Identifying Conversion to WET AMD

Take a step-by-step approach to early detection by learning signs of exudation and how to evaluate OCT findings.

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Gaining Ground on GA, p. 46
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—EARN 2 CE CREDITS
THE HORSEPOWER YOU NEED TO LOWER IOP

Powerful IOP reduction with excellent tolerability

VYZULTA delivered up to 9.1 mmHg mean IOP reduction from baseline in pivotal trials.

INDICATION

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

IMPORTANT SAFETY INFORMATION

• Increased pigmentation of the iris and periorbital tissue (eyelid) can occur. Iris pigmentation is likely to be permanent.
• Gradual changes to eyelashes, including increased length, increased thickness, and number of eyelashes, may occur. These changes are usually reversible upon treatment discontinuation.
• Use with caution in patients with a history of intraocular inflammation (iritis/uveitis). VYZULTA should generally not be used in patients with active intraocular inflammation.
• Macular edema, including cystoid macular edema, has been reported during treatment with prostaglandin analogs. Use with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.
• There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products that were inadvertently contaminated by patients.
• Contact lenses should be removed prior to the administration of VYZULTA and may be reinserted 15 minutes after administration.
• Most common ocular adverse reactions with incidence ≥2% are conjunctival hyperemia (6%), eye irritation (4%), eye pain (3%), and instillation site pain (2%).


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

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

Initial U.S. Approval: 2017

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

4 CONTRAINDICATIONS
None

5 WARNINGS AND PRECAUTIONS
5.1 Pigmentation
VYZULTA® (latanoprostene bunod ophthalmic solution), 0.024% may cause changes to pigmented tissues. The most frequently reported changes with prostaglandin analogs, including VYZULTA, should be informed of the possibility of increased pigmentation, including permanent changes. The long-term effects of increased pigmentation are not known.

Pigmentation of VYZULTA, the iris is likely to be permanent, while pigmentation of the pigmented tissues. The most frequently reported changes with prostaglandin analogs include increased length, thickness, and the number of lashes or hairs. Eyelash changes are usually reversible upon discontinuation of treatment.

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

5.3 Intraocular Inflammation
VYZULTA should be used with caution in patients with a history of intraocular inflammation. Untreated ocular inflammation may result in increased intraocular pressure. Patients who receive prostaglandin analogs, including VYZULTA, should be informed of the possibility of increased pigmentation, including permanent changes. The long-term effects of increased pigmentation are not known.

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

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

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

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

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

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

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
There are no available human data for the use of VYZULTA during pregnancy to inform any drug-associated risks.

Latanoprostene bunod has caused miscarriages, abortion, and fetal harm in rabbits. Latanoprostene bunod was shown to be abortifacient and teratogenic when administered intravenously (iv) to pregnant rabbits at exposures ≥ 2.8 times the clinical dose. Doses ≥ 2.0 μg/kg/day (23 times the clinical dose) produced 100% embryofetal lethality. Structural abnormalities observed in rabbit fetuses included anomalies of the great vessels and aortic arch vessels, domed head, sternbral and vertebral skeletal anomalies, limb hyperextension and malrotation, abdominal distension and edema. Latanoprostene bunod was not teratogenic in the rat when administered iv at 150 mcg/kg/day (67 times the clinical dose) (see Data). The background risk of major birth defects and miscarriage for the indicated population is unknown. However, the background risk in the U.S. general population of major birth defects is 2 to 4%, and of miscarriage is 15 to 20%, of clinically recognized pregnancies.

Data
Animal Data
Embryofetal studies were conducted in pregnant rabbits administered latanoprostene bunod daily by intravenous injection on gestation days 7 through 17, to target the period of organogenesis. The doses administered ranged from 0.24 to 80 mcg/kg/day. Maternal toxicity was produced at doses ≥ 300 mcg/kg/day on a body surface area basis. Embryofetal lethality (resorption and fetal death) and structural anomalies were produced at doses ≥ 300 mcg/kg/day (74 times the clinical dose). Malformations included anomalies of the sternum, domed head, forepaw hyperextension and hindlimb malrotation, vertebral anomalies and delayed ossification of distal limb bones. A no observed adverse effect level (NOAEL) was established at 150 mcg/kg/day (87 times the clinical dose) in this study.

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

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

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

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
Latanoprostene bunod was not mutagenic in bacteria and did not induce micronuclei formation in the in vivo rat bone marrow micronucleus assay. Chromosomal aberrations were observed in vitro with human lymphocytes in the absence of metabolic activation.

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

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

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


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Blue Light Lenses, Berry Extract Don't Help Digital Eyestrain

Dry eye symptoms did improve with oral omega-3 fatty acid supplementation.

There are currently no well-established clinical guidelines regarding the efficacy of various treatments for computer vision syndrome, or digital eyestrain; however, a number of options are directly marketed to patients. When assessing the efficacy and safety of these interventions, researchers uncovered no high-certainty evidence supporting the use of various therapies, such as blue-light glasses and oral berry extract. The findings were published recently in the *Ophthalmology* journal.

The study authors identified eligible randomized controlled trials, which were then appraised for risk of bias and synthesized. They assessed the certainty of the body of evidence and used standardized mean differences when differently scaled measures were combined.

The analysis included 45 randomized controlled trials with a total of 4,497 participants. Data revealed that there was no reduction in visual fatigue symptoms with blue-blocking glasses. Additionally, multifocal lenses did not improve visual fatigue scores when compared with single-vision lenses. Oral berry extract supplementation for four to 12 weeks did not improve visual fatigue and dry eye symptoms compared with placebo. The study authors also reported that this supplement had no impact on critical flicker-fusion frequency or accommodative amplitude.

The researchers, however, did observe an improvement in dry eye symptoms with oral omega-3 fatty acid supplementation for 45 days to three months. The study data also showed that oral carotenoid supplementation improved flicker-fusion frequency relative to placebo; however, the clinical significance of this is unclear.

“This review identified substantial inter-study variations in methodology and outcome measure selection,” the study authors wrote in their paper. “These findings indicate there would be benefit in developing a core outcome set for computer vision syndrome trials to standardize reporting in future studies and thus enable enhanced data synthesis in systematic reviews and meta-analyses; this would enable a clearer determination of the relative efficacy and safety of interventions to better inform clinical practice.”


**IN BRIEF**

- Treatment with Dexamethasone Alters Eye Growth. A recent animal study suggests that systemic use of dexamethasone interrupts emmetropization, according to findings presented early last month during the 2022 ARVO annual meeting in Denver.

  The researchers administered dexamethasone or vehicle daily to chicks during the development of monocular form deprivation myopia (the last seven days of a 17-day deprivation period). Occluders were removed on the last day of treatment, and chicks experienced unrestricted vision for a recovery period of about 20 hours.

  Data showed a significant decrease in choroidal IL6 gene expression in recovering eyes treated with dexamethasone vs. recovering eyes of vehicle-treated chicks. In their abstract, the study authors noted that they detected no significant differences in IL6 gene expression in the chorioids of control eyes between chicks treated with dexamethasone vs. vehicle were detected.

  The researchers reported a significant decrease in scleral proteoglycan synthesis in control eyes treated with dexamethasone compared with control eyes of vehicle-treated chicks. Despite this finding, they also observed that dexamethasone treatment led to a significant increase in scleral proteoglycan synthesis in recovering eyes relative to fellow controls.

  “Dexamethasone treatment reduced choroidal gene expression of IL6 in recovering eyes, resulting in a disinhibition of scleral proteoglycan synthesis during recovery from induced myopia,” the authors noted in their abstract. “These results provide additional support for a role of inflammation in visually regulated eye growth.”

  Summers J, Soriano D, Martínez E. Emmetropization is associated with a modified inflammatory response in the eye. ARVO 2022 annual meeting.
Diabetes Treatments Can Reduce AMD, POAG Incidence

Medications for diabetes demonstrate a protective effect against open-angle glaucoma and age-related macular degeneration (AMD), a study recently confirmed. While previous research suggested this, these studies hadn’t addressed confounding factors by indication. Using three Rotterdam Study (1990-2014) cohorts (n=11,260), researchers analyzed the association of diabetes medication use and common age-related eye diseases (open-angle glaucoma, AMD and cataract).

They reported that untreated type 2 diabetes was associated with a significantly higher risk of all three eye diseases, while the condition, when treated with metformin or other medication (insulin or sulfonylurea derivatives), was associated with a significantly lower risk of open-angle glaucoma or AMD, respectively.

Additionally, the cumulative lifetime risk for open-angle glaucoma was lower for individuals taking metformin than for individuals without type 2 diabetes. Individuals taking other medication also had a lower lifetime risk of AMD, the researchers reported. Diabetes medication wasn’t associated with cataract in the study, though diabetes itself was.

“Our findings accentuate the potential role of diabetes medication in the pathogenesis of open-angle glaucoma and AMD,” the researchers wrote. Based on these associations, they concluded that interventional clinical trials are warranted to confirm causality.”


FLACS, Phaco Similar in Safety and Efficacy, Says AAO

However, the laser procedure is less cost-effective, a literature review notes.

Using a laser to supplant or replace some manual aspects of cataract surgery sounds intuitively compelling, as the added precision may reduce adverse effects, improve visual outcomes or both. Though anecdotal experiences of individual surgeons and some published papers have argued for that conclusion, a recent American Academy of Ophthalmology report found that femtosecond laser-assisted cataract surgery (FLACS) and traditional phacoemulsification (phaco) cataract surgery have similar excellent safety and refractive outcomes; FLACS, however, typically costs more.

FLACS was introduced in 2011. Previous meta-analyses have reported high precision and a reduction in ultrasound energy delivered into the eye compared with phaco, but these benefits don’t always mean better outcomes or fewer complications. The Academy wrote in its report, “Since the Cochrane review in 2016, several rigorously conducted randomized clinical trials have been published with short- and long-term follow-up, making this an opportune time to revisit the data.”

The Academy conducted a PubMed search of FLACS studies in 2020. Of the 727 total abstracts identified, 12 met inclusion criteria. The studies reported no significant differences between FLACS and phaco in mean uncorrected distance visual acuity, best-corrected distance visual acuity or percentage of eyes within 0.5D or 1D of the target. Additionally, intraoperative and postoperative complication rates were similar. “In particular, most studies, including the most robustly powered RCTs, show no significant difference in endothelial cell loss between FLACS and phaco,” the report found.

Large randomized controlled trials in the United Kingdom and France reported that FLACS was less cost-effective than phaco. The Academy noted that this economic perspective is “a finding that may generalize to other countries with similar healthcare costs.”

2022 ORS Resident Case Report Contest Winners

The papers put two rare ocular conditions under the microscope: bilateral Bartonella henselae neuroretinitis and multifocal vitelliform dystrophy.

In April 2016, optometry lost a giant when the author of the seminal work Primary Care of the Posterior Segment, Larry Alexander, OD, died. In addition to being an optometric physician, author and educator at UAB School of Optometry, Dr. Alexander was a past president of the Optometric Retina Society (ORS). Each year, that group honors his legacy by accepting case reports from optometric residents across the country relating to vitreoretinal disease.

The two cases shown here, selected by the ORS Awards Committee, were co-winners of the sixth annual Larry Alexander Resident Case Report Contest. The contest is sponsored by Topcon, Visionix (Optovue) and Heidelberg.

“When reviewing submissions, we look for manuscripts that are well written, include high-quality images and provide new and innovative information to the community,” says Julie Rodman, OD, professor and chief of the Fort Lauderdale (Broward) Eye Care Institute at Nova Southeastern University in Florida, and ORS treasurer. “This year, our group honours his legacy by accepting case reports from optometric residents across the country relating to vitreoretinal disease.

The full text and images of both case reports are available on our website, reviewofoptometry.com.

Case 1: Bilateral Bartonella henselae Neuroretinitis
Claire Cordoba, OD, a primary care resident at the Indiana University School of Optometry, presented a case of an 18-year-old with severe bilateral neuroretinitis caused by Bartonella henselae, which causes 22,000 cases of cat scratch disease globally per year. She noted that ocular involvement occurs in 5% to 10% of affected patients and typically presents two to three weeks after systemic symptoms begin. The case report discussed which examinations to perform to ensure a proper diagnosis, as well as explained the various clinical characteristics of the condition including associated ocular signs and symptoms.

Among Dr. Cordoba’s conclusions from the case was that multiple differentials need to be considered when Bartonella is suspected in a patient, including HIV, HZV/HSV, leptospirosis, Lyme, syphilis, toxocariasis, toxoplasmosis and tuberculosis. She also emphasized the importance of early blood testing to test for Bartonella antibodies, which helps to identify the cause of the infection and begin treatment sooner to avoid potentially devastating visual outcomes.

Case 2: Multifocal Vitelliform Dystrophy
This case report by Keying Yan, OD, ocular disease optometry resident at the BronxCare Health System in New York, discusses a rare condition called multifocal vitelliform dystrophy (MVD), which presents as multiple yellow vitelliform lesions in the subretinal space. The case features a 67-year-old male with MVD who had asymptomatic but chronic, progressive lesions and describes appropriate diagnosis, treatment and management.

MVD can be either familial or sporadic, and the pathophysiology for multifocal vitelliform lesions remains unknown. Dr. Yan found that in most but not all cases, MVD is associated with BEST1 gene variation, referred to as multifocal Best disease. The report also noted that “lesions in patients without the genetic mutation tend to be smaller in size and higher in numbers.”

Though no treatment currently exists for MVD, Dr. Yan concludes that affected patients should be regularly monitored for potential secondary complications or the need for referral. In addition, she highlights the important role of research that can provide insight on the condition’s etiology and identify effective management techniques.

Photos of the patient in case 2 show scattered elevated, orange-yellow lesions with distinct borders, located along the superotemporal and inferotemporal retinal vascular arcades within the posterior pole.
 Genetic testing could change how you view their inherited retinal disease (IRD)

You may have the chance to end the diagnostic odyssey for your patients living with IRDs. Access free genetic testing options for eligible patients.

THE TIME TO TEST IS NOW
Visit [HCP.EW2K.com/RevOpt](HCP.EW2K.com/RevOpt) or scan the QR code to learn more.

*This initiative is open to US residents only, subject to the Terms and Conditions of the program.

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Acute Angle-Closure Crisis Often Missed, Study Says

More frequent use of gonioscopy for diagnosis and reducing the financial barriers of the technique could prevent condition-associated vision loss.

If an anatomic narrow angle is not appropriately diagnosed and treated, it can result in acute angle-closure crisis and lead to substantial vision loss. A recent retrospective study determined that in a group of Medicare patients, there appeared to have been multiple opportunities for interventions that may have averted the acute angle-closure crisis that ensued. In this cohort, only 67.5% consulted an optometrist or ophthalmologist at least once during the two-year lookback period. The research team believes that interventions targeted at addressing these risk factors and increasing eyecare access among high-risk groups may allow for better identification and treatment of these vulnerable patients.

A two-year lookback period from the date of initial presentation of acute angle-closure crisis was used to identify 1,179 patients who had at least one eyecare visit and received a diagnosis of open-angle glaucoma (OAG) or suspected OAG or took at least one medication associated with risk of acute angle-closure crisis. Of the patients who had at least one eyecare visit, those who underwent gonioscopy, received a diagnosis of an anatomic narrow angle before developing an acute crisis or both were identified. Characteristic clinical signs and symptoms of an acute attack include a mid-dilated pupil, elevated intraocular pressure, pressure-induced corneal edema, closed angles detected with gonioscopy, vascular congestion, eye pain, headache, nausea and/or vomiting.

The researchers noted that 39.4% of patients had OAG or suspected OAG, and 35.1% had received at least one medication associated with increased risk of acute angle-closure crisis before developing it. Of the 796 patients who consulted an optometrist or ophthalmologist in the lookback period, less than one-third underwent gonioscopy in the one to four weeks preceding the acute angle-closure crisis.

The researchers suggested potential reasons for the suboptimal rates of gonioscopy include prioritization of other components of the ophthalmic examination, use of alternate methods to characterize anterior chamber angle depth, patient’s refusal to undergo the examination owing to need for topical anesthesia and potential for ocular discomfort or financial barriers. In this case, all patients were covered under the same insurance provider. Therefore, lack of insurance was not a barrier to care.

“Educational initiatives aimed at cultivating awareness among optometrists, ophthalmologists and trainees on the importance of gonioscopy as a diagnostic tool may help address the underuse of the technique,” the study authors wrote in their JAMA Ophthalmology paper. “Reduction of financial barriers to gonioscopy, use of anterior segment imaging as adjunct testing and implementation of electronic health record reminders to flag patients at risk and facilitate timely and appropriate ophthalmic assessments may be associated with reduced incidence of acute angle-closure crisis.”


IN BRIEF

Glaucoma Affects Refractive Outcomes. New findings show that patients with glaucoma are more likely to end up with postoperative refractive surprises after cataract surgery, according to research presented in early May at the 2022 ARVO meeting in Denver. The researchers investigated one-month post-cataract refractive outcomes in glaucoma patients and non-glaucoma patients without visually significant comorbidities.

The retrospective cohort study included the first eye of 503 patients (354 without glaucoma and 149 with glaucoma). The researchers wrote in their ARVO abstract that 67.8% and 95.2% of control subjects fell within 0.50D and 1D of the target compared with 66.7% and 89.9% of glaucoma subjects, respectively. This comparison was significant for eyes within 1D of the target. Additionally, the researchers compared refractive outcomes between glaucoma types and noted no significant differences in the percentages of patients within 0.50D and 1D of the target.

As this study excluded patients with visually significant comorbidities, the researchers concluded that glaucoma likely plays a role in refractive outcomes that isn’t currently accounted for by intraocular lens calculations. Notably, they wrote that the increase in postoperative refractive surprise appears to occur regardless of glaucoma type.

To treat ocular inflammation and pain following ophthalmic surgery or ocular itching associated with allergic conjunctivitis.

DEXTENZA KEEPS PATIENTS SATISFIED†

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).

**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%).

**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.

*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.*

*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.

**References**

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It’s been shown that amblyopic children have reduced performance on visual attention and search tasks, but do amblyopic adults struggle in the same way? In a recent study presented at the 2022 ARVO meeting in Denver, researchers assessed visual acuity, binocular vision, higher-order executive function (selective and divided attention) and functional ability (fine motor skills and reading speed) in participants with and without anisometropic amblyopia. Their hypothesis, which the findings confirmed, was that amblyopic adults do indeed also show reduced performance in various tasks, including those that involve visual attention and visual search.

Twenty adults with anisometropic amblyopia and 10 controls participated. Fine motor skills, reading speed and visual attention and processing speeds were assessed, as well as visuo-cognitive search proficiency. All participants performed these functional tasks binocularly.

The mean visual acuity for amblyopic patients in this study was 0.51 logMAR. Amblyopes exhibited slower reading performance compared with controls (124 words per minute vs. 159 words per minute) and slower completion time on the T rail Making T ests compared with controls (amblyopes; T rail A- 58 seconds, T rail B- 73 seconds vs. controls; T rail A- 43 seconds, T rail B- 53 seconds). In addition, adult amblyopes performed significantly poorer on the fine motor skills subitems, such as making dots in a circle, transferring pennies and sorting cards. They also showed reduced performance in visual attention and visual search.

In the amblyopia cohort, visual acuity in the affected eye was a significant predictor of Useful Field of View performance. The study also determined that both visual acuity and binocular function scores were significant predictors of performance on T rail Making T ests.

The authors suggested these findings have important implications for understanding the impact of amblyopia on everyday function in adults.
Win Some, Lose Some with Statins

In vitrectomy patients, medication use was associated with higher chances of vitreous hemorrhage and edema but lower chances of retinal vascular occlusion and lens dislocation.

StatinS are one of the most prescribed medications in the world, notably for hypercholesterolemia treatment, and aid in primary and secondary cardiovascular disease prevention. Their use has been associated with lower rates of some ophthalmic interventions. Investigating long-term outcomes with pars plana vitrectomy after a year post-op, a recent study has determined a range of outcomes: an increased risk of developing vitreous hemorrhage, retinal edema and vitreous opacities but a decreased risk of retinal vascular occlusion and lens dislocation. These findings were presented at the 2022 ARVO annual meeting in Denver.

From a United States electronic health record network, the researchers identified 54,159 patients who had undergone vitrectomy and stratified them into statin vs. non-statin use cohorts. The team used propensity score matching to match the two cohorts for age, sex and other systemic comorbidities.

The cohort with prior history of statin use had a significantly higher risk of developing vitreous hemorrhage (risk ratio (RR): 1.15), retinal edema (RR: 1.15), macular puckering (RR: 1.21), intraoperative complications of the eye (RR: 1.47), glaucoma (RR: 1.12), vitreous opacities (RR: 1.42) and prosis (RR: 1.42).

The same group had a significantly lower risk of developing retinal vascular occlusion (RR: 0.7) and lens dislocation (RR: 0.75). No other significant differences were found between the two cohorts.

The researchers wrote in their abstract that they believe the increased risk of developing vitreous hemorrhage, retinal edema and vitreous opacities could possibly be due to statins’ biphasic effect on angiogenesis.


IN BRIEF

Moving Stimulus Increases Dynamic Range of Perimetry.

It’s been shown that perimetric sensitivities below -20dB are unreliable due to excessive variability. Increasing stimulus size to increase detectability extends this dynamic range, allowing testing for more severe glaucoma; however, larger stimuli overlap multiple nerve fiber bundles and may miss smaller defects. At the 2022 ARVO meeting in Denver, researchers proposed instead using moving stimuli to increase detectability and hence increase the dynamic range of perimetry in glaucoma.

A total of 152 participants with glaucoma or suspected of having glaucoma were tested in the study, with 52 undergoing retesting six months later. A Size V moving stimulus was designed to travel parallel to the average nerve fiber bundle orientation at each location, with speed proportional to local magnocellular ganglion cell spacing. Overall, 34 locations across the visual field were tested with moving and static stimuli, using an otherwise identical Zippy Estimation by Sequential Thresholding seen and not seen algorithm on a clinical perimeter.

The participants had an average mean deviation of -3.1dB from standard perimetry (interquartile range: -3.7dB to -0.3dB).

Sensitivities using moving stimuli were 1.8dB higher; this difference increased with damage and eccentricity. Test-retest limits of agreement among the 52 retested eyes were narrower for moving stimuli (-6.3dB to +6.7dB) than static stimuli (-12.7dB to +7.9dB), and test-retest variance was significantly smaller. Over half (53%) of the participants stated preferring the moving stimulus vs. 24% who preferred the static stimulus.

“Using a moving stimulus for perimetry increases sensitivities, and hence locations stay within the dynamic range longer, allowing reliable testing at locations with more severe damage without the problems caused by increasing stimulus size,” the study authors concluded in their abstract. “Since stimulus speed is a continuous variable, a clinical test could either use moving stimuli at all sensitivities or increase speed proportional to loss ensuring that early detection would be unaltered.”

Gardiner S, Mansberger S. Using moving instead of static stimuli to extend the dynamic range of perimetry. ARVO 2022 annual meeting.

Vitamin D Deficiency Affects Conjunctiva in Kids.

A prospective case-control study of 38 pediatric patients with vitamin D deficiency and 45 controls assessed TBUT, Schirmer-1 test compared, ocular surface disease index (OSDI) scores and conjunctival impression cytology results between groups.

The median TBUTs and Schirmer-1 test measurement were 10 seconds and 12mm in group one and 11 seconds and 15mm in group two. Median OSDI was 16 in group one and 17 in group two. According to conjunctival impression cytology, 25 samples in group one and 40 samples in group varied by grading score.

“More important changes in both histopathological and clinical findings occur in more severe vitamin D deficiency,” the study authors wrote in their paper. The differences can affect some tear function-associated clinical findings and clinicians should note the potential involvement, they explained.

High Prevalence of Refractive Errors Found in Children Born Preterm

Strabismus was also reported in a significant percentage of this patient population.

To better understand the prevalence of visual-sensory and oculomotor impairments among children born preterm, researchers recently analyzed data from a population-based cohort study. They observed a high prevalence of refractive errors and strabismus at age 5.5 among children born very and moderately preterm, according to findings presented in early May during the 2022 ARVO meeting in Denver.

Of 4,441 children in the dataset, the researchers clinically assessed 2,718. They included a sample of 592 full-term-born children as a reference group. The data revealed refractive errors in 43.1%, 35.2% and 28.4% of children born at 24-26, 27-31 and 32-34 weeks, respectively. Strabismus was reported in 19.5%, 14.8% and 8.3%, respectively. In children born at full-term, the prevalence of refractive errors and strabismus was 24.1% and 2.8%, respectively.

The study authors also reported severe/moderate visual deficiencies in 1.7% of those born at 24-26 weeks and in less than 1% for the other groups. They measured a 10/10 binocular visual acuity for 28.6%, 35.1% and 36% of patients born at 24-26, 27-31 and 32-34 weeks, respectively. For purposes of comparison, 10/10 binocular visual acuity was measured in 59.7% of the reference group. Additionally, the study showed that the presence of cerebral palsy at 5.5 years old had a strong association with visual deficiencies and suboptimal visual acuity compared with retinopathy of prematurity during the neonatal period.

