NEW DIRECTIONS IN GLAUCOMA CARE

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NEW DIRECTIONS IN GLAUCOMA CARE

Experts explain the latest thinking on nine ways your clinical responsibilities are changing. **PAGE 34**

**PLUS:**

*Breaking Down the Barriers to Success in Glaucoma*, PAGE 44
*A Guide to Seeing Existing Patients for the First Time*, PAGE 50
*MIGS: Your Role in the Post-op Experience*, PAGE 56
INDICATIONS AND USAGE
IYUZEH™ (latanoprost ophthalmic solution) 0.005% is a prostaglandin F2α analogue indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION
CONTRAINDICATIONS
Known hypersensitivity to latanoprost or any other ingredients in this product.

WARNINGS AND PRECAUTIONS
IYUZEH may cause changes to pigmented tissues. Most frequently reported changes are increased pigmentation of the iris, periorbital tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as IYUZEH is administered. Iris pigmentation is likely to be permanent. Eyelid skin darkening and eyelash changes may be reversible.
IYUZEH may cause gradual change to eyelashes including increased length, thickness, and number of lashes. These changes are usually reversible upon discontinuation of treatment.
IYUZEH should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation.

IYUZEH should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema. Reactivation of herpes simplex keratitis has been reported during treatment with latanoprost. IYUZEH should be used with caution in patients with a history of herpetic keratitis.

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

ADVERSE REACTIONS
The most common adverse reactions (5% to 35%) for IYUZEH are: conjunctival hyperemia, eye irritation, eye pruritus, abnormal sensation in eye, foreign body sensation in eyes, vision blurred, and lacrimation increased.

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

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

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

Initial U.S. Approval: 2022

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Pigmentation: Topical latanoprost ophthalmic products, including IYUZEH have been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, peribulbar tissue (eyelid), and eyelashes. Pigmentation is expected to increase as long as latanoprost is administered. The pigment change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of latanoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the peribulbar tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known. Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither new nor freckles of the iris appear to be affected by treatment. While treatment with IYUZEH can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

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

Intraocular Inflammation: IYUZEH should be used with caution in patients with a history of intraocular inflammation (iritis/uveitis) and should generally not be used in patients with active intraocular inflammation because inflammation may be exacerbated.

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

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

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

ADVERSE REACTIONS

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

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

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

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

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

POSTMARKETING EXPERIENCE

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

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

DRUG INTERACTIONS

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

USE IN SPECIFIC POPULATIONS

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

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

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

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

OVERDOSAGE

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

HANDLING THE CONTAINER

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

Manufactured for: Thea Pharma Inc. Waltham, MA.
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U.S. Patent N°. 8,637,054.
Revised: 04/2023
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FTC Votes to Require Rx Release Confirmation

The long-anticipated update goes into effect 60 days after publication in the Federal Register, which is expected “soon.”

Eye care practices will now be obliged to obtain a signed confirmation of receipt from each patient who’s given a copy of their spectacle lens Rx and keep this on hand for three years in order to be in compliance with the Ophthalmic Practice Rule (a.k.a. the Eyeglass Rule) of the Federal Trade Commission (FTC). The Commission announced the update on June 27. The requirement only applies to practices with an optical dispensary.

“For decades, the FTC’s Eyeglass Rule has promoted competition by ensuring that consumers can shop around for lower prices,” said Samuel Levine, director of the Bureau of Consumer Protection, in an FTC press release. “The FTC’s updated rule will strengthen compliance and make this market more fair and competitive.”

“Eyeglasses, like contact lenses, are the stuff of everyday life and kitchen-table budgeting,” wrote Commissioner Rebecca Kelly Slaughter in a separate statement. “The rulemaking record underscores how important the prescription-release requirement is to budget-conscious consumers, too many of whom have not benefited from it, even though it has been the law since 1978.”

“Despite the rule’s longstanding existence, prescribers have not always complied with the automatic release requirement,” the FTC statement says, adding that the agency “has sent warning letters to prescribers reminding them that they must provide patients with prescriptions at the end of an exam and cannot charge a fee or require eyeglass purchase for prescription release. But even so, surveys of consumers have repeatedly found that many consumers do not automatically receive their prescription following each refractive eye exam.”

The Commission began a review of the rule in December 2022 and invited public comment from consumers and practitioners on potential revisions needed to strengthen enforcement. In a letter to the FTC dated March 6, 2023, the American Optometric Association (AOA) voiced its concerns. “Doctors of optometry practices often do not have large teams of staff members,” noted the AOA’s letter. “Across the country, 91.9% of optometry practices have fewer than 25 employees. We understand that the FTC may view an additional form or documentation requirement to be a small update to the rule, but staffing challenges in medical practices cause serious issues that should not be dismissed lightly.” The AOA letter cited a recent study that found that staffing shortages led to increased medical errors for 34% of doctors worldwide. Such concerns do not appear to be addressed in the final rule or FTC statement.

“Too many officials and agencies remain out of touch with what we face every day in our practices, and the result can be an emboldened bureaucracy and schemes for burdensome new mandates,” says AOA President Steven T. Reed, OD, in a recent AOA article responding to the Eyeglass Rule update. “Our AOA will never stop fighting to change that and to stand up for the doctor-patient relationship as the foundation of optometry’s essential and expanding role in health care.”

In addition to the new confirmation requirement, other changes to the rule are as follows:

- The practice can provide the glasses Rx digitally if the patient agrees.
- Release of the Rx “must be provided immediately after the examination is completed” and the patient “must have their prescription before any offer to sell them glasses.”
- Presentation of proof of insurance coverage shall be deemed to be a payment for the purpose of determining when a prescription must be provided.
- The term “eye examination” will be changed to “refractive eye examination” throughout the text and emphasis will be placed on the need for prescribers to educate consumers that there can be a difference between an eye health examination and a refractive eye examination.

The FTC statement says the final rule “will be published in the Federal Register soon and will become effective 60 days after publication.”
Scope Bill Passed in D.C. Excludes Optometry

ODs’ right to prescribe controlled substances and manage glaucoma without MD oversight was removed from the legislation during amendments. Now, just two scope bills remain as contenders this year in Ohio and NJ.

In October 2023, Washington, D.C. introduced Council Bill 25-0545, which proposed an update to the District of Columbia Health Occupations Revision Act of 1985 to modernize the practice scope of numerous allied health professionals in the jurisdiction, including optometrists, podiatrists and pharmacists. The original document stated that if the proposed changes were granted, “the scope of optometry will authorize optometrists to prescribe controlled substances rational to the diagnosis and treatment of diseases of the human eye and its adjacent structures,” which would have encompassed the right to diagnose and treat glaucoma.

After several months of litigation, D.C. Mayor Muriel Bowser approved the bill in early June. Unfortunately for optometry, however, the language cited above that would have authorized ODs in D.C. to prescribe controlled substances was stripped during amendments and excluded from the enacted document.

“This decision was influenced by a range of factors, including expert testimonies, research findings and concerns regarding patient safety and public health,” stated the recent report from the D.C. Committee on Health. “The Committee received live or written testimonies from over 20 public witnesses, primarily ophthalmologists, strongly opposing the expanded scope of practice for optometrists,” it continued. One point of contention raised by the opposing side, the Committee explained, “was the disparity in training and education between optometrists and ophthalmologists,” an argument that organized medicine banks of the requirement for ODs to consult an ophthalmologist before initiating glaucoma treatment. In addition, OMDs testified that access to board-certified ophthalmologists is readily available within even the most underserved areas in D.C.

A plethora of evidence threatens the strength of this case against ODs. Washington D.C. is one of the few remaining areas in the country where optometrists are prohibited from prescribing controlled substances, accompanied only by Hawaii, Maryland and New York. In the remaining 47 states, ODs have consistently exemplified the safety and necessity of these expanded pharmaceutical privileges.

“The Committee received written testimony from numerous optometrists and a letter from the Association of Regulatory Boards of Optometry citing the necessity for optometrists to prescribe pain medication and advocating for the removal of consultation requirements before treating chronic open-angle glaucoma,” the Committee wrote in its report. “D.C. Health referenced similar actions in other states without reported issues.”

A spokesperson for the D.C. Department of Health also told Review of Optometry that the proposed bill failed to flesh out guidelines regarding telehealth, such as licensing requirements for out-of-state practitioners delivering virtual care to patients in D.C. In the coming months, the D.C. Board of Optometry will work on developing these policies and rules to prepare for the next legal endeavor to expand the practice scope for D.C. optometrists.

Remaining Active Scope Battles

Despite starting the year with more than a dozen pieces of legislation advocating increased practice privileges for ODs, just two remain on the docket for 2024. Ohio’s scope expansion bill, SB 129, has been moving at a slow but steady pace since its introduction last June. The legislation aims to add the state’s name to the current list of 12 where optometrists can perform laser procedures, including YAG capsulotomy, SLT and LPI. It would also permit Ohio ODs to remove benign lesions, cysts and skin tags, broaden pharmaceutical privileges, allow epinephrine injections and give the Vision Professionals Board more authority to establish training guidelines.

The Ohio Senate Health Committee heard proponent testimony in late April and opponent testimony last month. The state’s legislature is now in summer recess and will resume in autumn.

Like Ohio, New Jersey’s legislature also recently entered its summer recess. This state has two identical laser bills in the running—A-920 and S-354—proposing many of the same privileges as the bill in Ohio, including YAG capsulotomy, SLT, LPI, removal of styes and skin tags as well as an expansion of vaccine and prescription authority. Once the legislative session resumes in the fall, the New Jersey Society of Optometric Physicians is hopeful that the bills will continue moving forward in their respective committees. As of now, A-920 is on second reading in the Assembly Regulated Professions Committee, while S-354 rests in the hands of the Senate Commerce Committee.”
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In US, Laser Now Preferred Over Drops for POAG Among Younger Ophthalmologists

A recent survey assessed the practice preferences of ophthalmologists for the initial management of glaucoma. The researchers hypothesized that the multitude of options and accumulated evidence for primary open-angle glaucoma (POAG) treatment in the past decade will reflect a different preference pattern than reflected in a retrospective claims analysis of data from 2007 to 2014. Their study, published in Journal of Glaucoma, revealed that, for the first-line treatment of POAG, laser trabeculoplasty was more likely to be preferred over topical drops by US physicians who are relatively new in practice, have a larger glaucoma patient base and perform more MIGS.

The study determined to characterize primary treatment preferences (topical medication vs. laser trabeculoplasty or intracameral sustained-release implants) in POAG patients and determine factors related to primary intervention selection. A 33-question survey was distributed to an American Society of Cataract and Refractive Surgery database on treatment choices made by ophthalmologists for POAG. A total of 252/19,246 (1.3%) of surveys were returned.

Multiple logistic regression determined that 73.6% of respondents used topical medication as the first-line of treatment for POAG, while 26.4% preferred to start with laser treatment. Significant variables associated with the selection of laser (vs. drops) are practicing in the US (odds ratio [OR]: 2.85), more recent completion of ophthalmology residency (OR: 1.95), greater volume of MIGS (OR: 1.68) and a glaucoma patient base greater than 25% (OR: 2.21). For doctors preferring laser treatment as the first-line option, the leading indications for using Dursysta (bimatoprost SR, Allergan), a prostaglandin analog, are for patients who show intolerance to drops (19%), are non-responsive to SLT (17%) or wish to reduce medication dependence (17%). For MDs preferring primary topical treatment for POAG, the leading indications for using bimatoprost SR are for drop intolerance (25%), noncompliance (26%) or as an alternative to medication dependence (17.5%).

“It was also observed that the majority of either group, laser or topical drops first, preferred a trabecular meshwork bypass stent in cases of moderate POAG and visually significant cataract,” the study authors wrote in their paper. “[This finding] is likely reflective of a shift in preferred practice and community standards based on the relative safety and efficacy of this combined approach.”


Type 2 Diabetes Drug May Reduce RVO Risk

Retinal vein occlusion (RVO) is reported in 3.4% of patients with type 2 diabetes. The effects of different diabetes treatments on RVO risk remain unclear, leading researchers to perform a new study to compare the risk of RVO development in patients on sodium–glucose cotransporter–2 inhibitors (SGLT-2i) vs. dipeptidyl peptidase–4 inhibitors (DPP-4i). It revealed that patients on the former drug had a significantly lower risk than those on DPP-4i.

The nationwide retrospective cohort study used claims data from the National Health Insurance Research Database of Taiwan. More than 700,000 patients with type 2 diabetes were included, all of whom had no prior diagnosis of RVO and had newly commenced treatment with either SGLT-2i (n=123,567) or DPP-4i (n=578,665). Over a mean follow-up period of 1.6 years, the incidence of RVO was lower in patients newly receiving SGLT-2i (0.59 events per 1,000 person-years) compared to DPP-4i (0.77 events per 1,000 person-years). SGLT-2i users had a significantly lower risk of developing RVO compared to DPP-4i users (hazard ratio=0.76). This trend varied depending on RVO type, however; SGLT-2i use was significantly associated with a 29% reduced risk for branch RVO (HR=0.71) but not central RVO (HR=0.84).

To help explain this finding, the researchers noted in their paper that “arteriosclerosis and elevated blood pressure, which are crucial elements in RVO, tend to be more prevalent in cases of BRVO. SGLT-2i may have better pleiotropic effects in reducing blood pressure, BMI and blood lipids compared to DPP-4i; thus, its positive impact would be more noticeable in preventing BRVO.” These results suggest that SGLT-2i may be beneficial for reducing RVO risk in patients with type 2 diabetes.

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† High oxygen transmissibility promotes clear, white eyes during daily wear.
‡ During daily wear.
§ In the US market. Tylers Quarterly, December 2021 issue.
¹. CVI data on file, 2024. US industry reports and internal estimates.
². CVI data on file, 2020. Kubic masked online survey; n=404 US ODs who prescribe toric soft CLs.
³. CVI data on file, 2023. Based on number of US soft contact lens fits, including CooperVision-branded and customer-branded equivalent lenses. US industry reports and internal estimates.
⁴. CooperVision data on file 2021. Rx coverage database n=101,973 aged 14 to 70 years.
Chronic Pain May Share Pathway with Dry Eye

A large meta-analysis found the ocular surface disease was positively linked with more severe symptoms in these patients than in controls.

One recent meta-analysis examined multiple studies across databases to review the relationship between pain and dry eye. Specifically, researchers from Queensland University in Australia wanted to evaluate the relative contributions of objective and subjective indicators of dry eye disease (DED) in patients with chronic pain conditions vs. controls.

Included in the meta-analysis were 14 total observational studies encompassing 3,281,882 individuals. All included studies had the International Association for the Study of Pain International Classification of Disease (ICD)-11 codes for chronic pain conditions applied. Upon analysis, high-quality evidence supported that those with chronic pain were more likely to experience DED symptoms than controls, and these symptoms were more severe. Chronic pain patients also displayed more rapid tear film disruption and reduced tear production compared with controls with moderate quality evidence. Those with chronic pain also had lower basal tear production (anesthetized). However, tear film osmolarity did not display significant differences between the groups, and group differences for DED signs were not considered clinically meaningful.

In their discussion, the study authors elaborate that, despite the group differences for DED signs being statistically significant, they were arguably of subclinical effect size, suggesting dry eye symptoms in those with chronic pain may not be fully attributable to ocular surface pathology. Indeed, this discordant phenotype of DED of symptomatology but with minimal or no signs may reflect central and/or peripheral somatosensory nociceptive pathway dysfunction.

What’s more, rapid tear film instability in irritable bowel syndrome was revealed upon subgroup analysis, as was a higher tear film osmolarity in fibromyalgia than for other chronic pain conditions. These were clinically meaningful, but it should be noted that these instances may reflect inherent differences between various chronic pain conditions. Also clinically meaningful was the difference in DED symptoms for the Ocular Surface Disease Index between chronic pain patients and controls.

The increased prevalence and severity of DED symptoms in chronic pain conditions was not matched by clinical signs of the condition. Tear film osmolarity was not different between the groups and only a small, subclinical magnitude was observed with measures of tear break-up time and Schirmer Test 2. The only clinically significant one observed was a reduction in tear production (Schirmer Test 1).

Since these patients may be experiencing worse DED due to underlying nociceptive processing dysfunction or neuropathic mechanisms, the authors suggest that “highly symptomatic individuals with a chronic pain comorbidity may benefit from treatment targeting neuropathic and/or nociceptive mechanisms (such as a multimodal approach with initial use of anti-inflammatory agents and centrally acting medications including α25 ligand anticonvulsants, tricyclic antidepressants and serotonin-norepinephrine reuptake inhibitors, or improving physical activity, sleep and stress, respectively)” and also encourage a knowledge of mental health associations and a multidisciplinary management approach.

They also add that “clinicians managing patients with a chronic pain condition should be cognizant of associations with symptomatic DED and refer to optometry/ophthalmology when indicated.”

**IN BRIEF**

**Blood Pressure Medication May Increase POAG Risk.** Calcium channel blockers (CCB) are commonly prescribed to treat hypertension, but the literature suggests that these drugs may increase the risk of primary open-angle glaucoma (POAG). Since both of these often comorbid conditions are highly prevalent in Black populations, researchers turned to the NIH All of Us dataset, a cohort known for its demographic, geographic and medical diversity. They found that certain CCBs are associated with a significantly higher risk of POAG.

The retrospective study included 213,424 participants 40 years of age or older with no prior POAG diagnosis. In the cohort, 1.3% of patients were diagnosed with POAG and 98.7% were not. In the POAG group, the mean age was 73 years, 52.5% were female and 48.2% were white. Among those who developed POAG, 32.6% used one or more CCBs, 28.2% used a dihydropyridine CCB and 2.2% used a non-dihydropyridine CCB.

Bivariate analysis and multivariate adjusted analysis both showed use of any CCB—but especially dihydropyridine CCBs—was associated with increased risk of POAG.

The researchers wrote in their *Ophthalmology Glaucoma* paper that relationship between CCBs and ocular health is complex, but that use of these commonly prescribed antihypertensives may be associated with glaucoma. “A growing evidence base is needed to better understand how to balance treatment needs for glaucoma and hypertension, particularly in an aging population with growing prevalence and public health burden of both conditions,” they concluded.

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ORS Case Report Contest Winner Announced

Dr. Vasudha Rao of Palo Alto VA was honored for her paper on a case of “poppers” maculopathy.

The Optometric Retina Society (ORS) has announced this year’s winner of its annual Larry Alexander Resident Case Report Contest. Vasudha Rao, OD, an ocular disease, low vision and geriatric optometry resident at the Palo Alto VA, presented a case involving a 41-year-old white male with poppers maculopathy, a condition characterized by bilateral subfoveal ellipsoid zone disruption, yellow foveal spot and reduced visual acuity. Dr. Rao’s report discusses differential diagnoses based on macular OCT, the various manifestations of the condition and options for management.

This case was selected by the ORS Awards Committee as the winner of the seventh annual contest, named in honor of Larry Alexander, OD, who passed away in April 2016. Dr. Alexander had a distinguished career as an educator at the University of Alabama Birmingham School of Optometry, a prominent lecturer and, perhaps most notably, author of the seminal work Primary Care of the Posterior Segment. He was also a past president of the ORS. The group chose to honor his legacy by accepting case reports from optometric residents across the country relating to vitreoretinal disease.

