment findings can be seen below.

Take the Retina Quiz

1. Which of the following descriptions of the OCT images (Figures 1 and 2) is true?

a. There is a subretinal hyperreflective lesion.
b. There is hyperreflectivity of the outer retina.
c. There is intraretinal fluid.
d. There is vitreomacular traction.

2. What is the most likely diagnosis for this patient?

a. Berlin's edema.
b. Lamellar macular hole.
c. Solar retinopathy.
d. Vitelliform macular dystrophy.

3. What is the proposed mechanism for this patient's condition?

a. Inherited retinal dystrophy.
b. Mechanical trauma.
c. Photochemical toxicity.
d. Photothermal toxicity.

4. What is the most appropriate next step in the management of this patient?

a. Intravitreal anti-VEGF.
b. Intravitreal triamcinolone.
c. Observation and counseling.
d. Topical prednisolone acetate 1% four times daily for one week.

5. Which of the following statements is true?

a. The disease is inflammatory in nature and requires the use of an anti-inflammatory medication.
b. The disease is often progressive and there is no treatment; genetic testing is indicated.
c. The disease is often self-limiting but may result in permanent vision loss.
d. The disease is secondary to mechanical closed-globe blunt trauma.

For answers to the quiz, see page 114.

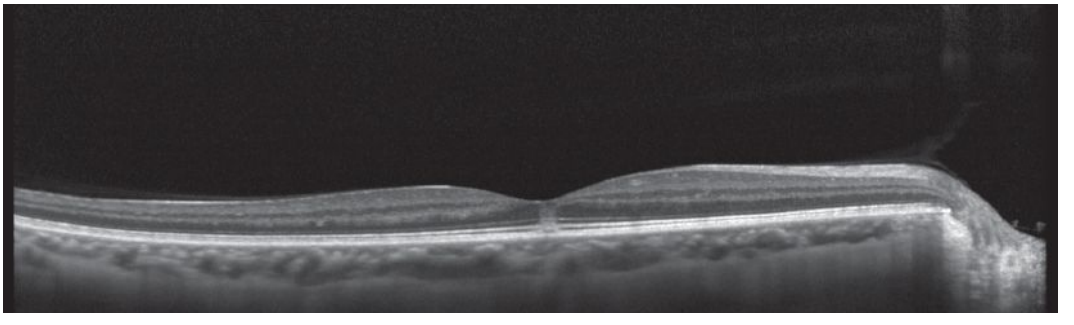

Fig. 1. Heidelberg Spectralis macular OCT of the right eye.

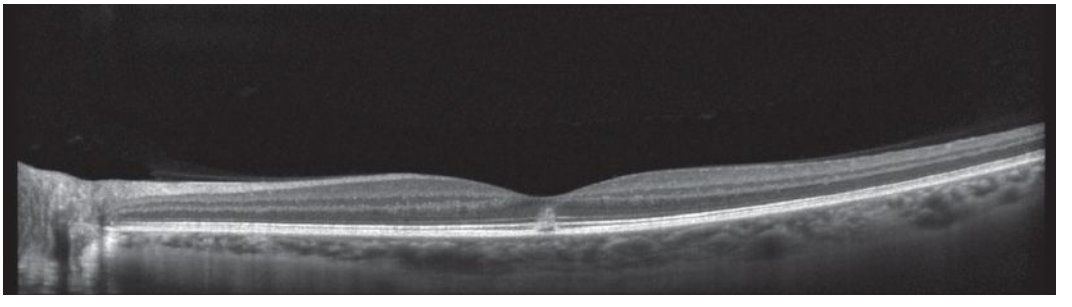

Fig. 2. Heidelberg Spectralis macular OCT of the left eye.