“We report in a large cohort of preterm-born children high prevalence of refractive errors and strabismus even in children born very and moderately preterm supporting a specific attention for these children,” the ARVO abstract noted. “Low prevalence of 10/10 visual acuity, even with glasses, at the age of reading and writing acquisitions could represent an additional challenge.”


### Gestation Period

<table>
<thead>
<tr>
<th>Gestation period</th>
<th>24-26 weeks</th>
<th>27-31 weeks</th>
<th>32-34 weeks</th>
<th>Full-term</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Refractive error</strong></td>
<td>43.1%</td>
<td>35.2%</td>
<td>28.4%</td>
<td>24.1%</td>
</tr>
<tr>
<td><strong>Strabismus</strong></td>
<td>19.5%</td>
<td>14.8%</td>
<td>8.3%</td>
<td>2.8%</td>
</tr>
<tr>
<td><strong>10/10 binocular VA</strong></td>
<td>28.6%</td>
<td>35.1%</td>
<td>36%</td>
<td>59.7%</td>
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Compared with those born at full-term, kids born prematurely have a greater risk for refractive error or strabismus and should be regularly monitored by an eyecare provider.

IN BRIEF

**High Prevalence of Corneal Guttata Found in Hispanic Cohort.**

Are some patient populations vulnerable to corneal endothelial compromise more so than others? Researchers in Mexico recently assessed the central corneal specular microscopy of healthy Hispanic adults and found a high prevalence of corneal guttata, outgrowths of Descemet’s membrane produced by distressed endothelial cells, with a higher preponderance in female patients. They presented their results in Denver at the 2022 ARVO annual meeting in early May.

The study included 702 eyes from 356 patients (55% female). The mean age was 70. The researchers considered endothelial pleomorphism if <50% of cells were hexagonal and polymegethism if the coefficient of variation was >40%.

The mean endothelial cell density was determined to be 2255.09 cells/mm², mean cell area was 458.85µm² and mean central corneal thickness was 522.37µm. Mean endothelial cell density and cell hexagonality in this Hispanic population were lower than in other reports, according to the authors. The study determined that 76% of the patients had a pleomorphic endothelium, with a significant difference in cell hexagonality between male and female patients. Also, 48% of patients had polymegethism and 18% had corneal guttata, with more than half (64%) of the corneal guttata patients being female.

“More information is needed regarding endothelial morphometric characteristics in Hispanics,” the researchers wrote in their abstract. “Knowing the average endothelial parameters in our population can allow us to predict whether the endothelial pump function will tolerate surgery performed on the eye before affecting corneal transparency.”

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2. CVI data on file 2016. Prospective, multi-center, subject-masked, bilateral, one month dispensing study in USA with Biofinity Energys® in existing Biofinity® sphere wearers. N=52. After 2 weeks. 3. After 1 week of wear. 4. On average, 86% strongly/somewhat agree. 5. CVI data on file 2021. Decision Analyst online survey of 1,027 Biofinity® wearers aged 16–65 years in USA, Japan, Germany, France and Spain. On average, 84% strongly/somewhat agree. ©2022 CooperVision 12493ROG 05/22
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Retina’s Renaissance—And Yours

You can track the evolution of optometry’s role in retina care by perusing our annual issues devoted to this category. It began rather humbly, 12 years ago, with just a photo essay of fundus images and an article pondering the implications of the original AREDS study. That’s about all optometry could do circa 2010: perform fundus exams (referring out most suspicious cases) and recommend AREDS vitamins.

Back then, most optometrists didn’t have an OCT, so even those interested in being more active in retina were stymied by significant barriers to entry. In 2010, AREDS2 hadn’t yet come out. There was only one FDA-approved anti-VEGF; Lucentis from Genentech, though off-label use of the same company’s Avastin was widespread. Lucentis and Avastin were pretty much identical in dosing and efficacy, so there wasn’t anything for ODs to weigh in on prior to referral. Anti-VEGF was primarily used for AMD; panretinal photocoagulation was still the mainstay for diabetic retinopathy. Throughout, the role of the optometrist is active and engaged in ways 2010 docs would marvel at.

In 2022, there’s more retina work to do than ever before. The pharmaceutical industry has noticed, too. I still remember the timidity of the drug manufacturers to support optometry’s use of even the most plain-vanilla topical antibiotics and anti-inflammatories in the 1990s. Nowadays, many of the big players in retina advertise their medications directly to optometrists in this publication and others. Retina dinner seminars for optometrists are both commonplace and uncontroversial.

Optometry, in short, has arrived.

For our 13th annual Retina Report this month, we delve into how ODs can take advantage of this rising stature with articles on dry and wet AMD, inherited retinal diseases and diabetic retinopathy. Throughout, the role of the optometrist is active and engaged in ways 2010 docs would marvel at.

Gene therapy for RP and Leber’s is a reality, and others are being explored.

For ODs in 2022, there’s more retina work to do than ever before. The pharmaceutical industry has noticed, too. I still remember the timidity of the drug manufacturers to support optometry’s use of even the most plain-vanilla topical antibiotics and anti-inflammatories in the 1990s. Nowadays, many of the big players in retina advertise their medications directly to optometrists in this publication and others. Retina dinner seminars for optometrists are both commonplace and uncontroversial.

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Reading over these stories one last time before press, I was struck by the level of sophistication in the discourse from our optometric authors. These aren’t E.Z Reader versions of retina articles you might see in ophthalmology publications; in fact, I’ll bet we could slip them into one of our company’s ophthalmology magazines and the MDs would only notice the difference if they looked at the byline. Too many heads would explode for this idea to be anything but a thought experiment right now. But one day, even ophthalmologists will come around and give you grudging respect in retina—provided you put in the work to earn it.
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The Next Frontier
Recent advances in retinal disease mean more opportunities.

In 2019 I completed a full-ceptorship at Retina Associates of Kentucky, one of the top 20 retina practices in the country. This reinvigorated my love for this area of practice. I’ve always felt that our profession can do so much in retina—and now we have to, since it’s such a common finding in clinical practice. Let’s look at some opportunities discussed in detail in this month’s issue.

Genetic Testing
Inherited retinal diseases are the next frontier. We’ve already seen treatments for rare hereditary retinal dystrophy, and many potential conditions ranging from Leber’s congenital amaurosis to retinitis pigmentosa are in the near future. What we can do today is begin to determine the role genetic diagnostics play and identify disease risk early. While most patients know it’s important to eat healthy, exercise, avoid excess blue light and take vitamins/carotenoids, knowing they have a gene that predisposes them to macular degeneration would most likely change their motivation to get healthier prior to developing symptoms. Millions of people use the DNA testing kit 23andMe to see what potential diseases they are prone to; a similar version for ocular diseases would have the same success.

Conversion from Dry to Wet AMD
Research shows that the entering visual acuity is the best determinant of success post-anti-VEGF therapy, meaning that a patient who is diagnosed with 20/200 vision is not likely to achieve 20/200 after therapy. On the other hand, an early diagnosis of wet AMD, also known as choroidal neovascularization, may allow your patient to achieve 20/20 vision.

Look for signs of fluid on the OCT, including subretinal fluid, intraretinal fluid and subretinal hyperreflective material. Even then, it can be difficult to discern and you may have to rely on traditional examination for exudates or hemorrhages in the macular region or apply newer technologies such as dark adaptation, OCT-A or refer the patient for fluorescein angiography.

What we can do today is begin to determine the role genetic diagnostics play and identify retinal disease risk early.

Age-Related Eye Disease Study 2
The results of AREDS2 confirm the value of nutritional treatment for AMD. I commonly see patients who have nothing more than a family history of AMD on AREDS2 formulations—this was not a group that was studied to show a decreased progression of disease. The patients you should recommend this formulation are those with intermediate stage AMD or greater. That is, patients who have at least one large drusen in the macula (large is defined as at the diameter of a blood vessel leaving the optic disc).

Patients with GA in one eye also showed decreased progression of AMD in the good eye with AREDS2 formulations. Everyone else, including those with early AMD or a family history of AMD, should be prescribed carotenoid or other nutritional formulations that are available. For example, PreserVision (Bausch + Lomb) for those that meet the AREDS2 criteria and Ocuvite (Bausch + Lomb) or your supplement of choice for those that do not.

Geographic Atrophy (GA)
With two new potential medications on the horizon, pegectacoplan (Apellis Pharmaceuticals) and Zimura (Iveric Bio), now’s a good time for an update on GA in macular degeneration. Since these will be the first therapeutics shown to slow GA progression, it’s important to start identifying these patients now. The key to success is to identify non-center involved GA with your OCT and refer to a retina specialist when these therapeutics become available. The grayscale OCT showing RPE loss will be key to GA diagnosis.

Diabetic Retinopathy (DR)
When a patient with proliferative DR (PDR) should be referred to a retina specialist is quite simple. Besides signs of PDR or diabetic macular edema (DME), if all four quadrants show signs of retinopathy (e.g., dot or blot hemorrhages, exudates) that’s the time to get a retina specialist involved. This will allow them to help care for the patient at an appropriate time and determine treatment. They can also assess for subtle DME and other treatable DR signs.

The vast majority of patients with dry AMD (particularly GA) and those with prediabetes or early diabetes primarily reside in optometry offices. Knowing how to manage these patients and doing so effectively is an ideal scenario for successful practice.
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Pop Quiz Time

Bet you didn’t see that coming.

Okay, kids, let’s switch it up a bit. Ready or not, it’s time for a pop quiz! I can’t think of a better way to get the day started, can you?!

Throughout my long, long education, one of the things I hated the most was the dreaded pop quiz. That, and meatloaf day in my grade school cafeteria. I am certain that most of my organs are still encased in Mrs. Frazier’s meatloaf, but that is a different column for a different day.

Today is pop quiz day! Cue the trumpet fanfare. No pressure, but make sure to choose your answers carefully…

1. Pigment in the peripheral retina is:
   a. Mrs. Frazier’s meatloaf.
   b. Something you knew back when you took the national boards.
   c. Evidence that you finally have a widefield retinal camera.

2. Which is better, number one or number two?
   a. Is this an eye question?
   b. If you get this wrong, the chair will shock you.
   c. Hyperopes either don’t know or lie like dogs.

3. What is corneal refractive therapy?
   a. Let’s start calling in orthokeratology again, okay?
   b. Harder to explain to a mom than it was a couple of years ago.

4. The number one problem in optometry is:
   a. 51 different laws.
   b. 50 different state boards.
   c. 49 different vision plans.
   d. 48-year-old post-LASIK patients.

5. Which is more important than a yearly eye examination?
   a. Fancy coffee every day.
   b. Whether you accept my insurance.
   c. Will slapping Chris.

6. Name the 2022 Final Four.
   a. COVID, Ukraine, inflation and Tarheels.
   b. Monovision, multifocals, pilocarpine and books on tape.
   c. Chevy, Ford, Dodge and that battery-powered one the rich dentists drive.
   d. Fluorescein, lissamine green, rose bengal and don’t wear a white shirt to your eye exam.

7. Which is the best reason for immediate referral?
   a. Retinal detachment.
   b. Metallic foreign body penetration.
   c. Unexplained sudden loss of vision.
   d. A patient who always no-shows.

8. Prevention of no-shows starts with:
   a. Explaining the reason the patient needs to return next year.
   b. Reminder calls, texts and cards.
   c. Scheduling offenders on the days your office is closed.

9. Which is the best reason to wear a mask in the office?
   a. To protect your patient.
   b. To protect you from your patient.
   c. Just look in a mirror and you will understand.

10. What you should never, never, never say to a patient:
    a. Never.
    b. Always.
    c. You have beautiful glands.

11. Explain blur.
    a. When things are hard to see.
    b. When you think you need a bigger TV.
    c. Job security.

12. The most difficult thing you may have to tell a patient:
    a. You have a tumor in your eye.
    b. You have macular degeneration.
    c. You need to start going to a different eye doctor, mom.

13. What is the wisest thing you have ever heard that helped your career?
    a. People are no damn good (thanks, Walt).
    b. Don’t marry for money. Hang around rich people until you fall in love with one of them (thanks, mom).
    c. Be who you are (a great title to a great song on a great album, “Cellular,” by a great songwriter, Monty Vickers, OD).
More Than a “Wow Factor”
Investing in New Technologies to Help Improve Patient Care—and Practice Profitability

Adding new technologies to is key to the continuous improvement of patient care at any optometry practice—and it is also a major investment. How can eye care professionals determine which technologies are worthwhile? 2022 Best Practices Honoree Melissa Tada, OD, of Mountain View Vision in Colorado Springs, Colo. shares how she evaluates new equipment, from how it fits in the budget to its impact on her practice's profitability, and ultimately, how it benefits her patients.

We've never been afraid to try new things—especially when it comes to investing in new technology. Since we have made this a priority for our practice, we set aside money every month to replace a piece of equipment or purchase something new. And while I recognize that other practices offer many of the same technologies as we do, our commitment to regularly updating our equipment with the newest, most advanced offerings has become a point of differentiation. We always aim to have something new to show our patients when they return, which is part of our “wow factor.”

For patient care, our retinal imaging equipment has made a significant impact on our practice. These real-time, cross-sectional images of our patients’ eyes enable us to look beyond their vision and into their overall health to help detect conditions like glaucoma, age-related macular degeneration, and more. The ability to see beyond what traditional instruments can reveal results in improved efficiency and outcomes, and assures our patients that they’re receiving a high level of care.

For us, it’s a three-step evaluation. First and foremost, we look to see if there is a need or demand for it in our practice. If it will benefit our patients or help streamline our internal processes, we proceed to the next step—the expected return on investment. Then finally, we simply consider whether we have space for a new piece of equipment. While it’s nice to purchase something new and shiny, it’s important to look at the bigger picture to see whether it’s right for the practice.

Since opening the doors 12 years ago, our specialty clinic has grown with every new piece of technology that we have brought in. At first, we were only able to offer eye drops, oral antibiotics, and warm compresses. Today, we can offer our patients advanced technologies and specialty services that have become a reputation-builder. People in our community know that if they want a high level of care, they can come to us to get it. As we look to the future, we’re striving to meet the needs of even more patients through our technological investments.

In terms of practice management, our commitment to purchasing new and improved technologies has helped to streamline our processes, moving patients through their appointments efficiently.

How do you utilize technology to set your practice apart?

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What technology has made the biggest impact on your practice?

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With so much technology available—and new products introduced regularly—how do you decide in which equipment to invest?

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How has your investment in new technologies contributed to your practice’s growth?

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3 Tips for Evaluating New Technologies:

1. **Research.** There will always be new “toys” coming to market, but it’s important to conduct thorough research to understand each and every technology before diving in.

2. **Have a Plan.** It’s easy to get caught up in whatever’s new in the moment. Identify the area(s) of the practice to which you’re committed to investing or expanding. Setting these priorities will help in knowing what types of equipment will support your business goals.

3. **Consider ROI.** The “wow factor” is great, but your investments in technology will always need to make sense from a financial perspective. Consider potential costs and insurance reimbursements to determine your return on investment.
Q My high-volume cataract surgeon is young but having early symptoms of a pinched nerve due to looking down through a microscope all day. Could 3D surgery have some big advantages?

A Over the past few years, 3D visualization systems have been developed that allow anterior and posterior segment surgeries to be performed while viewing a large 55” 4K monitor with 3D glasses rather than looking through a microscope. The Alcon NGenuity and Zeiss Artevo are the two systems in the United States that provide markedly enhanced depth of focus compared with using oculars on a traditional microscope.

“Though it may seem challenging to change from operating with oculars to looking at a monitor, most surgeons feel that it is an easy adjustment that does not require many procedures to feel comfortable,” according to Lawrence Woodard, MD, of Omni Eye Services of Atlanta.

The benefit of viewing the eye on a large, high dynamic range monitor is that the detail of all the ocular structures is significantly improved due to the added size and clarity of the tissues visible on the monitor. “This intuitively will lead to more precise surgery with the potential for fewer complications,” says Dr. Woodard.

Visualize and Follow Through

Improving visibility can give surgeons much more confidence when performing procedures, which may increase efficiency while also allowing more consistency from case to case. “The cornea, iris, anterior capsule and posterior capsule are all clearly in focus while I am working on the cataract,” Dr. Woodard says. “It is so much more accurate than 2D surgery through the oculars of a microscope, where one must rely on other cues to gauge depth within the eye.”

One of the biggest challenges during cataract surgery is identifying the thickness of the cataract. “This is critical because an error in judging the location of the posterior capsule can lead to a rupture of the capsule with vitreous prolapse into the anterior chamber, increasing the risk of undesired complications such as cystoid macular edema, retinal detachment and endophthalmitis,” Dr. Woodard notes. Any technology that could lessen the potential for complications would be welcome by surgeons.

An OR Aid

These 3D systems also allow surgeons to see pertinent information on the monitor during surgery. Parameters such as current ultrasound energy and fluid usage are visible in real-time, providing important feedback during the procedure. The surgeon can also view video overlays, which identify the axis of placement of a toric intraocular lens (IOL), crosshairs for centration of a multifocal IOL and data from intraoperative aberrometry. In addition, information from the clinic’s EHR (such as corneal topography, A-scans and OCTs) will be visible on demand on the monitor for the surgeon to view before or during the procedure.

Perhaps the most important benefit to 3D visualization is the dramatic impact that it has on surgeon comfort during a day in the operating room. Traditionally, surgeons must maintain the head and neck in a stationary position for multiple hours during the day while looking through the oculars of the surgical microscope. This continues week after week, month after month and year after year. The cumulative effect of this unnatural positioning is damage to the musculoskeletal system. Specifically, degenerative cervical disc disease and spinal stenosis are quite common in surgeons who operate frequently.

By no longer requiring surgeons to look through oculars, 3D systems significantly reduce the stress on the head and neck areas during surgery. The surgeon can sit in a more ergonomically neutral position while also enjoying the benefit of having a surgical chair with back support. This not only decreases stress on the neck and shoulders but also relieves pressure on the lower back that drastically reduces surgeon fatigue. These factors will prolong the longevity of a surgeon’s career while simultaneously improving quality of life.

Cataracts in IMAX

An innovative new visual technology can benefit the surgeon in the OR.

Dr. Ajamian is the center director of Omni Eye Services of Atlanta. He currently serves as general chairman of the education committee for SECO International and is vice president of the Georgia State Board of Optometry. He has no financial interests to disclose.
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The Stars in Our Eyes

Take a look at the spatial insight that the Van Orden star can offer.

In the June 2021 installment of Focus on Refraction, Drs. Harris and Taub gave an overview of the cheiroscopic trace in the article “Space: The Final Frontier.” They described how the cheiroscopic trace is a manifestation of the way that patients perceive space around them and direct their actions accordingly (in this case, tracing printed figures). They also showed how the cheiroscopic trace can be useful in detecting and managing aniseikonia. This month’s column will continue this theme by discussing another such technique, the Van Orden star.

What a patient produces during the Van Orden star task tangibly shows what they see. According to Kaplan and Lydon, “The Van Orden star probes the way we perceive, and mentally represent, the world around us. Execution of this pattern […] requires the individual to rapidly and accurately interpret what he sees, generate a motor response and maintain attention throughout. The appearance of his star pattern is fundamentally a predictor of the patient’s spatial behavior.” Spatial behavior is heavily influenced by ocular alignment, as will become more obvious through some examples.

The Procedure

The Van Orden star, like the cheiroscopic trace, is performed in a stand-up cheiroscope. The optics of the cheiroscope allow the patient to view each side of the test card separately, without fusion. This allows for the characteristic appearance to the finished trace: two sets of converging lines forming points. Careful interpretation of a patient’s star pattern gives us a great deal of insight into how they interpret space and whether there is any significant heterophoria or vertical deviation.

The test card for the Van Orden star is a horizontal rectangle that includes two vertical columns of pre-printed shapes placed 154mm apart. The patient stands in front of the cheiroscope and views the card through the oculars, where they will see one column of shapes with the left eye and the other with the right eye. Using two pencils, one for each hand, the patient will draw a series of lines on the card. They start by placing each pencil on the center target of each column. They will then draw a line with each hand, simultaneously, toward the center of the card until the pencils appear to touch each other. Once they have done this, they move the pencils so that the right-hand pencil is now on the top figure of the right-hand column of shapes, while the left-hand pencil is placed on the bottom figure of the left-hand column. From this position, they again draw a line with each hand toward the center until the pencils appear to touch.

Next, the pencils are moved such that the left-hand pencil is placed on the top figure of the left-hand column and the right-hand pencil is on the bottom figure of the right-hand column. The process is repeated, with the patient drawing lines toward the center and the pencils alternating between shapes until all corresponding shapes have been used.

![Fig 1. An ideal Van Orden star (A). Note the cleanly formed apices and vertical alignment. Dr. Schnell’s baseline Van Orden star showing vertical misalignment and esophoria (B).](image-url)
The Outcome

Ideally, a completed Van Orden star looks like what is shown in Figure 1A. The lines that the patient has drawn on each side meet in a definite point at a distance of approximately 37mm from the inside edge of the printed figures (a separation of 77mm). Various clinical presentations can change the appearance of the star, however. Among these are horizontal heterophorias, vertical deviations and central suppression of one or both eyes.

Let’s take a look at some examples of skewed or disorganized Van Orden stars and what they represent. To create these stars, I (Dr. Schnell) performed the test on myself with varying amounts of yoked prism in order to simulate different binocular conditions.

Before I started playing with the prism, I performed a baseline Van Orden star. Compared with Figure 1A, which shows perfect results, Figure 1B is evidence of both my esophoria and vertical deviation. The right side of the pattern is several millimeters below the left, with a horizontal separation of the apices of 63mm. You can also see that the point where the lines meet for each side is not precise, possibly indicating some instability of both fixation and alignment.

For the first set of Van Orden stars with prism, I wore 8° yoked and performed one star in each of the following base directions: right, left, up and down, followed by 8° base-in and base-out. Figure 2 shows the result with 8° base-right. While both sides of the star showed good apices, they were significantly closer to each other, at about 56mm compared with my baseline of 63mm. With 8° base-out, the apices were extremely far apart, at 110mm. Perceptually, as I was drawing the figures, the base-in setup made the two columns of figures appear to be much farther apart than they actually were, and the opposite was true for the base-out.

Another possible appearance occurs when the patient is showing a central suppression. In this case, one or both sides of the star will fail to come to a defined apex. As part of my experiment, I created a simulated central suppression OS with a piece of translucent tape on the left cheiroscope ocular, and sure enough, I had no definite apex to the star on that side. This is an easy-to-see manifestation of what can otherwise be a difficult clinical diagnosis.

The Message

While it isn’t necessary for eyecare practitioners to have a cheiroscope and run Van Orden star testing as part of their exam, this method can tell you a lot about a patient’s overall function. It offers a tangible representation of how space looks to them—from a phoria, vertical deviation or central suppression. It’s a quick look at what your patients are actually seeing and can help you decide on the best management.

Adding Lasers to Your Practice

Learn how you and your staff can prepare to incorporate this service when your state adds it to the clinical scope.

Setting Up for Success

As with any new service, there are logistical considerations to address when integrating laser procedures into clinical practice. These include determining if any additional education or certification is needed, purchasing the necessary tools and staff training, to name a few.

Specific education, training and certification requirements will vary state by state, so it lies on your shoulders as the OD to confirm which procedures are allowed under the legislation in your practicing state and which rules and regulations are in place. It’s also important to find out what is required in your state for an OD to maintain the necessary licensure and certification.

Regardless of your specific state’s requirements, Chris Wroten, OD, of the Bond-Wroten Eye Clinics in southeast Louisiana, highly recommends participating in continuing education courses that review laser protocols and procedures as you begin adopting these services. Check with your state’s optometric association to see if there are any trainings being offered.

In addition, take advantage of the expertise of your optometric colleagues, adds James Hunter, OD, an adjunct clinical professor at the Indiana University School of Optometry. “If you have a question or are unsure how to proceed, ask a fellow optometrist who is already offering these services,” he recommends. “Learning from one another helps us grow as individual practitioners as well as a profession as a whole.”

“Staff training is also important to ensure confidence in assisting with each procedure,” notes Joe Sugg, OD, immediate past president of the Arkansas Optometric Association. “We keep a step-by-step guide available for the staff to reference and have found staff members are as excited as we are to offer this care to our patients.”
Stocking the Equipment
Aside from the laser itself, there are very few additional things you will need to purchase that aren’t already on hand in the office, according to Dr. Wroten. “Laser lenses are required to perform SL T and LPI, but are optional for YAG laser posterior capsulotomy,” he explains. “The use of laser lenses necessitates having conditioning fluid on hand (e.g., Goniosol, Goniovisc, Celluvisc), while topical ocular hypotensives (e.g., brimonidine) and topical anesthetics (e.g., tetracaine, proparacaine) are also needed.”

As for the lasers themselves, there are several different companies that offer equipment to lease or purchase. “Some lasers are stand-alone for each type of procedure and others are combination lasers,” says Dr. Sugg. “It is up to the individual doctor to decide which laser type best meets the needs of their patients and the clinic space they have available to house the laser.”