“It is truly an honor to chair the Larry Alexander Case Report Contest, as it provides me with the unique opportunity to read case reports from residents nationwide,” says Julie Rodman, OD, professor and chief of the Fort Lauderdale (Broward) Eye Care Institute at Nova Southeastern University in Florida. “These residents are knowledgeable and amazing writers. There is no doubt that they are being provided with amazing clinical experiences. This year’s winner provided an outstanding report on poppers maculopathy.”

Dr. Rao’s case report notes that poppers maculopathy is a rare, bilateral condition most common in men that is associated with the use of nitrite alkyl inhalants, an angina drug often used recreationally to bring about feelings of euphoria. Poppers contain alkyl nutrients that induce an upregulation of nitric oxide synthase, which produces excessive nitric oxide. High amounts of nitric oxide can increase light response of cones, causing chronic activation and apoptosis of foveal cones. This theory, Dr. Rao’s report states, explains why excessive cone activation in poppers maculopathy can resemble photic maculopathy.

The paper on Dr. Rao’s case also emphasizes the importance of how this condition is reversible, as foveal EZ-RPE disruption on OCT and visual acuity loss often improve over time, and cessation of the illicit drug may improve visual and functional outcomes for patients.

The full text and images of Dr. Rao’s paper are available at reviewofoptometry.com.

OCT Predicts VF Status, May Reduce Need for Perimetry

The “structure vs. function” debate in glaucoma and other ocular conditions might one day be collapsed into a single concept that encompasses both, if emerging research bears fruit. One new study suggests it may in time be possible to reduce the frequency of visual field (VF) testing for glaucoma patients by using deep learning estimates of functional damage measured on spectral-domain OCT. In a new paper on AI efforts in glaucoma assessment, a research team from Switzerland explained, “It has now been shown that localized (glaucosmatous) defects of the retinal nerve fiber layer (RNFL) can be recognized reliably using SD-OCT even before VF defects become apparent in perimetry.”

To see whether this method of VF assessment is reliable enough for clinical practice and how it stacks up against standard automated perimetry (SAP) in the prediction of VF performance, the team of researchers performed a retrospective observational study. The cohort included 5,238 unique eyes classified as suspects or diagnosed with glaucoma. All patients underwent ophthalmologic examination consisting of SAP, macular OCT and peripapillary OCT on the same day. Deep learning models were trained to estimate VF mean deviation and cluster mean deviation using retinal thickness maps from seven layers: RNFL, ganglion cell layer and inner plexiform layer (GCL + IPL), inner nuclear layer and outer plexiform layer, outer nuclear layer, photoreceptors and retinal pigmented epithelium, choriocapillaris and choroidal stroma and total retinal thickness.

The results showed that the deep learning models trained on retinal thickness maps and optic nerve head scans could accurately predict VF parameters in glaucoma patients, achieving better performance than the baseline linear regression model. Specifically, the RNFL, GCL + IPL and total retinal thickness achieved the best performance of all the retinal layers in predicting the mean deviation of the VF. Moreover, combining macular and optic nerve head scans improved the accuracy of mean deviation.
and cluster mean deviation prediction in glaucoma patients.

The performance of the deep learning model may also be influenced by the severity and stage of glaucoma, the researchers suggested. Their evaluation determined that the model performed best in predicting early and moderate glaucoma, but its effectiveness diminished notably in instances involving both glaucoma suspects and those with severe glaucoma.

A noteworthy limitation of this study is its reliance on automatically extracted layer segmentations to generate thickness maps, which may subject the model to segmentation errors. The researchers note in their paper for *Translational Vision Science & Technology* that they plan to use unsegmented macular scans in a future investigation to eliminate this possibility.

“Accurate estimation of visual function from SD-OCT imaging can identify disease earlier and determine progression faster, enabling individualized VF testing frequency and reducing the overall need for VF tests,” the researchers summarized in their paper. “Deep learning models can estimate changes in VF results and postpone or recommend further testing, providing cost savings and standard metrics for monitoring patient visual function while reducing reliance on VF testing.”

The authors concluded that using their deep learning approach to extract relevant information from OCT images “could lead to new biomarkers for clinical decision-making and improve personalized patient care.”


In this image from the study, an AI technique called class activation mapping is used to highlight areas of peripapillary OCT scans that contribute to the patient’s visual performance as determined by standard automated perimetry (SAP). Examples of early (top row), moderate (middle) and advanced glaucoma (bottom) are shown. In time, the researchers believe, AI models will be able to predict VF status without need for the patient’s SAP data.
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Expanding Options for AREDS 2 in AMD: PreserVision Formulas

Dr. Jeffry Gerson, OD, FAAO

AMD is a leading cause of vision loss in Americans 50 years of age or older and the leading cause of blindness for those 65+. From 2022 to 2023, optometry was a leading specialty in managing patients with AMD, so optometrists' understanding of AMD is of vital importance.

Patients with AMD often manage multiple health conditions and health goals simultaneously. Four in 10 seniors suffer from 2 or more chronic health conditions, and on average, patients are trying to manage 6 health and wellness goals. Additionally, over 30% of patients 60 years and older take 5 or more prescription drugs a day, and more than 60% of those 65 years and older have 2 or more chronic conditions. Because of patients’ often complex daily regimens, eyecare providers (ECPs) can prioritize treatments that reduce overall patient burden, such as those that reduce the number of pills a patient has to take daily.

**Preservision** is made with your AMD patients in mind.

The Bausch + Lomb Preservision AREDS 2 formulas were developed based on 20 years of clinical research and contain the exact levels of nutrients recommended by the National Eye Institute to help reduce the risk of progression of moderate-to-advanced AMD. Bausch + Lomb has expanded the Preservision portfolio to include convenient forms that help the consumer experience and deliver added benefits to address multiple health needs of patients with moderate-to-advanced AMD.

**Preservision AREDS 2 Formula with OCUsorb**

Patients' ability to absorb and make use of nutrients diminishes with age. The Preservision AREDS 2 formula eye vitamins with OCUsorb contains a novel, patented formulation of micronized lutein and zeaxanthin that was clinically shown to enhance oral bioavailability, with two-times better absorption.

**Preservision AREDS 2 Formula Plus CoQ10**

People with AMD have increased risk of cardiovascular disease. Preservision AREDS 2 + CoQ10 contains the ocular benefits of the AREDS 2 formula plus 100 mg of high-quality coenzyme Q10 (CoQ10), an antioxidant that helps support healthy heart function.

**Empowering patient adherence**

Asking patients about their dietary and medication habits can help determine which AREDS 2 formula supplement may be appropriate for them. Optometrists have a unique opportunity not only to help patients with moderate-to-advanced AMD reduce their risk of progression but also to address the lifestyle challenges that may impede adherence to vitamin supplementation.

**ECP insight**

“I know my patients are dealing with multiple conditions, so I’m always looking for ways to make their lives easier. I want them to stay on their vitamin regimen, so I support options that reduce the number of pills they need to take.”

For patients with moderate-to-advanced AMD. For AREDS 2,$l_{	ext{final}}$ + zeaxanthin compared to original Preservision AREDS 2 Soft Gel.

*These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.*


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Andrew S. Gurwood, OD

We Welcome Your Comments!
Write to editor@reviewofoptometry.com
INTRODUCING

THE RYZUMVI™ DIFFERENCE

Reverse dilation and reimagine the post-dilation experience for patients.¹,²

RYZUMVI™ (phentolamine ophthalmic solution) 0.75%

1. RYZUMVI is the first and only relatively non-selective alpha-1 and alpha-2 adrenergic antagonist approved to reverse pharmacologically-induced mydriasis.¹

2. RYZUMVI reversibly binds to alpha-1 adrenergic receptors on the radial iris dilator muscle, thereby reducing pupil diameter, and indirectly reverses mydriasis induced by muscarinic antagonist effects on the iris sphincter muscle.¹

The onset of action after administration of RYZUMVI generally occurs in 30 minutes, with the maximal effect seen in 60 to 90 minutes, and the effect lasting at least 24 hours.¹

INDICATION
RYZUMVI™ (phentolamine ophthalmic solution) 0.75% is indicated for the treatment of pharmacologically-induced mydriasis produced by adrenergic agonists (e.g., phenylephrine) or parasympatholytic (e.g., tropicamide) agents.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions
• Uveitis: RYZUMVI is not recommended to be used in patients with active ocular inflammation (e.g., iritis).

• Potential for Eye Injury or Contamination: To avoid the potential for eye injury or contamination, care should be taken to avoid touching the vial tip to the eye or to any other surface.

• Use with Contact Lenses: Contact lens wearers should be advised to remove their lenses prior to the instillation of RYZUMVI and wait 10 minutes after dosing before reinserting their contact lenses.

Adverse Reactions
The most common adverse reactions that have been reported are instillation site discomfort (16%), conjunctival hyperemia (12%), and dysgeusia (6%).

Please see Brief Summary of Prescribing Information on the adjacent page and the full Prescribing Information at RYZUMVI.com.
**BRIEF SUMMARY:** Consult the full Prescribing Information for complete product information available at www.RYZUMVI.com

**INDICATIONS AND USAGE:** RYZUMVI is indicated for the treatment of pharmacologically-induced mydriasis produced by adrenergic agonists (e.g., phenylephrine) or parasympathomimetic (e.g., tropicamide) agents.

**CONTRAINDICATIONS:** None.

**WARNINGS AND PRECAUTIONS**
- **Uveitis:** RYZUMVI is not recommended when active ocular inflammation (e.g., iritis) is present because adhesions (synechiae) may form between the iris and the lens.
- **Potential for Eye Injury or Contamination:** To avoid the potential for eye injury or contamination, care should be taken to avoid touching the vial tip to the eye or to any other surface.
- **Use with Contact Lenses:** Contact lens wearers should be advised to remove their lenses prior to the instillation of RYZUMVI and wait 10 minutes after dosing before reinserting their contact lenses.

**ADVERSE REACTIONS**

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

RYZUMVI was evaluated in 642 subjects in clinical trials across various subject populations. The most common ocular adverse reactions reported in >5% of subjects were instillation site discomfort including pain, stinging, and burning (16%) and conjunctival hyperemia (12%). The only non-ocular adverse reaction reported in >5% of subjects was dysgeusia (6%).

**USE IN SPECIFIC POPULATIONS**

**Pregnancy:** Risk Summary: There are no available data with RYZUMVI administration in pregnant women to inform a drug-associated risk. In animal toxicology studies, when phentolamine was administered orally to pregnant mice and rats during the period of organogenesis skeletal immaturity and decreased growth was observed in the offspring at doses at least 24-times the recommended clinical dose. Additionally, a lower rate of implantation was seen in pregnant rats treated with phentolamine administered at least 60-times the recommended clinical dose. No malformations or embryofetal deaths were observed in the offspring of pregnant mice, rats, and rabbits administered phentolamine during the period of organogenesis at doses of at least 24-, 60-, and 20-times, respectively, the recommended clinical dose (see Data). RYZUMVI should only be used during pregnancy if the potential benefit justifies the potential risk to the fetus.

**Data Animal Data** Oral administration of phentolamine to pregnant rats and mice at doses at least 24-times the recommended clinical dose (based on a body weight per surface area (mg/m2) comparison with a 60-kg human) resulted in slightly decreased growth and slight skeletal immaturity of the fetuses. Immaturity was manifested by increased incidence of incomplete or unossified calcanei and phalangeal nuclei of the hind limb and of incompletely ossified sternebrae. At oral phentolamine doses at least 60-times the recommended clinical dose (based on a mg/m2 comparison with a 60-kg human), a slightly lower rate of implantation was found in rats. Phentolamine did not affect embryonic or fetal development in rabbits at oral doses at least 20-times the recommended dose (based on a mg/m2 comparison with a 60-kg human). No malformations or embryofetal deaths were observed in the rat, mouse or rabbit studies.

**Lactation:** Risk Summary: There is no information regarding the presence of phentolamine in human milk, the effects on the breastfed infants, or the effects on milk production during lactation to inform risk of phentolamine ophthalmic solution 0.75% to an infant. The developmental and health benefits of breastfeeding should be considered along with the mother’s clinical need for RYZUMVI and any potential adverse effects on the breastfed child from RYZUMVI.

**Pediatric Use:** The safety and effectiveness of RYZUMVI have been established in pediatric patients aged 3 to 17 years. No overall differences have been observed between pediatric and adult subjects.

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

**OVERDOSAGE**

No deaths due to acute poisoning with phentolamine have been reported. Overdosage with parenterally administered phentolamine is characterized chiefly by cardiovascular disturbances, such as arrhythmias, tachycardia, hypotension, and possibly shock. In addition, the following might occur: excitation, headache, sweating, visual disturbances, nausea, vomiting, diarrhea, or hypoglycemia. There is no specific antidote; treatment consists of appropriate monitoring and supportive care. Substantial decreases in blood pressure or other evidence of shock-like conditions should be treated vigorously and promptly.

**CARCINOGENESIS, MUTAGENESIS, IMPAIRMENT OF FERTILITY**

**Carcinogenesis:** Carcinogenicity studies with RYZUMVI have not been conducted.

**Mutagenesis:** Phentolamine was not mutagenic in the in-vitro bacterial reverse mutation (Ames) assay. In the in-vitro chromosomal aberration study in Chinese hamster ovary cells, numerical aberrations were slightly increased after a 4-hour exposure to phentolamine without metabolic activation, and structural aberrations were slightly increased after a 4-hour exposure to phentolamine with metabolic activation only at the highest concentrations tested, but neither numerical nor structural aberrations were increased after a 20-hour exposure without metabolic activation. Phentolamine was not clastogenic in two in-vivo mouse micronucleus assays.

**Impairment of Fertility:** The effect of phentolamine on female fertility has not been studied. Male rats treated with oral phentolamine for nine weeks (four weeks prior to mating, 3 weeks during the mating period and 2 weeks after mating) were mated with untreated females. At doses up to 648-times human therapeutic exposure levels at the Cmax, no adverse effects on male fertility parameters or on reproductive parameters in the untreated females mated with the treated males were observed.

**Marketing by:** Oyster Point Pharma, Inc., a Viatris company

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OVERVIEW

This comprehensive one-day event is designed to provide optometrists with a deep dive into ocular surface disease with an emphasis on dry eye, MGD, and blepharitis. Experts will share the latest data, research, and current treatment strategies. Numerous clinical cases will be shown to demonstrate critical advances in diagnostic and therapeutic options for ocular surface disease, MGD, and blepharitis.

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Get Going on Gonio

This simple procedure is essential to glaucoma patient care—and maybe to optometry’s wider ambitions, too.

Our annual glaucoma issue is always a great opportunity to take stock of optometry’s successes and struggles with this important responsibility. You don’t need me to tell you once again that the only way the burden of glaucoma care can be met is if ODs step up and fully embrace it (oops, I guess I just did).

Anyway, as this is the 30th Annual Glaucoma Report, I took a look at the slate of topics in our first one, published in 1995. There was no mention of OCT or MIGS, of course—two topics that are fully embraced today. But we included lots of discussion on disease pathophysiology, exam techniques and how to understand and use meds to lower IOP. Selective laser trabeculoplasty wasn’t mentioned but its precursor ALT was, mostly as an option for late-stage cases that might not be suitable for filtering surgery. And back in 1995, only 31 states allowed ODS to prescribe glaucoma meds, even topical ones (can you imagine?), so that topic was considered cutting edge by many.

Fast-forward to today and the newest legislative frontier is laser procedures, with 12 states currently allowing ODS to perform SLT and LPI. Topical meds, while clearly still a mainstay of care, are waning in importance as first-line SLT becomes more accepted and sustained-release drugs come into their own. Head-mounted visual field testers aim to take the sting out of perimetry, and there are hints that AI-powered OCT will one day be able to do to field testing what SLT and sustained-release are currently doing to old-school topical therapy.

But one topic that only got a cursory discussion in our 1995 series—gonioscopy—seems to still be a thorn in the side of ODs. It’s not cost prohibitive and doesn’t seem difficult to perform, but rates of gonioscopic evaluation have been low for decades. This is a detriment to both patients and the profession. One of the recent scope expansion bills that made the case for optometric laser responsibilities was shot down at least in part because of data its opponents provided—showing meager rates of gonioscopy as performed by ODs. “Why should we give them lasers when they don’t do gonio?” was the narrative spun by ophthalmology. And I have to say they’re right. I call out MDs for their spurious claims against optometry all the time but that one has the ring of truth to it.

However… it turns out that ophthalmologists aren’t exactly glued to their gonio lenses either. A few months ago, AJO published a study of almost 200,000 glaucoma patients/suspects and individuals with narrow angles seen by MDs. Only 20.4% had a record of gonioscopy having been performed on the day of diagnosis and 29.5% within six months. “The overall low rate of gonioscopy is striking,” the researchers wrote. “Gonioscopy represents a crucial junction in the glaucoma management algorithm where appropriate therapy could be prescribed to prevent permanent morbidity.”

Now, it’s possible that a bunch of those patients did in fact receive a gonioscopic exam and the practice simply didn’t note it in the record. Let’s hope so. Still, that’s not much consolation, as proper documentation is obviously critical to the long-term provision of care and as legal defense against a malpractice claim.

But, you know, two wrongs don’t make a right. Ophthalmology’s negligence here is no excuse for the same behavior in optometry. You can find gonio guidance on our website in several instructional articles linked to this article. Good luck!

Outlook

OUTLOOK

Editor-in-Chief
By Jack Persico

Get Going on Gonio

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But, you know, two wrongs don’t make a right. Ophthalmology’s negligence here is no excuse for the same behavior in optometry. You can find gonio guidance on our website in several instructional articles linked to this article. Good luck!
A 33-year-old Asian Indian woman was referred to me for an evaluation. She had a history of soft contact lens wear and although she had always corrected to 20/20 or better, noted that her vision had not been “crisp” for many years. By the time we saw her, she was very unhappy with her vision, particularly in the left eye, complaining of glare and “shadows.” She refracted to 20/20 OD and 20/20 OS, with normal to borderline keratometry readings and clear corneas.

Her contact lens history showed frequent small changes in the prescription and progression of myopia and astigmatism between ages 20-31. During that time, the contact lens prescription for the right eye changed from -1.25 sphere to -3.50 -0.75 x 020 and, for the left eye, from -1.00 sphere to -2.75 -1.25 x 140. Given that myopia typically stabilizes by about age 15, the degree of myopic progression in this patient’s 20s should have been a clue that something was not right.

The patient’s medical history included asthma, eczema, and seasonal allergies, for which she was treated with an inhaler, topical creams, anti-allergy shots, and eye drops. Keratoconus is associated with all three of these atopic conditions, although it is not entirely clear whether atopy and keratoconus share common causative factors or whether corneal ectasia is provoked by eye rubbing due to itching associated with allergies.