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

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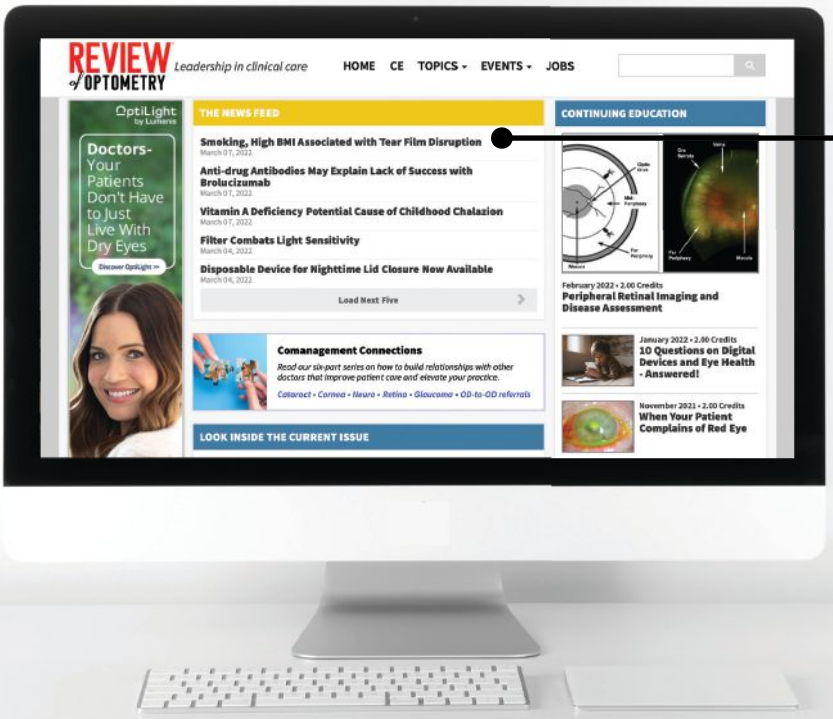

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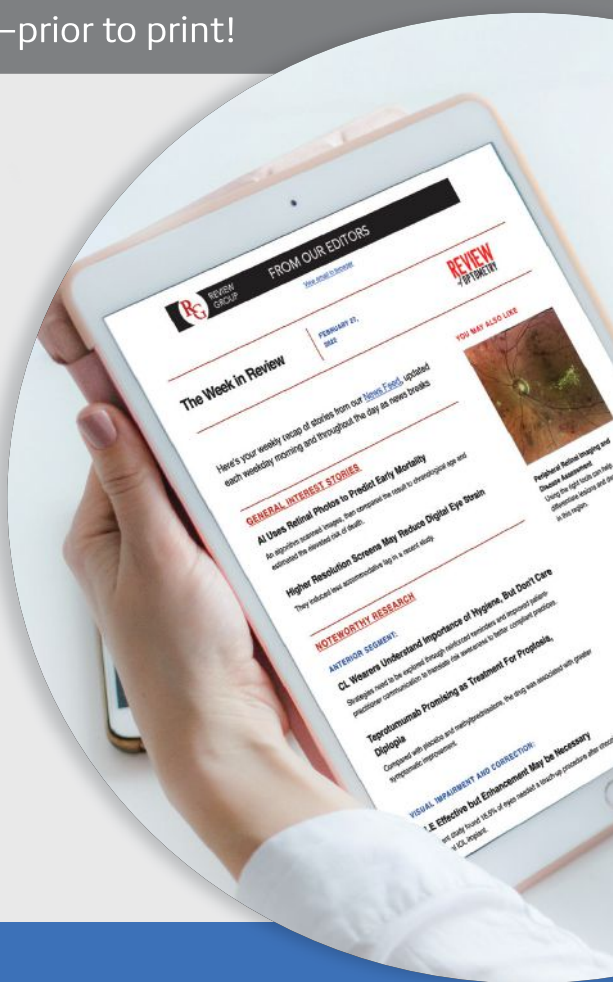