While lasers involve a significant financial investment, there are some misconceptions regarding their overall cost, according to Dr. Wroten. “Most new YAG/SLT combo lasers cost less than $40,000,” he notes, “which is much less than a new OCT scanner. Additionally, new standalone YAG lasers can be purchased for under $20,000, with refurbished, warranted units costing even less.”

You need not go it alone, he says. “Given their portability, multiple doctors/practices can purchase and share a laser, or laser rental services can be used where the laser is serviced, transported, set up and taken down by the rental company, and the doctor pays a per-patient usage fee,” he advises. “Keep in mind that while reimbursements vary by procedure type, carrier and geographic location, they are also significantly higher than for OCT procedures by comparison.”

For ODs who are hesitant to offer these new procedures due to cost, Dr. Lighthizer urges them to consider the professional value and satisfaction of adding a new service like lasers. “It is very rewarding—finances aside—to do something in the office that provides a great benefit for our patients,” he notes. “The more care you can provide for your patients—whether it’s a drop, oral medication or procedure—the more fulfillment you will have as a doctor, and the happier your patients will be.”

Virginia: A Recent Success Story
Thanks to a bill that passed in March of this year, optometrists in Virginia will now have the ability to perform three types of laser surgery—YAG capsulotomy, LPI and SLT. This scope of practice expansion is beneficial for both ODs and their patients, notes Lisa Gontarek, OD, president of the Virginia Optometric Association (VOA). Not only does this ensure timely care, but it also allows patients to remain in the care of a provider they know and trust.

“Because optometrists outnumber ophthalmologists 2.5 to 1 in Virginia, ODs are typically closer to patient’s homes and can get the patient in for treatment sooner,” says Dr. Gontarek. “This is especially beneficial in rural areas. As the largest state that permits optometrists to use lasers, we hope that our success in Virginia will help to pave the way for other states to expand their scope of practice as well.”

The bill will finally go into effect on July 1st after four years of planning and advocacy for scope expansion by the VOA. From the very beginning, they encouraged active members to complete an advanced procedure and laser certification course, explains Dr. Gontarek, who noted that by the time the bills were taken to the General Assembly, close to 150 doctors were already certified. The Virginia Board of Optometry is now working on setting a regulatory process, and once that is completed, the VOA will be able to help its members navigate the process of certification and implementation.

When asked what contributed to the success of Virginia’s legislative efforts, Dr. Gontarek emphasized the importance of an organized and well-executed plan that included a strong grassroots network, outstanding legislative committee leadership and a hardworking executive director and lobbyists, in addition to the full and loyal support of VOA members.

“It was a team effort from start to finish. I highly recommend that any state working toward scope expansion be fully prepared before pressing forward,” she says. “The process is a huge investment of time and money. It is just too important to take on halfheartedly.”
Another consideration for ODs is coding and billing. While this is fairly straightforward for laser procedures, Dr. Wroten explains that it may require amending some claims initially based on individual carrier requirements and/or insuring carrier protocols. For example, some insurers require a visual field and gonioscopy within the 12 months prior to SL T being performed.

**Practical Advice for ODs**

Before embarking on the task of incorporating lasers into your practice, again, it is important to consult your state board to determine the specific procedures that are permitted under your state’s scope expansion legislation.

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**OPTIMIZING LASER PROCEDURES: ADVICE FROM A PRO**

Looking for clinical tips and advice as you incorporate lasers into your practice? Dr. Wroten offers step-by-step recommendations to optimize three common ocular laser procedures below.

**YAG laser posterior capsulotomy.** The common initial laser settings for this procedure are single pulse, ~250μm posterior offset, starting energy of 1.2-1.8 mJ (higher for capsular fibrosis/denser opacification), moderate magnification and relatively high illumination for both the slit lamp light and for the focusing beam.

The most common YAG posterior capsulotomy treatment pattern is the cruciate/cross-shaped pattern; alternatively, the hinged, circular, spiral or star patterns may be used, all with the goal of creating a visible opening in the posterior capsule that is slightly larger than the scotopic pupil size (thus the surgery is performed with the pupil dilated). Intraoperatively, should the doctor have difficulty determining the focal plane due to reflections, one technique to assist is to focus the HeNe beam on the iris, then move over to the pupil without changing the plane of focus, and finally move the beam toward the patient to focus on the posterior capsule.

To decrease the chance of pitting the IOL, since there is a shockwave of energy that travels back toward the doctor from the laser’s focal plane, a posterior offset is often used. Additionally, the OD can intentionally defocus the HeNe beams behind the capsule initially, then pull the HeNe beam anteriorly to focus on the capsule before firing. If total energy used exceeds 100-150mJ in a single session, consider bringing the patient back on another day to finish. Whether or not to use a YAG laser capsulotomy lens is solely at the discretion of the doctor. Using a lens may increase accuracy, reduce the number of shots and totally energy required and provide better control of the eye during the procedure. On the flip side, it also adds time, requires conditioning fluid and increases the number of reflections in the doctor’s view.

**Selective laser trabeculoplasty (SLT).** Common initial energy settings include power at 0.8-1.0 mJ; moderate magnification and high illumination settings for the slit lamp and focusing beam; the counter is set to zero and the spot size and other laser settings are fixed. An SLT laser lens is necessary to visualize the angle of the eye and treatments are generally applied 360 degrees to the trabecular meshwork using adjacent, non-overlapping spots (typically about 100 shots total). The goal during surgery is to see tiny “champagne bubbles” in the anterior chamber when the laser is fired. Keep in mind that SLT is contraindicated for neovascular glaucoma, and energy settings can be decreased for patients with heavily pigmented trabecular meshwork.

**Laser peripheral iridotomy (LPI).** The common initial energy settings for this procedure are single, double or triple burst setting; energy = 2.5-3.0 mJ with no offset; and use of an iridotomy lens to focus laser energy, provide magnification and help identify an iris crypt (i.e., thin area of the iris) for creating the iridotomy. Keep in mind that an LPI can less commonly be performed using an argon laser, but settings will differ from the ones just outlined.

Pilocarpine may be used preoperatively to tighten the iris, and the iridotomy is created about one-third of the way from the limbus toward the pupillary margin, located at either 11:00 or 9:00 OD, and at either 1:00 or 3:00 OS, with some studies suggesting the chances of postoperative dysphotopsia are lessened with the 9:00 OD and 3:00 OS locations. The endpoint is reached when a “plume” of aqueous is observed entering the anterior chamber after a laser shot, then the opening is enlarged to approximately 1mm in diameter.

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Successful laser procedures begin with the basics, including something optometrists have been doing for years, according to Dr. Hunter, which is diagnosis. “For instance, the appropriate use of lasers in glaucoma is centered around the appropriate diagnosis of the type of glaucoma,” he says. “Then, the application of the laser treatment becomes the use of a slit lamp, which optometrists have used for decades, followed by applying the scientific-based settings for the laser for each individual condition.”

As with any intervention, a thorough medical history is required. “With rare exceptions, laser procedures are contraindicated if active intraocular inflammation is present, retinal issues exist (e.g., macular edema, macular hole,
epiretinal membrane), patients are unable to fixate or if corneal opacities prevent adequate visualization of the surgical site,” notes Dr. Wroten.

On the day of surgery, the laser should be properly focused by the doctor and the type of surgery, as well as the eye to be operated on, should be verified multiple times, according to Dr. Wroten. He also notes that appropriate informed consent should be obtained to include alternatives to the procedure and potential complications.

“After the laser counter is zeroed out and the laser settings are adjusted appropriately, the patient should be educated on what to expect during the surgery,” he explains. “For instance, YAG posterior capsulotomy is typically painless, but the patient may hear a ‘snap’ when the laser fires. SLT may produce a mild stinging sensation during the procedure with slight soreness the following day, and YAG LPI may also be slightly uncomfortable for the patient.” Eliminating surprises during and after the procedure will help ease a patient’s anxiety and increase their trust in you as their doctor.

On the day of the procedure, intraocular pressure (IOP) should be measured prior to surgery for YAG posterior capsulotomy, SLT and LPI to ensure it’s safe to proceed, advises Dr. Wroten. A topical ocular hypotensive—most commonly brimonidine—is instilled in the eye at least 20 minutes prior to surgery and then shortly after the procedure is completed.
dysphotopsia and floaters, in addition to how, when and whom the patient should contact if complications arise and when to return for follow-up. See the sidebar on the previous page for other clinical pearls from Dr. Wroten.

When performing YAG laser capsulotomy, Dr. Sugg emphasizes the importance of staying on plane and continually advancing the opening. “It’s always tempting to chase the capsule posteriorly and to try and make it look perfect, but it’s just not going to look as clean and perfect as you want it to immediately,” he explains. “If you keep moving on plane and advancing the capsulotomy, those capsular flaps will open and move further posteriorly with time, and it will look more like you want it to by the one-week follow-up appointment. This allows you to put less overall energy in the eye.”

Also, he urges ODs not to be afraid to increase the energy setting because this can allow for a more efficient capsulotomy, and you might actually put less overall energy in the eye by increasing the amount of energy per pulse.

“Regarding SLT, your ability to perform this procedure is tied directly to your gonioscopy skills,” Dr. Sugg says. “If you are confident in these skills, or if you take the time to become confident in these skills, then there really isn’t much more to performing an SLT. Of course, you must be familiar with the proper settings and how to adjust them.”

**Advocating for Change**

While scope expansion progress continues at a healthy pace, many states still do not recognize the full extent of education and training ODs possess to successfully perform laser procedures. Therefore, it is important that

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**LASER LAWS AND ACCESS TO CARE**

A recent study suggests that adding optometric laser privileges in Oklahoma, Louisiana and Kentucky has not expanded access to such care for patients, according to findings presented during the 2022 ARVO annual meeting in Denver.1

The data showed that optometrists cover an area similar to that covered by ophthalmologists for SLT and YAG procedures, according to the study authors. They reported that for SLT the percent of the population covered within 30 minutes of driving time by optometrists and ophthalmologists was 73.4% and 84.1%, respectively.

For YAG procedures, it was 84.8% for optometrists compared with 85.3% for ophthalmologists. The research also found that for both procedures, the percent of the population covered exclusively by optometrists was 5.6% compared with 6.1% by ophthalmologists.

These findings, the study authors conclude, suggest that expansion of laser authority for optometrists has not resulted in a statistically significant increase in access to these procedures for patients.

Commenting on these findings, well-known Kentucky optometrist Ben Gaddie emphasized that scope of practice legislation was never about replacing or overtaking the volume of laser being performed, but rather a way to augment the care delivered by their ophthalmological colleagues. “Access to care isn’t necessarily a volume game; keep in mind that there is a reason why these smaller population areas don’t have as much access,” says Dr. Gaddie. “In these settings, optometric laser care has been an essential benefit, and I can personally attest to this,” he notes. “Even in more metropolitan areas, patients don’t like to go through the hassle and expense of being treated in the physician-owned surgery center. They pay a facility charge and physician charge, as well as having to wait in an ASC setting. Patients appreciate having their own doctor perform the procedure right in the office.”

Over the last decade, Dr. Gaddie has witnessed firsthand the impact of expanded scope of practice in Kentucky. “We have an office in a county of 10,500 people where we are the only eye care providers in the county (we have an ophthalmologist that comes in and does cataract surgery twice a month) and the only providers in a contiguous six counties thereafter,” he notes. “The socioeconomic reality in many of our rural communities is that $5.00/gallon gas prices and a two-hour plus round-trip drive for a laser isn’t feasible. We are providing an alternative for those who don’t want to or can’t drive to Louisville or Lexington.”

1. Shaffer J. Evaluating access to laser therapy by driving distance using Medicare data and geographic information systems mapping. ARVO 2022 Denver.
optometrists continue to advocate for themselves and their profession.

Lisa V. Gontarek, OD, who serves as president of the Virginia Optometric Association, urges optometrists to get involved at the local, state and national levels. “Organized optometry is the only way we move our great profession forward,” she says, while noting that involvement looks different for everyone. “Some are able to do more than others, and that’s okay. Do what you can. We will always be stronger together.”

Actively advocating for optometric practice begins by joining your state association, notes Dr. Hunter, while also emphasizing the important role ODs play in the profession’s growth. Other ways to get involved include donating to state and AOA PAC, building relationships with legislators, participating in Legislative day or volunteering in your local optometry society.

“To keep optometry pertinent and at the forefront of the healthcare arena, it is incumbent upon us to keep moving our profession forward. In order to do that, we must educate the public and our patients about what we do,” says Dr. Gontarek. “While not all optometrists will necessarily incorporate every scope expansion into their practices, we should all support those who want to. Otherwise, our profession will become stagnant, and our patients will suffer for it.”

Continued Expansion

As the role of optometrists continues to grow with the ongoing scope of practice expansion, it is important that ODs take advantage of these practice authority wins. Dr. Lighthizer recognizes that incorporating laser procedures can be daunting, but he reminds optometrists that they have the knowledge and skills to be successful.

“Remember, this is within your education and training,” he says. “But, just because you have a laser and a patient doesn’t mean you have to perform that procedure. Take your time when you first start offering these services. Choose your patients wisely. It’s okay to start with straightforward cases and refer more complicated ones out until you build your confidence. And if you have no interest in providing these procedures, refer to your optometric colleagues who do.”

When ODs practice to the full extent of their clinical abilities, everyone benefits, notes Dr. Hunter. “As the general population continues to age, there is going to be an increasing need for eye care services, including laser treatments. Coupled with a decreasing number of ophthalmic surgeons, optometrists will need to expand within their scope of practice to meet this demand,” he says. “ODs are perfectly positioned to provide this care, and doing so offers significant value to our patients.”

Next month: Part 3 of this series will delve into glaucoma medication prescribing privileges and optometric glaucoma comanagement more broadly.
Bandage contact lenses (BCLs) are relatively low cost and can be used for a variety of therapeutic purposes. They heal injured corneal tissue and relieve pain and discomfort by protectively shielding the cornea from shearing forces of eyelids on blinking as well as from eye movements under the lids, thus preserving integrity of newly forming epithelial cell.1-7

BCLs also stimulate corneal metabolism, enhance corneal regeneration, increase epithelial adhesion, maintain hydration, reduce accumulation of collagenase, decrease edema and improve corneal transparency and vision.1,4,8 Future therapeutic considerations include the use of contact lenses as surgical adjuncts as well as vehicles for ophthalmic drug delivery.1,2,6

Common Uses
When the cornea needs protection from mechanical trauma during wound healing and a decrease in pain stimuli, BCL application can provide much-needed relief and respite.12-18

Contact lenses provide nearly instantaneous pain relief, as they protect exposed corneal nerves, preserve binocularity and cosmetics (unlike traditional pressure patches), improve visual acuity, can be combined with topical antibiotics for microbial prophylaxis and can be re-sterilized.6,15,19-21,23-25 Additional remedies, used alone or in

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combination, include topical steroids and metalloproteinase inhibitors, hypertonic solutions for corneal edema and oral doxycycline.\textsuperscript{14,19,24}

Numerous clinical studies have described BCL therapy for corneal defects. The time necessary for return to normal activities has been shown to be significantly less in patients treated with BCLs vs. pressure patching and bandage lenses combined with topical NSAID use was found to be more comfortable than pressure patching or BCL wear alone.\textsuperscript{15} One study indicated a more rapid recovery in patients with corneal erosions treated with BCLs vs. control, in which the compromised eye was treated by covering.\textsuperscript{25} Furthermore, BCLs were found to lessen pain and decrease corneal erosion size to a greater extent than pressure patching.\textsuperscript{16}

Another study, however, found no significant difference in pain relief and abrasion area between pressure patching, BCLs and ofloxacin ointment alone in the treatment of traumatic abrasions following corneal foreign body removal.\textsuperscript{24} One 1985 study demonstrated increased efficacy of ocular lubricants over BCLs for the treatment of RCEs; however, improved performance of BCLs seen in recent literature is likely due to newer lens materials with increased oxygen transmission that have since become available.\textsuperscript{18,26}

One such study demonstrated a comparable percentage of patients achieving complete resolution of RCEs between subjects treated with ocular lubricants vs. BCLs; however, patients receiving BCL therapy achieved complete resolution at a faster rate and with better initial pain scores.\textsuperscript{19} In another study—of 12 patients with a history of RCEs that previously failed conservative treatment with ocular lubricants and nightly ointments—application of an extended-wear BCL in combination with topical ofloxacin produced long-term symptom relief and prevented signs of recurrences at one year or more of follow-up.\textsuperscript{17}

Additionally, therapeutic BCLs have been indicated in children.\textsuperscript{27} One study of 29 pediatric eyes reported 93\% efficacy of extended BCL wear in conditions including corneal burn, erosions, ulceration, perforation, neurotrophic keratopathy, vernal keratoconjunctivitis, herpetic keratitis, keratouveitis, descemetocoele and exposure keratopathy.\textsuperscript{27} In one case, BCLs provided successful treatment of keratopathy secondary to lagophthalmos, thereby delaying more invasive tarsorrhaphy.\textsuperscript{27}

Conventional hydrogel soft contact lenses have been documented extensively in the healing of epithelial defects and were often worn on an extended wear schedule in conjunction with ocular lubricants.\textsuperscript{14} With the advent of silicone hydrogel (SiHy), conventional hydrogels became outmoded for therapeutic purposes, as the oxygen transmissibility (Dk/t) of SiHy superseded that of conventional hydrogels.\textsuperscript{14,15}

Post-Surgical BCLs
Soft bandage lenses are often used for wound coverage, such as placement after surgical procedures, including superficial keratectomy, phototherapeutic keratectomy and corneal collagen crosslinking.

Refractive surgery. Bandage contact lens application has been extensively noted in the postoperative management of photorefractive keratectomy (PRK), which typically results in ocular pain post-surgery due to corneal nerve damage and release of inflammatory factors.\textsuperscript{28-30} BCLs promote pain relief and speed re-epithelialization and may be used for three to five days post-PRK in concert with topical anesthetics, NSAIDs, artificial tears, oral analgesics and, in some cases, oral anti-convulsants.\textsuperscript{28-30} A multitude of studies have been conducted to determine the relative efficacy of various BCL materials and fitting parameters in speeding up recovery post-PRK.\textsuperscript{28,29,31-36} Materials have been shown to differentially impact re-epithelialization rate, epithelial defect size, pain, discomfort, foreign body sensation, epiphora and postoperative visual acuity.\textsuperscript{28,29,31-36}
Regarding fitting parameters, most patients preferred steeper base curve lenses, with the exception of patients with flattest K values preferring larger base curve lenses.28,37

The use of BCLs has also been noted in the postoperative management of flap-based refractive procedures (LASIK/LASEK) for the promotion of corneal wound healing and epithelial regeneration, proper epithelial flap positioning, corneal protection and relief of pain and discomfort.38-40 In order to minimize edema and hypoxia associated with BCL wear, higher Dk SiHys are preferred to traditional hydrogels and are able to satisfy corneal oxygen requirements during extended and overnight wear.38-42 Furthermore, Dk plays a role in corneal epithelial repair and pain relief post-surgery. Several studies have explored the relative performance of various SiHy materials following flap-based procedures, demonstrating that varying materials differentially affect re-epithelialization rate, pain and epiphora.38,39

To maximize pain relief with BCLs, fit tighter lenses with smaller base curves that minimize lens movement on the eye (albeit, ensuring adequate movement, stability and centration), as well as fit lenses with higher water content.38,39 Concomitant therapy with topical antibiotics, anti-inflammatories and artificial tears is recommended.39

Visual acuity may be worse in the immediate postoperative period for patients managed with BCLs, which may be due to increased corneal flap edema associated with BCL wear.40,42 Furthermore, higher asymmetry in corneal radii may exist temporarily due to BCL-induced warpage and mucoid secretions are higher in patients treated with BCLs.40,42

**Keratoplasty.** Postoperative use of BCLs in patients that have recently undergone a full- or partial-thickness keratoplasty has shown mixed results. Several studies have demonstrated the utility of BCL wear in maintaining epithelial integrity following penetrating keratoplasty;43,44 A risk for bacterial corneal ulcers was noted, however, in patients treated with BCLs after penetrating keratoplasty; this risk appeared to be intensified in immunosuppressed hosts.45

**Boston keratoprosthesis.** Boston Type 1 Keratoprosthesis (KPro; Mass Eye and Ear) is an artificial cornea that is placed when prognosis for a successful penetrating keratoplasty is guarded, as in patients with compromised host tissue or history of prior corneal graft rejection.46-48 Continuous BCL wear is essential for long-term management of KPro patients to maintain ocular surface hydration, minimize evaporative drying and prevent postoperative complications such as corneal melt.49-52 In order to preserve keratoprosthesis function and maintain adequate lens retention, it is imperative to establish a suitable BCL fit, with modification of contact lens parameters such as base curve and diameter often necessary.48,49,53

**Corneal collagen crosslinking (CXL).** This surgical procedure, which aims to stop the progression of keratoconus, necessitates the use of BCLs to promote re-epithelialization following complete removal of corneal epithelium.54-56 Due to absence of epithelium, microbial colonization and infection pose a concern.54,55 One study found that 16.7% of eyes treated with CXL experienced bacterial colonization and recommended the prophylactic use...
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- Practice Workflow Implementation
- Remote Patient Management
- Vision Alert Management

of postoperative topical antibiotics to prevent infection.\textsuperscript{54} Another concluded that forgoing BCL application as well as delaying use of steroids until epithelialization occurs may reduce risk of microbial keratitis; however, the authors noted that it was impossible to discern whether risk of microbial keratitis increased from use of BCLs, steroids or a combination thereof.\textsuperscript{55}

\textbf{Cataract extraction.} Bandage contact lenses offer ocular surface protection in the immediate postoperative period following cataract surgery.\textsuperscript{57} Patients often experience post-surgical discomfort secondary to corneal incisions.\textsuperscript{57} One 2018 study found that BCLs can successfully control postoperative pain and discomfort, protect the cornea from exposure during recovery from corneal incisions and improve delivery of antibacterial drops.\textsuperscript{57} Furthermore, medications for cystoid macular edema (CME) following cataract extraction may result in keratoconjunctivitis medicamentosa.\textsuperscript{58} In these cases, bandage contact lens wear was shown to mitigate corneal epithelial disease—which may, in turn, improve tolerance to CME medications.\textsuperscript{58}

\textbf{Pterygium excision.} Bandage lenses have been recommended in the postoperative management of pterygium excision due to their ability to hasten corneal healing and alleviate discomfort.\textsuperscript{59-61} BCL wear, however, has not shown superior comfort post-pterigium excision when compared with patching; furthermore, studies have shown that patching confers the added benefits of relief from photophobia and improved sleep quality, albeit at the expense of binocularity and cosmesis.\textsuperscript{60,62,63}

\textbf{Post-trabeculectomy.} Bandage contact lenses have demonstrated superior utility relative to traditional suturing and patching in the post-surgical management of trabeculectomies, which may result in complications including filtration bleb leakage and anterior chamber shallowing.\textsuperscript{64-69} The concurrent uses of topical antibiotics, steroids and cycloplegics have been recommended when covering bleb leaks with BCLs, as well as conjunctival coverage extending 2mm to 3mm superior to the limbus to prevent air bubble formation.\textsuperscript{64,65} Large-diameter BCLs have also shown efficacy in managing early onset hypotony secondary to surgical filtration procedures such as trabeculectomies, with intraocular pressures rising 5mm Hg to 12mm Hg following BCL application.\textsuperscript{70}

\textbf{Corneal laceration.} In one case of severe laceration, bandage lens wear was shown to prevent complete extrusion of ocular contents, including of the crystalline lens, allowing for a short delay of necessary evisceration.\textsuperscript{71} In another case, a perioperative BCL was placed during pars plana vitrectomy in the setting of corneal laceration, stabilizing the anterior chamber, maintaining a closed environment and improving surgical visualization.\textsuperscript{72} In instances of small, perforating corneal injuries, BCL wear has been shown to be an effective alternative to surgical intervention with the added benefit of precluding complications associated with suturing.\textsuperscript{73}

\textbf{Novel and Additional Uses}

Bandage contact lenses have also shown utility for improving the ocular surface in certain situations and for other conditions.