Corneal topography and tomography was performed in this patient for the first time at age 33, during her first pregnancy. This corneal imaging ultimately confirmed the diagnosis of keratoconus; the left eye (Fig 1) was determined to be worse than the right and progressive. Unfortunately, cross-linking of the left eye had to be delayed due to the patient’s pregnancy. The delay in treatment due to pregnancy was unfortunate and could have been avoided with earlier diagnosis.

The patient underwent FDA-approved iLink® cross-linking in her right eye at age 33, during her first pregnancy. This corneal collagen cross-linking for the treatment of progressive keratoconus and corneal ectasia following refractive surgery.

REFERENCES:

Could it be KC (KERATOCONUS)?

KC File #3: KC Masquerading as Myopia

Gloria “Gadget” Chiu, OD, FAAO, FSLs, Los Angeles, CA

Dr. Chiu is a paid consultant for Glaukos.

Findings can reduce corneal stiffness and cause or exacerbate an ectatic response. iLink cross-linking is contraindicated during pregnancy because of the unpredictability of corneal changes and unknown effect on the fetus of topical drugs used during and after cross-linking.

Following unsuccessful fits with toric soft and hybrid lenses, a scleral lens was able to eliminate the shadows and higher order aberrations she was experiencing in the left eye. After delivery, the patient underwent FDA-approved iLink® cross-linking in her left eye. Both eyes have now been stable for about 7 years, and she wears toric soft contact lenses OU comfortably. She has been prescribed antihistamine eye drops and counseled to not rub her eyes. We continue to monitor her and have begun monitoring her now 7-year-old son for signs of KC.

This case illustrates that KC can present with 20/20 vision, low myopia and mild astigmatism, and no obvious changes at the slit lamp. Complaints of “shadows” and vision that is not crisp were key clues, especially in an atopic patient with progressing myopia. The delay in treatment due to pregnancy was unfortunate and could have been avoided with earlier diagnosis.

By following the KC clues that are hiding in plain sight, you can help patients get diagnosed and treated earlier, taking one more concern off your patients’ plate as they become parents themselves. Visit iDetectives.com to learn more.

#FollowTheClues

INDICATIONS: Photrexa® Viscous (riboflavin 5'-phosphate in 20% dextran ophthalmic solution) and Photrexa® (riboflavin 5'-phosphate ophthalmic solution) are indicated for use with the KXL System in corneal collagen cross-linking for the treatment of progressive keratoconus and corneal ectasia following refractive surgery.

IMPORTANT SAFETY INFORMATION: Corneal collagen cross-linking should not be performed on pregnant women. Ulcerative keratitis can occur. Patients should be monitored for elimination of epithelial defects. The most common ocular adverse reactions were corneal epithelial defects. Other ocular side effects include punctate keratitis, corneal striae, dry eye, corneal epithelial defect, eye pain, light sensitivity, reduced visual acuity, and blurred vision. There are no data on the side effects of the corneal collagen cross-linking treatment. For more information, go to www.fda.gov/ucm/groups/fdagov-public/@ucm_398015-25.

You are encouraged to report all side effects to the FDA. Visit www.fda.gov/medwatch, or call 1-800-FDA-1088.
The Blue Light Controversy

Exposure affects more than just the eyes.

There is no way to deny the potential impact of blue light, given the digital era we are in. To put this into perspective, there are approximately 340 million Americans, yet 383.4 million cellular mobile connections.1 The average American spends over seven hours a day looking at a screen, with Gen Z averaging nine hours per day.2 Can this incredible shift in blue light radiation have an impact on our ocular or more generalized health?

Not Proven, Yet

One area that can’t be proven is the negative impact of blue light on the retina. While it is certainly possible, studies would require decades to prove. I believe this controversy pushed people away from the entire subject of blue light regardless of the volume of exposure. As optometrists, we must know the impact of light on the eye and general health. There is a wealth of proven studies to guide us and significant options to help patients ranging from screen protectors (Eyesafe) to high energy visible light-blocking lenses.

Negative Impacts

We know that blue light exposure influences sleep patterns, which can lead to issues ranging from dry eye disease to obesity. A systematic review examined 24 high-quality studies and found that blue light exposure from electronic devices significantly disrupted sleep by increasing sleep latency and decreasing sleep quality. The suppression of melatonin production, a hormone essential for sleep regulation, was consistently lowered. The review highlighted the need for practical measures to mitigate blue light exposure, especially in the evening.3

Looking more specifically at late-day exposure, another study explored the effects of short-wavelength light from devices on melatonin suppression and sleep disturbances. It concluded that pre-bedtime exposure to blue light from electronic devices delayed melatonin secretion, disrupted circadian physiology and reduced sleep quality.4

A similar study found that reading on a smartphone without a blue light filter before bedtime reduced sleep quality and increased morning cortisol levels, affecting overall sleep physiology and alertness.5,6 Yet another article, from the Sleep Foundation, explains that blue light suppresses melatonin production and delays sleep onset, leading to reduced sleep quality.7

The question is: Does this lack of quality sleep have repercussions, or does blue light exposure alone lead to other diagnoses, including diseases and disorders such as depression, obesity and even cancer? A study involving over 85,000 participants found that high nighttime light exposure increased the risk of depression by 30%, while bright light during the day reduced depression risk by 20%. Similar patterns were observed for other mental health issues including anxiety and post-traumatic stress disorder.8 Furthermore, another study indicated that blue light exposure is linked to associated with increased risks of depression and other mood disorders, including bipolar disorder. It even suggests that reducing blue light exposure could be beneficial for one’s mental health.9

“...We are aware that blue light exposure late in the day can affect circadian rhythms; this demands that we educate our patients."

Another study explored the connection between light pollution and obesity and found that nocturnal light exposure is linked to an increased risk of obesity and related diseases. It also discusses how nighttime light exposure might contribute to cancer risk.9 One more study worth mentioning found that higher levels of light exposure at night were associated with a 21% higher risk of obesity and related metabolic disorders, suggesting a strong link between blue light exposure and type 2 diabetes.9,10

When I was young, in my residency and fellowship it was considered a badge of honor to be the first one to arrive at the clinic in the morning and the last one to leave. I recall times when I covered call and slept on a cot at the clinic for multiple days. I only wish I knew then what I know today—that quality and duration of sleep not only would have helped me retain more information and be more productive, but also decrease long-term risks...
Learn how to quickly identify ideal patients for punctal occlusion success. Protocols regarding punctal dilation, anesthetic, which drops to use and which punctal plug to select will be reviewed. Understanding the newest punctal plug innovations from tapered 180 day plugs to FormFit will be expounded on, so your patients can benefit from this very important dry eye disease treatment.

Learn how to optimize staff training and management for punctal plug therapy and reimbursement in the practice. This course covers all compliance forms, communication, marketing and the important code management for a successful transition to this valuable dry eye treatment.

The course covers staff education and marketing to make OTC dry eye management successful in the practice. Coding and billing using Evaluation & Management codes will be addressed in detail as well as the Oasis tools and resources.

Presented by:

Paul M. Karpecki, O.D., FAAO

With over 20 years experience running some of the largest dry eye clinics in the United States, Dr. Karpecki is a leader and pioneer in this dedicated area of optometry. He is a noted educator and author, having delivered over 1000 lectures and authored over 1000 papers on the subject of Dry Eye Disease - a condition that can negatively affect not only a patient’s vision but also their quality of life.

John W. Lahr, O.D., FAAO

Dr. John Lahr is a recognized educator on topics of nutritional supplementation, ocular surface disease, intraocular and refractive surgery, co-management, eye care coding and billing and other areas of clinical care. He was an original member of the Clinical Practice Guidelines Committee of American Optometric Association (AOA) to develop practice standards and protocols for the optometric profession. Dr. Lahr served on the AOA’s Eye Care Benefits Executive Committee for ten years and as optometry’s first representative to the American Medical Association’s CPT coding committee. He has provided guidance and consultation in multiple roles for the past 45 years.
ranging from metabolic health issues to cardiovascular disease and cancer.\textsuperscript{11} The difference today is we have the sleep-deprivation knowledge and are aware that blue light exposure late in the day can affect circadian rhythms; this demands that we educate our patients.

The National Institutes of Health National Heart, Lung and Blood Institute outlines how sleep deficiency affects overall health. It can impair learning, decision-making and emotional regulation and is linked to increased risks of obesity, diabetes, heart disease, high blood pressure and stroke. Proper sleep is essential for physical health, including maintaining a healthy hormone balance and immune function.\textsuperscript{12}

Further research showed a statistically higher risk of cancers such as those of the breast, colon, ovaries and prostate. The interplay between sleep and cancer is also significant during treatment, as sleep problems can persist long-term and impact survivors’ quality of life.\textsuperscript{13}

So, while we may never know the effects of blue light exposure on the retina, we can be assured our recommendations to block or limit exposure late in the day will have a significant effect on our patients’ cognitive ability and risk of diseases such as cancer, mental illness, cardiovascular disease and diabetes.

Mental Block

Misconceptions remain on using this long-standing glaucoma treatment in patients with heart disease.

I have a patient who has early glaucoma and a “heart condition.” I am hesitant to start a beta-blocker, but should I be?

“Recently, two different practitioners asked me whether they could use a topical beta-blocker to treat their patient’s open-angle glaucoma (OAG),” says Richard Madonna, OD, professor of optometry at SUNY College of Optometry and glaucoma expert. “One of the patients had a history of a relatively recent but mild myocardial infarction, while the other had hypertension and symptomatic ischemic heart disease.” Questions on this usage can arise from time to time, so a review may be helpful.

Beta-blockers prevent the neurotransmitters norepinephrine and epinephrine from binding to beta-adrenergic receptors. Their primary use is in the management of cardiovascular disease. They treat ischemic heart disease by binding to beta-1 receptors in the heart, reducing heart rate and contractility, which reduces the demand for oxygen by the heart and improves coronary blood flow. This makes the heart more efficient and decreases ischemic symptoms (angina). Blood pressure is reduced by the slowed heart rate, the reduced force of blood being pumped by the heart and the blockade of beta-2 receptors in blood vessels, which causes vasodilation. Beta-blockers also influence beta-receptors in the lungs, leading to bronchoconstriction and difficulty breathing in susceptible individuals. Central nervous system effects such as depression, drowsiness and lethargy have also been noted but tend to be less frequent or significant.

Potential Contraindications

Topical beta-blockers lower intraocular pressure (IOP) by reducing aqueous production via their effects on beta-receptors in the ciliary body. They were first-line therapy for OAG since the approval of timolol in 1978 until they were supplanted by prostaglandin analog therapy around the turn of the current century. Beta-blockers remain one of the most frequently prescribed topical agents because of their efficacy, excellent local side effect profile, once (or twice) per day dosing, generic availability, nominal cost and efficacy when added to prostaglandin analog therapy. However, topical beta-blockers can be absorbed into the bloodstream and affect other tissues by causing unwanted beta-blockade. According to Dr. Madonna, topical beta-blockers are contraindicated when treating patients with bradycardia, second- and third-degree heart block and uncompensated congestive heart failure, where the cardiac effects of beta-blockade may cause significant adverse effects. “Note that these cardiac conditions do not include hypertension or ischemic heart disease, conditions in which beta-blockers are a mainstay of systemic treatment,” he adds. “There is no contraindication to the use of topical beta-blockers in glaucoma therapy in a patient with either of these conditions.”

“A bigger question for eye doctors,” says Dr. Madonna, “is the effect of systemic beta-blockers on IOP-lowering.” Most studies have shown that systemic beta-blockers lower IOP by less than 0.50mm Hg in patients who are not on topical beta-blockers. A recent population-based study showed that systemic beta-blockers lowered IOP by 0.33mm Hg. This small IOP reduction probably accounts for the lower odds ratio of having glaucoma in patients taking systemic beta-blockers as compared with those not on them. Physicians are also commonly confronted with patients taking systemic beta-blockers and wonder if it will reduce the efficacy of topical beta-blockers’ ability to lower IOP. While the literature is not completely clear on this, it appears that the IOP-lowering effect of topical beta-blockers is dampened when patients are on systemic beta-blockers, but the effect varies between individuals, the baseline IOP, and the type and dosage of the systemic beta-blocker.

“Topical beta-blockers remain a common glaucoma treatment, yet misconceptions about their use in patients with heart disease persist,” Dr. Madonna says. “Be aware of when topical beta-blockers are absolutely contraindicated but also when they are safe.”


About Dr. Ajamian

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

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The Struggle is Real

Is there anything more annoying than those who don’t pick up after their dog? These patient interactions are a close second.

There is a mighty struggle going on in this country. It is a battle between good and evil. It stinks. Yes, I am referring to the war between people who pick up their dog’s poop and those who do not.

This brings to mind the struggle with other equally annoying events in our offices. Pick your favorite response to these patients’ comments:

1. “I just want a copy of my prescription” and, of course, its devilish addendum, “Oh, and can you give me my PD?” (as they ponder inside, “What’s a PD anyway?”)
   a. You mean you are buying glasses from a place that doesn’t know how to take a PD?
   b. No problem, of course, and don’t forget to come back for your exams once every 10 years.
   c. Unfortunately, our office policy is that we only see one family member each year. Maybe Susan can come next year.

2. “I can’t see out of my new glasses” (which they got online).
   a. Well, here’s your old prescription that you could see 20/50 out of and your new ones that you can see 20/20 out of. Which do you like?
   b. Oh, as we explained at your exam (see your initials here?) we offer free rechecks for patients who purchase from us but it’s $80 cash for the doctor to recheck prescriptions purchased elsewhere. There’s an ATM across the street.
   c. You’re the one who chose “number one” instead of “number two,” not me.

3. “Can you give me a couple of contact lens trials for my vacation this week?”
   a. You mean like we did the last time you were here for your examination in 1999?
   b. Ummm, no.
   c. Well, we never, ever have completed an exam and finalized a contact lens prescription for you, but what the heck, here’s an old pair of mine that might hold you over.

4. “My teenage daughter wears glasses, so she has to see an ophthalmologist.”
   a. Who’s the ophthalmologist? I never met one who actually sees a glasses patient.
   b. I will pray about her eye disease.
   c. Let me get this straight. You think the tech who determines the prescription is an ophthalmologist?

5. “We have to change doctors because your office is 15 minutes away.”
   a. How often do you take your kids to the mall every year? You do realize the mall is 30 minutes away, right?
   b. Our time is certainly very important. Do you use Facebook?
   c. How’s your dentist in Houston?

6. “Do you offer a senior citizen discount?”
   b. Yes, but we call it “Medicare.”
   c. No, but some burger places might.

7. “Do I have to wear my glasses?”
   a. Only when you want to see something.
   b. Only when you are wearing shoes.
   c. Only if you have a grain of sense.

8. “My insurance only pays once every two years.”
   a. That’s awesome! You get 50% off every single year!
   b. That’s because eyes only change once every 729 days.
   c. That’s because they truly, truly care about you.

9. “Can I have Lasix (sic)?”
   a. I guess, but you may pee a lot.
   b. It’s cheaper than bumetanide.
   c. Why not just drink cranberry juice?

10. “I hate that puffer.”
    a. You’d be OK with me poking you in the eye, though?
    b. Join the club.
    c. We still feel strongly that it’s the best way to make you holler out loud.

There are many more in our world, but no matter how these battles unfold, we will survive. Except, of course, those creatures who do not pick up their dog’s poop. They will ultimately suffer. I will personally see to it.

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The Struggle is Real

Dr. Montgomery Vickers

Dr. Vickers received his optometry degree from the Pennsylvania College of Optometry in 1979 and was clinical director at Vision Associates in St. Albans, WV, for 36 years. He is now in private practice in Dallas, where he continues to practice full-scope optometry. He has no financial interests to disclose.
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†In a chronic dry eye patient usage study, participants from a variety of socioeconomic backgrounds answered questions about their experience with iVIZIA lubricant drops. In the study, 203 chronic dry eye patients, 28-80 years old, switched from their dry eye artificial tears to iVIZIA for a month.
‡To limit blurriness when using contact lenses, remove contacts, apply drops, then insert contacts.
Anatomical Anomaly?

Almost half of the population possesses a cilioretinal artery, which has implications in certain conditions.

One of the most unique features of an ophthalmologic exam is the ability to observe ocular vasculature in real time. This differs from the rest of the body in which advanced ultrasonographic or imaging techniques are necessary to observe this feature. As such, the examination of ocular vasculature—particularly in the retina—is often what feeds us information regarding the health of the entire body. The retina is also unique in that it has a dual blood supply, which is often impacted in vascular disease. Moreover, the retina can exhibit congenital anomalies of its vasculature, differentiating one person’s retinal vasculature from another. The most common of these congenital anomalies is the cilioretinal artery.

Vascular Divisions

A cilioretinal artery can be readily observed upon ophthalmic examination and is present in a significant proportion of healthy eyes. Besides making note of this anomalous vessel or vessels upon examination, it is important to understand its significance and how it may or may not impact retinal disease. To do this, reviewing the normal retinal vascular supply and branches is essential.

The retina and surrounding ocular structures are supplied by branches from the ophthalmic artery (OA), which is the first branch of the internal carotid artery. The internal carotid artery first leaves the cavernous sinus and almost immediately branches into the OA intracranially until it enters the both the dura and optic canal. The OA then branches into several divisions that supply various areas around the eyes and face. Two unique branches of the OA are responsible for nourishing the outer retina and choroid (posterior ciliary arteries) and the inner retina (central retinal artery; CRA).1

Usually, the first of these branches is the CRA, which is responsible for supplying the inner retina and is critical for vision. A different branch of the OA, known as the posterior ciliary arteries, supplies the outer retina and choroid. Unlike the CRA, though, these posterior ciliary arteries are not terminal—they instead divide into multiple, shorter branches to supply the proximal choroid and optic nerve head. It then pierces the sclera and continues as long posterior ciliary arteries, which supply the distal choroid. When these branches anastomose behind the lamina cribrosa, they form the circle of Zinn. The congenital anomaly known as the cilioretinal artery belongs to the posterior ciliary artery system, deriving directly from the choroid rather than the CRA and its branches.2

Presentation

When performing a retinal examination using a condensing lens or via indirect or direct ophthalmoscopy, it is the CRA and its branches that are readily visible. The choroidal vasculature is not as easily delineated, being much deeper. However, the cilioretinal artery can also be viewed in this manner despite its derivation from the posterior ciliary artery system or choroid. It appears as a hook-like vessel coming from the edge of the optic disc resembling a “walking stick.” Although in gross appearance it can look like the rest of the CRA’s branches, it would best be distinguished using fluorescein angiography. Since the basis of fluorescein angiography is in the timing of vascular filling, with the choroidal flush occurring first, the cilioretinal artery would fill right along with it and significantly earlier than the arterial phase.2

Clinical Implications

Cilioretinal arteries are rather prevalent and are documented in up to 49.5% of the population—arguably, not an “anomaly” at all. They are often found as solitary vessels that appear unilaterally. Most commonly, cilioretinal arteries are located on the temporal edge of the optic disc. Because of its location, it has a significant role in the circulation of the macula and, very rarely, the entire retina.2

The greatest significance of the cilioretinal artery has been documented in CRA occlusions. These are visually devastating, irreversible and, for the most part, untreatable. However, in eyes with a patent cilioretinal artery supplying the macula, vision can be spared and even return completely back to baseline following this occlusive event. The reason for this goes back to the dual vascular supply—the CRA and its branches are impacted.
but the posterior ciliary and choroid are not, allowing for continued perfusion from the cilioretinal artery to the area of the macula. Conversely, having a cilioretinal artery can also mean having an additional vessel that is at risk for an occlusive event in vascular disease, which would then impact the macula and visual acuity if present.