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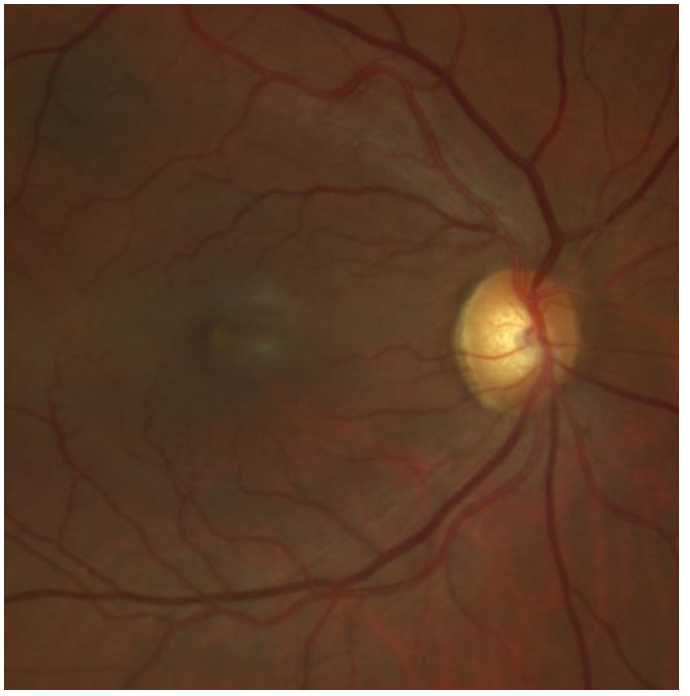

Fig. 3. Zeiss Clarus fundus photo of the right eye.

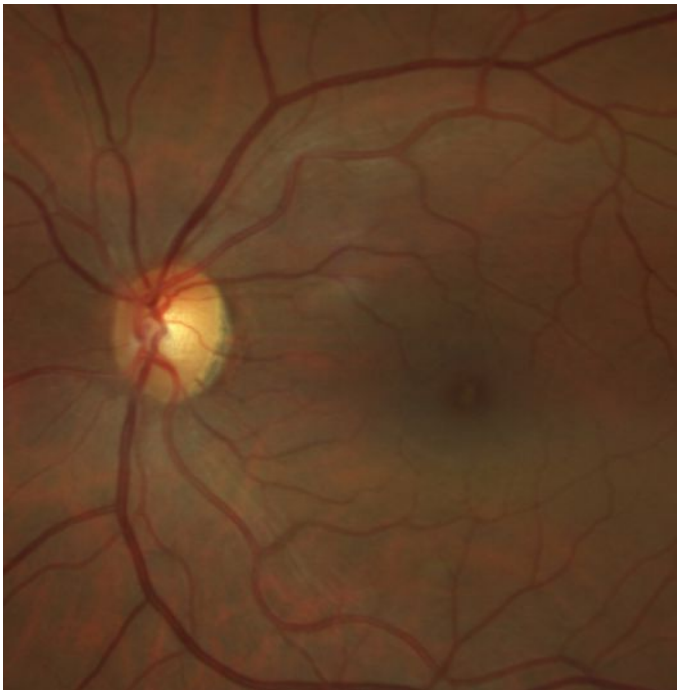

Fig. 4. Zeiss Clarus fundus photo of the left eye.

Diagnosis

Fundus examination revealed bilateral white punctate foveal lesions in both eyes (*Figures 3 and 4*). Additionally, there was a small hyperpigmented flat choroidal lesion along the superotemporal vascular arcade without overlying deposits or fluid, consistent with a choroidal nevus (*Figure 3*). The optic nerve, retinal vasculature and retinal periphery were all otherwise normal (*Figures 3 and 4*).

Ancillary testing with retinal OCT revealed bilateral, hyperreflective subfoveal outer retinal disruption involving the photoreceptor inner segment and outer segment (IS-OS) layers OU (*Figures 1 and 2*).

Upon further questioning, the patient admitted to a recent compulsion to sungazing for minutes at a time over the last few months while photographing nature. Most recently, she endorsed a history of sungazing for three consecutive minutes the day before she noticed her symptoms starting. She adamantly denied any hallucinogenic or mind-altering drugs.

The patient was diagnosed with solar retinopathy and photokeratitis.