\textbf{Dryness.} Silicone hydrogel BCL wear can improve discomfort from ocular dryness after cataract surgery by increasing stability of tear film and promoting corneal healing.\textsuperscript{74,76} Improved TBUT scores, Schirmer 1 scores, fluorescein staining, inflammatory biomarkers, OSDI and subjective evaluation scores were noted for patients treated with BCLs.\textsuperscript{74,76}

For patients with filamentary keratitis in aqueous-deficient dry eyes, higher water content, higher Dk contact lens materials have been reported to be therapeutic, while thicker, lower Dk and hydrogel materials have been noted to cause filamentary keratitis, with long-term use of BCLs being contraindicated in aqueous tear-deficient eyes.\textsuperscript{77}

In patients with dry eye associated with Sjögren’s syndrome, application of BCLs has been shown to significantly improve BCVA, OSDI, corneal staining, TBUT, comfort and quality of life.\textsuperscript{78} This approach also proved superior to autologous serum drops in certain instances.\textsuperscript{73} The combination of BCL use with autologous serum drops has been suggested for the treatment of severe dryness and has further proved valuable for the recovery of persistent epithelial defects with subsequent improvement in BCVA.\textsuperscript{75,78,81}
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Furthermore, BCL use in sedated and mechanically ventilated patients has been shown to limit exposure keratopathy to a greater degree than ocular lubricants, with BCLs significantly promoting healing of preexisting corneal defects.82 Bandage lenses have also shown utility in the treatment of congenital cornea anesthesia, a rare clinical condition which results in impaired healing of the corneal epithelium and may progress to keratopathy and/or corneal perforation.83

**Graft-vs.-host disease.** Several studies report on the role of BCLs in the treatment of ocular surface disorders secondary to graft-vs.-host disease (GVHD). Ocular GVHD can result in minor conjunctivitis and/or keratoconjunctivitis sicca, or can be severe, with cicatricial findings and/or corneal perforation; superficial punctate keratopathy and filamentary keratitis are often noted.84,85 When initial treatments alone may not sufficiently mitigate symptoms or when scleral lens wear is difficult due to high cost, time or availability limitations, soft BCLs may be considered as an alternative.84,86 BCLs have been found to promptly improve subjective symptoms, visual acuity and ocular surface integrity in patients with ocular GVHD, as well as reduce frequency of topical lubricant instillation.84,86

**Bullous keratopathy.** BCL wear has been shown to promote healing of this chronic corneal condition that results in formation of painful epithelial bullae secondary to endothelial dysfunction and subsequent corneal edema.86,87 BCLs prevent lid interaction with exposed corneal nerves, minimizing corneal edema and contributing to relief of pain, photophobia, blepharospasm and epiphora.86,87 SiHy material has been shown to outperform conventional soft lens materials in terms of comfort, while no significant difference was found in terms of pain relief, fit, movement or buildup of deposits.86

**Infectious keratitis.** Bandage contact lens use has been shown to improve ocular surface abnormalities secondary to adenoviral keratoconjunctivitis.88 In concert with adjuvant therapies including preservative-free artificial tears, topical antibiotics, ganciclovir, povidone-iodine and steroids, BCLs can promote pain relief by resolving epithelial defects, filamentary keratopathy and epithelial edema.86

**Conjunctival protection.** Soft BCLs have been implicated in the treatment of several conjunctival conditions. One study demonstrated the value of short-term large-diameter BCL wear in resolving symptoms of severe acute superior limbic keratoconjunctivitis (SLK), although recurrences were likely to occur and treated for the long term by other means.89 Unilateral BCL wear was found to contribute to bilateral symptom relief in SLK, possibly mediated by a bilateral decrease in reflex blinking.90 Bandage lenses have also demonstrated mechanical shielding of the cornea from irregular palpebral conjunctiva in a case of primary conjunctival amyloidosis, conferring significant symptom relief.90 Further, BCLs were shown to prevent post-surgical symblepharon reformation after chemical burn of the external eye.90

**Drug Delivery**

Extensive research recognizing the abilities of BCLs to function as drug delivery systems has been documented due to their superior drug bioavailability relative to eye drops and availability for use on an extended wear schedule.82-86 Eye drops confer low drug bioavailability due to precorneal loss and poor corneal absorption, leading to increased frequency of dosing, side effects and poor medication compliance.82-86

Desired properties of drug delivery devices include easy, comfortable and controlled administration over an extended period of time with preservation of vision and ocular function.85 Several types of BCL drug delivery systems have been described; these include soaking contacts in drug solution, instilling eye drops over bandage contact lenses already in place on the eye, molecularly imprinting drug site polymers onto contact lenses, loading colloidal nanoparticles onto contact lenses to control drug release, preparing contact lenses with hydrophilic and hydrophobic phases, integrating vitamin E within lenses to create drug transport barriers and incorporating microemulsions, liposomes or micelles into the contact lenses.82-86

In April 2021, Johnson & Johnson Vision Care announced FDA approval of Acuvue Theravision with Ketoti- fen, a drug-eluting contact lens made of etafilcon A material, intended for allergy relief. This is currently the only medication-releasing contact lens available. Despite these innovations, optical and physical properties of contact lenses may be impacted

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*The use of BCLs has also been noted in corneal protection from the ocular adnexa, such as in the case of trichiasis.*
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and drug-loading and release capacity remains limited, thereby limiting commercial use of drug delivery by means of BCLs.92,93

Complications

While bandage contact lenses play a significant role in the protection and healing of numerous ocular surface conditions, they are often used on an extended, overnight wear schedule and bacterial colonization as well as complications including corneal edema, neovascularization, stromal infiltrates, endothelial polymegathism and infectious keratitis have been reported.97-103

In a retrospective study of 6,685 eyes from 2019, researchers found that infectious keratitis following BCL wear was diagnosed in 0.13% of eyes, which is lower than other studies.98,99 Of the eight patients diagnosed with infectious keratitis, five displayed poor compliance with BCL wear, either by overextending lens wear or noncompliance with drop regimen.99 Additional risk factors included post-keratoplasty BCL wear and older age.99 Although treatment of corneal ulcers was shown to be successful with antibiotic therapy, corneal scarring and poor visual outcomes were common.104 Biofilm formation over BCLs has also been noted in the setting of KPro. One study found prophylactic vancomycin and linezolid therapy to be relatively effective in preventing biofilm growth of BCLs worn over KPro at one month.104

Given the risks associated with bandage lenses, be vigilant to identify and prevent complications, with heavy emphasis on patient education to promote good compliance and ensure successful outcomes.90,99 Daily contact lens checks are recommended, as well as handling of lenses by the clinician.

Takeaways

With the advent of newer technology and materials, clinical use of contact lenses for the treatment of ocular surface conditions has increased considerably. Soft bandage contact lenses remain a popular option for the treatment of corneal defects and confer the added benefit of visual improvement. In many cases, BCLs can lead to complete resolution of corneal conditions and may preclude surgical intervention. Continued innovation in the manufacturing and application of contacts will likely expand their roles and result in enhanced patient outcomes.1

If you identify new or changing signs or symptoms, consult with an eye doctor who specializes in TED right away.1,14

For patients with Graves’ disease (GD), Thyroid Eye Disease (TED) may be hiding in plain sight.1,2

Up to 50% of patients with GD may develop TED, a separate and distinct disease which can progress if left untreated. Look out for the early signs and symptoms 3-7:

- Proptosis1
- Sensitivity to light12
- Diplopia3
- Grittiness8-11
- Dry eyes8-11
- Pain or pressure behind the eyes1,13

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Published March 7, 2023 • By Staff
BRONYM, NEWS
Smoking, High BMI Associated with Disruption
Interferometry identified these populations as at-risk

Researchers recently found that smokers and individuals with a high BMI showed significantly lower fRIP layer thickness and tear meniscus height scores compared with controls. They noted that their assessment of tear film parameters supports the findings of previous studies that implicates smoking and other risk factors for dry eye.

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New drugs continue to emerge at a steady rate for neovascular macular degeneration (nAMD). The past two years alone have seen a refillable port delivery system, a biosimilar anti-VEGF and a new therapeutic, Vabysmo (Genentech/Roche).

Geographic atrophy (GA), on the other hand, has been plagued by failed treatments for a disease that has no proven therapeutic intervention. The unmet need is high. For eyecare providers, it is gut-wrenching to watch GA patients eventually succumb to severe loss of central acuity, while at the very least, we have treatment to offer to those who develop nAMD. But is there hope on the horizon? We will dive into the elusive disease of GA to break down the complex pathophysiology and provide insight on potentially promising treatments and updates in multimodal disease monitoring.
We are focused on developing treatments for patients suffering from retinal diseases with significant unmet medical needs.

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Pathophysiology Breakdown

The mechanisms of dry AMD and GA are complex and multifactorial. Genetics, aging and environmental stressors are all thought to contribute. The first clinically visible sign of dry AMD is the accumulation of drusen, an extracellular deposit composed of lipids, proteins and debris. Photoreceptor outer segment turnover from aging and retinal pigmented epithelium (RPE) stress leads to lipofuscin deposition. These by-products of oxidative stress, among others, are thought to lead to inflammation through the complement cascade and the NLRP3 inflammasome. As dysfunction occurs in these pathways, inflammation induces the retinal cell death that is distinctive to GA.

Complement Cascade

Understanding the pipeline therapeutics, in turn, necessitates a refresher on the complement cascade. This is an immune response to recognize and remove pathogens and cellular debris. Over 50 proteins make up the cascade, which ultimately lead to the formation of the membrane attack complex (Figure 1). There are three pathways: classical, lectin and alternative, which converge into the formation of a protein complex—the C3 convertase. The path travels from there toward the C5 convertase and the membrane attack complex, which creates a pore on pathogen material to facilitate its cell lysis.

In AMD, the complement cascade is activated by inflammation, reactive oxygen species and macrophages. As well, genetic polymorphisms result in complement dysfunction. Most notably, Y402H, a variant in complement factor H, has been linked with GA and found to be present in half of individuals with AMD.

Therapeutic Pipeline

There are multiple therapeutic contenders targeting all aspects of the complement cascade. By inhibiting C3 cleavage, pegcetacoplan (APL-2, Apellis Pharmaceuticals) stops the downstream progression of the complement cascade. After a successful Phase II study, FILLY, pegcetacoplan moved into phase 3 studies, OAKS and DERBY. In the OAKS 12-month results, those randomized to monthly injections of 15mg/0.1 mL pegcetacoplan had a 22% reduction in GA growth compared with every-other-month treatment at a 16% reduction. DERBY narrowly missed its primary endpoint to significantly reduce GA lesion growth. Of important note, when data from the two Phase III trials were pooled, pegcetacoplan performed better for extrafoveal GA, decreasing lesion growth by 26% (monthly) and 23% (every-other-month). However, the combined trial data also noted increased conversion to nAMD of 6.0% (monthly) and 4.1% (every-other-month) compared to a rate of 2.4% in the sham arm.

In a March 2022 press release, Apellis announced 18-month data for DERBY and OAKS. In pooled analysis, the reduction of GA lesion growth in monthly treatment went from 13% in months zero to six to 21% in months 12 to 18. In the EOM group, the decrease in growth went from 12% in months zero to six to 17% for months 12 to 18. The company noted its plans to submit for a new drug approval to the FDA in the second quarter of 2022.

Also gaining promise in clinical trial is a C5 inhibitor, avacincaptad pegol (Zimura, Iveric Bio). In the Phase III trial GATHER1, avacincaptad pegol met its primary outcome to slow the growth of extrafoveal GA in both the 2mg and 4mg doses of intravitreal injection. The 2mg group saw a 27.4% reduction in GA growth, and a 27.8% reduction was observed in the 4mg treatment arm. However, the treated arms did show high rates of conversion to choroidal neovascularization (CNV) compared with sham. The CNV conversion rate at one year was 2.7% in the sham arm compared to 9% and 9.6% in the 2mg and 4mg groups, respectively. This increased at the 18-month mark to 11.9% and 15.7%, respectively, while sham rates did not change.

A second Phase III trial (which anticipates completion next year) is GATHER2, evaluating just the 2mg dose against sham. Participants randomized to treatment will receive 2mg intravitreal injection monthly for year one and then will be randomized for year two to receive treatment either monthly or every-other-month.

As the closest of the Phase III candidates, will either of these drugs have enough positive data to garner an FDA approval? If so, how will they be used? The answer will depend on how much these drugs slow GA growth (extrafoveal in particular), the risk of conversion to nAMD and the treatment burden for patients. Will there be enough gain to be worth the frequent treatment? Some would argue that with no other treatment available for GA, anything is better than offering nothing to slow down a visually debilitating disease.

Other contenders targeting the complement cascade include NGM621 (NGM Biopharmaceuticals), a human-
ized IgG1 monoclonal antibody that inhibits cleavage of C3. In contrast to other complement-targeting drugs, NGM621 is not pegylated, which could play a role in not eliciting the conversion to nAMD. Phase II trial, CATALINA, is underway for NGM621 with an enrollment of 320 participants estimating topline data in late 2023.11

ANX007 ( Annexon Biosciences), a monoclonal antibody antigen-binding fragment, binds to C1q to inhibit downstream components of the classical pathway. It is recruiting for Phase II trial, ARCHER.12 Table 1 provides a summary of active clinical trials for GA.

Non-complement Contenders

Even though therapeutic intervention for GA may seem to be just focused on the complement cascade, other targets and mechanisms continue to be explored. Oral treatments, which are of particular interest in an optometric setting, are also under exploration, including the anti-inflammatory effects of doxycycline (Oracea) in a Phase III trial called ToGA.13

Another potential oral GA treatment, ALK-001 (C20-D3-vitamin A, Alkeus Pharmaceuticals), is in a Phase III trial known as SAGA.14 ALK-001 targets modulation of the visual cycle by slowing the formation of vitamin A dimers, thought to be toxic to the retina.15 Alkeus is also exploring the drug for macular atrophy caused by Stargardt’s disease, which is now in recruitment for the Phase II TEASE trial.16

A familiar drug, brimonodine, has also been trialed due its known cytoprotective and neuroprotective properties.17 The Brimonidine Drug Delivery System (Brimo DDS), a biodegradable intravitreal implant, showed statistically significant reduction in GA growth at three months that waned over the course of the Phase II trial.17

Gene therapy and stem cell transplantation also show promise in GA but are in far earlier stage development.

Targeting Risk Factors

Until a treatment is approved for GA (and even after), patient counseling should focus on modifiable risk factors. Smoking is at the top of that list. Evidence shows that current smoking, not just former, is linked to development of advanced AMD.18 Obesity and alcohol consumption have also been suggested to contribute.19,20 Counseling patients on lifestyle choices may help to lower the risk for GA development and progression.

Vitamin supplementation continues to be a hot button topic for any stage of AMD. What combination of vitamins? What dose? Is genetic testing necessary prior to recommending? These questions continue to linger. The risk reduction found in the original AREDS, for intermediate AMD patients on a combination of high-dose antioxidants and zinc, was only statistically protective toward reducing development of nAMD.21 Even in AREDS2, the addition of lutein, zeaxanthin and omega-3 fatty acids did not show additional protection for nAMD or GA.22 However, the AREDS2 participants were a well-nourished and well-educated population.

This raises the question: would our patients with AMD and poor dietary habits benefit more from supplementation? Twenty years after the original AREDS, it’s still not clear if a specific supplement can target GA. A healthy diet, on the other hand, does show a clear role in reducing the incidence of AMD.23 In particular, a Mediterranean diet rich in fruits, vegetables, legumes and fish has been linked to a decreased incidence of GA.24,25 Until a treatment can also be offered, the chairside discussion for patients with GA and dry AMD alike should focus on modifiable risk factors, diet and supplementation.

Multimodal Imaging

On fundus exam and color photos, GA appears as well-defined areas of RPE loss with increased visibility of the underlying choroidal vasculature. Atrophy can occur as a unifocal lesion or multifocal lesions, and the latter is known to progress at a faster rate and go on to involve the fovea quicker.15,26,27 Natural history studies have observed a variable rate of progression of GA.

### Table 1. List of Active Trials for GA

<table>
<thead>
<tr>
<th>Drug</th>
<th>Target</th>
<th>Trial (Phase)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PEGCETACOPAN (APL-2, Apellis)</td>
<td>C3</td>
<td>OAKS (3), DERBY (3)</td>
</tr>
<tr>
<td>AVACIRCAPTID PEGOL (Zimura, Iveric Bio)</td>
<td>C5</td>
<td>GATHER2 (3)</td>
</tr>
<tr>
<td>NGM621 (NGM Biopharmaceuticals)</td>
<td>C3</td>
<td>CATALINA (2)</td>
</tr>
<tr>
<td>GEM103 (Gemini Therapeutics)</td>
<td>CFH</td>
<td>ReGatta (2a)</td>
</tr>
<tr>
<td>ANX007 (Annexon Biosciences)</td>
<td>C1q</td>
<td>ARCHER (2)</td>
</tr>
<tr>
<td>IONIS-FB-LRx (Ionis Pharmaceuticals)</td>
<td>Complement factor B gene</td>
<td>GOLDEN (2)</td>
</tr>
<tr>
<td>ALK-001 (Alkeus Pharmaceuticals)</td>
<td>Formation of vitamin A dimers</td>
<td>SAGA (3)</td>
</tr>
<tr>
<td>DOXYCYCLINE (Oracea, Galderma Laboratories)</td>
<td>Anti-inflammatory</td>
<td>TOGA (3)</td>
</tr>
<tr>
<td>FHTR2163 (Genentech)</td>
<td>High-temperature requirement protein A1 (HTRA1) inhibition</td>
<td>GALLEGÓ (2)</td>
</tr>
<tr>
<td>ELAMIPRETIDE (Stealth Biotherapeutics)</td>
<td>Mitochondrial dysfunction</td>
<td>ReCLAIM-2 (2)</td>
</tr>
<tr>
<td>BRIMONIDINE (Allergan)</td>
<td>Cytoprotective, neuroprotection</td>
<td>BEACON (2)</td>
</tr>
<tr>
<td>GTO005 (Gyroscope Therapeutics)</td>
<td>Gene therapy targeting complement system</td>
<td>FOCUS (1/2): HORIZON and EXPLORE (2)</td>
</tr>
<tr>
<td>HMR59 (Janssen pharmaceuticals)</td>
<td>Gene therapy targeting complement system</td>
<td>NCT03144999 (1)</td>
</tr>
<tr>
<td>OpRegen (Lineage Cell Therapeutics)</td>
<td>Stem cell transplant</td>
<td>NCT02286089 (1/2a)</td>
</tr>
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</table>
lesions ranging from 0.53-2.6mm²/year (median of 1.78mm²/year) with larger lesions expanding at a faster rate.\textsuperscript{17,26-29} Color photography serves as a useful tool to image drusen over time, particularly monitoring for drusen regression. The regression and collapse of drusen has been linked to the development of GA, as well as nAMD (Figure 2).\textsuperscript{30,31}

Fundus autofluorescence (FAF), in particular, highlights the distinct atrophic patches, which image as a dark hypofluorescence due to the loss of RPE cells and absence of lipofuscin. The junctional zone, the edge between GA lesions and the intact outer retina, provides insight into progression rate. On FAF, GA lesions without fluorescence at the junctional zone show a slower rate of change, progressing at a rate of 0.38 mm²/year, compared with banded and diffuse patterns of hyperautofluorescence which progressed at 1.81 and 1.77mm²/year, respectively.\textsuperscript{29} Simply put, hyperautofluorescence around GA lesions is a poor prognostic sign for fast progression.

SD-OCT provides insight into the status of all the retinal layers. The structural changes in GA are most prominent in the outer retina as disruption and/or loss to the external limiting membrane (ELM), ellipsoid zone (EZ) and RPE/Bruch’s membrane complex. Because of the outer retinal loss, there is subsequent hypertransmission through to the choroid.

GA Biomarkers

It has been well-established that risk factors of large, soft drusen and pigmentary abnormalities signify a higher risk for progression from intermediate AMD to GA. Other high-risk biomarkers have risen over the past decade, particularly with the widespread use of multimodal imaging that correlates to a high risk for GA development. If a treatment for GA becomes approved, recognizing risk factors and the earliest signs of GA will become even more critical. A recent collaborative effort by the Classification of Atrophy Meeting (CAM) group took to defining biomarkers and nomenclature in GA, emphasizing SD-OCT to recognize biomarkers and differentiate the extent of atrophy as it progresses.\textsuperscript{32}

Hyperreflective foci. This finding is only appreciated on SD-OCT as punctate intraretinal lesions often located at the apex of drusen.\textsuperscript{33} They can be isolated or in a cluster. Hyperreflective foci often correspond clinically to focal hyperpigmentation and likely represent pigment granules. The foci originate in the outer retina and can migrate inward over time. An AREDS2 ancillary study of SD-OCT found the presence of hyperreflective foci in dry AMD is associated with a five-times higher risk of GA within two years.\textsuperscript{34}

Subretinal drusen deposits (SDD). These are an atypical form of drusen that are also referred to as reticular pseudodrusen. The former term was chosen by the CAM group as the preferred nomenclature, as it correctly identifies the known histologic location of the deposits in the subretinal space above the RPE layer.\textsuperscript{35} It is challenging to distinguish SDDs from true drusen when visualizing on color photography but rather best appreciated with SD-OCT to confirm the subretinal location. In the earliest development of SDD, SD-OCT shows a granular hyperreflective deposit below the EZ.\textsuperscript{35} As SDDs progress, the material accumulates into small mounds that break through the EZ.\textsuperscript{35}

FAF is also sensitive in detecting SDDs. Individually, an SDD is hypo- or isoautofluorescent with a hyperautofluorescent surrounded in a target shape. Collectively, this forms a diffusely reticular pattern. The presence of SDDs represents a higher risk of progression to advanced AMD, particularly GA.\textsuperscript{33,36-38}

Hypertransmission defects. Hypertransmission occurs as disruption to the RPE develops, leading to increased OCT reflectivity in the choroid. Hypertransmission defects can be seen on individual OCT B-scans as areas of increased choroidal reflectivity or on en face choroidal slabs. Even though the overlying RPE may appear intact, hypertransmission indicates loss of integrity to the RPE. Hypertransmission defects, even as a stand-alone finding, portend a high risk of progression towards nascent GA.\textsuperscript{39}

In the CAM group definitions, hypertransmission defects were emphasized as an importance characteristic to define incomplete RPE and outer retinal atrophy (iRORA) and complete RPE and outer retinal atrophy (cRORA).\textsuperscript{32,35}

Nascent GA/iRORA. In 2014, the term nascent GA was used to describe an SD-OCT biomarker that showed in a
longitudinal study to impend a 78-fold risk for transition to GA. This was defined as a “subsidence,” or collapse of the outer plexiform layer (OPL) and inner nuclear layer (INL) and a hyporeflective wedge-shaped band within the OPL. Taking this a step further, the CAM group established the preferred term iRORA by adding the presence of a choroidal hypoperfusion defect, signs of photoreceptor degeneration and RPE attenuation/disruption to the definition. The terms are synonymous, both indicative of the precursor changes seen prior to the development of complete atrophy.

**cRORA**. The progression of iRORA, typically in the timeline of one to two years, leads to a complete loss known as cRORA. This represents an endpoint in the development of atrophy in GA, which the CAM group defines as:

- A region of choroidal hypertransmission of at least 250μm in diameter.
- A zone of attenuation or disruption of the RPE of at least 250μm in diameter.
- Evidence of overlying photoreceptor degeneration:
  - subsidence of the inner nuclear layer (INL) and outer plexiform layer (OPL)
  - thinning of the outer nuclear layer (ONL), disruption of ELM or disintegrity of EZ
  - thinning of the outer nuclear layer (ONL), disruption of ELM or disintegrity of EZ

**Evidence of overlying photoreceptor degeneration:**
- subsidence of the inner nuclear layer (INL) and outer plexiform layer (OPL)
- thinning of the outer nuclear layer (ONL), disruption of ELM or disintegrity of EZ

**Takeaways**

There is an unmet need to serve our patients with GA, to give them hope that their disease can be slowed and their functional vision maintained for a longer time period. The trials reviewed here provide optimism that the retina world may be moving in that direction. If an intervention is approved, optometry will be on the forefront to educate and refer the proper patients, which means understanding GA and therapeutic targets. Optometrists would need to recognize early GA and high-risk OCT biomarkers to help identify at-risk intermediate AMD patients for early invention before advanced atrophy sets in.


**TABLE 2. DEFINITIONS OF IRORA AND CRORA**

<table>
<thead>
<tr>
<th>IRORA</th>
<th>VS.</th>
<th>CRORA</th>
</tr>
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<tbody>
<tr>
<td>A region of choroidal hypertransmission</td>
<td>A region of choroidal hypertransmission of at least 250μm in diameter</td>
<td>A zone of attenuation or disruption of the RPE of at least 250μm in diameter</td>
</tr>
<tr>
<td>A corresponding zone of attenuation or disruption of the RPE, +/- basal laminar deposits</td>
<td>Evidence of overlying photoreceptor degeneration: subsidence of the inner nuclear layer (INL) and outer plexiform layer (OPL)</td>
<td>Evidence of overlying photoreceptor degeneration: ONL thinning, ELM loss, EZ or interdigitation zone (IZ) loss</td>
</tr>
<tr>
<td>Evidence of overlying photoreceptor degeneration: subsidence of the inner nuclear layer (INL) and outer plexiform layer (OPL)</td>
<td>-thinning of the outer nuclear layer (ONL), disruption of ELM or disintegrity of EZ</td>
<td>-no signs of RPE tear</td>
</tr>
</tbody>
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Fig. 4. (A) Color fundus photos of a 90-year-old Caucasian female with bilateral GA AMD. The images on the left are baseline and on the right are 29 months later. (B) FAF images on the left highlight hypoautofluorescence of multifocal lesions of GA in both eyes (OD>OS) that on the right side have expanded and coalesced over time. (C) SD-OCT image of the right eye (top left) shows an area of cRORA (white arrows) that expanded to a much wider lesion (top right). The left eye OCT at baseline (bottom left) did not have cRORA, which then developed after 29 months (bottom right).
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IDENTIFYING CONVERSION TO WET AMD

Take a step-by-step approach to early detection by learning signs of exudation and how to evaluate OCT findings.