One study also documented the significance of cilioretinal arteries in pathologic myopia, concluding that the presence of one in highly myopic eyes was associated with higher axial lengths and worse glaucomatous optic neuropathy. This correlation is not fully understood but is likely a result of blood flow dynamics affecting the optic nerve.

Another area of research is the impact of cilioretinal arteries in age-related macular degeneration (AMD). The outer retina and choroid are often implicated in the pathogenesis of AMD. It has been theorized that the additional circulation provided by a cilioretinal artery could enhance oxygen tension in the macular area and be protective against the development of choroidal neovascular membranes. It has been documented that the presence of a cilioretinal artery reduced the risk of developing late-stage AMD and resulted in lower rates of neovascular membranes.

This vascular anomaly we come across routinely on retinal examination bears a great deal of significance. Understanding the intricacies of retinal vascular supply and identifying these unique features can potentially aid in the prediction of retinal disease and progression.

JOAG Misdiagnosed as Amblyopia

Reduced visual acuity requires a good explanation.

In this current issue, one of us (SB) co-authored a CE article entitled “When It’s Not Amblyopia: The Differential of Functional vs. Pathological Vision Loss.” This, as well as many of our prior columns, highlight some of the significant issues that arise when pathological vision loss is missed because functional vision loss (amblyopia) is the suspected diagnosis. It seems, unfortunately, to be a recurrent problem in eyecare. In this month’s case, the misdiagnosis of amblyopia in a young girl sadly resulted in blindness in one eye and significant field loss in the other eye.

Case

An 11-year-old girl presented for an eye examination because the mother reported that her eyes were not straight. She had been noticing this for a while and was becoming concerned.

Entering uncorrected visual acuities were 20/100 in OD and 20/20 OS. Cover test revealed a right exotropia at distance and at near. The refractive error was OD: -0.75-0.75 x 90, with best-corrected visual acuity (BCVA) of 20/70 and OS: -0.50 sphere, with BCVA of 20/20. The eye doctor in this case used a “check-off” type of recording form in which the results were not written out but checked off, indicating (according to the doctor in his deposition) that the test was performed and the results were normal. At this visit, everything was “checked,” including the disc, macula and tonometry.

Phorias at distance and near were attempted but not measured due to suppression of the right eye in the phoropter. A Keystone Visual Skills test was also performed, and the doctor noted “Dog over Pig” for Card #1, in which one eye sees the dog and the other eye sees the pig and “three ball fusion response at distance and near.” On the phoria cards at distance, the doctor noted that the arrow pointed to #15 (one eye sees the arrow and the other eye sees numbers), indicating a high exophoria or an underconvergence response, and at near, the arrow pointed to between #6 and #7, indicating an ortho to slight exophoria response.

The diagnosis was not indicated, but the eye doctor wrote in the chart, “VT (vision training) suggested—no decision.” Apparently, the doctor thought the patient had a functional reason for the vision loss, namely exotropia, and suggested vision training.

The patient never returned for VT (it was later learned that the parents thought the fee for VT was too expensive) and presented for another eye examination over two years later. Her chief complaint at this visit was that when she covers the left eye, the right eye is blurry. BCVAs were 20/400 OD and 20/20 OS. At this visit, instead of using a check-off form, ophthalmoscopy results were written and were recorded as “OD extreme cupping” and “OS moderate cupping.” Tonometry readings, performed by non-contact tonometry, were 51mm Hg OD and 49mm Hg OS. The patient was immediately referred to an ophthalmologist, diagnosed with end-stage juvenile open-angle glaucoma (JOAG) OD and advanced JOAG OS. Despite medical and surgical intervention, the glaucoma progressed, resulting in hand-motion vision in the right eye with no remaining visual field and 20/20 in the left eye with a 30% reduction in the visual field.

Malpractice Allegation and Outcome

The eye doctor was sued for failure to detect the glaucoma two years earlier. The case was settled for $350,000 two days before a jury trial.

Fig. 1. Cupped out disc in end-stage glaucoma, with corresponding 10° visual field in another patient.

Reduced visual acuity requires a good explanation.

JOAG Misdiagnosed as Amblyopia

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

About Drs. Sherman and Bass

Fig. 1. Cupped out disc in end-stage glaucoma, with corresponding 10° visual field in another patient.
You Be The Judge
Considering the facts presented thus far, opine on the following questions:

- Did the eye doctor have a reason to diagnose amblyopia, since the patient had a right exotropia and not an exophoria on cover test?
- Did the results on the Keystone Visual Skills test support a diagnosis of amblyopia?
- Should the eye doctor have recorded quantitative data for IOP measurement and optic nerve head findings, or is a checkmark enough when findings are normal?
- Are the patient and her parents responsible for not returning for the recommended vision training, which would have given the doctor another opportunity to reassess the situation?
- Is the eye doctor culpable for malpractice, since he failed to diagnose glaucoma in a young child, which is a very rare condition?
- Is tonometry the standard of care prior to the teenage years?
- What would a like practitioner under like circumstances have done on the first visit?

Our Opinion
JOAG is rare, with a reported prevalence of one in 50,000 in the US.¹ It occurs in individuals younger than 40 years of age.² Therefore, when a young child presents with reduced vision in one eye, end-stage JOAG is not foremost as the likely explanation for reduced visual acuity. However, before amblyopia can be diagnosed, certain criteria apply.

One of us (JS) reluctantly opined that the eye doctor had no explanation for the reduced visual acuity in the right eye. “Reluctantly” because this case dates back four decades, and it was unclear what a “like practitioner” would have concluded under like circumstances. The standard of care continues to evolve, and today this would clearly be a violation of the existing standard of care.

While strabismus existed, most patients with exotropia can and do alternate, unless the turn is so large that the exotropic eye is completely suppressed. The eye doctor noted on Keystone Skills that there was no suppression, since the child saw both the dog and the pig, as well as the arrow and numbers on the phoria card. Therefore, the turn was not large enough for suppression, and the exotropia was very unlikely the reason for the reduced visual acuity in the right eye. There was only a slight difference in refractive error between the two eyes, and therefore, refractive amblyopia was not the reason for the reduced visual acuity. The eye doctor failed to record the pressures in the eye on the first visit, noting tonometry as “checked” and neither did he record any details about the discs and maculas at this initial examination.

Discussion
The eye doctor is culpable on a few issues:

First, he had no good explanation for the reduced visual acuity in the right eye. There was no significant anisometropia, and the strabismus was an exotropia, not an esotropia. If the child was able to perceive two targets on the Keystone Skills battery, then she was not suppressing. And most exotropes can and do alternate. This is important to remember when attributing decreased visual acuity to exotropia.

Second, the eye doctor did not record the appearance of the optic nerve heads in his initial examination or his tonometry findings but instead checked it off in his record. These “checks” were of no help in his defense since they did not indicate a quantitative amount that could have been compared from one examination to the next.

Third, he did not specify a diagnosis in his initial examination, and he did not specify a recall date except to write “VT suggested—no decision.” Children with reduced vision in one eye should be monitored closely if they are not referred and if the cause is not evident.

Since there was no other reason for the reduced acuity in the right eye, it is likely the child already had end-stage glaucoma in her right eye at the initial examination as the visual acuity was already affected. Likely, the disc was already cupped out, since the VA was reduced (Figure 2). Since the visual field in the left eye was reduced by 30%, she likely had moderate glaucoma in the left eye two years later (Figure 2). But more important, the delay of two more years resulted in a further decrease of central vision in the right eye and additional loss of visual field in the left eye—her only good seeing eye.

This case dates back decades, but knowledge of such cases will likely prevent similar cases in the future.

NOTE: This article is one of a series based on actual lawsuits in which the author served as an expert witness or rendered an expert opinion. These cases are factual, but some details have been altered to preserve confidentiality. The article represents the authors’ opinion of acceptable standards of care and do not give legal or medical advice. Laws, standards and the outcome of cases can vary from place to place. Others’ opinions may differ; we welcome yours.
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The most common adverse reactions reported in 82% of TYRVAYA treated patients was sneezing. Other common adverse reactions that were reported in >5% of patients include cough (16%), throat irritation (13%), and instillation-site (nose) irritation (8%).

USE IN SPECIFIC POPULATIONS
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All pregnancies have a risk of birth defect and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively.

Data: Animal Data: Pregnant rats and rabbits received varenicline succinate during organogenesis at oral doses up to 15 and 30 mg/kg/day, respectively. While no fetal structural abnormalities occurred in either species, maternal toxicity, characterized by reduced body weight gain, and reduced fetal weights occurred in rabbits at the highest dose (4864 times the MRHD on a mg/m² basis).

In a pre- and postnatal development study, pregnant rats received up to 15 mg/kg/day of oral varenicline succinate from organogenesis through lactation. Maternal toxicity, characterized by a decrease in body weight gain, was observed at 15 mg/kg/day (1216 times the MRHD on a mg/m² basis). Decreased fertility and increased auditory startle response occurred in offspring at the highest maternal dose of 15 mg/kg/day.

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

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

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

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Over the last few decades, there have been many shifts in optometry’s approach to glaucoma diagnosis and management, resulting from an influx of new research and technology-driven knowledge. Below, we address several of the ongoing conversations that are allowing clinicians to develop a more up-to-date approach to glaucoma.

1. What is a “glaucoma suspect”?

One barrier to success in classification, risk identification and subsequent surveillance of our patients comes from a lack of clarity of the term “glaucoma suspect,” which is widely, but likely inconsistently, used in glaucoma nomenclature. Does family history—amongst a myriad of other risk factors—truly make someone a glaucoma suspect, or does accurate labeling of someone as a glaucoma suspect require signs consistent with actual glaucomatous optic nerve head damage, whether that be thinning of inferior- or superior-temporal rim and retinal nerve fiber tissue?

The authors of one recent editorial point out that the term “glaucoma suspect” is ambiguous and cannot be exclusively categorized as either a disease state or a risk factor. Broadly included under the umbrella of glaucoma suspect are both those with clinical findings suggestive of, but not yet definitive for, glaucomatous optic neuropathy, as well as those possessing traits and risk factors for glaucoma but lacking features even remotely suggestive of characteristic optic nerve head damage. The authors state that the vagueness of the term leads to incorrect diagnosis, errant treatment decisions and inappropriate follow-up intervals, confusion amongst providers and the resultant risk of negatively affecting the patient’s sense of wellbeing. They propose abandonment of the term “glaucoma suspect” in favor of the more refined descriptions of such patients as having either features of glaucomatous optic neuropathy (FOG) and/or glaucoma-related risk factors (GRFs). This type of classification is illustrated by flowchart in Figure 1. Differentiating these two, as opposed to the current lumping of them together, is not a controversial subject, but rather one that provides an opportunity to define everyone’s overall condition, allowing for a more accurate reflection of the current optic nerve status and future risk to said status. Embracing the terms FOG and GRFs presents an opportunity to improve necessary care while reducing unnecessary care. Figure 2 illustrates two instances when these terms more aptly fit patients’ status.

2. What are the limitations of tonometry?

As a reminder, intraocular pressure (IOP) is a GRF but not part of the definition of glaucoma. IOP has a wide distribution of normative values and therefore may vary per individual. The Ocular Hypertension Study demonstrated that a high IOP (≥24mm Hg) is a concern for increased risk of conversion to glaucoma, particularly when the corneal thickness is thinner than average. Focusing on a single IOP reading at an exam—or even three readings over the course of a year—concentrates attention on merely a snapshot of the patient’s true IOP range.

All tonometry methods, including the traditional gold standard, Goldmann...
applanation tonometry (GAT), have inaccuracies in measurement based on corneal thickness variations. IOP is also prone to diurnal/nocturnal variation. Furthermore, Valsava maneuvers, body position changes (heart elevated higher than head) and physical pressure on the eye can all increase IOP. This affects parameters used in clinical decision making, such as Tmax (highest IOP without treatment) and treatment IOP target range, because research has shown patients with higher IOP peaks and wide IOP ranges are more likely to progress.

Since the true IOP disparity is not observable in-office, 24-hour or continuous IOP devices have become available as a new evaluation modality. iCare Home was the first FDA-approved device in 2017 with portability and easy use for patients. The prescribing doctor is able to review the readings and make decisions based on the fluctuations, specifically at the highest peak reading. Unfortunately, this device does not take a continuous measurement, nor does it track IOP when the patient is sleeping. As with all tonometry methods, iCare is also influenced by corneal properties and does not always correspond with GAT.

Triggerfish is a soft contact lens that takes a continuous 24-hour measurement, but it records changes in the corneoscleral junction curvature in millivolt equivalents (mV eq) rather than millimeters of mercury (mm Hg) as with IOP measurements. This variable might be superior to GAT for glaucoma monitoring but requires more research to verify its influence on risk of progression. Another advantage of a 24-hour device is that patients may be more inclined to use their glaucoma drops knowing their IOP is being measured outside the office.

If and when to use these remote monitoring devices is up to the prescribing doctor. If pursued, it would be wise to attain these measurements prior to treatment and/or as a tool to evaluate a treatment’s effect. Per the manufacturer website, iCare Home 2 must be prescribed and can be ordered via the company website; one-week rental of the device via a distributor costs around $250 and insurance may cover the product.

Another consideration when applying IOP as a GRF is that it is not the only force in play around the optic nerve head; both ocular perfusion pressure and cerebrospinal fluid pressure have been implicated in glaucoma but are less easily measurable.

3. How is corneal hysteresis relevant?

Traditionally, pachymetry has been considered the critical corneal metric to include in the baseline testing of glaucoma and ocular hypertensive patients. However, studies on corneal hysteresis (CH) over the last decade show that the relationship between the cornea and glaucoma involves more than just corneal thickness, as it is unlikely to indicate how the eye adapts to the multiple forces to which it is exposed. CH is a biomechanical property that reflects the cornea’s ability to absorb and release energy created by applana-
dysregulation has been implicated in glaucoma research, especially in patients with low IOP. Optic disc hemorrhage, reduced mean and diastolic ocular perfusion pressure, isolated vasospastic conditions—such as migraines and Raynaud’s syndrome—vascular dysregulation found in Flammer syndrome and presence and enlargement of parapapillary atrophy in patients with glaucoma all suggest that vascular dysregulation plays a role in the pathogenesis of the disease.

Multiple technologies have been used in research trying to measure blood flow in glaucoma, including laser speckle flowgraphy, intravenous fluorescein and indocyanine green angiography, laser Doppler flowmetry and retinal flowmetry; with some studies showing reduced optic nerve and peripapillary blood supply; others even demonstrate a correlation between the extent of blood flow disturbance and disease severity. Although each technology has contributed to understanding the role of vascular dysregulation on glaucoma, each has its own unique limitations and all have shown an inconsistent or lack of ability to obtain accurate, reproducible and quantitative information.

OCT angiography (OCT-A) has emerged as a technology that provides non-invasive, high-quality imaging of the retinal and choroidal microvasculature that is reproducible and can provide quantitative data allowing for inter-visit comparisons. OCT-A studies over the last decade have consistently demonstrated a reduction in the peripapillary and both the para- and perifoveal capillary networks in patients with open-angle glaucoma compared with healthy controls. This reduced capillary density is in direct proportion to the severity of disease and its rate of progression. It also aligns with topographical structural loss and actually has a stronger correlation with functional testing than structural OCT measurements.

Another benefit of OCT-A lies in cases where typical structural testing has reached its measurement floor due to severe stage or in eyes with high myopia not amenable to consistent machine segmentation. It also may be able to demonstrate medical or surgical success by confirming an increase in vessel density post-treatment and may even provide a marker of retinal ganglion cell dysfunction prior to cell death.

A report by the American Academy of Ophthalmology concluded in 2021 that peripapillary, macular and choroidal vessel density parameters may complement functional and structural OCT measurements in the diagnosis of glaucoma. More recently, the authors of one study concluded that longitudinal OCT-A measurement complemented OCT structural measurements and, when combined, these measurements improved the accuracy of detecting visual field progression vs. either OCT-A or OCT alone. OCT-A has also shown to be repeatable for most platforms, which is necessary for any technology to be usable in monitoring disease progression. However, OCT-A tends to have longer scan acquisition time than OCT and therefore increased chance of fixation drift and motion artifact, which must be factored into analysis. Mammadinezhad et al. have recently shown that to detect progression, the average optimal OCT-A test frequency is two tests per year. This is the same number of tests per year that is recommended to minimize the time required to detect structural OCT.

One of the major limitations in using OCT-A for monitoring disease is that not every platform has a substantial enough software package allowing for quantitative data to be measured and compared (Figure 3). Ultimately, the research shows that OCT-A can be a complementary piece in glaucoma diagnosis and management. As the technology becomes more widespread, how important OCT-A becomes in our glaucoma care remains to be seen.

5. What should be considered first-line therapy?

Topical glaucoma medications have been regarded as first-line treatment for glaucoma for decades. As of recently, selective laser trabeculoplasty (SLT) has been accepted as an appropriate first-line treatment as well. Unfamiliar procedures and devices may seem daunting to recommend but could be superior treatment in early cases.

Glaucoma drops not only require consistency of instillation but also disrupt the ocular surface, which leads to dry eye symptoms, thus contributing further to patient nonadherence. In addition, patients may have pre-existing dry eye or be on multiple glaucoma meds. In response, practitioners may switch to prescribing a different class, a more consistent brand or even preservative-free options. However, chronic use of the active drug is often the culprit of imbalance in ocular surface homeostasis. Recommending aggressive dry eye therapy may further impair patient adherence due to multiple treatments.
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References:
2. Steger et al. An Evaluation of the Efficacy and Safety of Timolol Maleate 0.5% Microdrops Administered with the Nanodropper®. Ophthalmology. 2024.

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and increased costs, negatively affecting quality of life.\textsuperscript{35}

To mitigate this, new drug delivery options and laser procedures offer excellent first-line treatment options with the understanding that drops or further procedures may still be necessary. The shift to a modern approach requires a fresh perspective and a different conversation with our patients.\textsuperscript{36}

Clinicians’ hesitation to SLT as first-line therapy may stem from past approaches to treatment. SLT’s predecessor, argon laser trabeculoplasty (ALT), was introduced in 1973 and was the predominant form of therapeutic glaucoma laser for decades until SLT received FDA approval in 2001.\textsuperscript{37} Since 2011, research has demonstrated strong evidence that SLT provides safe and effective 24-hour IOP control in patients with primary open-angle, juvenile open-angle, pigmentary and exfoliation forms of glaucoma as well as in patients with ocular hypertension.\textsuperscript{37}

In spite of this effectiveness, medical therapy has remained the most common initial IOP-lowering intervention, with SLT often used as a supplement.\textsuperscript{38} Although practitioners have both advocated for and employed SLT over the last 20 years, there was lack of strong evidence that challenged medical therapy as first-line treatment until recently.