Discussion

Solar retinopathy describes a type of photic retinopathy resulting in retinal injury secondary to a photochemical reaction.[1,2] It has also been termed solar retinitis, photoretinitis, foveomacular retinitis or eclipse burn/retinopathy.[1-4] In contrast with photothermal or photocoagulative retinal injury, which occurs at a thermal threshold of greater than 10°F above the body's temperature, photochemical toxicity occurs with less than 10°F change in body temperature.[1,2,4]

Solar viewing through a 3mm pupil produces a 7.2°F rise in retinal temperature (less than a threshold for photothermal damage), but sustained viewing for greater than 90 seconds exceeds the threshold for photochemical damage. Of note, solar viewing through a dilated 7mm pupil produces a 39.6°F increase in retinal temperature, far exceeding the threshold for photothermal damage.[1,2,4] That being said, momentary solar observation or looking up at the sky on a bright sunny day is typically safe.[2]

Solar retinopathy is primarily associated with solar eclipse viewing and sungazing in the setting of religious events, rituals, psychiatric illness, consumption of hallucinogenic drugs (*e.g.*, LSD) and hypoglycemia, but can also be caused from exposure to laser pointers.[1,3,4] The severity of injury is dependent on age, duration of exposure, intensity of light source, spectral content and even refractive error.[1,3,4] Higher energy, shorter wavelength light (*i.e.*, UV radiation) carries greater potential for phototoxicity than visible light.[1,2,4] Younger age or clearer crystalline lens status may allow for greater transmission of hazardous UV radiation. Furthermore, emmetropia and low hypermetropia also result in increased relative light focus onto the retina.[1,4] Other predisposing factors may include chorioretinal hyperpigmentation, higher body temperature and systemic photosensitizing agents such as tetracycline antibiotics or psoralen.[1,2,4]

Visual symptoms typically develop within hours of solar exposure and include central or paracentral scotoma, chromatopsia, metamorphopsia, photophobia, as well as headache or periorbital ache.[1,2,4]

Solar retinopathy generally presents with bilateral, foveolar lesions that

may be asymmetric with greater severity in the more dominantly fixating eye.[3,4]

Diagnosis is essentially based on clinical exam with supportive history. Visual acuity is typically reduced to 20/40 to 20/70 at presentation.[4] Acute solar maculopathy will show a white, yellow, red or gray foveolar lesion OU.[3-5] The exam often evolves over the first two weeks with fading of the original lesion and development of retinal pigment epithelial (RPE) mottling and/or atrophy adjacent to or in place of the original lesion.[1-5]

Ancillary testing may be acquired, and OCT is thought to be the most helpful imaging modality.[5] Acutely, OCT will show hyperreflectivity of the IS-OS and RPE layers extending from the outer retina toward the inner retina, while focal IS-OS and RPE loss can be seen in the chronic phase (*i.e.*, focal hypertransmission on OCT).[2-6] Fluorescein angiography may be normal during the acute phase but can evolve within weeks to hyperfluorescence in the form of a window defect, corresponding with the area of hypertransmission seen on OCT.[2-5] Fundus autofluorescence is a less useful diagnostic tool as it often only shows isoautofluorescence, but acute central hypoautofluorescence with a surrounding hyperautofluorescent ring at the site of the lesion has been reported.[7]

Treatment

Solar retinopathy is a self-limiting disease, and there are no proven therapeutic interventions available.[1,2,4,5] Often, vision can improve to 20/20 to 20/40 or near baseline levels over a period of weeks to three to six months.[1,2,4] Counseling is necessary to discourage further sungazing or eclipse viewing without proper eye protection.[2,4] If psychiatric illness is suspected, a psychiatric referral may be indicated.

This patient was counseled on the potential for permanent vision loss and discouraged from continuing such behavior. She was offered a psychiatric referral but declined. Copious lubrication with preservative-free artificial tears hourly for five days was recommended to address the photokeratitis. ■

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ABOUT THE AUTHOR

Dr. Aboumourad currently practices at Bascom Palmer Eye Institute in Miami. He has no financial disclosures.