BY CAROLYN MAJCHER, OD, ELAINE PETRY, OD, AND SWETA DAS, OD TAHLEQUAH, OK

AGE-RELATED MACULAR DEGENERATION (AMD) IS THE THIRD LEADING CAUSE OF BLINDNESS WORLDWIDE AND THE LEADING CAUSE OF LEGAL BLINDNESS AMONG PEOPLE AGED 65 YEARS AND OLDER IN THE UNITED STATES.1-3 IT IS ESTIMATED THAT APPROXIMATELY HALF OF ALL CAUSES OF SEVERE VISION LOSS (20/200 OR WORSE) IN US INDIVIDUALS LIVING OVER THE AGE OF 40 ARE CAUSED BY AMD.4,5 ONLY ABOUT 10% TO 20% OF INDIVIDUALS WITH AMD HAVE THE EXUDATIVE FORM OF THE DISEASE, THE ADVANCED CONDITION ACCOUNTS FOR THE MAJORITY—90%—OF AMD-RELATED SEvere CENTRAL VISION LOSS.3,6

AMD IS A COMMONLY ENCOUNTERED DISEASE, ESPECIALLY IN DEVELOPED COUNTRIES. IN POOLED DATA FROM THE US, NETHERLANDS AND AUSTRALIA, THE PREVALENCE OF AMD WAS 4.6% AMONG INDIVIDUALS AGED 75 TO 84 YEARS AND 13.1% AMONG INDIVIDUALS OVER THE AGE OF 84 YEARS. THIS SAME STUDY FOUND THAT NEOVASCULAR AMD WAS PRESENT IN 0.17% OF INDIVIDUALS AGED 55 TO 64 YEARS AND 5.8% FOR THOSE OLDER THAN 85.7,8 DUE TO A GROWING PROPORTION OF OLDER ADULTS IN THE US THE PREVALENCE OF AMD IS EXPECTED TO RISE, AND THE NUMBER OF CASES OF ADVANCED AMD IS ESTIMATED TO INCREASE FROM 1.7 MILLION IN 2010 TO 3.8 MILLION IN 2050.4,7,9

AMD IS AN ACQUIRED DEGENERATIVE MACULAR DISEASE USUALLY AFFECTING INDIVIDUALS OVER THE AGE OF 55 YEARS. IT IS CHARACTERIZED BY PATHOLOGIC ALTERATIONS OF THE OUTER RETINA, RETINAL PIGMENT EPITHELIUM (RPE), BRUCH’S MEMBRANE AND CHORIOCAPILLARIS COMPLEX INCLUDING DRUSEN FORMATION AND PIGMENTARY CHANGES.1,3 AMD IS A PROGRESSIVE DISEASE, AND IN ADVANCED STAGES, CENTRAL GEOGRAPHY ATROPHY AND NEOVASCULARIZATION—EITHER CHOROIDAL OR SUBRETINAL—MAY DEVELOP AND REDUCE VISION.3

NEOVASCULAR AMD IS CAUSED BY PROLIFERATION OF NEW AND ABNORMAL BLOOD VESSELS, USUALLY ORIGINATING FROM THE CHORIOCAPILLARIS, THAT INVADE THE SUB-RPE AND/OR SUBRETINAL SPACE THROUGH A DISRUPTED BRUCH’S MEMBRANE.1,7,10 NEOVASCULAR MEMBRANES MAY BE EXUDATIVE OR NON-EXUDATIVE. THESE FRAGILE ABNORMAL VESSELS LACK A PROPER INNER BLOOD-RETINA BARRIER AND MAY LEAK OUT FLUID CONTAINING PROTEIN AND LIPIDS OR BLOOD.3,7,11 WHEN LEAKAGE OF FLUID OR BLOOD OCCURS AND A NEOVASCULAR COMPLEX IS FOUND, THE TERM EXUDATIVE NEOVASCULAR AMD IS MOST APPROPRIATE.

INTERESTINGLY, FEW CASES OF NON-NEOVASCULAR, YET EXUDATIVE, AMD HAVE BEEN REPORTED, WHERE INTRARETINAL FLUID WAS FOUND WITHOUT EVIDENCE OF NEOVASCULARIZATION OR RETINAL VASCULAR ABNORMALITIES TO ACCOUNT FOR SUCH. LIKE NEOVASCULAR EXUDATIVE AMD, NON-NEOVASCULAR EXUDATIVE AMD ALSO APPEARS RESPONSIVE TO ANTI-VEGF THERAPY.12

EARLY DETECTION OF EXUDATIVE AMD IS OF UTMOST IMPORTANCE SO THAT TREATMENT MAY BE INSTITUTED WITHOUT DELAY AND VISION CAN BE SAVED.
Step 1: Identify Eyes at High-risk

We know that not all patients with AMD will convert to the exudative and highly vision-threatening form of the disease. Therefore, it is important to be familiar with high-risk clinical features so that individuals at high-risk for conversion can be identified. Patients that exhibit these high-risk AMD phenotypes should be monitored in-office more frequently and educated on symptoms of conversion and provided with self-screening tools. Recommending dietary and lifestyle modifications, such as smoking cessation, as well as vitamin supplementation when appropriate, may also reduce the risk of exudative conversion.

Fundus findings that increase the risk for exudative conversion include large-sized drusen (especially soft subtype), as well as RPE clumping and pigment migration anteriorly into the retina (Figure 1A). Eyes with intermediate non-exudative AMD, or AREDS category 3, are at greater risk for conversion to advanced AMD, which occurs in approximately 18% of cases within five years, compared to those with early stage non-exudative AMD. \(^4,11\) Intermediate stage dry AMD is defined as the presence of either (1) extensive medium-sized drusen (63-124 µm in diameter), (2) at least one large sized druse (≥125 µm in diameter) or (3) non-central geographic atrophy. \(^4,13\) Among patients that already have neovascular AMD in the fellow eye, the risk for neovascularization in the eye with non-exudative AMD is very high, approximately 42% at five years. \(^7,14\)

There are certain drusen subtypes that pose a greater risk for future neovascularization including soft drusen and subretinal drusenoid deposits, also referred to as reticular pseudodrusen. With OCT, soft drusen appear as round, mound-shaped elevations of the RPE from Bruch’s membrane that are filled internally with drusenoid material that is homogenous (uniformly reflective) and relatively dark or hypo-reflective (Figure 1B). Subretinal drusenoid deposits are characterized on OCT as nodular, hyper-reflective deposits that rest on the anterior surface of the RPE. Research has shown that eyes with a combination of both soft drusen and subretinal drusenoid deposits are at highest risk for conversion to neovascular AMD. \(^15\) Although more research is needed, lower macular pigment optical density and impaired dark adaptation may also pose an increased risk for AMD progression. \(^10,17\)

The American Optometric Association Clinical Practice Guidelines advise that patients with soft confluent drusen and granular pigmented degeneration be monitored at four to six month intervals. \(^2\) Similarly, the American Academy of Ophthalmology Preferred Practice Patterns recommend that “patients at exceptionally high-risk (e.g., the presence of advanced AMD in one eye and large drusen with RPE changes in the fellow eye) may be examined more frequently (i.e., every six to 12 months) in an effort to detect asymptomatic CNV at a treatable stage.” \(^14\)

With the advent of OCT angiography (OCT-A) we now know that non-exudative neovascular membranes exist in eyes with AMD and is an entity that poses a greater risk for future exudative conversion. \(^18-20\) Nonvascular AMD and exudative AMD are not synonymous terms, and the presence of exudation is the main factor in determining whether anti-VEGF therapy is indicated.

A non-exudative neovascular membrane is characterized by the presence of a well-defined neovascular complex via OCT-A in a treatment naïve eye that has no signs of exudation via ophthalmoscopy, such as exudate or hemorrhage, and no fluid on structural OCT imaging. \(^18-20\) This vascular anomaly is present in approximately 10% of eyes with intermediate AMD are already exudative in the fellow eye. \(^18-20\)

Non-exudative neovascularization carries with it a substantial risk for conversion to the exudative form of the disease, and research suggests that the risk of conversion to exudative AMD in eyes with nonexudative choroidal neovascularization (CNV) is about 15 times greater than those without. \(^18-20\) Although most retina specialists are not treating non-exudative neovascular membranes, there may be value in referring to them, especially if the
membrane is identified in the better seeing eye of a monocular patient.4,18-20

Figure 2 depicts the left eye of an asymptomatic 68-year-old previously diagnosed with dry AMD bilaterally. Baseline exam revealed best-corrected acuity of 20/40 in the left eye. Color photography revealed macular pigmentary changes and noncentral geographic atrophy (Figure 2A). Structural OCT showed an irregular and shallow PED with medium internal hyperreflectivity and no fluid in the nasal fovea (Figure 2B). The 3mm OCT-A outer retina choriocapillaris en-face display revealed a well-defined sub-RPE neovascular membrane with adjacent choriocapillaris nonperfusion (Figure 2C). On the corresponding OCTA B-scan overlay, the PED appeared internally vascu-
larized and was red (Figure 2D). The patient was diagnosed with a non-exudative neovascular membrane in the left eye and told to follow-up in three months.

He returned six months later reporting stable vision. Acuity and ophthalmoscopy were unchanged; however, repeat structural OCT revealed new subretinal and intraretinal fluid overlying the PED (Figure 2E). Repeat OCTA showed that the neovascular membrane was slightly larger with a peripheral fringe of lacy capillaries morphologically suggestive of exudative activity (Figure 2F). The patient was referred to a retinal specialist and treated with anti-VEGF.

**Step 2: Recognize Symptoms of Exudative Conversion**

It is important to educate all patients with AMD, as well as your office staff, regarding symptoms of exudative conversion and the need for prompt examination, typically within 24 hours of onset, when they occur. Symptoms of dry-to-wet conversion tend to develop rather rapidly over the course of days to weeks and are more severe and unilateral in nature compared to those caused by progression of non-exudative AMD.1,3,7 They may include painless and new-onset metamorphopsia, loss or blurring of central vision, and sudden development of a new central scotoma (positive scotomas that a patient is aware of may be caused by hemorrhage).4,7,10 Micropsia may also occur in the setting of serous macular detachment.10

At home self-screening is strongly encouraged, and patients should be provided with an Amsler grid and near acuity chart, as well as educated on how to properly use these screening tools. Consider mobile applications and prescription devices for those at particularly high-risk for conversion, such as those with intermediate stage non-exudative AMD who still have useful vision in at least one eye.

Providing the patient with written information on symptoms suggestive of exudative conversion and educating
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the patient’s loved ones not may be of particular benefit since AMD affects the elderly who may also suffer from memory loss. Home self-screening tools do not replace the need for frequent in-office examinations, since patients may be asymptomatic at the time of exudative conversion. This is an ideal time to catch and treat exudation so that vision can be preserved.

**Step 3: Perform a Thorough Fundus Exam**

In those previously diagnosed with AMD or new patients complaining of central vision loss and/or metamorphopsia, dilated slit lamp biomicroscopy should be performed using a low powered noncontact pre-corneal lens, such as a 60D lens, that enhances stereopsis. Every attempt should be made to maximize stereopsis during biomicroscopy, especially when you don’t have access to OCT.

The central portion of the contact Goldmann 3-mirror is also of benefit in detecting subtle outer retinal thickening but should be performed after ancillary imaging tests are completed. It is very important to note that OCT does not replace the need for fundus examination since sub-RPE hemorrhages, suggestive of exudation and a need for treatment, are often invisible on OCT.

The fundus and OCT features of active wet AMD occur because of fluid or blood leakage. Fluid or blood commonly accumulate in the sub-RPE, subretinal and intraretinal spaces, but preretinal and vitreous hemorrhage are less common features of exudative AMD that have been reported. The clinical manifestations of neovascular and/or exudative AMD include the following:

**Hemorrhage.** As previously mentioned, hemorrhage from exudative AMD can occur at any depth location; it may be sub-RPE (resulting in a hemorrhagic PED), subretinal, intraretinal and less commonly preretinal or vitreous. Biomicroscopy and fundus photography are superior to OCT in the detection of hemorrhage, which is a relatively common manifestation of neovascular AMD that is suggestive of active exudation. Recall that the retina itself is translucent; therefore, a small, shallow subretinal hemorrhage will appear brightly red on fundus exam (Figures 6 and 7). On the other hand, a large collection of subretinal blood will be darker red. Subretinal hemorrhages are redder and brighter compared to the dark green sub-RPE hemorrhages, which are masked by RPE pigment. Visualizing unobscured retinal blood vessels anterior to the hemorrhage can help differentiate subretinal hemorrhages from nerve fiber layer and preretinal ones.

**Pigment epithelial detachment (PED).** This is defined as a separation of the RPE from Bruch’s membrane and is a common finding in both dry and wet AMD forms. There are various types of PEDs: fibrovascular, hemorrhagic, serous and drusenoid. Use of multimodal imaging—OCT, OCT-A, fluorescein angiography (IVFA) and indocyanine green angiography (ICG)—is beneficial and sometimes necessary to differentiate various types of PED.
Drusenoid PEDs are associated with intermediate stage dry AMD and formed by coalesced soft drusen, while hemorrhagic and fibrovascular PEDs are always associated with exudative and/or neovascular AMD. Clinically drusenoid PEDs appear as yellow-white areas of RPE elevation with possibly scalloped borders and intralesional spots of hyperpigmentation (Figure 1A). Fibrovascular PEDs result from a type 1 neovascularization complex that proliferates between Bruch’s membrane and the RPE. Clinically, they manifest as a mostly opaque area of RPE elevation often with an irregular surface contour that may contain a mix of blood, fibrotic tissue and fluid (Figure 3).1,11

Hemorrhagic PEDs appear as round or oval-shaped dark-green colored elevations of the RPE with discrete borders.1,3

Serous PEDs result from serous fluid accumulation between the RPE and Bruch’s membrane. Clinically they appear as well-demarcated, dome-shaped, yellowish-orange elevations of the RPE (Figure 4).3 While serous PEDs may be a manifestation of non-exudative AMD due to compromise of the outer blood-retinal barrier, they are more often a manifestation of exudative AMD and should greatly raise suspicion for the presence of neovascularization until proven otherwise.1,21 When a serous PED is found, multimodal imaging, often including IVFA and ICG, must be performed to look for a treatable neovascular source.11

Grey-green subretinal/sub-RPE thickening. Occasionally, and especially in cases of subretinal (type 2) neovascularization, the neovascular complex itself may be visualized with biomicroscopy as a grey-green or pinkish-yellow plaque-like membrane (Figure 5A).1,7,10 When a neovascular complex is exudative, which is often the case, the area of grey-green thickening may be surrounded by hemorrhage, exudate and/or fluid (Figure 6).10

Exudate. Fluid that leaks out from incompetent neovascular vessels contains high density lipoproteins, which may deposit and become trapped within the retina (intraretinal exudate) or under the retina (subretinal exudate).1,10 Exudate alone, without fluid, does not indicate that a neovascular membrane is currently exudative and requires treatment. The amount of exudate may actually increase with successful anti-VEGF therapy and will likely remain for a lifetime. Clinically, it can be difficult to differentiate drusen from exudate since both tend to be yellow-white in coloration. Drusen are located deeper in the retina while exudate exuded from leaky neovascularization is often more superficial and located intraretinally or subretinally.1 Drusen also tend to be more diffusely distributed throughout the macula and posterior pole, while exudate tends to be more localized within clusters.22 When in doubt, OCT can be very valuable in depth localizing an unknown yellow-white lesion.

Fibrovascular disciform scar and RPE tear. Subretinal/sub-RPE fibrosis and scarring as well as an RPE tear are also manifestations of exudative AMD found in later stages of the disease.3,11

Step 4: Use Multimodal Imaging
Incorporating techniques such as color fundus photography, fundus autofluorescence (FAF), OCT, OCT and IVFA/ICG (when appropriate and within scope) can greatly benefit your evaluation of eyes with AMD.

OCT. This is generally considered standard of care in the evaluation of AMD and can greatly facilitate the clinician’s ability to detect the earliest neovascular and exudative AMD possible, refer for prompt treatment and prevent future vision loss. It is also of great value in monitoring for exudative recurrence and serves as guide during anti-VEGF therapy. The sensitivity for neovascularization detection with structural OCT alone is excellent and is even better when used in combination with OCT-A.4,23 It is important when reviewing OCT data to scan through the entire cube, looking for fluid and RPE elevation, rather than just one central raster B-scan. Before detailing structural OCT features suggestive of exudation, understand the OCT classification system of choroidal CNV that divides into various subtypes depending upon the anatomic location of the membrane itself.
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IF YOU SEE OR SUSPECT DIABETIC RETINOPATHY

EDUCATE PATIENTS
- Your early and frequent discussions about progression of disease, timely referral, and potential treatment options can empower patients

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

IMPORTANT SAFETY INFORMATION

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

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

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

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

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

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

BRIEF SUMMARY—Please see the EYLEA full prescribing information available on HCPEYELEY.US for additional product information.

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

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

2 CONTRAINDICATIONS

3 DOSAGE AND ADMINISTRATION

4 WARNINGS AND PRECAUTIONS

5 ADVERSE REACTIONS

6 ADVERSE REACTIONS

7 USE IN SPECIFIC POPULATIONS

8 LACTATION

9 PATIENT CONSENT

10 FUNCTIONAL STATUS

11 PRECAUTIONS

12 PATIENT CONSENT

13 FUNCTIONAL STATUS

14 PRECAUTIONS

15 PATIENT CONSENT

16 FUNCTIONAL STATUS

17 PRECAUTIONS

5.1 Endophthalmitis and Retinal Detachments

5.2 Increase in Intraocular Pressure

5.3 Thromboembolic Events

5.4 Ocular or Periocular Infections

5.5 Hypersensitivity

5.6 Retinal Edema

5.7 Other Ocular and Systemic Adverse Reactions

6 CLINICAL TRIALS EXPERIENCE

7 SAFETY INFORMATION

8.1 Pregnancy

8.2 Lactation

8.3 Females and Males of Reproductive Potential

8.4 Pediatric Use

9.1 Pregnancy

9.2 Lactation

9.3 Female or Male Reproductive Potential

9.4 Pediatric Use

10.1 General Use

10.2 Use in Specific Populations

10.3 Use in Special Populations

11.1 Description

11.2 Safety

11.3 Tolerability

11.4 Use in Clinical Studies

11.5 Use in Patients with Known Risk of Vascular Endothelial Growth Factor Inhibitor-Related Adverse Reactions

12.1 General Use

12.2 Use in Specific Populations

12.3 Use in Special Populations

13.1 Description

13.2 Safety

13.3 Tolerability

13.4 Use in Clinical Studies

13.5 Use in Patients with Known Risk of Vascular Endothelial Growth Factor Inhibitor-Related Adverse Reactions

14.1 General Use

14.2 Use in Specific Populations

14.3 Use in Special Populations

15.1 Description

15.2 Safety

15.3 Tolerability

15.4 Use in Clinical Studies

15.5 Use in Patients with Known Risk of Vascular Endothelial Growth Factor Inhibitor-Related Adverse Reactions

16.1 Description

16.2 Safety

16.3 Tolerability

16.4 Use in Clinical Studies

16.5 Use in Patients with Known Risk of Vascular Endothelial Growth Factor Inhibitor-Related Adverse Reactions

17.1 Patient Counseling Information

17.2 In PHP A/EYELEA® (aflibercept) Injection full prescribing information.
**Type 1 (occult).** This type of CNV membrane is in the sub-RPE space between Bruch’s membrane and the RPE and is the most common type of CNV present in neovascular AMD, found in 80% of cases. They are often consistent with occult leakage patterns (late leakage of an undetermined source) on conventional IVFA. Via structural OCT, type 1 CNV manifests as a fibrovascular PED (Figures 2E and 3). On OCT-A they appear as an ill-defined network of vessels and are usually larger membranes with mature feeder vessels (Figure 2F). Type 1 CNV membranes are often mature, poorly respond to anti-VEGF therapy and have a worse visual prognosis compared to type 2 CNV.4,10

**Type 2 (classic).** This type of CNV is characterized by proliferation of neovascular tissue above the RPE, in the subretinal space. Type 2 membranes are consistent with classic leakage patterns of well-demarcated hyperfluorescence on conventional IVFA. Using structural OCT, type 2 neovascularization is often characterized by a subretinal hyporeflective mass resting on top of the RPE and frequently has overlying intraretinal fluid (Figure 6). These membranes are usually well-defined complexes with OCT-A.

**Mixed Type 1 and 2.** CNV membranes may be partially located beneath the RPE and in the subretinal space. Mixed types are sometimes subclassified as predominantly classic (Figure 7). They can also be minimally classic when the subretinal component is either greater or less than 50% of the total lesion area.4,10

**Figure 7** depicts the right eye of a 73-year-old who was being monitored closely for intermediate dry AMD in both eyes prior to the COVID-19 pandemic. During the pandemic, she cancelled two appointments. Fifteen months after her last exam, she presented as a walk-in complaining of decreased vision in her right eye for at least six months. Her Snellen distance acuity in the right eye had declined from 20/20 to 20/100.

**HOME MONITORING FOR AMD**

As mentioned in step 1, there are mobile applications and prescription devices for patients at particularly high-risk for conversion. Recent and exciting advances in home monitoring systems using preferential hyperacuity perimetry (PHP) and OCT technology allow for earlier detection of new CNV or worsening of pre-existing CNV, thus leading to earlier treatment, better visual outcomes and improved cost-effectiveness.1,4 Home monitoring devices have the potential to detect new CNV membranes when they are smaller in size, compared to conventional periodic follow-up visits and patient-reported changes with Amsler grid monitoring.1 CNV is traditionally diagnosed during a scheduled follow-up visit or patient-directed visit due to new onset of visual symptoms. However, in the majority of these cases, patients present to the clinic after losing a substantial amount of vision as opposed to when minimal change in acuity has occurred.1 Home telemonitoring systems, in addition to periodic visits, can help bridge this gap by providing cost-effective increased access to quality eye care to patients with AMD.1 Furthermore, home monitoring systems may be the most efficient and effective way to closely monitor patients with or at high-risk for exudative conversion in the era of COVID-19 related cancellations of non-emergency office visits.1

The ForeseeHome AMD Monitoring System (Notal Vision) is an FDA-cleared home telemonitoring device that uses PHP and is intended to augment, not replace, in-office eye exams. The device is only available by physician order and is installed temporarily in the patient’s home. Eligible patients must have been diagnosed with at least intermediate stage nonexudative AMD and have best corrected acuity of 20/60 or better in at least one eye. During the test, the patient uses a mouse to click where a wave or bump appears along a dotted line and each test takes two to three minutes. The test results are compared to a normative database and the patient’s own personal baseline. If a significant change is detected, the clinician is alerted so that the patient can be scheduled for prompt in-office examination.

The AREDS2 HOME (Home Monitoring of the Eye) study showed that functional vision of 20/40 or better at conversion was maintained in 94% of patients using ForeseeHome compared to 62% without.6 More recently, real-world data analysis showed that 81% of patients with intermediate stage nonexudative AMD using the device maintained acuity of 20/40 or better at the time of exudative conversion.6 This is a much greater percentage than what real-world data from the IRIS registry found among patients not using the device.6,8 The IRIS registry data analysis showed that only 34% of patients had acuity of 20/40 or better when first diagnosed with exudative AMD.6,8

The newer Notal Home OCT device allows patients to complete OCT testing independently within their homes. It incorporates artificial intelligence machine learning software that performs automated analysis of the scans taken. The device received breakthrough device designation by FDA and was found to be more accurate in diagnosing subtle intra and subretinal fluid with a sensitivity of 82.2% than that of retina specialists’ at 46.8% but with slightly lower specificity of 86.5% when compared to retina specialists at 97%.1 The Notal Home OCT is user-friendly and able to obtain reliable scans. A study completed on version 2.5 prototype of Notal OCT device showed 91% of 301 participants were successfully able to operate the device, and in 88% of 531 eyes analyzable images were obtained.1,5

Fundus examination revealed central gray-green subretinal thickening with surrounding subretinal hemorrhage and minor exudate superiorly (Figure 7A). Her structural OCTs showed a mostly serous multi-lobed PED (white arrows) that became shallower inferiorly with overlying hyperreflective subretinal mass (subretinal neovascular membrane, yellow asterisk) and significant intraretinal cystic edema (Figure 7B). There was also some subretinal fluid (red arrows).

The 6mm OCT-A outer retina choriocapillaris enface display revealed a mature neovascular complex with large feeder vessels (Figure 7C). OCT-A B-scan overlay shows that the large feeder vessels are in the subretinal space above the PED (Figure 7D). Inferiorly, the subretinal mass is red and highly vascularized, suggestive of a subretinal neovascular membrane (Figure 7D).

**Type 3 (retinal angiomatous proliferation).** This is characterized by deep intraretinal neovascularization that often anastomoses with a sub-RPE neovascular membrane. Other structural OCT features suggestive of neovascular and/or exudative AMD include:

**Fluid.** Fluid at any level on OCT, including intraretinal (Figure 6), subretinal (Figure 2E and 3), and subRPE (serous PED, Figure 4) is suggestive of active exudative AMD. With OCT, fluid is hyporeflective or dark, and this imaging is superior to ophthalmoscopy in the detection of fluid.