The SLT vs. Medical Therapy for Initial Treatment of Glaucoma Study and, more famously, the Laser in Glaucoma and Ocular Hypertension (LiGHT) trial found that SLT provided IOP control equivalent to medications, with both studies concluding SLT to be a safe and effective first-line treatment.\textsuperscript{39,40}

Additionally, at the six-year mark of the LiGHT trial, patients who received SLT initially had less disease progression, required fewer incisional glaucoma surgeries and had quality-of-life metrics equivalent to patients initially started on drops.\textsuperscript{40} The evidence supporting SLT as first-line therapy has proved powerful enough that the UK’s National Institute for Health and Care Excellence has recently upgraded SLT to become its preferred first-line treatment. This sentiment has extended also to the European Glaucoma Society, which has updated its guidelines to include SLT as a first-line option. What’s more, a 2024 report by the American Academy of Ophthalmology’s Ophthalmic Technology Assessment Committee concluded that there is level 1 evidence substantiating SLT as an appropriate primary intervention strategy.\textsuperscript{37,41-42}

Thus, recommending SLT as first-line to eligible patients has now become part of the standard informed consent process and is no longer considered controversial. Note that although in most trials SLT is as effective as topical therapy, SLT, like medication, is not effective on every eligible patient; when it is effective, that effect is not permanent and treatment may need repeating, as studies show treatment duration will vary from patient to patient.\textsuperscript{37,43}

As optometrists become more involved in both recommending and performing SLT, we must continue to exert caution in our conversations with patients, clearly elucidating that SLT is not a cure but rather a tremendous drop-free, repeatable option to help slow the progression of their glaucoma.\textsuperscript{44,45} Furthermore, a retrospective study published in 2018 found that lower energy (0.4mJ/spot) 360° SLT when repeated annually had better outcomes than standard SLT settings applied on an as-needed basis.\textsuperscript{46}

The ongoing Clarifying the Optimal Application of SLT Therapy trial is comparing this novel treatment approach to standard SLT application. When the results are published, they may dictate how often optometrists should perform or refer for this procedure.\textsuperscript{47}

### 6. What are the sustained-release drug options?

With rising concern of the lower statistical likelihood that patients are both adherent to taking their drops and reliably instilling them, as well as the question of how much medication actually impacts the targeted mechanism inside the eye or bioavailability, comes the exploration of other therapeutic modalities. Sustained-release devices address the above concerns but can be limited to a niche category of patients who may respond well to ocular hypotensive medications but are not candidates for other avenues of therapy, such as laser trabeculoplasty or traditional incisional surgery like minimally invasive glaucoma surgery. This may simply be due to apprehensiveness about surgery, incompatible insurance coverage or costs regarding use of an ambulatory surgery center. The simplest approach to differentiating sustained-release devices is to distinguish by delivery location: ocular surface (i.e., adnexa, puncta) or intraocular (i.e., iridocorneal angle, trabecular meshwork).

**Ocular surface.** Sustained delivery to the ocular surface has been conceptualized as early as the inferior fornix-situated Ocusert (Alza Corporation) in 1975.\textsuperscript{48} The pilocarpine-impregnated elliptical plastic membrane proved that IOP could be controlled effectively without drops, but it required weekly replacements and was reported to cause unrelenting foreign body sensation. Conjunctival fornix-based medications have been explored as of 2024, including the preservative-free Bimatoprost

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**Fig. 3.** Patient with glucomatous damage to the superior arcuate bundle (dotted oval) shown on Hood thickness report (left). OCT-A of circumpapillary vessel density shows corresponding superior loss of vessel density (solid ovals) using OCT-A platform with analytics package and progression software.
Ocular Ring (Allergan) and the Topical Ophthalmic Drug Delivery Device (prostaglandin and timolol, Amorphex Therapeutics) with the latter lasting 90 days before needing replenishment and the former lasting six months with a slow decline in the amount of medication delivered, starting from 35µg/day and tapering off to only 6µg/day.49,50 Neither inserts have yet begun Phase III trials.49,50

Drug-eluting devices have also been explored in the puncta with Evolute (travoprost, Mati Therapeutics), the subconjunctival space via injection by Vi-Sci’s Eye-D (latanoprost, BioLight Life Sciences) and via soft contact lens delivery by LL T-MTT1 (bimatoprost, MediPrint Ophthalmics).51 Logistically, ocular surface-based eluting devices pose a myriad of questions about efficacy—will a patient feel an insert fall out? What would the cost be to replace it for the patient? What material works best for eluting medication? How will this impact patients who already have ocular surface disease?

**Intraocular.** The intraocular sustained-release devices may be superior in reliability, adherence and consistency. These medications are delivered directly into the eye, thus removing reliance on patient adherence and accuracy of alternate ocular surface therapies. To date, there have been several iridocorneal injectables: Durysta (bimatoprost, Allergan), OTX-TIC (latanoprost, Ocular Therapeutix, Phase II) and the ENV515 (latanoprost, Envisia Therapeutics, Phase II). Durysta is currently the only FDA-approved sustained-release therapy that can be implanted in-office; however, this will depend on the comfort level of the physician and appropriate scope of practice laws (Figure 4).52 Durysta offers a 30% reduction in IOP for the course of three to four months for the average patient, with some patients benefiting much longer. However, Durysta is currently FDA-approved for a single insertion within the lifetime of the patient.

In clinical experience, patients tolerate the procedure well with minimal inferior circumlimbal injection as the pellet settles inferiorly. However, providers should be aware that the pellet presence can affect corneal endothelial cell count (ARTEMIS-1 showed a 10.2% incidence of ≥20% endothelial cell density loss with a 10µg implant) and can potentially maneuver its way to the posterior chamber in patients with compromised or absent lens capsules.53 The biggest hurdle patients and physicians will face is that Durysta is FDA-approved (and reimbursed by insurance) for just a single administration to each eye. Therefore, surgeons will have to transfer the full cost to the patient if a patient succeeds with Durysta and requests another insert months or years later.

Last to consider is the trabecular meshwork implant iDose TR (travoprost, Glaukos).54 The intracameral iDose elutes 75mcg of the drug from a titanium implant that is inserted through the trabecular meshwork and anchored to the sclera, eluting travoprost for several months up to three years per current FDA trials comparing 12 month data. It is contraindicated in those with Fuchs’ endothelial dystrophy or with history of any corneal transplant but does boast a robust safety profile with minimal adverse effects per Glaukos. The device is visible upon slit lamp exam and much like other injectables, it can migrate or become dislodged. Thus, it is imperative to check patients at regular intervals.55 It is expected to launch this year, with a single implant costing $13,950.

### Table 1. VRVF’s on the Market

<table>
<thead>
<tr>
<th>VRVF Model</th>
<th>Manufacturer</th>
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<td>Advanced Vision Analyzer</td>
<td>Elisar Vision Technology</td>
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<tr>
<td>C3 Field Analyzer</td>
<td>Remidio &amp; Aalfaleus Technology</td>
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<td>VF2000</td>
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<td>Vivid Vision Perimeter</td>
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**7. To LPI or not to LPI?**

What is the best approach to managing primary angle-closure suspects? Figure 5 delineates these patients into primary angle closure, primary angle-closure glaucoma and acute angle-closure crisis categories.56 The approach is contingent on accurate assessment of the angle along with risk factor analysis.

Gonioscopy remains the accepted method for visibly evaluating the structures of the anterior chamber angle and the interaction between those structures and the iris. Unfortunately, per surveys and retrospective research, gonioscopy is the most underused test in a glaucoma risk assessment.57,58 Without it, the common diagnosis of primary open angle glaucoma cannot be assumed based on Van Herick angle estimation and IOP expectations. It is critical to understand that angle closure can not only be acute or chronic but also may or may not be associated with elevated IOP or glaucomatous damage.59

While the standard of care for an acute angle-closure crisis (AACC) has not changed (topical/oral aqueous suppressants to lower IOP followed by an iridotomy), the protocol for primary angle-closure suspects is less standardized. The management approach also varies widely among eyecare practitioners. Based on risk vs. benefits, laser peripherial iridotomy (LPI) was historically...
Favored over observation. The confusion exists because of the inability to predict likelihood of AACC. The Zhongshan Angle-closure Prevention 14-year trial demonstrated that inci
dence of primary angle closure was three times lower after LPI—primarily a lower risk of syn
drome formation, which may be of little clinical significance.60

The researchers concluded, however, that prophylactic LPI for primary angle closure is not recommended, as the long-term risk of progression is still low at 1.4% per eye per year.60 An additional consideration is that participants were of Asian descent, and this ethnicity has an even higher risk of developing angle-closure crisis or glaucoma compared with other ethnicities.60

Multiple observational studies indicate that primary angle-closure suspects without increased IOP or posterior syn
drheia rarely develop acute angle-closure or chronic glaucoma. Low-risk patients can be monitored closely without laser intervention. If choosing to monitor, the patient should be warned of AACC symptoms—sudden blur, halos around lights, eye pain, periocular headache, nausea and eye redness—so that they seek immediate care.

Patients that may benefit from a prophylactic LPI include those with AACC in the contralateral eye or anticholinergic/4desernergic medications that may induce a pupillary block. Other common risk factors include Asian or Inuit descent, hyperopia or short axial length and cataract progression. The patient’s health status, location and occupation can each complicate the process of seeking urgent ophthalmic care, which can also influence the decision.

Despite potentially superfluous procedures, the complications of LPI are minimal.9 Vertical dysphotopsias (i.e., glare, halos, lines, ghosting) have a low incidence rate of 2% to 3%, theorized to be caused by light scatter from the upper eyelid and tear film bisecting the iridotomy opening.64 However, current literature does not show a significant relationship between iridotomy location and dysphotopsia rates.51-63

Per the EAGLE study, removal of the lens via cataract surgery or clear lens extraction lowered IOP more effectively (mean IOP 1mm Hg difference) than LPI in patients with primary angle closure or primary angle-closure glaucoma. Phacoemulsification leads to widening of the anterior chamber and reduction of IOP; with similar or even superior outcomes compared with LPI. This approach should be highly considered for patients that are eligible for cataract surgery.64,65

8. What are the benefits vs. limitations for virtual reality visual field testers?

Glaucoma management requires both observation of the structural and functional changes. Technology has advanced the ability to detect structural change, yet functional testing has changed very little. Automated perimetry enables physicians to perceive glaucoma progression but has always been critiqued for the large size of the machine, the learning curves for administering and performing perimetry by staff and patient alike—and of course the biggest hurdle—the reliability of the patient during the test.

There has always been a desire to better map the functional changes in optic neuropathies with more ease. So-called virtual reality visual field (VRVF) instruments are portable, chargeable devices that can be used for patients who may not physically fit in a traditional visual field due to disability, wheelchair or being bedridden. A list of ones available can be found in Table 1. The majority possess glaucoma threshold capability and present visual stimuli in the same visual positions as standard automated perimetry (SAP).66 The ability for the target and field to move with patient eye movement allows for less patient error when compared with static fields that produce high false positives when the patient cannot help but search for the stimulus, even when instructed against it.57,68

These head-mounted, gaze-tracking devices accomplish the basic needs of mapping a visual field. VRVFs also have a lower cost compared to purchasing a new or even used Humphrey Field Analyzer. Certain devices, such as the VirtualEye, will even perform pupillometry and color vision testing, which can streamline the patient’s screening/workup. The VisuAll (Olleyes) employs a unique pediatric, game-like strategy to keep engagement of the patient.69 In an attempt to detect early functional loss, nGoggle has been exploring visual evoked potential, which provides an objective map of functional loss.70,71

Per manufacturer websites, most VRVFs are also capable of presenting information in other languages, which can improve the reliability and inclusivity for non-English speaking patients. Cost is of course a factor as well. Many companies offer monthly subscription-based plans.

Despite the future of VRVFs being promising, there are several factors left
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to consider. Each company provides its own algorithms for threshold testing, which are based on the heavily studied and performed SAP. Although most variables, such as stimulus size, are comparable, some programs do not possess the same standards, such as different types of luminance.

There are different biases among each VRVF reference database; do they compare to the databases we are all familiar with? There is also lack of progression analysis with several VRVFs, which is considered essential to check for stability over time, as well as lack of generated structure-function overlay reports such as the PanoMap (Cirrus HD-OCT, Zeiss) or GMPE Hood Glaucoma Report (Heidelberg Spectralis, Heidelberg Engineering).

As time progresses and data becomes more established, the ability of these tests to stretch beyond in-person testing could be considerable. Home-based testing is becoming more prevalent in various aspects of healthcare; blood pressure and blood glucose monitoring allow the patient to be more mindful and present in their health. Why should ocular disease be any different? The advent of home-monitoring is enticing, but reliably must be considered. Regardless, visual field progression can be detected much more quickly and efficiently, hastening an office visit for more aggressive treatment.

### 9. Is the transition to SITA FASTER seamless?

Released in 2019, the SITA Faster testing strategy was an important addition. This newer development reduces patient test burden over the original SITA test by cutting testing time by close to 60% as well as providing denser sampling of potentially damaged retinal ganglion cells with the 24-2C grid. Accordingly, transitioning from the original SITA Standard to SITA Fast and now to SITA Faster when doctors upgrade their software seems sensible. SITA Faster is not, however, infallible—studies show a 30% to 49% unreliable rate compared with a smaller 10.8% to 16.6% rate with SITA Standard, caused by initial low sensitivity measurements and relatively more severe global indices.

Luckily, SITA Standard and SITA Faster have similar test-retest variability, comparable sensitivity and specificity and overall agreement amongst most field parameters. Pham et al. in 2021 showed transition from SITA Standard to SITA Faster showed similar mean deviation results in mild stage disease and in suspects but problematically resulted in higher mean deviation in moderate and severe stage disease, possibly masking disease progression. Recent research from the same group showed also that in the transition, applying traditional SITA Standard criterion (Hodapp-Parrish-Anderson criterion) to SITA Faster test data can result in an artificially “better” result and subsequent misclassification of disease severity and misdiagnosis of the rate of disease progression.

These researchers have proposed that when assessing tests using SITA Fast and SITA Faster strategies, modified criteria would better reflect disease severity and assessment of the rate of progression (Table 2). From a practitioner standpoint, more accurate information provides a more accurate perception of the disease state and helps drive timely intervention. As we transition to newer strategies—even if they are on the same platform—we need to be vigilant in our practices in attaining sufficient information to determine change once we transition strategies rather than assuming older data will blend perfectly with the new.

### Takeaways

GRFs play a major role in predicting whether our patients will develop disease and consequently how they may progress. However, this does not automatically mean a patient has or will get glaucoma, changing how we use the term “glaucoma suspect.” While IOP is currently the only modifiable risk factor, the dynamics of tonometry, the value of CH and the potential of vascular etiology should also be considered.

Exhausting all topical treatment options before suggesting a procedure no longer serves our glaucoma patients. Recent research demonstrates the benefits of SLT and sustained-release drugs as first-line options, but communicating these options effectively is needed to align with modern care. With better understanding of primary angle closure, there has been less peripheral iridotomy referrals which will continue to decrease as practitioners improve gonioscopy skills and consider monitoring closely or cataract extraction. Lastly, understanding updates to visual field testing algorithms and innovative virtual reality fields will allow doctors to better care for their patients.

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**Gonioscopy Essentials**

This procedure requires a dark room with a shortened light beam to avoid touching the pupil to minimize pupillary constriction and simulate the naturally dilated state of the iris and pupil.

- Three-mirror scleral gonioprism offers optimal views and prohibits indentation.
- Four-mirror corneal gonioprism allows compression gonioscopy to determine if angle closure is appositional or synechial.
- Anterior segment OCT can be used as a supplementary test but cannot replace gonioscopy for diagnosis.
- Van Herick technique is insufficient to determine angle closure.

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| TABLE 2. GLAUCOMA STAGING BY HPA CRITERIA WITH PROPOSED MODIFICATIONS |
|---------------------------------|----------------|----------------|----------------|
|                                 | Early         | Moderate       | Severe         |
| SITA Standard (HPA)             | below -6 dB   | between -6 and -12 dB | above -12 dB   |
| SITA Fast (proposed)            | below -5.3 dB | between -5.3 and -10.8 dB | above -10.8 dB |
| SITA Faster (proposed)          | below -5.2 dB | between -5.2 and -10 dB | above -10 dB   |
A s the global population ages and the prevalence of glaucoma rises, the need for effective and accessible management strategies has never been more critical. Optometrists are uniquely positioned to lead the charge in the early detection and comprehensive management of this sight-threatening condition. With their specialized training, widespread accessibility and a patient-centered approach, ODs are indispensable in the fight against glaucoma.

“It is essential for optometrists to take the lead in glaucoma management,” notes Jackie Burress, OD, who practices at the Jack C. Montgomery VA Medical Center in Muskogee, OK. “We are on the frontline of eye care for the vast majority of patients. Optometrists are well-trained to provide exceptional glaucoma care, graduating from school with knowledge about anatomy, physiology, visual field interpretation and OCT analysis.”

And the role of the OD is set to get even more central to glaucoma care. “In many states, we also have the privilege of performing selective laser trabecu-lopasty (SLT) procedures to allow our patients to choose the treatment option that works best for them,” Dr. Burress continues. “This is even more important now with the number of ophthalmologists declining, restricting access to care.”

Integrating glaucoma management into optometric practice, however, has its challenges, and some optometrists may be hesitant to expand their services. Below, we delve into the psychological and logistical barriers to success, while also highlighting strategies to help ODs step into a leadership role for the treatment of this growing cohort of patients.

**Key Obstacles to Overcome**

Optometrists often find themselves at the crossroads of expanding their practice to include more specialized care such as glaucoma management. This transition is not without its hurdles, and there are a number of reasons why ODs might opt out of providing glaucoma care.

Psychologically, the shift demands a significant change in mindset. Optometrists must not only enhance their knowledge and skills to diagnose and manage a chronic, progressive condition like glaucoma but also build the confidence to assume greater responsibility for their patients’ long-term ocular health. This can be daunting, as it requires overcoming self-doubt, managing patient expectations and staying updated on the latest advancements.

Logistically, the incorporation of glaucoma care can involve substantial adjustments in practice infrastructure. Optometrists must invest in advanced diagnostic equipment, adhere to regulatory requirements and potentially hire or train additional staff.

Understanding these barriers is vital to address the hesitations optometrists face and develop strategies that can support them in growing their practices to include glaucoma care.

**Lack of confidence and fear of failure.**

Managing glaucoma requires specialized knowledge and skills. Optometrists may feel uncertain about their ability to accurately diagnose and treat this condition, fearing potential misdiagnosis or inadequate patient care.

“I believe that the greatest hurdle to new graduates is the lack of confidence in their diagnostic skills,” says Dr. Burress. “One of the best ways to learn more about disease management is to pursue an optometric residency after graduation.” There are many disease-based residencies available in a variety of practice styles, including those with the Department of Veterans Affairs in VA hospitals, optometry/ophthalmology combined practices and even private practice optometry clinics.
These afford optometrists interested in disease management more experience with complicated cases to improve their diagnostic skills and learn more about the management of these patients. If a residency is not right for that individual, though, there are numerous other resources available in the form of continuing education and hands on workshops to further strengthen one’s skills.