PRODUCT REVIEW

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▶CONTACT LENSES

Scleral Lens with Simpler Fitting Process

A new addition to the growing scleral lens market aims to address a common challenge that eyecare providers face: achieving the optimal fit. The Europa Tangent—the second scleral lens design to join the Europa line by Visionary Optics—allows for independent adjustment of parameters in the central, limbal and landing zones using a three-zone fitting system, developers say.

The design of the customizable lens was inspired by profilometry data from more than 10,000 fittings, the company explained in a press release. The lens has one landing zone curve, which the company says was engineered to follow the natural slope of the sclera. It also has a softer landing zone, patterned after the free-form design used in the company's Latitude scleral lenses. The smoother transition to the landing zone is intended to help eliminate compression and blanching that sometimes occur during the fitting process.

The developers suggest the lens may be a practical option for providers in search of a more streamlined, easy-to-understand process for fitting patients with scleral lenses.

▶PHARMACEUTICALS

Three Atropine Formulations Now Available

Growing interest in myopia management is bringing ophthalmic mainstay drug atropine renewed attention, as the agent has a role to play in slowing the condition's development. Optometrists can now order atropine in one of three concentrations from compounding pharmacy ImprimisRx, which has just launched three 5ml bottles at strengths of 0.01%, 0.025% and 0.05%, each priced at $39. The company says the drops do not contain preservatives or boric acid, have a pH of 5.5 and may be stored at room temperature for up to 180 days.

▶IMAGING TECHNOLOGY

Two Next-Generation OCT Models Debut

The capabilities and precision of spectral-domain OCTs in today's market are continuously advancing. Joining the line-up is a new high-resolution imaging system from Visionix, marketed as the Optovue Solix FullRange OCT. The company is also offering a second device called Optovue Solix Essential, which—aside from its inability to perform multimodal imaging—still shares many of the same features as the full-range model.

The Solix OCT scans at an ultra-high speed of 120kHz, according to the company press release. Visionix notes that both devices feature company-designed software, coined "iWellness" and "AngioWellness," that can be used to assess and monitor patients with diabetes or glaucoma suspects by combining structural data on retinal and ganglion cell thickness with objective metrics on retinal vasculature. The software also uses FAZ analytics to reveal early indicators of diabetes-related ocular changes.

Both the FullRange and Essential platforms can perform advanced glaucoma screening using technology such as AI segmentation. With the full-range system, the repeatability and reproducibility of glaucoma analytics are two times better than in the previous model, Visionix says. Both platforms also use pachymetry and epithelial thickness mapping to aid in the assessment of anterior pathologies such as keratoconus and dry eye, the press release notes.

The more feature-loaded of the two, Solix FullRange, can perform the following functions for anterior segment assessment, according to the device brochure:

- Single-scan imaging for visualization of the entire anterior chamber from the front of the cornea to the anterior of the lens or entire crystalline lens.
- Angle structure visualization and quantification.
- A 10mm corneal layer map showing epithelial, stromal and total corneal thickness with change analysis.
- External IR imaging to display the structure of the upper and lower lids.

As for the posterior segment, Visionix says that the FullRange platform features AngioVue OCT-A software for 3D visualization and quantification of retinal vasculature. A montage feature also enables widefield visualization of the peripheral retina. The company notes that the technology can allow for accurate retinal analysis even in highly myopic patients.

For ODs who aren't interested in multimodal imaging but still desire a fast and advanced OCT, the Solix Essential might be the better choice, as it includes the same anterior and posterior segment OCT and OCT-A capabilities. ■