**Hemorrhage.** A hemorrhage must be quite large to be visualized with OCT. Because blood is pigmented, it is hyperreflective and may block light transmission posterior to it (produce a posterior shadowing artifact). Ophthalmoscopy and color photography are superior to OCT in detection.

**Exudate.** Exudate may be intraretinal or subretinal. The exudative material itself is hyperreflective and is often associated with posterior shadowing. Anterior RPE pigment migration, a high-risk nonexudative AMD phenotype, may appear similarly on OCT imaging; thus, comparing OCT and photography is sometimes needed to determine whether intraretinal hyperreflective foci represent exudation or pigment migration.

**Pigment epithelial detachment (PED).** As mentioned previously, there are various types of PED and differentiating them with multimodal imaging is critical to determine whether or not the clinician should suspect exudation/neovascularization and refer out.11 Enhanced-depth imaging or swept-source OCT can be of value in differentiating different PED types since they improve posterior image resolution.11 Drusenoid PEDs are associated with non-exudative AMD and appear as round elevations of the RPE, filled with homogeneous and uniformly mildly hyperreflective drusenoid material (Figure 1B). Purely drusenoid PEDs should not be associated with intraretinal or subretinal fluid.

In contrast, fibrovascular PEDs that contain type 1 neovascularization exhibit variable (non-homogenous or non-uniform) internal reflectivity, which may include horizontally oriented multilaminate hyper-reflective sheets due to the lateral proliferation of new blood vessels (Figure 3).10,11 The elevation of the RPE is also often irregular in contour or the PED is multilobulated.10

Hemorrhagic and fibrovascular PEDs are always associated with exudative and/or neovascular AMD.

Serous PEDs exhibit a smooth, dome-shaped elevation of the RPE and are internally dark or optically empty since they are filled with clear fluid (Figure 4).10 Bruch’s membrane is often visible at the base of the PED as a thin hyperreflective line.10 While serous PEDs may be a manifestation of dry AMD, they are more often a manifestation of wet AMD and should be evaluated with fluorescein angiography and indocyanine green angiography to look for a treatable neovascular source.11,21

**OCT-A.** This instrument allows the clinician to directly visualize the choroidal neovascular membranes themselves, not just the secondary effects such as fluid identified with structural OCT.22-27 Performing OCT-A provides high-resolution, detailed images of CNV complexes, allowing the clinician to assess their shapes and morphologic patterns.1,28 In fact, the sensitivity and specificity for CNV detection using a combination of cross-sectional and en-face OCT-A imaging analysis approaches that of IVFA.21 OCT-A is also the only modality that can directly image high-risk nonexudative neovascular membrane. Therefore, OCT-A should be performed periodically in eyes clinically graded as having intermediate stage non-exudative AMD to look for early neovascularization.

The outer retina or outer retina choriocapillaris preset en-face display was
specifically designed to aid in detection of CNV (Figures 2C, 2F, 5C and 7C). The segmentation boundaries vary depending upon the OCT brand, but typically include some combination of photoreceptors, RPE and choriocapillaris (Figure 5D). OCT-A can also be of great value in differentiating vascularized (Figure 2) from non-vascularized PEDs (Figure 1).11

Fluorescein angiography and indocyanine green angiography. Although invasive, fluorescein angiography can add value in detecting and classifying neovascular membranes as well as determining the degree of exudative activity.1 Indocyanine green angiography is of particular use in imaging the choroidal vasculature and is important in the diagnosis of polypoidal choroidal vasculopathy, which is considered a subtype of AMD.4

Step 5: Refer for Treatment
Intravitreal anti-VEGF is the standard first-line therapy for treating wet AMD, and early detection and prompt treatment results in better visual outcomes.4 Immediately refer to a retina specialist, if available, or an ophthalmologist experienced in retinal disease whenever a diagnosis of new onset exudative AMD is made or highly suspected.1,4 The consultative exam should be scheduled within a few days and no longer than one week from the diagnosis.

Step 6: Prepare for the Long Haul
Patients who have undergone anti-VEGF therapy and are either no longer receiving injections or receiving injections on an as-needed or treat-and-extend protocol may still suffer a relapse that requires prompt treatment or an injection sooner than was originally planned. Patients with worsening symptoms should be promptly examined and if new or worsening exudative fundus or imaging features such as hemorrhage or fluid are found, the managing ophthalmologist or retinal specialist should be informed.

Prompt treatment of wet AMD is associated with better long-term visual outcomes, and many cases of severe loss can actually be prevented through early detection and referral.1,4 Recognizing fundus findings suggestive of exudation, such as hemorrhage and exude, and using imaging technologies, especially OCT, will allow earlier detection of exudation in hopes that your patients’ vision can be saved.■

Genetic Testing in Retina: Practical Applications

Consider offering this option to your patients and aid them in taking the next steps of management.

With the ongoing growth in scientific knowledge about the genetic causes of ocular disease and the current developments in gene therapy, it is becoming increasingly important for optometrists to be up-to-date on the latest developments in genetic testing and genomics research.

Genetic testing can be beneficial for patients with an inherited retinal disease (IRD) to obtain a more accurate genetic diagnosis, provide a more precise prognosis and facilitate gene-specific treatment and management options. For instance, a confirmation of pathogenic RPE65 gene mutations is necessary for patients with retinitis pigmentosa (RP) or Leber’s congenital amaurosis to be eligible for Luxturna (Spark Therapeutics) gene therapy. There are dozens of ongoing interventional clinical trials, including gene therapy, gene editing and antisense oligonucleotide-based therapy, which require confirmation of a genetic diagnosis. Patients and family members can also benefit from genetic counseling and appropriate referrals for beneficial resources, such as support groups and low vision rehabilitation.

Genetic Testing

The process of complete genetic testing is much more involved than simply obtaining a saliva sample and shipping it to a lab. Unlike a COVID test, which provides a straightforward positive or negative result, there are more factors that play a role in inherited retinal diseases.

The American Academy of Ophthalmology’s (AAO) Task Force on Genetic Testing published Recommendations for Genetic Testing of Inherited Eye Diseases in 2014. The document recommends provider-ordered testing through a Clinical Laboratory Improvement Amendments (CLIA)-certified laboratory for conditions for which the causative gene(s) have been identified. Direct-to-consumer testing should be avoided. Furthermore, the document outlines five parts of genetic testing: “(1) the clinical determination that a genetic eye disease is likely to be present, (2) the molecular investigation of genomic DNA samples […] (3) the analysis of the resulting molecular data in the context of relevant published literature and public databases using appropriate statistical methods, (4) the interpretation of the data in the context of the clinical findings and (5) the counseling of the patient about the interpreted findings and their implications.”

If considering implementing genetic testing within a clinical practice, optometrists should have a plan to address all five components.

Part 1: Clinical Exam. The initial examination is of course necessary to identify a tentative diagnosis or several
differential diagnoses. Depending on the eye condition, the examination may include additional testing such as imaging, visual fields and electroretinography. The AAO’s Recommendations on Clinical Assessment of Patients with Inherited Retinal Degenerations provides a good outline of clinical testing for IRDs.²

It is important to use clinical examination and differential diagnoses to select an appropriate genetic test panel. The panel should include genes known to be associated with the differential diagnoses. For instance, a patient suspected to have X-linked RP should be tested with a panel that includes the many genes known to be associated with RP. In particular, the panel should be checked to include the RPGR gene, which accounts for a majority of X-linked RP cases.

However, testing more genes is not always better. In fact, it is recommended to order an inherited retinal dystrophy panel rather than whole-exome sequencing for a patient with clinical signs of an inherited retinal dystrophy. Ordering an appropriate panel increases the chances of a clinically useful result while limiting the possibility of unrelated secondary findings.

Parts 2 and 3: sample collection and laboratory analysis. There are many different laboratories and test panels to select from. One important recommendation is to work with a CLIA-certified laboratory. Two examples of commonly used test panels include the Blueprint Genetics Retinal Dystrophy Panel and the Invitae Inherited Retinal Disorders Panel. Both encompass 330+ genes associated with inherited retinal disorders. In addition to out-of-pocket and insurance billing options, these panels are currently supported by sponsored no-charge testing programs.

Specialized equipment for genetic testing in-office is minimal. Clinicians can request specimen collection kits directly from the testing laboratories. Saliva and buccal swab samples are the most commonly obtained in optometric practice. Saliva samples require the patient to spit in a tube and buccal samples typically require multiple cheek swabs. Patients should not eat, drink or chew gum prior to saliva sample collection.

Laboratory testing may take two to four weeks. The ordering practitioner and patient may be able to access the results through the respective laboratory’s online portal.

Part 4: genetic report interpretation in the context of clinical findings. Upon receiving the genetic test report, it is important to interpret the results within the context of the patient’s clinical findings, including ocular signs, medical history and family history.

A positive result indicates that a pathogenic variant or mutation was found in one of the genes tested. It is important to confirm if the identified whole blood, buccal swab and saliva sample collection tubes.

Family pedigree of three brothers diagnosed with choroideremia confirmed with genetic testing. Applying the X-linked recessive inheritance pattern indicates that a daughter of one patient is a carrier for choroideremia; her two young sons each have a 50% probability of having inherited choroideremia.
pathogenic variant(s) correlate with the clinical diagnosis or if they are secondary findings unrelated to the condition in question. Keep in mind that a pathogenic variant must be present on both alleles of a gene to cause an autosomal recessive condition, whereas only one pathogenic variant must be present to cause an autosomal dominant condition.

A negative result merely indicates that no pathogenic mutations were found in the tested genes. Since genetic test panels are constantly growing and improving, retesting in the future may be indicated. Likewise, a patient with a negative result obtained several years ago with a limited test panel may benefit from updated testing.

Genetic test results may also indicate several variants of uncertain significance. These are periodically reclassified as we gain more knowledge about variants. Therefore, genetic test reports are not “static” and may be updated over time. The practitioner may need to counsel the patient as changes are made and reports are updated.

A family pedigree can be useful to confirm the inheritance pattern if needed. Likewise, if genetic testing confirms diagnosis of a condition with a known inheritance pattern, the pedigree may be useful for identifying at-risk relatives. Familial variant testing may be indicated and can be ordered after a variant of interest has been identified in the affected family member.

**Part 5: patient counseling.** It is important to allot sufficient chair time to discuss results and further management with the patient. This can include discussion of eligibility for FDA-approved gene therapy (currently only available for RPE65-associated retinal dystrophy), interventional clinical trials (gene therapy, gene editing, antisense oligonucleotide-based therapy, etc.) and natural history studies. The database clinicaltrials.gov is a great resource to search for current trials.

Inform patients about joining a research database such as the Foundation Fighting Blindness My Retina Tracker Registry to be updated on relevant research studies.

In addition to the patient education provided in-office, it is important to provide patients and family members access to counseling with a certified genetic counselor. No-cost genetic counseling may be available when using select sponsored panels.

**Counseling and Management**

Genetic testing by itself may not adequately represent the entire clinical picture for any individual patient. Some conditions have large genotypic and phenotypic heterogeneity. As such, patients may have a similar phenotype or clinical presentation, but have different affected genes. For instance, there are over 60 different genes known to be associated with non-syndromic RP. On the other hand, some patients may have identical mutations on the same affected gene but have very different clinical presentations, even within the same family.

Furthermore, while the diagnosis and prognosis of some monogenic conditions can be easily predicted by one gene, other conditions are more complex and may be affected by a combination of multiple genes and/or environmental factors.

Therefore, prognosis and management should be individualized, taking into account both genetics and clinical findings. Once a patient’s specific pathogenic mutation(s) have been identified, literature searches of recent research can be used to provide the most up-to-date management recommendations. For instance, lifestyle modifications such as smoking cessation are recommended for certain conditions.

Patients identified with syndromic conditions may benefit greatly from increased screening, monitoring and medical management of the known systemic risks associated with their condition. For instance, a child diagnosed with Joubert syndrome
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would benefit from being monitored for kidney disease and a patient diagnosed with Stargardt’s disease may be advised to avoid vitamin A supplementation.

Confirmation of a progressive vs. nonprogressive condition and the projected impact on vision can be crucial for counseling the patient and family on prognosis and future management. This can help direct planning for appropriate low vision aids and assistive technology.

Regardless of the diagnosis, remind patients that annual eye exams are still important to monitor eye health. Even if there is no currently available FDA-approved treatment for the genetic cause of a patient’s particular eye condition, there may be a clinical trial in the near future. Regularly scheduled exams also allow patients to be updated on new and upcoming advances in treatments and low vision aids.

Patients with vision loss may greatly benefit from low vision services to maintain independence and be prescribed devices for school, work and activities of daily living. For example, a patient with RPGR X-linked RP would benefit from eye exams and referrals to monitor for cataracts, find out about the latest in assistive technology and receive information on the several ongoing RPGR clinical trials.

**Implementing Testing in Practice**

Genetic testing for IRDs can be implemented in optometric practice with relatively little equipment. Regardless, management of rare dystrophies can still be daunting in a practice that does not regularly see this patient population. It is advised to keep in mind the extensive amount of counseling and chair time needed to provide comprehensive care for patients with IRDs.

Thankfully, there are a growing number of patient and doctor resources such as the Foundation Fighting Blindness Open Access Genetic Testing Program (www.fightingblindness.org/open-access-genetic-testing-program) and the Spark Therapeutics ID Your IRD Gene Testing Initiative (www.invitae.com/en/idyourird). Currently, these programs cover the cost of genetic testing lab fees and provide free genetic counseling for qualified patients with inherited retinal dystrophies. Foundation Fighting Blindness offers genetic counseling through InformedDNA, and ID Your IRD offers genetic counseling through Invitae. Without these programs, the cost of testing can be a significant barrier for patients.

If offering genetic testing through a sponsored program, optometrists must check that the patient meets the program’s eligibility criteria. Optometrists can bill for exam fees and any associated testing but cannot charge for the sponsored lab testing.

Optometrists should consider the scope of practice and any relevant laws governing lab testing and genetic testing within their state. Also, educate staff members on genetic testing policies as well as privacy and confidentiality concerns with regards to genetic information.

**Patient Preparation**

Informed consent and patient education are important parts of genetic testing. It is important to ask patients their goals for genetic testing and to discuss reasonable expectations.

For example, if a patient diagnosed with cone dystrophy is interested in genetic testing because they heard about a gene therapy “cure for blindness,” it would be important to discuss that there is no current cure for cone dystrophy. However, genetic testing is indicated to help the patient learn more about the genetic cause of their cone dystrophy and may qualify them for future clinical trials.

Patients should be informed that genetic testing may not provide a definitive answer; the genetic test result is only one component of the clinical picture. Even with

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Fundus autofluorescence imaging of a child with achromatopsia confirmed with genetic testing. The diagnosis helped provide the family with assurance of likely stable vision and appropriate recommendations for school, including prescribed low vision aids and discontinuation of Braille training. Genetic test results were also used to refer the patient for an achromatopsia gene therapy clinical trial.
A genus of herbaceous flowering plants

Many flowers have 4 or 5 petals and 4 or 5 stamens or stigmas. The term "flower" is used to describe any plant part that bears reproductive parts. Flowers can be classified based on their structure and function. For example, some flowers have both male and female parts, while others have only one type of reproductive structure. These reproductive structures are typically arranged in a way that promotes pollination and fertilization. Understanding the structure and function of flowers can help us appreciate the beauty and diversity of plant life.

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our current test panels, a causative mutation may be identified in 60% to 80% of patients with inherited retinal dystrophies. Depending on the eye condition, there can be a significant possibility that the test may not yield a positive result. For instance, approximately only three-quarters of cases of Leber’s congenital amaurosis can be attributed to causative mutations. Nonetheless, genetic testing for these patients is highly recommended for the possibility of being positive for RPE65 gene mutations and qualifying for gene therapy. On the other hand, the known genes associated with achromatopsia account for almost all cases. Therefore, a patient with achromatopsia tested with a comprehensive panel is almost certain to receive a positive test result.

Patients with a family history of IRD but without any signs or symptoms may inquire about genetic testing. In this case, it is more effective to first test the affected family member to identify the causative mutation(s) before testing unaffected individuals who are interested in carrier status.

Testing is indicated when the possible benefits outweigh the potential cons. Inform patients about the possible implications of genetic test results for the patient and family members. Special considerations need to be taken into account when testing children and minors. For instance, clinicians and parents may need to weigh delaying testing to respect a minor patient’s autonomy against the potential benefits of earlier testing for particular adult onset conditions.

Patients should be made aware of the increased possibility of secondary findings when running broader genetic tests. Patients may also need to be informed about the implications of genetic testing on insurance, as genetic discrimination protections vary by state. Various publications, such as the American Medical Association’s Code of Medical Ethics, can serve as an ethics guidance resource for clinicians.

Validity and Utility of IRD Testing

There are three considerations to note when assessing the accuracy and value of genetic testing: analytical validity, clinical validity and clinical utility.

**Analytical validity** is how well a test can accurately detect the presence of the genetic variants. It is recommended to use CLIA-certified labs to ensure analytical validity. Additionally, confirming that the panel selected includes the genes known to be associated with the differential diagnoses will help ensure an appropriate genetic test.

**Clinical validity** refers to how accurately the genetic variant predicts presence, absence or risk of the ocular condition. Clinical validity can vary depending on the condition in question. Some genes are associated with multiple different inherited retinal conditions; therefore, diagnosis will rely heavily on other clinical testing. Some conditions exhibit variable expressivity or reduced penetrance, meaning some patients with the pathogenic mutation may present with a much milder presentation compared to other patients with the same mutation, or without any signs or symptoms at all.

**Clinical utility** refers to whether the test provides meaningful clinical impact to patient management. As we learn more about the genetic basis of inherited retinal dystrophies and as we develop more treatments, the clinical utility of genetic testing will only continue to grow.

**Key Takeaways**

Optometrists play an important role in educating patients with IRDs about the possibilities of genetic testing, ongoing clinical trials and the development of future treatments. Either conducting genetic testing in-office or referring patients for testing, optometrists can use genetic information to provide valuable insight for diagnosis and prognosis for patients with IRDs.

Genetic test results when combined with clinical examination findings and genetic counseling can help patients understand inheritance risks and inform important treatment decisions. Identifying a patient’s pathogenic variants is crucial for determining eligibility for gene therapy and genotype specific clinical trials.

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www.vistatrialhcp.com
Based on the 2022 National Diabetes Statistics report from the CDC, 37 million people in the United States have diabetes mellitus (DM). This number is expected to increase to 55 million by 2030. Diabetes is the leading cause of lower-limb amputations and kidney failure. It is also the leading cause of blindness in working-age adults. Additionally, 11.7% of US adults with diabetes had vision disability, including blindness, in a survey conducted in 2018. Nearly half of patients with diabetes will have diabetic retinopathy (DR) by 2030.1,2

As first-line primary eyecare providers, optometrists play an important role in recognizing DR earlier on, educating patients on the risk factors for diabetes and DR, evaluating the staging of DR and deciding how often to follow-up with patients, as well as when to refer to a retinal specialist.

This article will provide an overview of diabetes, explain the pathophysiology/staging of DR and offer advice regarding what ODs should know, say and do at each stage of the disease.

Types of Diabetes
There are three major types of diabetes: type 1, type 2 and gestational, and it is important that ODs have a clear picture of each.3

Type 1 DM. This is typically, but not always, diagnosed before the age of 30 and was formerly known as juvenile-onset or insulin-dependent diabetes. This type of diabetes accounts for 5% to 10% of the DM population. The mechanism of type 1 DM is the destruction of pancreatic beta-cells (autoimmune reaction) to the degree that ultimately no endogenous insulin is produced.

Type 2 DM. This is the major diabetes type in the US population (90% to 95%). It is typically, but not always, adult-onset, might be without symptoms and usually is characterized by slow progression. Its mechanisms include reduced pancreatic beta-cell insulin secretion, overlaid on top of insulin resistance. Insulin-sensitive tissues become unable to respond to insulin appropriately.4

Gestational DM. This very common subtype of diabetes occurs in 2% to 10% of pregnancies, per the CDC. Gestational diabetes typically resolves by itself after delivery, but both the mother and baby have a higher chance of developing type 2 diabetes in the future (up to 50% maternal risk).

Prediabetes. Based on a CDC report, there are 96 million people in the United States (around 30% of the country’s population) with prediabetes. This is defined as glucose levels higher than normal but not high enough to reach the numeric threshold for diagnosis of diabetes. The pathology includes insulin resistance or beta-cell failure.
to compensate, just as in type 2 diabetes. These patients may have impaired glucose tolerance, impaired fasting glucose or glycated hemoglobin (A1c) levels above normal (5.7% to 6.4%). Fortunately, prediabetes often can be reversed or its progression to type 2 DM slowed by lifestyle modification. ODs should encourage patients to work with their primary care providers (PCP) in order to prevent the possible progression of prediabetes into type 2 diabetes.

Risk Factors For DM/DR
Both DM and DR have the same risk factors, including family history of diabetes/DR, hypertension, cardiovascular disease, abnormal blood lipid level, prediabetes, gestational diabetes, obesity, longer DM duration, older age (>45), smoking, physical inactivity and race.

Nearly 100% of type 1 and 60% of type 2 diabetes patients will develop DR. Controlling for risk factors is one of the most important ways to reduce the incidence of diabetes complications. For example, the risk of DM microvascular complications is reduced by 40% for every 1% absolute decrease in A1c level. At the same time, the risk of diabetes-related microvascular complications is reduced by 12% for every 10mm Hg reduction in systolic blood pressure in hypertensive patients. Early detection of diabetes and appropriate treatment can reduce the risk of DR.

Pathophysiological DR Findings
The early physiological change in retinal vessels in DR—reduced retinal blood flow—starts from endothelial vasodilator dysfunction in retinal arterioles. The detailed mechanism is an impairment of the vasodilator, nitric oxide and overexpression of the vasoconstrictor. This decreased retinal blood flow leads to retinal tissue ischemia and, ultimately, to vessel leakage.

The pathological changes in the retinal vessels in DR include basement membrane thickening, pericyte loss and epithelial tight junction loss. The last pathological change is the loss of endothelial cells coupled with capillary closure.

The pathological pathways of DR include both inflammatory and angiogenic processes, with both neuronal and vascular injury/dysfunction. The molecular pathways of DR include oxidative stress, with activation of the sorbitol pathway, renin-angiotensin system, diacylglycerol-protein kinase C pathway and advanced glycation endproduct pathway, as well as raised vascular endothelial growth factor (VEGF) levels.

Chronic hyperglycemia and hypertension induce oxidative injury, then microthrombi formation followed by cell adhesion molecule activation/leukostasis and additional cytokine activation in a vicious

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Estimated Time to Complete Activity: two hours

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

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

• Explain the pathophysiology and staging of diabetes.
• Determine their role in the management of these patients at each stage.
• Comanage diabetic retinopathy patients effectively.
• Communicate with patients about diabetes and diabetic retinopathy.

Target Audience: This activity is intended for optometrists engaged in managing patients with diabetes.

Accreditation Statement: In support of improving patient care, this activity has been planned and implemented by PIM and the Review Education Group. PIM is jointly accredited by the Accreditation Council for Continuing Medical Education, the Accreditation Council for Pharmacy Education and the American Nurses Credentialing Center to provide CE for the healthcare team. PIM is accredited by COPE to provide CE to optometrists.

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cycle. All of these pathways/mechanisms induce further retinal damage. The detailed pathway can be found in the included table.

Prevalence of DR
In the United States, 40% of diabetes patients (age ≥40) have some degree of DR, whereas 8% have vision-threatening DR. The American Academy of Ophthalmology’s 2016 preferred practice patterns for DR state that about 60% of type 1 diabetes patients will develop any stage of DR within 10 years, whereas 53% to 84% of type 2 diabetes patients will develop DR within 19 years. Approximately 20% of type 1 diabetes patients and 14% to 25% of type 2 diabetes patients will develop diabetic macular edema (DME) after 10 years. The most common cause of vision loss in diabetes is DME.

Stages of DR
To effectively care for their patients, optometrists need a clear understanding of the stages of DR. However, grading systems vary slightly depending on the source. For example, the International Council of Ophthalmology (ICO) published guidelines for diabetic eye care in 2017 and defined mild nonproliferative DR (NPDR) as “microaneurysms only.” Since the American Optometric Association (AOA) is one of the most prominent organizations supporting optometry, it is reasonable to follow the 2020 edition of the AOA clinical practice guidelines on DR staging, a modified version of the Early Treatment Diabetic Retinopathy Study (ETDRS).

Mild NPDR. This stage includes at least one microaneurysm without additional significant retinopathy stages. Its underlying pathological features include increased vascular permeability due to the loss of capillary pericytes with vascular outpouching that results in its characteristic appearance. Microaneurysm formation is the earliest clinical characteristic of DR, but only 5% of mild NPDR cases will develop proliferative DR (PDR) within a year. Moderate NPDR. This includes microaneurysms, dot or blot hemorrhages (from leaking microaneurysms or retinal capillaries in deeper retinal layers), cotton wool spots (formerly called “soft exudates,” arising from disruption of axoplasmic flow in the nerve fiber layer), mild venous beading (a biomarker of retinal ischemia) and intraretinal microvascular anomaly formation (IRMA). The latter phenomenon, IRMA, provides a “shunt” from the nonperfused retina to the perfused retina (either from remodeling of
existing vessels or new growing vessels). IRMA is thought to be the “germ beds” of incipient neovascularization and commonly results in neovascularization elsewhere due to retinal ischemia. It always occurs within the intraretinal layers and is very difficult to detect in early stages without fluorescein angiography. Its role is to supply retinal areas of nonperfusion in DR.