Adding glaucoma care into clinical practice can be overwhelming, even for the most seasoned optometrists, adds Michael Chaglasian, OD, associate professor at the Illinois College of Optometry and chief of staff of the Illinois Eye Institute. Dr. Chaglasian is also the current president of the Optometric Glaucoma Society (OGS). No matter the level of experience, he recommends that optometrists join or form their own discussion groups. “This provides a space for optometrists to talk about cases and ask detailed questions,” he says. “What does this mean on the OCT? What is this visual field? What’s the best eye drop? What are the treatment options?”

While continuing education is important, discussion groups allow ODs the opportunity to get more individualized support and advice on specific patient cases. Dr. Chaglasian notes that the OGS developed work discussion groups for just this reason. “The nuances of individual patients can be challenging to navigate and support from your peers is an invaluable resource.”

Going hand in hand with this lack of confidence is a fear of failure. “In my experience, there seems to be a fear of failure mentality among many primary care optometrists,” says Eric Schmidt, OD, founder of Bladen Eye Center in Elizabethtown, NC. “What happens if the patient doesn’t respond to the therapy that I prescribe? What if their disease gets worse?” Such lingering worries may discourage some ODs from taking a more active role. Dr. Schmidt advises taking it in stride, as this is inevitable in many cases.

“A patient may progress on your watch, but that doesn’t equate to failure. It is a part of the disease process and we must be prepared to take the necessary next steps, whether that be additional medication or surgical intervention,” he advises. “Glaucoma is not a disease we can cure; however, it can be managed successfully. The medications at our disposal today are very good, and if we do our job—diagnose, stage and treat to the target pressure—we should be able to control the vast majority of glaucoma patients.”

**Contending with a chronic condition.** Unlike acute eye conditions that may resolve quickly, glaucoma demands a long-term commitment, meticulous monitoring and adaptation to evolving patient needs and treatment protocols. This not only takes a toll on patients but also on eyecare providers committed to providing exceptional patient care and outcomes.

“The chronicity of glaucoma management can most definitely cause stress to providers, especially in the event of patients trending negatively with an impact in their vision and quality of life;
most notably when it affects a person’s later years,” says Brian Fisher, OD, supervisor at The Villages VA Outpatient Clinic in The Villages, Florida. “We are fortunate at our practice to have the vision impairment service team, which provides social work support to our patients, and a well-equipped and trained blind rehabilitation program. In the event of poor visual outcomes, our patients can attend an inpatient blind rehabilitation center to help improve their activities of daily living,” he notes. “Having these lines of support provides hope and reassurance not just for the patient but for the provider, too.”

While Dr. Burress acknowledges that it can be emotionally exhausting when you have a compliant patient with great intraocular pressures (IOPs) that still continues to progress, she tries to find the positive and talk to the patients about how to maximize the vision they do have.

“Thankfully, I do have some wonderful ophthalmologists who specialize in glaucoma care for me to refer those patients to,” she says, while also noting that working with a low vision referral center is another valuable resource.

“It helps get your patients the tools they need to still function and be independent despite their vision loss,” Dr. Burress explains. “Also, always share these challenging cases with your trusted colleagues. A fresh pair of eyes may help you think of a different management strategy or at least emphasize the fact that you have done all you can do for a patient.”

Successful management of a chronic condition is a team effort that includes ODs and their staff as well as patients and families. “Treating ocular disease does require empathy and compassion for your patients,” says Dr. Burress. “It is important to let the patients know that they are important to you, and you want them to see clearly for as long as possible. Let them know you are in this with them.”

**Equipment needs.** To effectively manage glaucoma, optometrists need a range of advanced diagnostic and monitoring equipment. Key pieces of equipment include OCT, gonioscopy lens, fundus camera, tonometry and pachymeter. For some ODs, especially those in smaller practices or ones that don’t see a large amount of elderly people, the cost of these devices may be prohibitive.

“Diagnostic equipment for glaucoma equipment today has more options, is less costly and generally easier to use,” says Dr. Chaglasian. “If you know how to use the equipment, it can make an individual a near expert. While this equipment is an investment, it comes with significant benefits for the success and growth of your clinical practice.”

For ODs who are not ready—or are unable—to purchase the necessary equipment, there are creative ways to start glaucoma management. For instance, mobile technology companies allow ODs to rent an OCT for a day, or they could partner with a fellow optometrist in the area who has an OCT in-house.

Lack of familiarity with use and interpretation of OCT scanning can also be an impediment. Manufacturers provide ample training on their devices to ease newcomers into adoption. Table 1 lists common reasons for poor scan acquisition that practices, and particularly techs, must learn to be adept at spotting and correcting.

“I know equipment issues can also be a factor that makes an optometrist want to refer disease patients to another provider. It is important to take advantage of OD-to-OD referrals in this case,” says Dr. Burress. “Often times, another local provider is happy to perform testing you don’t have in your office, such as an OCT, which can then be sent back to the referring provider for review/interpretation.”

While lack of equipment is a hurdle that must be overcome, it does not have to be a reason to forgo glaucoma management altogether.

**Medication costs and accessibility.** Glaucoma meds can come with a high
cost, and limited coverage for certain
drugs can affect accessibility and adher-
ence. Navigating these challenges may
make some ODs question whether or
not they want to dive into glaucoma
management. However, this is not an
insurmountable issue and ODs have the
resources to meet medication-related
challenges head on.

For Dr. Fisher, the main logistical
issues for his glaucoma practice are
the costs of topical medications and
access to certain classes of newer drugs/
formulations, such as approval for
Vyzulta (latanoprostene bunod, 0.024%,
formulations, such as approval for
access to certain classes of newer drugs/
the costs of topical medications and
issues for his glaucoma practice are

A new laser procedure called direct
SLT (Belkin Vision) does not require
a gonio lens, lowering the learning
cost. Some even speculate that a laser
law may not be required for an OD to
perform this procedure; obviously, check
with your state authorities before diving in.

Insurance and reimbursement.
Navigating the complexities of medical
insurance, billing and coding is essential
for effective glaucoma management in
optometry. By staying informed about
insurance coverage, using accurate codes
and maintaining thorough documenta-
tion, optometrists can streamline and
improve reimbursement.

ODs who have limited experience
with medical plans might be hesitant to
move forward with glaucoma manage-
ment, but Dr. Schmidt encourages his
fellow optometrists not to let concerns
around insurance and reimbursement
hold them back from practicing to their
full potential.

“It is really incumbent upon our
profession to get credentialed with
Medicare, Blue Cross, UnitedHealthcare
and the rest,” he notes. “If you are not
credentialed, then you cannot provide
this medical eyecare that your patients
need and our asking for, and this is a
disservice not just for your patients but
for your practice as well.” Getting your
practice onto medical insurance plans
benefits many more patients than just
those with glaucoma and should be a
priority regardless, he says.

Legal concerns and liability. Dr.
Schmidt is often asked, “If I start treat-

ing glaucoma, does that increase my
liability?” And while the answer is yes,
he urges ODs not to let that stop them
from incorporating management of this
condition into their clinic practice. “If
you maintain quality care and manage
your patients properly, the likelihood
of an issue arising is low,” he notes.

“Additionally, your professional liability
insurance should already cover this.”

While the glaucoma management
does come with potential liability is-
issues, these risks can be mitigated with
diligent practice and proactive strate-
gies. This includes adhering to a high
standard of care, maintaining thorough
documentation and fostering clear
patient communication. Ultimately, safe-
guarding patients’ vision while protect-
ing your professional practice requires a
balanced approach of clinical excellence
and legal awareness.

Patient compliance. This is a critical
factor in the successful management of
glaucoma, but ensuring patient adher-
ence to prescribed therapies and follow-
up appointments remains a significant
challenge for optometrists.

“Compliance issues are a recurrent
frustration when treating glaucoma
patients,” says Dr. Burress, while em-
phasizing the importance of trust and
honesty between you and your patients.

“Let them know you are in this journey
with them and educate them that you
can’t treat their glaucoma to the best of
your ability, unless they are honest about
their medication compliance.”

Many times, she notes, education
about your concern for their vision
and the possibility of them losing it is
equal to help with compliance. An-
other avenue for patients who struggle
with compliance is SLT, suggests Dr.
Burress.

While all optometrists should be
concerned about how to improve
compliance, that is not a reason to
avoid managing glaucoma patients, says
Dr. Schmidt. “When caring for these

A newer technique known as direct SLT obviates the need for
a gonio lens by delivering laser energy directly through the
limbal area. This may allow more optometrists to transition their
practices to offering SLT, as the learning curve may be
lower in traditional SLT.
As sustained-release drug delivery becomes more commonplace in glaucoma care, patient adherence to daily drug instillation regimens will become less of a concern. Some states even allow optometrists to perform the procedure. These images show Dr. Nate Lighthizer implanting the device. OD-to-OD referrals can help optometrists who lack experience or legal status to deliver such high-level care to their patients.

patients, a decent portion of every visit should reiterate the importance of using their drops as well as educating patients on glaucoma and the consequences of noncompliance.

“We are here to not only provide comprehensive care but also to support patients on what can be a very overwhelming and life-changing journey,” he continues. “I would argue that, as primary eye care providers optometrists are the ones best suited to take a leadership role in the management of these patients.”

Clinical Pearls for Success
Optometrists should, according to Dr. Fisher, consider the following viewpoints to optimize the treatment of glaucoma patients:

• Detect early to prevent functional vision impairment and disability.
• Maintain visual abilities for patients to live independently and stay physically active.
• Reduce psychological stress.
• Negate the medication and medical costs.

“Optometrists’ primary goal in the management of glaucoma is to ensure a lifetime of visual function to meet patients’ visual demands,” he notes. “No perfect formula exists to determine which therapeutic approach is best. By evaluating patients’ risk for visual decline, medication adherence and burden, along with the pros and cons of surgery, clinicians can individualize a therapeutic plan to address any apparent progression and preserve vision as long as possible.”

Dr. Burress emphasizes the significance of the initial diagnosis. “Spend time explaining the disease process with them and that IOP needs to be reduced to prevent progression and vision loss,” she suggests. “Let them know that medication is going to be a lifelong commitment.” Also remember to explain side effects of the medications, such as latanoprost causing conjunctival erythema and increasing the pigmentation of the iris, or potential ocular surface irritation from preserved topical drugs.

“Gonioscopy is important,” she emphasizes. “This lets you know the anatomy of the eye and correctly identify the type of glaucoma. It also lets you know if the patient is a good candidate for an SLT procedure.” You’ll need to perform this routinely as you take on more glaucoma patients (see the online version of this article for a link to a primer on gonioscopy technique and interpretation).

Additionally, she advises ODs not to forget about serial tonometry if you have a patient who is progressing, but IOPs are always great at your exam time. “People often schedule exams for the same time of day. While the normal diurnal curve shows the majority of patients have the highest IOP reading in the morning, I have seen some with higher IOPs in the afternoon. Everyone is unique and needs to be treated as such.”

Takeaways
Both patients and optometric practice as a whole benefit when ODs take a leadership role in glaucoma management, leveraging their accessibility and ongoing patient relationships to ensure timely diagnosis and effective treatment.

“It is critical for ODs to take the lead in glaucoma management. Glaucoma is a visually devastating disease with minimal symptoms until it reaches the advanced stage,” Dr. Fisher emphasizes. “Early detection is imperative, and management can help stave off progression and ensure a lifetime of preserved vision.”

By stepping up to this challenge, optometrists can significantly enhance patient outcomes, reduce the burden on the healthcare system and fulfill an essential role in the health and vision of their patients. No matter the hurdle, integrating glaucoma care into clinical practice is possible. ODs have the skills and knowledge to ensure their patients have optimal outcomes while simultaneously enhancing the field of optometry at large.

“There is such a great opportunity for optometrists to step up in even larger numbers to address the growing need of glaucoma care,” concludes Dr. Chaglasian. “Much of glaucoma care and management is relatively straightforward and not as complex or risky as people may think. It is a rewarding area of care that ODs are equipped to handle and can be easily implemented into their practices.”
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- Babak Kamkar, OD

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- Nancy Tanchel, MD

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Inheriting a patient with a pre-existing glaucoma diagnosis can feel like stepping into the middle of a complex story. While their medical history provides valuable context, their current experience with the disease, anxieties and treatment adherence may take several visits to uncover. This initial encounter presents a unique challenge for clinicians and requires a nuanced approach to navigate their current needs while respecting existing management plans.

Records Review
When assuming the care of new patients, whether they’re suspected of having glaucoma or are already undergoing treatment, it’s crucial to thoroughly review all available past information.

Encouraging patients to sign medical records release forms can help in obtaining their previous records and test results, yet there are still some limitations. One challenge is the lack of consistency among practitioners in how they interpret test results and document their findings, which can complicate the continuity of care. In optometry and ophthalmology, there’s a broad range of electronic health records systems, and some practitioners still rely on paper charts, necessitating ongoing maintenance of physical copies over the years. Relying on paper charts can lead to issues such as legibility challenges and printing errors, which makes it harder to interpret the information. Additionally, when practitioners receive information via fax, the quality of black and white images may restrict the optical coherence tomography (OCT) details available, including average retinal nerve fiber layer (RNFL) thickness, symmetry and thickness and deviation maps (Figure 1). Speaking with the patient’s pharmacists may give key insight to compliance, information about their past providers and expected treatment regimen.

Glaucoma is a multifactorial disease in which demographics such as age, race, sex, family history, geographic location, ocular perfusion pressure and systemic disease act as risk factors for development. Other important factors include a careful angle assessment and whether there are characteristics that might indicate aggressive glaucomas like pseudoxefoliation or pigmentary. Additionally, understanding how to use objective elements including intraocular pressure (IOP), pachymetry and corneal biomechanics, OCT and visual fields is vital for a confident diagnosis and management.

IOP
In evaluating glaucoma patients for the first time, understanding this measurement is critical, as it’s the primary modifiable risk factor in the progression of glaucomatous optic neuropathy, with all treatments aiming to lower it. IOP fluctuates throughout the day due to circadian rhythms.

Despite patients typically being seen two to six times a year, this provides only a limited number of data points. For instance, even if a patient is seen four times a year, we’re only measur-
ing IOP for a mere four seconds out of over 31 million seconds in a year. This scarcity of data can pose challenges when initiating or adjusting therapies, particularly since the method we use to measure IOP, such as the Goldman applanation tonometer, introduced in the 1950s, has known inaccuracies. Factors such as corneal thickness, previous surgeries, edema or astigmatism can affect readings. Inconsistent readings can also arise between doctors and technicians.

Identifying the maximum IOP (Tmax) remains a crucial step for assessing open-angle glaucoma (OAG) risk due to its ability to indicate large diurnal fluctuations. When searching old records, Tmax should be a priority. Other factors include which instrument was used to measure IOP and the time of day tested. Additionally, regulating the autonomic nervous system is vital for accurate IOP measurements. During the Valsalva maneuver, there’s heightened autonomic nervous system activity, affecting heart rate variability and possibly blood flow, which can raise IOP. Recent findings suggest that incorporating “365 breathing” into glaucoma treatment, along with standard therapies, leads to significantly lower IOP and cortisol levels and improved autonomic regulation.

To enhance the reliability of IOP measurements, it’s advisable to take multiple readings and calculate an average, assess the tear film height (0.2mm to 0.5mm average) to ensure there is neither an excess or insufficient fluorescein before measurement, ensure patients don’t hold their breath and be cautious of any orbital pressure when holding eyelids during measurements.

**Pachymetry and Corneal Biomechanics**

Average central corneal thickness (CCT) as measured by pachymetry is estimated to be between 540µm to 550µm. Thicker corneas tend to overestimate measured IOP, while thinner corneas tend to underestimate IOP. Pachymetry has also been shown as an independent risk factor for the development of glaucoma, with lower CCT being a larger risk factor for glaucomatous progression.

Other corneal biomechanics are important to consider, including the influence of corneal hysteresis (CH), which determines the cornea’s ability to dissipate energy. Eyes with lower CH have a higher likelihood of developing glaucoma and a faster rate of progression by visual field.

**OCT**

This technology has become a main tool in monitoring glaucomatous progression and enjoys widespread acceptance. While OCTs from prior providers may give additional information, new scans will generally need to be performed because of both manufacturer nuance and baselining for future progression analysis.

Using OCT as a differentiator of non-glaucomatous vs. glaucomatous optic neuropathy (NGON vs. GON) requires attention to several details. While assessing the optic nerve head (ONH), cup-to-disc asymmetry <0.2 in the absence of disc asymmetry remains a hallmark of glaucomatous change. The cup-to-disc ratio relative to optic nerve size is also of significance with superficial optic disc areas averaging from 2.1mm² to 2.35mm² on OCT in a normal Caucasian population. Large discs will physiologically correspond with larger cups, and smaller discs are more likely to have smaller cups. RNFL thickness and deviation maps are especially useful in diagnosing early glaucomatous slit defects.

While OCT is commonly used, there are weaknesses to this technology such as having no consensus on what constitutes progression. There is also no general agreement on the number, frequency or spacing of scans to detect progression. As a result, over- or under-identifying change can have significant unintended consequences on patient outcomes.

It is important to acknowledge that clinical information obtained from OCT is relative to the reference database, which may or may not align with a given patient’s specific demographics.
(e.g., age, race, disc area, axial length). The “ISNT rule” characteristically describes normal optic nerve disc rim thickness in which divided sectors expected thicknesses are as follows: inferior (I) is greater or equal to superior (S) greater or equal to nasal (N) greater or equal to temporal (T). Beneficially, it is independent of race and is useful for differentiating glaucomatous optic nerves. When using the ISNT rule as it applies to OCT, one may need to consider nerves with oblique insertion, segmental disc hypoplasia and high myopia or extensive peripapillary atrophy.

Macular changes can be especially useful to assist in correlating RNFL defects. Ganglion cell analysis (GCA) provides the ability to divide the central macula into critical zones. The presence of a temporal raphe sign is highly indicative of glaucoma. It has been suggested that macular thickness varies with respect to various glaucomatous risk factors. Among patients with pseudoxfoliation syndrome (PXS) and ocular hypertension (OHT), the inner retinal layers appear most thin in the patients with ocular hypertensive PXS, with normotensive PXS and OHT groups following in a respective order.

However, not all arcuate-shaped RNFL loss indicates glaucomatous progression. Multiple macular RNFL defects in the absence of ONH cupping may be more suggestive of hypertensive or diabetic changes in non-glaucomatous eyes. Confounders may exist in this region including areas where prior vitreomacular traction then released as well as NGON (uveitis, ischemic optic neuropathy, etc.) induced RNFL edema with subsequent resolution.