Practice For Sale

BY ANDREW S. GURWOOD, OD

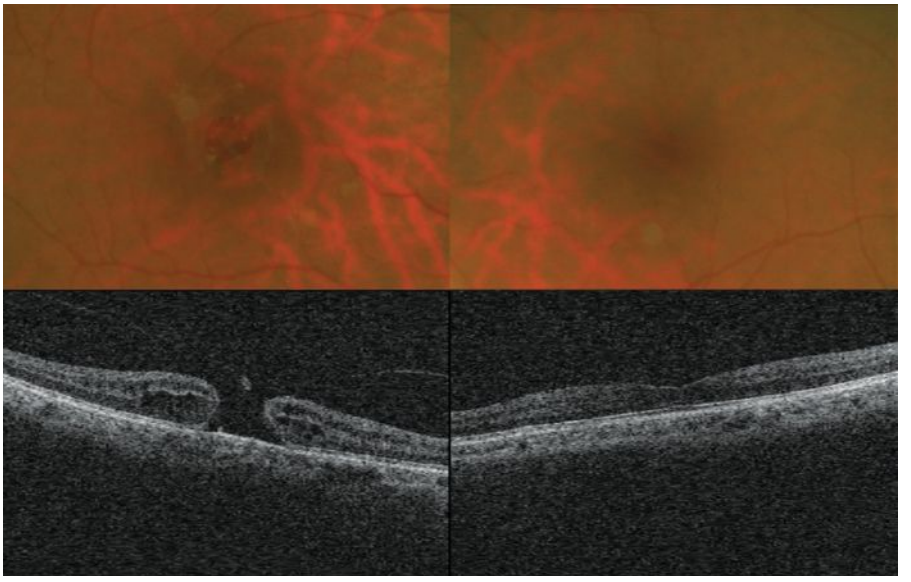
DIAGNOSTIC QUIZ

In the Thick of It

Retinal exam points toward a likely culprit for this patient's severely reduced visual acuity.

A 68-year-old African American female presented to the clinic for a routine eye examination with a chief complaint of blurred vision in the right eye of six months' duration.

Her ocular history was remarkable for slightly enlarged cup-to-disc ratios and previously identified but untreated cataracts OU. Discussion of her systemic history revealed no reports of hypertension, diabetes or other illnesses. The patient denied any past ocular trauma or allergies to medications or environmental substances.



While the retinal findings above should be fairly clear, it is appropriate to consider whether or not the patient's circumstances add additional complexity to the management of the case. Read the online discussion of this case for a thorough assessment of options.

Clinical Findings

Her best uncorrected entering visual acuities were 20/150 OD and 20/25 OS at distance and near with no improvement upon pinhole or refraction. Her external exam was normal with the exception of the facial Amsler grid OD, which demonstrated central distortion. There was no afferent pupillary defect.

Biomicroscopy uncovered normal anterior segment tissues with grade II nuclear sclerotic cataracts in both eyes. Her intraocular pressures measured 16mm Hg by Goldmann applanation. The pertinent posterior segment findings are demonstrated in the photographs.

For More Information

Additional testing included a traditional Amsler grid, formal automated perimetry, additional funduscopic examination with a 90-diopter lens completing the Watzke-Allen sign (a vertical strip of light perceived by the patient as "broken" or distorted), OCT testing and laser interferometry to assess best acuity.

Your Diagnosis

What would be your diagnosis in this case? What is the likely prognosis? Which interventions, if any, would you recommend? To find out, please read the online version of this article at www.reviewofoptometry.com. ■

About Dr. Gurwood Dr. Gurwood is a professor of clinical sciences at The Eye Institute of the Pennsylvania College of Optometry at Salus University. He is a co-chief of Primary Care Suite 3. He is attending medical staff in the department of ophthalmology at Albert Einstein Medical Center, Philadelphia. He has no financial interests to disclose.

Retina Quiz Answers (from page 108)—Q1: b, Q2: c, Q3: c, Q4: c, Q5: c

NEXT MONTH IN THE MAG

In April, we present our annual issue devoted to corneal disease. Articles will include:

- A Game Plan for Treating Corneal Infections
- Know Your Options for Managing Recurrent Erosion
- Trauma Care: Advice on Managing Corneal Injuries, Abrasions and Foreign Bodies

Also:

- How to Handle Non-Ocular Emergencies in the Office
- Should You Prescribe a Glaucoma Drug for Ocular Hypertension?

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