Approximately 12% to 27% of moderate NPDR cases will develop PDR within one year. Vascular closure (retinal nonperfusion) typically develops in patients with greater than moderate NPDR.

Severe NPDR. This stage carries a high risk for development of PDR and consists of at least one of the following: severe microaneurysms and dot or blot hemorrhages in all four retinal quadrants, definite venous beading in two or more quadrants or prominent IRMA in one or more quadrants (4:2:1 rule). IRMA is very hard to be detected clinically; therefore, once it is visible the patient likely has prominent IRMA. Severe NPDR has a 50% risk of developing into PDR within one year.

Very severe NPDR. This stage includes two or more of the criteria of severe NPDR but without neovascularization. Very severe NPDR has a 75% of risk of developing into PDR in one year.

PDR. This stage is characterized by neovascularization (growth of new vessels) on the retinal surface, optic nerve or anterior segment (iris or angle). Neovascularization with inflammatory cells and fibrovascular proliferation may induce vitreous hemorrhage or retinal detachment.

PDR staging in the 2020 AOA guidelines only consists of high-risk stages and doesn’t include mild and moderate stages, as does the 2017 ICO. High-risk PDR has at least three of the following four risk factors:

1. Presence of any pre-retinal or vitreous hemorrhage.
2. Presence of moderate or severe new retinal vessels.
3. Presence of any pre-retinal or vitreous hemorrhage.
4. Presence of moderate or severe new retinal vessels or new vessels greater than half the disc area in size.

DME

This complication can occur during any stage of DR. It is characterized by intraretinal fluid leaking within the macula, with or without lipid exudate or cystoid changes, due to breakdown of the blood-retinal barrier. Common pathological changes associated with DME may include disruption of the perifoveal capillary network and capillary nonperfusion, widening of the foveal avascular zone and macular ischemia, though these features are also found in patients with DR without DME. The underlying mechanisms for DME include ischemia, oxygen-free radicals/oxidative stress that increase capillary permeability, production of pro-inflammatory cytokines and elevated levels of VEGF that further promote vascular leakage.

Clinically significant macular edema (CSME) is defined by at least one of the following three features: 1. Thickening of the retina at or within 500µm (or one-third of the disc diameter) of the center of the macula. 2. Hard exudates at or within 500µm of the center of the macula associated with thickening of the adjacent retina. 3. An area of retinal thickening one disc diameter or larger, part of which is within one disc diameter of the center of the macula.

It is important to note that the term “CSME” has largely become an anachronism with the advent of OCT. DME is now defined as center-involved (thickening or intraretinal fluid within the central 1mm subfield on OCT) or non-center-involved (thickening or fluid within other OCT subfields).

Treatments For DR/DME

There are a number of medical and surgical treatment options available for these conditions, and it is important ODs recognize the best approach for each of their patients.

Intravitreal anti-VEGF injection. Ischemia induces VEGF production, which causes angiogenesis and induces retinal neovascularization in diabetes. In the endothelial cells of retinal vessels, VEGF regulates tight junctions, impairment of which damages the blood-retinal barrier. Given this biology, anti-VEGF injections were developed, tested and proved to help reduce retinal vascular leakage and neovascularization.

For DME, and depending on study-specific visual acuity gains or anatomic improvement of macular thickening, anti-VEGF injections may help improve visual outcomes for cases of moderate to severe NPDR.
demonstrate a 10% to 70% success rate, which is better than laser treatment.25,26 A general principle is that patients treated earlier for DME achieve superior outcomes. The use of anti-VEGF agents has been shown to preserve and improve vision in patients with DME.

The scope of treatment of VEGF in DR includes DME or CSME, PDR and severe or very severe NPDR, though both ranibizumab and aflibercept have FDA approval for treating any level of DR with or without DME. Faricimab-svoa was recently approved for the treatment of DME with dual action mechanisms to inhibit VEGF and angio-poiten.27 Anti-VEGF therapy is the initial treatment choice for center-involved macular edema with vision impairment, with possible subsequent or deferred focal laser treatment. Earlier treatment with these intravitreal injections could prevent vision-threatening complications from developing later on, reduce the need for potential future treatment and promote better visual acuity. Anti-VEGF injections can regresses the severity of moderate to severe NPDR without DME and far better preservation of the visual field (as expected) and significantly lower risk for developing center-involved DME or requiring vitrectomy in the anti-VEGF group.30 However, intravitreal injections of anti-VEGF agents still carry a risk for complications such as subconjunctival hemorrhage, vitreous hemorrhage, cataract, endophthalmitis, retinal tear/detachment, eye pain, secondary glaucoma, etc. If patient compliance is poor, there is an increased burden of care and need for concern.

Neovascularization of the iris involves the blood vessels growing on the anterior surface of the iris as a result of retinal ischemia. This condition is more likely to occur near the pupillary border. It is important to detect whether the angle is involved or not by performing gonioscopy. Hyphemas can be seen. Treatment for neovascularization of the iris is PRP with or without an anti-VEGF injection.

Neovascular glaucoma is a secondary form with neovascularization of the iris and high intraocular pressure (IOP). It is the result of posterior segment ischemia (diseases like PDR, central retinal vein occlusion, central retinal artery occlusion and ocular ischemic syndrome with abundant VEGF). Treating an ischemic retina includes anti-VEGF (induce the regression of neovascularization) and PRP.31 IOP treatments include IOP-lowering meds, glaucoma filtering surgeries, etc.

**Intravitreal corticosteroids.** Steroids have been used in controlling both the inflammatory and angiogenic processes of diabetic retinal disease. Their use is generally limited to pseudophakic patients or those with persistent or refractory DME (typically in combination with anti-VEGF therapy). Sustained-release corticosteroids like dexamethasone or fluocinolone are commonly used in patients who exhibit a sub-optimal

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This patient with moderate to severe NPDR developed CSME.

Severe NPDR based on hemorrhages and microaneurysms in four retinal quadrants.
response to anti-VEGF, but they carry an increased risk of steroid-induced glaucoma.

**Laser photoocoagulation.** Focal/grid macular laser treatment is limited to the treatment of focal, extrafoveal DME or for patients who show poor response to or cannot tolerate injections of anti-VEGF agents. PRP has been the standard of care for managing PDR and very severe NPDR by treating areas of capillary nonperfusion adjacent to areas of perfused retina, thereby lessening the production of VEGF, subsequent neovascularization and preventing retinal vessel leakage. PRP can be particularly valuable in conjunction with anti-VEGF therapy for patients with high-risk PDR.

**Vitrectomy.** Surgical removal of the vitreous is used for treating vitreous hemorrhage, DR with fibrosis, tractional retinal detachments and vitreous traction with persistent DME. The complications of vitrectomy are similar to those of intravitreal injection of anti-VEGF agents. The risk of retinal detachment with anti-VEGF injections varied from tractional retinal detachment (5.2%) to rhegmatogenous retinal detachment (one per 7,500).33,34

**Role of the OD**

As primary eyecare providers, optometrists have an important role to play in every stage of the disease.

**DM without retinopathy.** ODs should be able to recognize the symptoms of DM, which can include thirst, hunger, fatigue, frequent urination, blurry vision, weight loss, slow wound healing and pain or numbness in the limbs, especially as some patients don’t know that they have the condition. The American Diabetes Association estimates that 7.5 million adults with type 2 diabetes are unaware they have diabetes. ODs should send these suspected DM patients to their PCP for evaluation. Even though many PCPs refer their patients with diabetes to optometrists for a dilated fundus exam, it is estimated, for example, that only 50% of Texas patients adhere to yearly eye exams.39 ODs should always encourage diabetes patients to get annual eye examinations and to do so on time.

ODs need to screen for a history of diabetes or prediabetes, perform a comprehensive dilated eye exam and educate patients about the risk factors for DR/DME. Additional education should include the possibility of refractive fluctuation with both poor and improving blood glucose control and the potential symptoms of retinal disease, though it is critical to teach patients that DR is asymptomatic at its earliest stages.

Finally, it is important that ODs send a diabetes eye exam report to the PCP and other diabetes care providers. For new diabetes patients, unbiased, evidence-based educational materials from the AOA, National Eye Institute, patient advocacy organizations and pharmaceutical companies can help build a good doctor-patient relationship.

**Mild NPDR.** Optometrists must communicate with PCPs and educate patients on the importance of controlling risk factors to reduce the risk of DR progression. Management includes glycemic control, smoking cessation, optimally managing both blood pressure and dyslipidemia, cardiovascular risk reduction, physical exercise and weight management. HbA1c accounts for 10% of DR risk, and hypertension plus dyslipidemia accounts for less than 10%.36,37 The probability of mild NPDR progression to PDR is 5% in one year per ETDRS data.14

The presence of hemorrhage anywhere, asymmetric hyperopic shift or any signs of DME warrants additional macular OCT/fundus photography. ODs should document whether the patient has DME/CSME or not. Referral to a retinal specialist within two to four weeks is indicated for center-involved DME and CSME. Patients should be followed up in one year or sooner if there is no DME, and sooner if their A1c is changing rapidly or they have poor metabolic control.

**Moderate NPDR.** ODs should educate these patients about the...
importance of blood glucose/pressure/lipid control and the possibility of progression to PDR (12% to 27% of cases in one year). Fundus photography can detect most DR and document its severity and the presence of neovascularization. Macular OCT can facilitate the recognition of subtler DME. Communication with the PCP/internist/endocrinologist on ocular findings and recommendations/follow-up is critical.

Follow-up every three to nine months in the absence of DME is warranted. Similar to mild cases, patients should be referred to a retinal specialist within two to four weeks if center-involved DME or CSME are present. Follow-up should be sooner if A1c is changing rapidly or in patients with poor metabolic control. Patients with non-center-involved DME should be watched closely—every one to six months—by the OD or referred to a retinal specialist.

All patients with DR or DME referred to a retinal specialist should also be reappointed with their optometrist to verify completion of the initial referral, ongoing therapy and surveillance for worsening disease and/or treatment-related adverse events (e.g., glaucoma, cataract, etc.). Evidence suggests that even retinal specialists tend to undergrade NPDR severity (accurate staging is best facilitated by widefield fluorescein angiography), so any patient with moderate or worse NPDR should be considered for referral as they may, in fact, have worse disease severity than that diagnosed by clinical examination.

Severe NPDR/very severe NPDR/non-high-risk PDR. As these stages of DR portend much higher risk of severe vision loss, patients require careful education and appropriate referral. In addition to routine dilated fundus exam, macular OCT and fundus photography to document disease severity, gonioscopy should be performed if there is any sign of retinal or iris neovascularization to rule out angle neovascularization and help diagnose secondary glaucoma (always measure IOP in these patients). Document the stage of DR and presence of any DME/CSME (more likely as DR severity worsens) carefully. Communicate with the PCP/internist/endocrinologist/cardiologist/nephrologist about the ocular finding, referral to a retina specialist and probable treatment.

The PANORAMA study showed that proactive intravitreal aflibercept for moderately severe to severe NPDR cases reduces the risk of progression to vision-threatening complications. It also showed that good blood glucose control was not protective against subsequent progression to PDR, center-involved DME or anterior segment neovascularization in patients with moderately severe or severe NPDR, so don’t base referral decisions on diabetes control, but rather, disease severity. Patients with multiple complications, especially cardiovascular disease, poor cognition, multiple comorbidities and shortened lifespan, should not be instructed to attempt tight blood glucose control without the oversight of their treating diabetes physicians. These patients should be referred to a retinal specialist within two to four weeks, per AOA clinical practice guidelines.

While it remains a clinical judgment call for physicians on the most appropriate time to refer severe-stage
referral and earlier intervention with anti-VEGF due to findings of PAN-ORAMA and Protocol W. The AOA clinical practice guidelines currently state “follow-up every three to four months in consultation with an ophthalmologist experienced in the management of diabetic retinal disease is advisable for patients with severe or very severe NPDR.” Follow-up with the OD is prudent to ensure completion of the initial referral, ongoing therapy and surveillance for worsening disease and/or treatment-related adverse events.

**High-risk PDR.** These patients require prompt referral to a retinal specialist within 24 to 48 hours for treatment to preserve vision and reduce the high probability of blindness over five years (50%). Optometrists should continue to follow these patients to ensure adherence to the treatment regimen, address any primary care needs and provide or refer for vision rehabilitation, if necessary.

**Tele-screening and Artificial Intelligence (AI)**

These technologies will likely assist with earlier identification and accurate staging of diabetic retinal disease. Two AI systems are currently approved in the United States for autonomous detection and grading of DR and DME, and multiple other systems are in development with varying degrees of sensitivity and specificity.

Teleretinal DR screening programs are another option for reaching underserved populations. They have been employed for more than a decade and require a photographer/technician to capture retinal images (often without dilation) which are then sent to a certified image reading center where ophthalmologists, optometrists and clinical personnel judge the presence or absence of DR/DME, grade DR severity and personalize decisions for follow-up, in-person clinical examination and referral to a retinal specialist.

Teleretinal screening may be faster and more accessible, often reducing travel time, and can be more convenient than traditional in-office examination. However, it also has shortcomings, including equipment and training expenses and non-readable or non-gradeable images due to small pupil size, media opacities or poor field of view.

**Takeaways**

ODs are in the perfect position to play a key role in the management of diabetes patients. Therefore, they must have a comprehensive understanding of not only the disease but also what steps to take during every stage.

The author thanks Paul Chous, OD, for his contributions to this article.

OBTOMETRIC STUDY CENTER QUIZ

1. Which percentage of moderate NPDR cases will develop into PDR in one year?
   a. 5%.
   b. 12% to 27%.
   c. 52%.
   d. 75%.

2. Which percentage of severe NPDR cases will develop into PDR in one year?
   a. 5%.
   b. 12% to 27%.
   c. 50%.
   d. 75%.

3. Which percentage of very severe NPDR cases will develop into PDR in one year?
   a. 5%.
   b. 12% to 27%.
   c. 52%.
   d. 75%.

4. Which is not one of the risk factors for developing DR?
   a. Obesity.
   b. Hypertension.
   c. Hyperthyroidism.
   d. Cardiovascular disease.

5. The most distinguished retinal vascular finding for PDR is which?
   a. Reduced blood flow rate.
   b. Neovascularization.
   c. Increased vascular permeability.
   d. Vascular closure.

6. The most distinguished pathological finding for moderate to severe NPDR is which?
   a. Reduced blood flow rate.
   b. Neovascularization.
   c. Increased vascular permeability.
   d. Vascular closure.

7. The most distinguished pathological finding for mild NPDR is which?
   a. Reduced blood flow rate.
   b. Neovascularization.
   c. Increased vascular permeability.
   d. Vascular closure.

8. Which is not involved in the mechanism of DME?
   a. Macular ischemia.
   b. Disruption of the perifoveal capillary net and capillary nonperfusion.
   c. Widening of the foveal avascular zone.
   d. Increased blood flow.

9. The mechanisms of both DR and DME include which?
   a. Inflammatory and angiogenic processes with raised VEGF levels.
   b. Oxidative stress, the sorbitol pathway, advanced glycation end-products.
   c. The diacylglycerol-protein kinase C pathway activation.
   d. All of the above.

10. The definition of mild NPDR includes which?
    a. IRMA.
    b. Dot or blot hemorrhages.
    c. At least one microaneurysm.
    d. Preretinal hemorrhages.

11. The definition of moderate NPDR includes which?
    a. Neovascularization of the disc.
    b. Dot or blot hemorrhages.
    c. At least one microaneurysm.
    d. Preretinal hemorrhages.

12. The definition of severe NPDR includes which?
    a. 4:2:1 rule.
    b. Dot or blot hemorrhages.
    c. At least one microaneurysm.
    d. Preretinal hemorrhages.

13. The definition of PDR includes which?
    a. Within 24 to 48 hours.
    b. Within two to four weeks.
    c. Within one month.
    d. Within three months.

14. When should you refer DME or CSME patients (except those with high-risk PDR) to a retinal specialist?
    a. Within 24 to 48 hours.
    b. Within two to four weeks.
    c. Within one month.
    d. Within three months.

15. The scope of treatment of anti-VEGF in DR includes which?
    a. Severe or very severe NPDR.
    b. PDR with risk of progression.
    c. DME or CSME.
    d. All of the above.

16. How often is it recommended by the AOA to monitor a patient with moderate NPDR without DME or CSME?
    a. Every month.
    b. Every three months.
    c. Every six to nine months.
    d. Every 12 months.

17. Which patient does not require a referral to a retinal specialist?
    a. Severe or very severe NPDR.
    b. Early PDR with risk of progression.
    c. High-risk PDR.
    d. Mild and moderate NPDR without DME or CSME.

18. How soon do you need to refer a high-risk PDR patient to a retinal specialist?
    a. Within 24 to 48 hours.
    b. Within two to four weeks.
    c. Within one month.
    d. Within three months.

19. Which percentage of moderate NPDR cases will develop into PDR in one year?
    a. 75%.
    b. 52%.
    c. 12% to 27%.
    d. 5%.

20. The role of the OD in seeing DM patients includes which?
    a. Encourage achievement of metabolic goals.
    b. Perform an annual dilated fundus exam and educate patients on the risk factors and DR progression ratios.
    c. Document, communicate with PCP about dilated fundus exam findings, arrange proper follow-up schedule and refer to an ophthalmologist on time.
    d. All of the above.
Examination Answer Sheet
Staging of Diabetes and Diabetic Retinopathy
Valid for credit through June 15, 2025

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

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

Answers to CE exam:
1. A  B  C  D  E  F  G  H  I  J
2. A  B  C  D  E  F  G  H  I  J
3. A  B  C  D  E  F  G  H  I  J
4. A  B  C  D  E  F  G  H  I  J
5. A  B  C  D  E  F  G  H  I  J
6. A  B  C  D  E  F  G  H  I  J
7. A  B  C  D  E  F  G  H  I  J
8. A  B  C  D  E  F  G  H  I  J
9. A  B  C  D  E  F  G  H  I  J
10. A  B  C  D  E  F  G  H  I  J
11. A  B  C  D  E  F  G  H  I  J
12. A  B  C  D  E  F  G  H  I  J
13. A  B  C  D  E  F  G  H  I  J
14. A  B  C  D  E  F  G  H  I  J
15. A  B  C  D  E  F  G  H  I  J
16. A  B  C  D  E  F  G  H  I  J
17. A  B  C  D  E  F  G  H  I  J
18. A  B  C  D  E  F  G  H  I  J
19. A  B  C  D  E  F  G  H  I  J
20. A  B  C  D  E  F  G  H  I  J

Post-activity evaluation questions:
21. Explain the pathophysiology and staging of diabetes.
   Rate how well the activity supported your achievement of these learning objectives. 1=Poor, 2=Fair, 3=Neutral, 4=Good, 5=Excellent
   1  2  3  4  5
22. Determine their role in the management of these patients at each stage.
   1  2  3  4  5
23. Comanage diabetic retinopathy patients effectively.
   1  2  3  4  5
24. Communicate with patients about diabetes and diabetic retinopathy.
   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.)
   A I do plan to implement changes in my practice based on the information presented.
   B My current practice has been reinforced by the information presented.
   C I need more information before I will change my practice.
   D I need more information before I will change my practice.
   E 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): __________

Post-activity evaluation questions:
27. If you plan to change your practice behavior, what type of changes do you plan to implement? (Check all that apply.)
   A Change in diagnostic methods
   B Change in vision correction offerings
   C Change in current practice for referral
   D More active monitoring and counseling
   E Other, please specify: ______________________

28. How confident are you that you will be able to make your intended changes?
   A Very confident
   B Somewhat confident
   C Unsure
   D Not confident

29. Which of the following do you anticipate will be the primary barrier to implementing these changes?
   A Formulary restrictions
   B Insurance/financial issues
   C Patient adherence/compliance
   D Lack of interprofessional team support
   E Other, please specify: ______________________

30. Additional comments on this course: __________________________________________________________________________________

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31. The content was evidence-based.
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Not-So-Simple Simplex

Science and strategy are needed to manage HSV epithelial keratitis and prevent deeper penetration.

An 88-year-old man presented with a mildly red and irritated left eye. He had a previous history of dry eye syndrome for which he used Cequa (cyclosporine 0.09%, Sun Pharma) BID OU. His uncorrected acuity was 20/30 OD and 20/25 OS. Neuro-ocular screening was normal in each eye. His right eye was normal, but he manifested a paracentral dendritic lesion on his left cornea along with a grade 1 conjunctival injection and an accumulation of endothelial inflammatory cells. There were rare cells and mild flare in his left anterior chamber. His intraocular pressure was 11mm Hg OD and 12mm Hg OS. Corneal sensitivity testing revealed a subjective decrease of 20% in his left eye.

His medical record revealed that he had a previous episode of dendritic keratitis followed by a prolonged course of diffuse epitheliopathy and corneal non-healing approximately two years earlier with another practitioner in the practice. He was diagnosed with herpes simplex dendritic keratitis and prescribed Valtrex (oral valacyclovir, GlaxoSmithKline) 1000mg BID and Zirgan (topical ganciclovir ointment, Bausch + Lomb) five times daily OS. He was told to continue his Cequa as prescribed and to be seen in one week.

While the diagnosis and initial management was straightforward, his history of epitheliopathy and prolonged corneal healing was somewhat troubling.

A Latent Infection

Herpes simplex virus (HSV) is a common pathogen and frequent source of ocular infection. Nearly 60% of the American population is seropositive for HSV-1, and another 17% is seropositive for HSV-2. Initial ocular infection by HSV tends to be seen in younger patients at an average age of 24. Recurrence of HSV has been associated with causative factors that include fever, hormonal changes, ultraviolet sun exposure, psychological stress, ocular trauma, trigeminal nerve manipulation, steroid use, ocular surgery, exposure to ultraviolet radiation, immunosuppressive agents and glaucoma treatment with prostaglandin analogs.

Epithelial dendritic keratitis is the second most common ocular manifestation of HSV, occurring in 12.2% of cases overall, while stromal keratitis was more prevalent at 25.4%. HSV epithelial keratitis presents as a unilateral red eye with a variable degree of pain or irritation. Vision may or may not be affected, depending upon the location and extent of the corneal lesion. Bilateral HSV keratitis may be encountered in a small percentage of cases, though it is more common in children and those with immune or atopic disease. The hallmark finding in HSV keratitis involves a dendritic ulceration of the corneal epithelium, which may be accompanied by a stromal keratitis in more severe presentations. Secondary anterior uveitis is often encountered with the keratitis, particularly when treatment is delayed. Other epithelial manifestations include geographic ulcers, marginal ulcers, neurotrophic ulcers and diffuse epitheliopathy.

HSV keratitis can be caused by either type 1 or 2 herpes simplex. The virus is transmitted via bodily fluids and affects the skin and mucous membranes of the infected host. Primary herpetic infections are generally encountered in children and young adults. HSV establishes what is known as a lytic and latent infection. Latent reactivation occurs intermittently and chronically—a life-long source of recurrent infection. After resolution of the initial infection, the herpes virus migrates along local nerves to regional ganglia and remains dormant until reactivated by specific stimuli. On average, patients experience recurrences at a rate of 0.6 episodes per year. While many of the ocular manifestations related to HSV are immune (e.g., delayed hypersensitivity reaction) or inflammatory in nature (e.g., stromal and disciform keratitis, iridocyclitis), epithelial keratitis represents infection by live virus.
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Answered by Dr. Mile Brujic, OD, FAAO

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penetration into deeper corneal tissues with subsequent scarring and vision loss. The treatment of choice consists of topical and oral antiviral therapies. Historically, Viroptic (trifluridine 1%, Monarch) has been the standard treatment. The initial dosage of trifluridine is one drop every two hours up to nine times daily for HSV epithelial keratitis; as regression of the dendrite ensues, the dosage may be tapered to Q3H to Q4H until complete resolution is seen, over a period of seven to 10 days.15,17

Zirgan, an alternative to corneotoxic trifluridine, requires less frequent initial dosing at just five times daily until the corneal ulcer heals and then three times per day for another seven days. Ganciclovir demonstrates greatly reduced corneal toxicity as compared with trifluridine because it is only taken up by virus-infected cells.14,19 Cycloplegia may be initiated, depending upon the severity of the uveitic response and the patient’s subjective discomfort.