Visual Fields
Functional testing by visual fields is subjective, time-consuming and too often unreliable. Despite those limitations, they often help determine whether the patient has glaucoma or comorbidity. Scotomas (in arcuate or isolated fashion), nasal steps and generalized depressions are most likely seen in glaucoma. Studies suggest that performing multiple visual fields on the same day (frontloading) may enhance reliability in testing and yield more confident diagnosis. Past vasculopathies can confound glaucoma diagnosis. While fields from prior providers may add additional insight, like with OCTs, new fields should be taken to help with future progression analysis.

While the World Glaucoma Association recommends at least four visual fields in the first two years and possibly six if the patient is at risk for rapid progression, greater than 75% of glaucoma patients receive less than one field per year.

Making Decisions
In many scenarios, the optometrist must decide: should treatment be continued, changed or discontinued altogether? Several factors may arise to lead practitioners to one decision or another.

Case 1: Continue Treatment. An 83-year-old woman with Alzheimer’s reported to the clinic accompanied by her husband. She was previously diagnosed with primary open-angle glaucoma (POAG) by a prior optometrist who had since retired. She was being treated with Xalatan (latanoprost, Pfizer) qhs OU. Her husband had expressed concerns regarding compliance due to her resistance to his administration of drop therapy. He also expressed the patient could not sustain long office visits without agitation.

The patient’s last Humphrey visual field (HVF) was performed in 2020 without glaucomatous defects. Their last OCT was performed in 2022 and demonstrated excellent reliability with robust RNFL on all clock hours and an average RNFL thickness of 90um and average cup-to-disc ratio of 0.57 for both OD and OS. Her IOP was measured at 12.0mm Hg OD and 14.0mm Hg OS with Ocular Response Analyzer at 9:46am. Her RNFL appeared robust for age-expected norms without suggestion of any slit or wedge.
defects (Figure 2). On RNFL GPA, the HVF was clear without glaucomatous defects in the right eye, while the left eye suggested a superonasal defect mimicking a nasal step on the gray scale but falling short of cluster criteria on the pattern deviation plot (Figure 3).

Modification or discontinuation of therapy could have been a possibility, but given the husband’s personal experience with glaucoma and the longevity of care with another provider, a mutual decision was made to continue with treatment to the best of their ability and monitor diurnal IOP closely. Had the patient’s glaucoma state been more severe or risked fixation, changing treatment options may have been considered. In this case, the patient and her husband were assured that quality of vision had a high chance of preservation given the patient’s structural stability. Keeping the treatment the same allows providers the opportunity to focus on building the patient’s trust and respect up to the same level they once had for their past providers.

Future considerations could include therapeutic alternatives such as selective laser trabeculoplasty, Durysta (intracameral bimatoprost, AbbVie) and/or MIGS procedure(s). These all reduce the burden of compliance.

In general, removing the burden of medication compliance also reduces risk for falls and motor vehicle accidents. Fall risk in the elderly population has been positively correlated with visual field loss secondary to glaucoma.20 Elderly with glaucoma were 1.65-times more likely to be involved in a motor vehicle collision than elderly without glaucoma when visual acuity and contrast were corrected for.21

Case 2: Adjust Treatment. A 40-year-old Asian woman recently moved to the area and reported a previous diagnosis of glaucoma made by her general ophthalmologist. She reported excessive fatigue over the last several months. Her records indicate that she was diagnosed with POAG in 2018 and treated with 0.5% timolol bid OU. Previous records reported “large cupping with mild OCT dropout

OU” with a Tmax of 19mm Hg OU and pachs of 577 and 605. Visual field report stated, “Central 30-2 Sita-fast presents as normal.” We were not able to get the actual structural or functional test results. While it is impossible to know by chart review exactly what led a previous provider to make the diagnosis, it appears that large cupping and possible OCT thinning were the key factors, despite the relatively young age, moderate to thick pachs and low Tmax.

At our exam, her corneal-corrected IOP was 16.0mm Hg OD and 17.1mm Hg OS. Her refractive error was -1.00D OD and OS correctable to 20/20. OCT revealed large cups and large discs. Her RNFL and ganglion cell complex (GCC) showed reasonable thickness with no evidence of glaucomatous structural loss (Figure 4). The visual field was unremarkable, with no evidence of glaucomatous functional loss. Gonioscopy revealed angles open to ciliary body with grade 1 pigmentation of trabecular meshwork and no synechiae.

We explained that either her glaucoma is extremely well controlled or that it is possible that she may not need treatment. We also explained that her timolol treatment may be

Fig. 3. Superior nasal defect that falls short of cluster criteria.

Fig. 4. 5 RNFL and GCC of OCT show reasonable thickness without a glaucomatous pattern.
contributing to her fatigue. We discussed using a different drop vs. a complete discontinuation of treatment. She felt most comfortable switching to a different drop, and we started her on tafluprost. One month later her corneal-corrected IOP decreased to 13.2 mm Hg OD and 14.1 mm Hg OS, and she reported a significant reduction in fatigue. We will continue to monitor every six months.

**Case 3: Discontinue Treatment.**
A 49-year-old African American woman who recently moved to the area reported a previous diagnosis of POAG with a family history of glaucoma (sister, mother and paternal grandmother). She brought in paper records from her previous general ophthalmologist. The records, while barely legible, indicate that she was diagnosed as a POAG suspect based on large cupping (cup-to-disc ratio listed as 0.7 OD and OS), an asymmetric IOP of 15 mm Hg OD and 22 mm Hg OS by Goldmann, family history and “possible progression by Heidelberg Retina Tomograph.” There was a notation of “gonio—open to CB.”

We did not receive any of the actual test results, and there were no test reports in the records we received. The patient was then started on bimatoprost qhs OU, which lowered the pressure to the low to mid-teens. The patient was followed for several years, with no further notes indicating progression.

At our exam, best-corrected visual acuity was 20/20 OD and OS. Her refractive error was -2.00 OD and -1.75 OS. Corneal compensated IOP by Ocular Response Analyzer was 11.8 mm Hg OD and 13.7 mm Hg OS on treatment. Corneal pachymetry was 489 µm OD and 488 µm OS. Corneal hysteresis was 10.8 and 10.7. Cup-to-disc ratio was estimated at 0.7 OD and OS (Figure 5). OCT showed thick nerve fiber layer and GCC with a large disc area of 3.17 mm² OD and 3.05 mm² OS (Figure 6). Visual field was unremarkable OD and OS. The angles were open to ciliary body with grade 1 pigmentation of trabecular meshwork with no synechiae. The patient mentioned her eyes were becoming redder and more irritated. Biomicroscopy revealed grade 1 superficial punctate keratitis and bulbar conjunctival injection.

While she had large cupping, she also had a large disc, and her nerve fiber layer and GCC was unremarkable with excellent symmetry. We explained that she may not need treatment and that it would be reasonable to discontinue. She agreed. One year later, all testing was stable off treatment.

**Balancing Underdiagnosis and Overdiagnosis**
Glaucoma, the leading cause of blindness for adults over 60, often progresses silently. While underdiagnosis remains a major concern (estimates suggest up to 78% of cases are missed), recent studies highlight a growing issue: overdiagnosis.28-30

The challenge lies in the complexity of the disease itself. The optic nerve can vary greatly in appearance, and interpreting tests such as OCT requires significant expertise. This complexity was highlighted by Claude Burgoyne, MD, at a previous Optometric Glaucoma Society Meeting, who compared interpreting OCT scans to the work of a radiologist, suggesting a need for subspecialization within the field.

Comorbidities such as retinal artery and vein occlusion, anterior ischemic optic neuropathy, demyelinating disease, neurosarcoid, toxic optic neuropathy, traumatic optic neuropathy, sexually transmitted disease and tumors can all masquerade as glaucoma and must be carefully ruled out.

Adding to the difficulty, factors like family history can be a double-edged sword. While it’s a known risk factor for glaucoma, individuals with a family history were also 8.69-times more likely to be overdiagnosed.29,31 Similarly, cataract surgery emerged as another risk factor for overdiagnosis, especially when combined with family history.29

The legal landscape in optometry further complicates matters. Since most negligence cases involve missed diagnoses, the stakes are high for optometrists.32 This might lead them to err on the side of caution and diagnose glaucoma even with unclear test results.

While OCT is a valuable tool for early detection, its overuse can lead to unnecessary testing and potentially overdiagnosis. This could occur if optometrists routinely include OCT in basic wellness exams for healthy patients who may not require it. Higher amounts of hyperopia and myopia are known to displace the nerve fiber layer bundles nasally and temporally respectively. This may lead practitioners into diagnosing “red disease,” which means that the OCT database flags normal patients. Conversely, OCT’s in which the database shows green may lull the practitioner into a false sense of security when the patient has
by the recognition of silent progression and the imperative for timely detection, optometrists are challenged to navigate the intricate terrain of diagnostic precision. Acknowledging the dual specters of underdiagnosis and overdiagnosis, glaucoma clinicians must take a nuanced approach, fostering a balance between proactive vigilance and judicious restraint in optometric practice. ■


**Takeaways**

Through illustrative cases, this article delineates the intricate dance of clinical judgment, balancing the patient’s needs, treatment efficacy, and potential risks. However, this narrative extends beyond individual cases, delving into the broader issue of underdiagnosis and overdiagnosis in glaucoma care. Driven...
As eyecare providers, we know far too well how important compliance is in glaucoma management, and it’s hard enough having patients use their drops consistently and keep their appointments.

In theory, glaucoma drops sound simple and straightforward; however, drops come with an array of troubles. Topical medications can be difficult for the patient to obtain due to several pharmacy and insurance obstacles. Many branded medications need prior authorizations and/or coupons to make them affordable. Additionally, large chain pharmacies prioritize generics over branded medications and have the ability to override our prescriptions if we do not mark “dispense as written.”

All drops also have potential ocular and/or systemic side effects that can make them intolerable or unsafe to use. Even if the drug is affordable and tolerable, sometimes the medication doesn’t reduce the intraocular pressure (IOP) effectively, leaving us trialing different agents and/or adding more drops to a patient’s regimen. Lastly, after all of the above, patients can have difficulty remembering to instill their drops or physically getting drops in their eyes.

In this day and age, no matter what stage of open-angle glaucoma (mild to severe) patients have, there are many options available that reduce our reliance on drops. These treatments—selective laser trabeculoplasty (SLT), minimally invasive glaucoma surgeries (MIGS) and sustained-release drug delivery—can potentially reduce the number of drops or eliminate the need for daily drop dosing entirely.

In many cases, IOP is reduced and/or medications are eliminated. If patients do not require topical therapy after the procedure, we recommend IOP checks at least every six months to monitor for increasing IOP. Medical reduction, in particular, will result in happier patients who are appreciative of not having to deal with eye drops. The duration of effect of SLT is substantial, with most treatment effect lasting two to three years on average. The major benefit of SLT is that the procedure can be repeated, potentially providing years of glaucoma control without dependence on eye drops.

In the few cases where IOP does not respond to SLT treatment and drops are either not working or not tolerated, then MIGS should be considered. Glaucoma patients who develop cataract and are in need of intraocular...
lens replacement are also an ideal use-case for MIGS, as a surgical procedure is already needed and the drainage implant or technique is additive to it rather than a primary surgery.

**MIGS**
The popularity of MIGS has risen because the traditional surgical options for glaucoma were tube shunts and trabeculectomies. These procedures are wrought with complications, have prolonged healing time and involve large wounds requiring sutures through the conjunctiva. In contrast, MIGS are significantly safer, have a quick recovery time and are sutureless, since they are performed through clear cornea.

Categorizing MIGS can take many different approaches. MIGS is performed as a standalone procedure or in conjunction with cataract surgery; the latter is typically performed when there is phacomorphic component to a patient’s glaucoma or the cataract is visually significant and patient symptomatic. The majority of MIGS are performed via an *ab interno* approach.

The two main two categories of MIGS are trabecular stents—iStent infinite (Glaukos) and Hydrus Microstent (Alcon)—or trabecular stripping procedures (goniotomy or Omni canaloplasty/trabeculotomy). There is also the Xen Gel Stent (AbbVie), which we place in its own category because it lowers IOP by shunting aqueous fluid to the subconjunctival space.

Below, we will give general recommendations and complications to look out for with these procedures in the postoperative period. It’s important to note that all surgeons have their own protocol. We recommend establishing a good relationship and communicating with your referring surgeon, which will allow you to know each other’s thought processes and preferences for postoperative management, especially if complications arise.

**MIGS Options**
There are a multitude of options in this category, and their popularity ebbs and flows based on a combination of individual surgeon preference/experience and documented outcomes in the literature influencing uptake. Below, we will limit our discussion to those most popular at our clinic.

**Goniotomy or trabeculotomy with canaloplasty (Omni procedure)**
Both goniotomy and Omni procedures have been a popular choice by surgeons. I (Dr. Yadgarov) especially like the Omni due to its dual mechanism of canaloplasty and trabeculotomy. You can explain this to patients as a “Roto-rooter” plumbing procedure that helps the drainage of aqueous fluid. The Omni procedure typically works the day following surgery, but if there is inflammation, its full effect may take up to four to six weeks post-surgery.

CPT code: 0671T.

**Indication:** Open-angle glaucoma of any stage, in patients who have failed prior medical or surgical intervention.

**Global post-op period:** If performed standalone, there is no global period, so visits after surgery can be billed as office visits. If performed in conjunction with cataract surgery, then standard 90-day post-op is valid.

**Recommended post-op visits:** Day one, week one, month one.

**iStent infinite**
This product is the first standalone implantable device for patients with primary open-angle glaucoma and, since its creation, Glaukos has continued to improve upon its design. Surgeons can insert up to three iStents into an auto-injector system approximately six clock hours around Schlemm’s canal. The stents are designed to lower IOP by restoring the natural physiological outflow of aqueous humor.

CPT code: 65820 or 66174 (coordinate with surgeon).

**Indication:** Open-angle glaucoma of any stage, not controlled on eye drops or not tolerant of eye drops.

**Global post-op period:** 90 days.

**Recommended post-op visits:** Day one, week one, month one.

**Hydrus Microstent**
This is by far the largest-sized MIGS option available. The device covers 90° within the angle and bypasses the trabecular meshwork to help outflow via Schlemm’s canal. It can only be inserted during cataract surgery.
**Feature MIGS POST-OP**

**CPT code:** 66991  
**Indication:** Mild-to-moderate open-angle glaucoma.  
**Global post-op period:** 90-day post-op due to conjunction with cataract surgery.  
**Recommended post-op visits:** Day one, week one, month one.

**Xen Gel Stent**
While some consider the Xen implant to be a MIGS treatment, most doctors have this procedure in its own category due to the mechanism of action and complications that can arise, as well as revisions necessary to maintain function.  
**CPT code:** 66183.  
**Indication:** Refractory glaucoma, including cases where previous surgical treatment has failed, cases of primary open angle glaucoma and pseudoexfoliative or pigmentary glaucoma with open angles that are unresponsive to maximum tolerated medical therapy.  
**Post-op period:** 90 days.  
**Post-op visits:** Day one, week one, week three, then monthly.

**Post-op After Cataract Surgery and MIGS**
Adequate IOP reduction can often be unpredictable and treatment effects can wane quickly. Here’s what follow-up visits should consist of:  
**Day one.** Just like a typical cataract surgery patient, this visit consists of a vision and an IOP check. NaFl dye should be instilled to confirm a negative Seidel test. If IOP is elevated on day one, it is either due to retained viscoelastic or a weakened trabecular outflow system. We do not recommend burping the wound unless IOP >40mm Hg (to avoid causing inadvertent hyphema). For IOP between 21mm Hg and 30mm Hg, we recommend a short course of a single, quick-acting IOP-lowering drop, such as dorzolamide or brimonidine/timolol; there is no harm using a combination drug like these. For IOP between 30mm Hg and 40mm Hg, we recommend a combination IOP-lowering drops and seeing the patient several days later (before a typical one-week visit). For IOP greater than 40mm Hg, either burp the paracentesis wound or use oral acetazolamide (two 250mg tablets BID) for the first three days along with a combination IOP-lowering drop and see the patient back in two to three days.  
**Week one.** This visit is needed to make sure the patient is healing appropriately as a patient would post-cataract surgery. You also want to check to make sure the IOP is at an appropriate target. We recommend gonioscopy at this visit to confirm the glaucoma stent device inserted during surgery is in good position and open and not obstructed.  
**Weeks three and four.** Depending on previous healing and findings at the previous visit, sometimes patients need to return sooner than one month. This is a good visit to determine how well the IOP is controlled; mild glaucoma patients whose IOPs are controlled and on less or no glaucoma medications can potentially return after the three-month global period to re-establish glaucoma care with new baseline testing.  
**Month two.** For moderate to severe primary open-angle glaucoma patients, we recommend this visit to allow a second IOP check to confirm stability of glaucoma control.  
**After 90 days.** We recommend obtaining updated glaucoma testing to re-establish glaucoma care or establish new baselines if drops were discontinued or reduced.

**Postoperative Drops**
Broad-spectrum antibiotics QID five days to one week (unless dropless surgery is performed) are recommended, along with topical steroids (again, unless the patient had dropless surgery) and glaucoma drops. Mild-to-moderate glaucoma patients on one medicine can typically stop their glaucoma medicine one day after surgery. If the patient had been on multiple topical medications, it is recommended to stop one bottle and re-assess IOP after a few weeks of recovery. Our office typically stops the prostaglandin class first due to possible

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*Photo Credit: Katie Harris, OD*

This patient has a more translucent limbus where the Hydrus Microstent is visible on slit lamp within the nasal angle. This should not be a cause for alarm. Of note, observe the significant conjunctival injection and faint hyphema at the stent opening, which warrants a topical steroid to control the inflammation.
pro-inflammatory characteristics of the drop. If IOP continues to be low, another bottle can be trialed off.

For severe glaucoma patients, we caution to not stop all medicines, as these patients usually have a weakened trabecular outflow system and need MIGS as well as medical therapy to maintain IOP stability. Most severe patients need to stay on at least one medication to maintain a stable and low enough target pressure. However, if the patient is able to discontinue all medications, we recommend IOP checks every three to four months to detect elevating IOP or fluctuations.

Early Complications of MIGS
Postoperative management is more complex than other MIGS procedures due to the risk of complications and need for additional intervention.

**Postoperative inflammation.** This is more common when cataract surgery is combined with glaucoma procedures. A slit lamp examination can reveal one or more of the following: diffuse or, more commonly, limbal conjunctival injection, cells in the anterior chamber and corneal edema.

In some cases, a topical steroid dosed QID is needed (sometimes Q2H if there is also fibrin or significant pain). Also, the IOP can rise depending on amount of inflammation, but don’t be afraid to use steroids during the inflammatory phase; prednisolone acetate is usually sufficient enough. Difluprednate can also be used dependent of severity if the inflammation seen. Dosing can range from QID to Q2H dependent on severity. Steroid response typically takes many weeks to set in.

**Hyphema.** This typically occurs with trabecular stripping MIGS procedures such as goniotomy or trabeculotomy (Omni procedure). A slit lamp examination can reveal visible blood on the corneal endothelium or angle. If we do not see an obvious hyphema within the angle on slit lamp, we are highly suspicious of a microhyphema when we see 4+ cells in the anterior chamber on a post day one or week one visit. Gonioscopy can be performed during the week one visit to confirm a small hyphema in the inferior angle or a hyphema along the nasal trabecular meshwork. Postoperative hyphemas usually self-resolve (unless the IOP is persistently high).