Oral antiviral agents can also effectively treat HSV epithelial keratitis, generating pharmacotherapeutic levels in the tears.18,21 Management options for HSV epithelial keratitis include acyclovir 200mg to 400mg five times daily, valacyclovir 500mg to 1000mg three times daily and famciclovir 250mg to 500mg two to three times daily for 21 days. The Acyclovir Prevention Trial (APT of the HEDS II) demonstrated that oral antiviral medications may further serve a preventative role by reducing the frequency and severity of recurrent infectious outbreaks.22 Acyclovir 400mg BID is the most commonly used regimen for prophylactic suppression, but valacyclovir 500mg once daily may also be used.23

Judicious topical steroid use can be a beneficial adjunct when used under the umbrella of a topical or oral antiviral agents, following several days of effective antiviral therapy; this is particularly true in cases of associated stromal inflammation.24

When managed appropriately, HSV epithelial keratitis resolves without scarring, although there is potential with recurrent disease to develop neurotropism and persistent epithelial non-healing.25 In such cases, amniotic membranes may assist with returning the eye to normal homeostasis.26,28 Autologous serum can also be beneficial in promoting corneal healing.29,30 Blood serum contains many growth factors, and autologous serum eye drops are useful in corneal re-epithelialization when a patient’s serum is diluted by 20% or 50% to create the eye drops and used every three hours daily.31

Latent reactivation occurs intermittently and chronically— a life-long source of recurrent infection.

Follow-up
When the patient returned one week later, his right eye was unchanged, but his acuity had dropped to counting fingers at two feet in his left. The dendritic pattern was now gone, but there was dense, diffuse corneal epitheliopathy across the entire cornea, similar to the course he had previously. There was still a significant endothelialitis present. To reduce toxicity issues, topical ganciclovir was discontinued while the oral valacyclovir was continued. He was prescribed a topical steroid-antibiotic (tobramycin-dexamethasone) combination QID OS. An amniotic membrane was placed on his eye.
Upon his last follow-up eight weeks after his initial presentation, his ocular inflammation resolved on topical steroids, which had been discontinued as had the valacyclovir, and he reported a great improvement in all findings though he was still on gabapentin for post-herpetic neuralgia.32

Dear Colleagues,

I am thrilled to welcome you to our New Technologies & Treatments in Eye Care conference series - in person for 2022!

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Sincerely,

Paul M. Karpecki, OD, FAAO
Kentucky Eye Institute
Lexington, Kentucky
Chief Clinical Editor
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A 54-year-old Caucasian female was referred to determine whether she should be treated for glaucoma. The referring provider did a great job in the preliminary evaluation, obtaining multiple IOP measurements over a three-month period, visual field studies, OCT imaging and gonioscopy, yet the question remained to begin therapy or not.

Patients like these are seen every day in glaucoma clinics and, in many cases, the decision to begin intervention or passively monitor is based primarily on clinical judgement.

The Case
This particular individual was taking no meds other than vitamins and OTC supplements and reported no allergies to medications. There was the possibility of a history of glaucoma in her family, but the details were not clearly elucidated. Entering visual acuities through mildly hyperopic astigmatic and presbyopic correction were 20/20 OD, OS and OU. Pupils were EERR with no APD, and EOMs were full in all positions of gaze. The patient was not refracted, as the purpose of the initial visit was a second opinion regarding glaucoma.

Previous IOP readings were, on average, 24mm Hg OD and 25mm Hg OS, as reported by the referring provider. We obtained similar IOPs of 23mm Hg OD and 24mm Hg OS. Previous pachymetry readings were 540μm OD and 533μm OS, again consistent with our readings. Threshold visual fields were normal.

A slit lamp exam of the anterior segments was essentially unremarkable, with clear corneas, quiet chambers, open angles and no transillumination defects or Krukenberg spindles OU. Gonioscopy demonstrated wide open angles with a flat iris approach, minimal trabecular pigmentation and no angle abnormalities.

Through dilated pupils, the patient’s crystalline lenses were clear OU. Stereoscopic examination of her optic nerves demonstrated a cup-to-disc ratios of about 0.40 x 0.35 OD and 0.40 x 0.40 OS. The neuroretinal rims were plush and well perfused and deemed to be of average size. Her retinal vascular evaluation was entirely normal, as was her macular evaluation. Mild vitreous syneresis was observed. Her peripheral retinal evaluation was unremarkable.

Discussion
With a questionable family history of glaucoma and IOPs in the mid-20s, certainly there is a risk for glaucoma. But what was most concerning for the referring provider were some of the OCT findings obtained; namely, the optic disc metrics.

It’s common knowledge that different providers subjectively looking at the optic nerves of the same patient may very well judge the cup-to-disc ratio differently. This inherent confounder is common, especially when you see a patient of a previous provider. This was the case with the referring provider, as they had inherited the patient from another OD who had their own method of interpreting her optic nerve characteristics.

Naturally, with the heavy reliance on OCT technology in evaluating glaucoma patients, much of the subjectivity of optic nerve parameters is eliminated by the objective measurements that OCT provides. However, the interpretation of these objective measurements remains subjective in nature, and different clinicians looking at the same OCT readings may come to different conclusions.

This is one of the reasons why you need to know and thoroughly understand the details that your OCT technology is providing you. I’ve previously mentioned the tendency to overly rely on reference databases and cautioned against doing so. But what happens when some of the OCT findings are suggestive of the presence of disease while other parameters are...
not? This is where your interpretive skills come into play, and those skills must be shaped by an understanding of the information the OCT provides.

At the end of the day, there are many very good OCT devices on the market, and they do provide reliable data that is objective in nature. How they generate that information varies somewhat from company to company; thus, understanding how your particular instrument processes data is critical.

Of course, OCT’s evolution has moved from a single analysis of the circumpapillary RNFL thickness to analyses that include not only the RNFL but also the macular ganglion cell layer, as well as metrics associated with the optic disc itself. When these objective findings match our subjective finding from the physical exam, formulating an assessment is easy. But when they don’t, then we must use our clinical judgement.

The majority of the OCT findings in this patient are representative of a healthy glaucoma suspect (Figure 1). The RNFL metrics are good, as are the ganglion cell metrics. With a cursory view of the OCT report, there may not be any suspicion; however, after closely examining the optic nerve metrics, a different picture emerges (Figure 2).

While both my and the referring doctor’s physical exam of the right optic nerve seemed to indicate a relatively healthy appearing structure, the OCT results demonstrated a different interpretation of the cup-to-disc ratio. And this is where the devil is in the details. As we move away, gradually and albeit slowly, from using the subjective cup-to-disc ratio as a solid metric on physical exam, OCT—by its inherent objectivity—aims to provide a reliable and repeatable metric of the cup-to-disc ratio, unbiased by subjectivity. But we need to keep in mind how OCT calculates this ratio and recognize that each OCT does it differently.

The basis of OCT interpretation of the optic nerve itself, and namely the neuroretinal rim tissue, is predicated upon identification of Bruch’s membrane opening (BMO), which frankly is very easy with OCT. The BMO is not identifiable at the slit lamp. Essentially, the BMO is the de-facto limit of the optic canal. In other words, all axons of ganglion cells exit the eye at the optic nerve medial to the BMO, making this structure the passage through which the axons are traveling. When an OCT calculates cup-to-disc ratio, this is effectively the optic disc size.

But what about the cup size? How is that determined? Again, the devil is in the details. I’ve heard comments from some providers who are not fond of OCT’s generated cup-to-disc ratio. The reasons cited are often related to the ratio not matching the in vivo appearance. In many instances, they won’t match up, especially since we can’t see the BMO in vivo at the slit lamp.

With the Maestro OCT (Topcon) used in this case, the calculated cup-to-disc ratio is based on the BMO and a plane 120μm anterior to the BMO. The cup size is larger than our subjective in vivo estimation (Figure 3).

It is very important to note that the BMO generally does not change over time, whereas—should glaucoma progress—the neuroretinal rim would thin and, thereby, the OCT-calculated cup-to-disc ratio would naturally enlarge. But the disc itself does not enlarge. And therein lies the value of the OCT-calculated ratio: it readily shows change should the disease progress. And given the technology’s resolution, that change would be visible on OCT well before we would see it in vivo.

Where the difficulty comes in is in the initial set of scans, especially if our subjective interpretation of the cup-to-disc ratio differs significantly from the objective ratio calculated by OCT, as it does in this case. Don’t dismiss the calculated cup-to-disc ratio in these cases, as we cannot visualize in vivo the BMO, while OCT can. But do use the OCT-generated ratio to assess for change over time, which is what we are all looking for in the long-term management of our glaucoma patients.

**Takeaways**

So, what is this patient’s diagnosis? I believe she is a glaucoma suspect with no frank OCT or visual field evidence of damage; therefore, she will only be monitored. While the OCT results seem to conflict with our exam findings, they just present the case in a different fashion than we can see in vivo.

Moving forward, the patient will be seen by the referring provider who will ultimately be looking for progression on OCT in the macular ganglion cell layer, RNFL, and neuroretinal rim cup-to-disc ratio.
Night Moves

Inadequate lid closure, caused by nocturnal evaporative stress, may be the reason for your patient’s dry eye.

We often think about our dry eye patients’ daytime experiences and how these may exacerbate their symptoms. But in fact, the greater culprit may be lurking in a patient’s nighttime environment. Consider that 61% of symptomatic dry eye patients across the spectrum of disease severity have compromised lid closure.1

If you have a patient whose dry eye is not improving despite treatment, it’s time to consider inadequate eyelid closure, sometimes referred to as nocturnal lagophthalmos. This form is far less obvious, as this under-identified and under-treated condition is caused by nocturnal evaporative stress (NES) and is highly prevalent in refractory dry eye.1

Causes

Our eyes don’t produce as many tears while we’re sleeping, which automatically puts patients in a dry eye state during sleep.2 Closed lids protect the eye from desiccation.3 However, many patients’ lids don’t adequately close at night. Several factors contribute to the development of NES, many of which are directly linked to inadequate lid seal (ILS). These include floppy eyelid syndrome, surgical cosmetic procedures and injections, lid deformities, age-related lid laxity, dermatochalasis, senile ectropion and Graves’ disease.3,4

In addition, patients with NES often have another condition, such as meibomian gland dysfunction (MGD), that contribute to the disease. Environmental factors likewise should be considered. A fan in the bedroom, CPAP devices or forced air heat can make symptoms worse. Newer research indicates that even in the majority of patients who show no apparent lid abnormalities, insufficient lid seal is present and leads to nighttime dryness.5

Diagnosis

Despite our busy schedules and heavy patient loads, investigating NES in new dry eye patients as well as refractory cases is time well spent. This can be as easy as asking patients how their eyes feel when they first wake up. If they say their eyes feel fine in the morning but get worse throughout the day, we can usually rule it out. Conversely, if the patient indicates their eyes feel particularly bad upon waking, ILS is the likely diagnosis.

The Korb-Blackie light test is probably the most simple and straightforward way to detect ILS if you feel the need for a confirmatory test beyond morning symptoms. This test helps you determine whether a patient’s seemingly closed eyelids are actually protecting the ocular surface and preventing evaporation during sleep.6 Simply darken the room and place a transilluminator against the patient’s closed outer upper eyelids. As you direct the light toward the interpalpebral fissure, look for light leakage along the lid and between the lashes.6 Repeat on the second eye.

The Korb-Blackie light test can detect ILS by determining if the patient’s closed lids are protecting the ocular surface and preventing evaporation during sleep.

Treatment

If you are trying to treat a patient’s ocular surface disease but not managing their ILS, there is an uphill battle...
to climb, as you’re often treating the resulting inflammation, corneal staining or desiccation, MGD and blepharitis without treating the cause. For that reason, a treatment that addresses the lids would be ideal; however, until now, these options were limited.

Other than surgery, there’s sleep masks, but they only work for select patients. Sleep masks don’t address the cause—ineffective light seal—but they may provide a brief moisture chamber if the patient is able to maintain them throughout the night. Other options include instillation of gels or ointments before bed, but these don’t create a long enough seal to prevent NES. A re-evaluation of the bedroom environment can also help, such as eliminating ceiling fans, but many patients say it helps them sleep. Directing all fans and vents away from the bed and keep bedding pillows and mattresses clean and as free from dust mites as possible can help.

There’s also a daily disposable lid seal, SleepTite, which is a single-use, hypoallergenic, latex-free device intended to hold the eye closed to prevent NES due to inadequate lid closure. Each card has two eye covers that can be applied universally to either eye. Instructions are straightforward and it’s best to begin with having the patient close one eye overnight. Patients are instructed to place the eye cover over the closed eye. The tab can be oriented laterally or medially for best fit. Gently seal the cover by running a finger around the entire edge of the oval. Upon awakening, the patient easily removes the eye cover by gently grasping the colored tab and pulling in a downward direction so that the eye is not opened during removal. The device should then be discarded. If they find they are not getting up often during the night and the device is working well for them, they can transition to bilateral placement.

In my experience, not only has this product been the single most effective treatment for recalcitrant dry eye, it has also changed people’s lives and their need for chronic therapy. Many even comment that it has allowed them the best sleep they’ve had in decades, likely due to the lack of light entering the eye. By treating the cause of ocular surface desiccation and MGD, you can often relieve these patients of multiple adjunctive therapies.

We only recently discovered that inadequate lid closure occurs in patients who appear to have normal lid structure and performance. It’s a seemingly small discovery, but it’s one that can make a significant difference in patient outcomes and is likely to be the number one cause of morning symptoms in those who don’t respond to ocular surface disease therapies.

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Hole in One

The recently approved Evo Visian ICL comes with a central port that allows aqueous movement, eliminating the need for a PI.

BY AMANDA GROENHUYZEN, OD
SAN ANTONIO, TX

Most patients seeking to eliminate the need for glasses or contact lenses turn to corneal refractive procedures (LASIK, PRK, SMILE), but high myopes are often best served by a phakic IOL such as Staar Surgical’s Visian posterior chamber implantable collamer lens (ICL). The procedure, which is reversible, preserves corneal integrity and accommodative function while correcting up to -16D of myopia.

Traditionally, the implantation of an ICL requires an iridotomy to allow aqueous flow around the lens and prevent pupillary block complications. Now, patients have the option to have ICL surgery without the need for an iridotomy with the recent FDA approval of Staar’s newest version, called the Evo Visian. This lens has been shown to reduce the incidence of post-surgical complications while maintaining positive visual outcomes equivalent to conventional ICLs.

What is EVO ICL?

Like the previous generation Visian, this posterior chamber phakic IOL is made of a biocompatible collagen/polymer (hence, “collamer”) material. However, the new Evo (short for “evolution”) lens features a unique design that includes a 360μm central port. This allows sufficient aqueous flow, eliminating the need for the pre-op iridotomy. The procedure only takes five to 10 minutes and offers patients a quick visual recovery time. Although the Evo lens has been used around the world for many years, it only recently gained FDA approval; it’s indicated for patients 21 to 45 years of age with a spherical equivalent of -3D to -20D and up to 4D of astigmatism.

Due to the ICL’s ability to correct large amounts of myopia and astigmatism, it has often been shown to produce postoperative vision that is better than pre-op vision.

Safety and Effectiveness

The central port design of the Evo ICL allows for improved circulation of aqueous around the crystalline lens, allowing for improved circulation of aqueous and preserving accommodative function, and has reduced the incidence of postoperative increased intraocular pressure and pupillary block.

In fact, only one case of pupillary block has been reported in 4,196 eyes with over one year of follow-up. This design has also resulted in less visually significant anterior subcapsular cataract formation compared to earlier ICL models, due to the efficient fluid dynamics around the anterior lens capsule.

The question we all want to know is, does this central port impact vision? The current peer-reviewed data shows the port does not significantly alter the optical performance of the Evo lens compared to conventional ICLs, with studies demonstrating equivalent optical quality variables.

Postoperatively, uncorrected visual acuity averages 20/19, with a range of 20/12 to 20/27. Patients with either design report similar instances of initial glare, halos and ring-shaped dysphotopsias at night, with these visual symptoms disappearing over time for up to one year.

For those with moderate to severe myopia with or without astigmatism, the Evo ICL has demonstrated safety and efficacy in minimizing or eliminating the hassle of corrective lenses. It is a well-established, flexible solution to preserve accommodative function, protect corneal and lens integrity, and provide clear vision.


ABOUT THE AUTHOR

Dr. Groenhuyzen is a refractive surgery and ocular disease resident at Parkhurst Nuvision in San Antonio, TX.
Sunset Glow

Fundus and OCT imaging uncovered this rare, inflammatory disease.

By Rami Aboumourad, OD

A 42-year-old Dominican male presented with eight days of vision loss and photophobia of the left eye. He denied any associated flashes, floaters, recent trauma or similar symptoms in the right eye, which was asymptomatic. His past medical and ocular histories were unremarkable, and he was not taking any prescription or over-the-counter medications. He had no known environmental or drug allergies. An extended review of systems revealed he experienced onset of unilateral hearing loss two years prior.

His uncorrected visual acuity was 20/20 in the right eye and 20/800 in the left eye with no pinhole improvement. His pupils were equally round and reactive without a relative afferent pupillary defect. Confrontation visual field and extraocular motility testing were both normal, and the intraocular pressure was 15mm Hg in both eyes.

The anterior segment examination was normal in both eyes except for 1+ anterior chamber cell OS. Posterior segment findings were significant for trace vitreous cells with no vitreous haze in both eyes. Fundus photography (Figures 1 and 2) and OCT images (Figures 3 and 4) were obtained.

Take the Retina Quiz

1. Which of the following descriptions of the OCT retinal imaging is false?
   a. There are multifocal neurosensory retinal detachments.
   b. There are multifocal bacillary layer detachments.
   c. There is choroidal thickening and infiltration.
   d. All of the above are true.

2. What is the most likely diagnosis for this patient?
   a. Endogenous endophthalmitis.
   b. Sympathetic ophthalmia.
   c. Toxoplasmosis.

3. What is the most appropriate next step in the management of this patient?
   a. Hospital admission for blood cultures, intravenous anti-infectives and intravitreal anti-infectives.

Figs. 1 and 2. Clarus fundus photography of the right eye (left) and left eye (right).

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.
b. Initiation of anti-tuberculosis medications.
c. Initiation of anti-toxoplasmosis medications.
d. Initiation of immunosuppressive therapy.

4. Which of the following statements is true?
   a. Sugiura sign describes depigmentation of the eyelids.
   b. There is a strong association across most populations with HLA-B51.
   c. “Sunset glow” describes the clinical picture of optic nerve pallor with peripapillary choroidal depigmentation, which appears as red-orange.
   d. Patients with this condition often have a history of penetrating ocular trauma.

5. Which of the following is NOT a common complication of this patient’s condition?
   a. Macular neovascularization.
   b. Neovascular glaucoma.
   c. Posterior subcapsular cataract.
   d. Subretinal fibrosis.

For answers, see page 98.

Diagnosis

The fundus exam revealed focal, peripapillary, hypopigmented and granulomatous lesions around both optic nerves with overlying subretinal fluid. There is also clearly evident fluid underneath the macula in the left eye and fluid just nasal to the fovea in the right eye (Figures 1 and 2).

From the OCT images, we were able to anatomically visualize the serous neurosensory retinal detachments and confirm another interesting finding. Looking more closely you can see that the retinal pigmented epithelium (RPE) is not detached from Bruch’s membrane and, even more significantly, neither are the inner and outer photoreceptor segments (IS/OS junction). Instead, it appears the detachment is at the level of the external limiting membrane (ELM) and the IS/OS junction. These are referred to as bacillary layer detachments. OCT also shows choroidal thickening and infiltration in both eyes (Figures 3 and 4).

The clinical presentation and review of systems were most consistent with Vogt-Koyanagi-Harada (VKH) disease. The plan was to start 60mg of oral prednisone and prednisolone acetate 1% every two hours in both eyes; however, the patient was sent to have blood drawn right away to rule out infectious etiologies (syphilis and tuberculosis) prior to taking his first dose of prednisone, which came back negative. He was followed closely and demonstrated an adequate response to therapy with resolution of subretinal and intraretinal fluid; however, there was incomplete resolution of the choroidal thickening and infiltration. Vision in the right eye remained stable, and the left eye improved to 20/20.

Discussion

VKH disease is an immune-mediated condition against melanocyte-containing tissues (e.g., uvea, skin). Ophthalmic involvement typically presents as a bilateral, granulomatous, non-necrotizing posterior or panuveitis, and extraocular involvement may include dysacusis, poliosis, alopecia and vitiligo. Its incidence is variable as it tends to affect populations or races containing more pigment such as Asians, Hispanics, American Indians and Asian Indians. In the United States, VKH accounts for only 1% to 4% of all uveitis referrals. There may be a female predilection, and it often presents in the second to fifth decade of life.

Classically, the disease progresses through four well-defined stages: (1) prodromal, (2) acute uveitic, (3) chronic-recurrent and (4) convalescent. The prodromal phase manifests as a nonspecific viral illness that lasts a few days. Symptoms can include malaise, headache, dizziness, fever, neck stiffness and auditory disturbances (tinnitus and dysacusis). The acute uveitic phase follows the prodromal phase with photophobia and blurred vision. Clinical findings of this stage include bilateral granulomatous posterior or panuveitis, choroidal thickening, multifocal exudative retinal detachments and optic nerve hyperemia and edema.

While recurrent exudative retinal detachments are uncommon, the chronic recurrent phase typically
involves a smoldering panuveitis with acute episodic flares of granulomatous anterior uveitis that may be resistant to corticosteroid therapy.\textsuperscript{2,3} Complications of recurrent and smoldering inflammation include cataract formation, uveitic glaucoma, posterior synechiae, chorioretinal atrophy and subretinal neovascularization.\textsuperscript{2,3} The convalescent stage of the disease is predominantly characterized by degeneration of the skin and choroid. This stage consists of poliosis, vitiligo, alopecia and most notably, the “sunset-glow” fundus, which describes a red-orange appearance of a pale optic nerve surrounded by peripapillary/juxtapapillary chorioidal depigmentation.\textsuperscript{2,3}

The exudative process in VKH classically causes detachment of the neurosensory retina from the RPE, as well as bacular layer detachments (BALADs), which is what was seen in our patient.\textsuperscript{4,5} While BALADs were initially described as multilobulated serous retinal detachments due to the presence of subretinal fibrin and septae, advances in OCT technology have allowed better structural analysis.\textsuperscript{4,5} The term BALAD describes intraretinal separation where the photoreceptor inner segments are detached from the outer segments and underlying ELM.\textsuperscript{4,5}

**Treatment**

The mainstay of treatment for the acute uveitic phase is aggressive systemic and topical corticosteroid use.\textsuperscript{2} Initial treatment can be 60mg to 100mg per day of prednisone or a 200mg intravenous loading dose of methylprednisolone for three days with an oral taper; patients require a prolonged taper often for longer than six months.\textsuperscript{2} The chronic-recurrent phase of the disease is less responsive to corticosteroid therapy and often requires the use of other biologic or cytotoxic immunosuppressive agents (e.g., azathioprine, cyclophosphamide, mycophenolate moftil and tacrolimus).\textsuperscript{2} Patients can often regain visual acuity of 20/40 or better barring any complications as previously mentioned.\textsuperscript{2}


**ABOUT THE AUTHOR**

Dr. Aboumourad currently practices at Bascom Palmer Eye Institute in Miami. He has no financial disclosures.
Join Review Education Group and MedscapeLIVE! this December for the West Coast Optometric Glaucoma Symposium (WCOGS) and Retina Update 2022. The conferences will be co-located at the Hilton La Jolla Torrey Pines in La Jolla, California. Attendees are encouraged to participate in both symposia to greatly enhance their learning experience.

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www.reviewedu.com/winteroptometry
A 69-year-old white male presented for a routine eye exam without any ocular complaints. His ocular history was remarkable for a superficial corneal foreign body with removal and no complications over five years ago. His systemic history was remarkable for hypertension and benign prostatic hyperplasia, for which he was properly medicated. He reported no allergies.

Clinical Findings
The patient’s best-corrected entering visual acuity measured 20/20 OD and 20/20 OS at distance and near. His external examination was normal, confrontation visual fields were full and there was no afferent pupillary defect. The anterior segment biomicroscopic exam demonstrated normal structures with mild cataracts and Goldmann applanation pressures that measured 13mm Hg OU. The pertinent fundus findings from the dilated posterior segment examination are demonstrated in the photographs.

For More Information
Additional tests for this case might include a spectral-domain or swept-source OCT of the optic nerve OS to determine the depth of tissue and vasculature involvement, Amsler grid testing OU to rule out metamorphopsia OS, B-scan ultrasonography OS to better understand the extent of the lesion and visual field testing to rule out any functional deficits.

A frequency-doubling perimetry test was completed and found to be normal, OU. Referral to a retina specialist is prudent even in the event the diagnosis is known.

Your Diagnosis
What would be your diagnosis in this case? What is the patient’s likely prognosis? To find out, please read the online version of this article at www.reviewofoptometry.com.

Dr. Gurwood thanks Oskar Shura, HBSc, Virginia Donati, OD, FCOVD, and Michelle McKenzie, OD, FCOVD, for contributing this case.

An otherwise routine visit reveals a suspicious finding. What is the appropriate course of action?

Retina Quiz Answers (from page 94)—Q1: d, Q2: d, Q3: d, Q4: c, Q5: b

NEXT MONTH IN THE MAG
In July, we present our annual glaucoma report. Articles will include:

• Advanced Glaucoma Management: How to Handle Endstage Patients
• Effective Follow-up Care Strategies for MIGS Patients

Also in this issue:
• Vital Dyes for Dry Eyes: How to Read Staining Patterns Better
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