We recommend staying on prednisolone three to four times a day until most of hyphema has resolved, which typically takes one to two weeks. If still present, be cautious with steroids, as IOP will start to rise after two weeks of use. After most of the hyphema has resolved, a standard or a quick steroid taper can be initiated. If the IOP rises, start topical medications and see the patient back within two to three days. If the IOP is still high (>21mm Hg) despite escalating treatment, reach out to the surgeon to discuss whether an anterior chamber washout is best.

We also recommend patients sleep at a 45° incline (with an extra pillow under their head at night) to help the blood settle quicker.

**Steroid response.** This is not a common occurrence, as most patients are tapered off within a month before the steroid response has time to kick in, but it does occur in those who have an inflammatory predisposition. If IOP rises within a few weeks of steroid use,
we recommend adding quick-acting combination glaucoma drugs and not stopping the steroid until the anterior chamber cell has substantially resolved, and then tapering. Once the patients is tapered off the steroid, the glaucoma drugs can be trialed off.

We recommend seeing the patient back in a few weeks to make sure the IOP is controlled. If topical medications are not controlling IOP, communicate with the surgeon.

**Infection.** Postsurgical endophthalmitis is extremely rare. Ensuring there are Seidel negative wounds and that the patient is following proper instructions and wearing an eye shield at night is important.

**Malpositioned stents.** Occasionally, due to the microinvasive nature of procedure, trabecular stents may not be positioned perfectly into the trabecular meshwork. These stents do not cause any associated ocular issues and can be left in place as long as they are not causing corneal endothelial disruption. A scenario that is typical for a malpositioned stent is when IOP does not lower much despite the MIGS malpositioned stent is when IOP does not lower much despite the MIGS.

Gonioscopy after the week is important.

**Malpositioned stents.** Occasionally, due to the microinvasive nature of procedure, trabecular stents may not be positioned perfectly into the trabecular meshwork. These stents do not cause any associated ocular issues and can be left in place as long as they are not causing corneal endothelial disruption. A scenario that is typical for a malpositioned stent is when IOP does not lower much despite the MIGS procedure. Gonioscopy after the week one visit can confirm this scenario.

**Xen-specific Complications**

Hypotony (IOP <6mm Hg) and elevated IOP are two complications patients may experience after implantation of the Xen stent. Hypotony is most commonly experienced and we tend to describe this to the patient as the stent is working “too good.” It’s usually temporary and dilation is needed to detect choroidal detachment. If the anterior chamber is shallow or there are choroidal detachments, starting a cycloplegic agent like atropine and increasing topical steroid tends to help these eyes recover quicker. In some cases, it’s critical to consult a surgeon.

Elevated IOP usually happens due to scarring around the stent. If the IOP is >13mm Hg at any of the visits or IOP is trending upwards, we recommend reaching out to the surgeon to assess if a minor Xen revision is needed with the surgeon to improve Xen stent flow and open the stent back up.

**Long-term Complications**

While rare, there are some possible hurdles patients may experience down the road that they need to be aware of.

**Best-corrected visual acuity loss.** This is a rare but serious complication that can arise in patients with moderate to advanced glaucoma who have field loss close to central fixation or extensive ganglion cell damage preoperatively. Procedures that drop IOP significantly, such as the Xen stent, can occasionally “snuff out” the central vision and result in worsened final visual acuity than what the patient started with.

Counseling patients appropriately is imperative to ensure realistic expectations and assess patients’ risk tolerance. To potentially reduce this risk, avoid the Xen stent in eyes with extensive ganglion cell damage—unless IOP is high—in which case, after appropriate counseling and acceptance of risk, surgery is recommended to prevent glaucoma progression.

**Endothelial cell loss.** Any device inserted within the anterior chamber can potentially cause endothelial cell loss. Both iStent and Hydrus have long-term data that show no significant endothelial cells over two to five years.

**Failure of MIGS.** No glaucoma treatment is permanent. It is important and prudent that patients understand MIGS or any glaucoma procedure doesn’t last forever and IOP can still rise over time. It is also imperative they understand that even with MIGS and stopping their glaucoma medicines, they still need to show up to clinic at least twice a year (more often dependent on glaucoma severity) to have their glaucoma monitored. If IOP does rise over time, despite MIGS, eye drops may need to be restarted to avoid the chance of glaucoma progression.

**Takeaways**

The optometric profession has evolved from the early days of a “glasses-only” specialty, as many states now allow ODs to provide more advanced medical care, including minor surgical procedures. With all of these expansions, one of the most powerful advantages optometrists have is the ability to maintain care of their own patients by performing postoperative care.

Glaucoma, in particular, is undergoing an interventional renaissance and partnering with your local glaucoma specialist will greatly benefit your patients. MIGS postoperative care is a critical element in a patient’s glaucoma journey, and we encourage each of you to be a part of that experience.

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A patient with unilateral or bilateral vision loss can be a challenge for the eyecare practitioner. Is there a functional reason or disease process causing the loss of vision? While most times the reason is quite apparent, there are times when the diagnosis is not so obvious. If a practitioner diagnoses disease and there is a functional issue, that is not going to adversely affect the patient’s vision or life. However, if the reverse conclusion is made and the patient is diagnosed with a functional problem, e.g., amblyopia but there is an underlying disease process, the result can have significant effects on a patient’s vision and even life.

The misdiagnosis of amblyopia is costly. For the patient, it can mean wasted time pursuing treatment for a functional problem when they may have a condition that can result in permanent loss of vision and in some cases even death. For the eyecare practitioner, it can mean loss of reputation and career.

This article will review the American Optometric Association (AOA) Guidelines for the criteria that support amblyopia (amblyogenic factors) and will then cover case presentations that exemplify how the practitioner can best differentiate functional vision loss from pathological vision loss.1

**AOA Guidelines**

Amblyopia consists of more than reduced visual acuity and has a constellation of symptoms and clinical findings including increased difficulty with crowding effects, abnormal spatial distortions, unsteady and inaccurate or eccentric monocular fixation, poor tracking ability, reduced contrast sensitivity and inaccurate accommodative response.1-5 Functional amblyopia can be a result of form deprivation, (e.g., cataract, ptosis, etc.), constant unilateral strabismus and amblyogenic refractive error either high isoametropic or anisometropic (Table 1).1,6

The key is assessment of the patient. A careful history is critical. Age of onset of the condition is also important. While amblyopia can still develop up to six to eight years of age, if the child presents with sudden worsening of visual acuity; after this age, a thorough clinical evaluation must be performed to rule out other causes of vision loss.1 Visual acuity needs to be assessed based on the child’s age and ability to perform the test. When Snellen visual acuity testing is not feasible, tests of forced preferential looking (e.g., Cardiff Cards, Teller Acuity Cards) or matching, (Lea Symbols, HOTV chart) in young children may be an alternative.7

Testing visual acuity through a neutral density filter may be helpful in ruling out amblyopia. The visual acuity will usually be the same in amblyopia; whereas if the vision drops significantly, a disease process may be suspect. Refractive error assessment should be performed under noncycloplegic and cycloplegic conditions. Retinoscopy can be a valuable tool to give clues to ocular health (like keratoconus with scissor reflex or detecting
media opacity) in addition to dioptic refractive value. While tropicamide can be used as a cycloplegic agent, in cases of strabismus and/or latent hyperopia, cyclopentolate is the drug of choice for controlling accommodation to assess refractive error. Monoculomotor deviation can be an adjunct cause of reduced acuity in patients with amblyopia. Fixation assessment can be performed by monocular visuscopy, with the calibrated target in the ophthalmoscope. More recently, studies have reported using optical coherence tomography (OCT) to assess eccentric fixation in children. Oculomotor deviation should be carefully assessed objectively. This should include a slow cover test to allow the fixing eye to pick up fixation; be mindful of both vertical and horizontal deviations. Small angle deviations, not clinically visible to cover test, may be revealed with ancillary sensorimotor fusion testing such as no stereopsis on random dot stereopsis and a failure to make a compensatory vergence movement with a 4° prism. Normal stereopsis in a patient over eight years of age with recent onset best-corrected visual acuity (BCVA) loss should be suspect for disease.

Ocular health assessment should be carefully performed to ensure that there are no abnormalities. Under standard pupillary light testing, look for evidence of any pupillary abnormality. Amblyopia is a condition affecting form sense, not light sense, so pupil responses should be normal. Color vision testing is an underused test that is easy to perform and can signify inherited retinal and optic nerve disease. Color vision in amblyopia is normal, so a patient with bilateral reduced vision and reduced color vision is a red flag for a possible inherited retinal disease such as cone dystrophy. Careful slit lamp examination is imperative to assess the ocular corneal surface for any pathology and corneal topography should be assessed in cases where scissoring of retinoscope images was detected, or in cases of prominent corneal nerves and/or when a Fleischer ring is detected on the corneal surface—these may be signs of early keratoconus. Dilation should be performed, and a careful assessment of the lens should be conducted to rule out any lenticous or subluxation. Subluxation can typically be viewed through a dilated pupil with Bruckner reflex on ophthalmoscopy, which may pick up subtle subluxations. Careful assessment of the macula and optic nerve is necessary when ruling out disease. Attention to the vasculature is also important since attenuated arterioles in a young individual could be a sign of retinitis pigmentosa. Unilateral hemorrhage and exudation in a young individual, especially a male, could signify Coats’ disease.

Fig. 1. Fundus photography reveals what appears to be a smaller optic nerve head in the left eye, suspicious for optic disc hypoplasia.
Technology and Differential Diagnosis

Supplemental testing in amblyopia should be ordered when there are no amblyogenic factors associated with the decrease in vision as previously described. Testing includes static visual field testing, OCT of the retina and optic nerve fiber layers, fluorescein angiography and fundus photography, including fundus auto-fluorescence imaging for inherited retinal diseases that affect the outer retina, such as retinitis pigmentosa (RP), Stargardt’s disease and cone dystrophy. Referral for electrodagnostic testing such as visual evoked potential (VEP) and electroretinography (ERG), electro-oculography and/or neuroimaging are other tests that are important in ruling out retinal and visual pathway disease.

Misdiagnosis of amblyopia is often the result of the failure to use or to refer for many of these available technologies. For example, many practitioners rely on confrontation visual fields (CVF) using fingers as a sufficient screener for visual field defects. Unfortunately, CVF using gross targets will only demonstrate abnormalities in cases of absolute field loss, such as in stroke, and end-stage glaucoma and inherited retinal degenerations. Relative field loss will be more difficult to detect. In the case of unilateral visual acuity loss due to an early space occupying lesion affecting the visual pathways, some form of static perimetry will be sensitive enough to pick up an early defect. VEP testing allows for objective testing of visual function and can be performed using patterned and non-patterned (flash) stimulation. Amblyopia is a disease of form sense, hence responses to pattern VEPs are reduced in amplitude and delayed, depending on the degree of amblyopia. However, responses to flash stimulation should be normal. If not, then the practitioner should suspect visual pathway disease. In young patients, space occupying lesions must be ruled out and neuroimaging may be necessary. ERGs are ordered when hereditary retinal diseases are suspected, such as RP, X-linked juvenile retinoschisis, cone dystrophy and Stargardt’s disease.

Misdiagnosed Ocular Diseases

A consistent number of ocular disease conditions have been misdiagnosed as amblyopia, especially in young children, based on the referrals we have received. These conditions include, but are not limited to:

- Keratoconus
- Lens anomalies
- Inherited retinal disease, including inherited macular diseases
  - Stargardt’s disease
  - RP and its related syndromes
  - X-linked juvenile retinoschisis
  - Cone dystrophy
- Coats’ disease (unilateral vascular anomaly often seen in young males)
- Congenital optic nerve head anomalies and inherited optic nerve disease
  - Dominant optic atrophy
  - Optic nerve hypoplasia
- Juvenile glaucoma
- Visual pathway disease, including undiagnosed space occupying lesions
The following cases demonstrate how the proper use of technologies helped to differentiate functional from pathological vision loss.

Case 1. Optic disc hypoplasia or refractive amblyopia?
A six-year-old was referred for amblyopia. His BCVA was 20/20 in the right eye with a +3.00D and 20/70 in the left eye with +6.25-1.00x90 after cycloplegic refraction. There was no strabismus present on cover testing. As per standard of care, the patient was dilated. Retinal evaluation revealed asymmetric optic nerve head size with the left nerve being smaller when compared with the right (Figure 1). The patient was referred for imaging to rule out functional vs. pathological component. OCT was performed but imaging from the left eye was unsuccessful (Figure 2). The patient returned a couple of weeks later, and the OCT image was repeated in the left eye only indicating a normal nerve with normal RNFL.

This patient does have amblyopia secondary to anisometropia with a stronger prescription on the left eye.

Case 2. Bilateral refractive amblyopia?
A 13-year-old girl was referred for corneal topography secondary to high cylinder and the provider was "unable to refract past -6.00D cylinder, no lens attachment available, possible keratoconic component." BCVA was 20/30 in the right eye with +2.75-6.50x180. Visual acuity in the left eye was 20/25 with +3.25-6.00x015. Pinhole was done at this visit, and no improvement was noted. Slit lamp examination and dilation were unremarkable. Pentacam corneal topography demonstrated high astigmatism in both eyes but regular corneas (Figure 3a). The patient was diagnosed with refractive amblyopia in both eyes because of the high astigmatism.

The patient was referred for vision therapy three years later with complaints of eye strain and "history of refractive amblyopia." BCVA was stable in the right eye at 20/30; however, the spectacle refraction had an increase of cylinder to +3.50-7.25x180. The left eye had a stable acuity of 20/30 and relatively stable refractive error of +2.50-6.75x005. A repeat of the Pentacam corneal topography was performed, and there was an increase in corneal cylinder of 1.4D in the right eye and 0.9D in the left eye, which is highly suspicious (Figure 3b). Gas permeable (GP) contact lenses were trialed, and the patient’s visual acuity improved. The patient was then subsequently fit with bitoric GP contact lenses with a final visual acuity that was 20/20 in the right eye and 20/25+ in the left eye.

While a formal diagnosis of keratoconus cannot be made in this case, the corneal topography is highly suspicious. BCVA cannot be assessed accurately unless you have attempted a GP lens. And unfortunately, this 13-year-old could have had better visual acuity in both eyes two years earlier if a GP lens was trialed. While these lenses may not be comfortable for young people, they deserve an attempt for the best possible visual acuity instead of being diagnosed with amblyopia. In this case, vision training is not necessary and would not have helped improve the vision.

In a separate unrelated case, a young woman in her 20s presented to an eye doctor who was temporarily covering for the regular eye doctor that day. The patient had complained of reduced vision in one eye for several weeks and was only correctable to 20/40 in the affected eye. The patient was a soft contact lens wearer. The eye doctor who was temporarily covering for the regular eye doctor concluded that the reduced vision was due to contact lens-induced corneal distortion. He advised the patient to discontinue her contact lens wear for one week and return when the regular eye doctor was there. The patient never returned, but as
her vision continued to deteriorate in the affected eye, she went to several other specialists until she found an optometrist who performed a static visual field test, which revealed bitemporal hemianopic field loss due to what was ultimately determined to be a pituitary adenoma.

The patient sued all the eye doctors who had seen her prior to her visit with the optometrist who was the only one to perform the correct test, i.e., a static visual field test. And she also sued the eye doctor who saw her for only one visit as a temporary stand-in for the regular eye doctor. What could this eye doctor have done on that visit? Since the eye doctor suspected visual acuity loss secondary to “distortion from her contact lenses,” he could have placed a trial GP lens on her eye which would have become her “new cornea.” An improvement in the VA would have supported a corneal etiology for the reduced vision. In this case, however, the BCVA would not have improved because the patient had a space occupying visual pathway lesion that was the cause of the reduced vision. Therefore, using trial GP contact lenses can help weed out pathologies believed to be due to corneal issues.

Case 3. Bilateral refractive amblyopia with learning disability? An 11-year-old asymptomatic male was referred for a vision training work-up for possible refractive amblyopia and poor test taker with a history of learning difficulties. There was no family history of eye disease, and the patient reported no eye health history. The patient’s current prescription was OD +1.50−1.75x175 and OS +1.75−2.25x165. BCVA was 20/40 in each eye. The referring provider noted that the examination was unremarkable and that the macula was “clear.” The patient had not been dilated.

Examination through a dilated pupil revealed attenuated arterioles, lack of a foveal reflex but no pigment abnormalities (Figure 4). Fundus autofluorescence (FAF) imaging revealed areas of hypo autofluorescence (AF) in the posterior pole and a central, small hyper-AF ring in each eye (Figure 5). A macular OCT revealed a thickened macula in each eye with evidence of cystoid macular edema (CME). ERG testing revealed extinguished responses under both photopic and scotopic conditions. Genetic testing revealed two pathogenic variants in CRB1 which is associated with several autosomal recessive (ar) diseases including arRP. In this case, the genetic testing confirmed the clinical characteristics. CME is a late-stage development in arRP and the small hyper-AF ring seen in the FAF imaging confirms this is late-stage RP. Unfortunately, standard treatment of CME, including intravitreal injection of a steroid medication, failed to improve the CME.

Although the patient had a moderate degree of astigmatism, the numbers did not meet the criteria for refractive amblyopia. Therefore, the diagnosis of “possible refractive amblyopia” was not confirmed but we were able to correctly diagnose advanced RP. Not all patients with RP present with the typical bone-spicule pigmentation, especially in some pediatric cases.

All patients deserve a correct and timely diagnosis. Although there currently is no medical treatment, clinical trials are underway and during this patient’s lifetime, there may be treatment for him. Instead of vision training, this patient is better served by a low vision consult.

Case 4. Possible bilateral amblyopia without pathology? A 31-year-old Hispanic female was referred for “possible bilateral amblyopia without pathology.” She reported decreased vision in both eyes for as long as she could remember. There was no family history of a similar issue. When she was younger, she had a
full battery of tests, including an MRI to determine why she had reduced vision. None of these tests helped determine the cause. She was becoming concerned because now she has noted difficulty distinguishing colors on her computer screen. The referring doctor noted that her “ocular health was normal with a clear macula, and no pallor noted.” The doctor had performed a 30º visual field test which was noted to be “full OD and OS.”

At her exam, BCVAs were 20/40 OD through a +0.50 sphere and 20/60 OS through plano –0.25x5. Pupils were normal, corneas and lenses were clear. Examination of the retinas revealed temporal pallor of both optic nerve heads, greater in the left eye (Figure 6). A 10º Octopus M TOP visual field test revealed small central scotomas in both eyes, greater in the left eye (Figure 7). An OCT of the RNFL revealed thinning along the clock sectors representing the papillomacular bundle RNFL in both eyes (Figure 8). Due to the suspicion of a hereditary optic neuropathy, genetic testing was performed, which revealed a pathogenic variant in the OPA1 gene, which is associated with dominant optic atrophy or Kjer’s disease.15

The visual field performed in the referring doctor’s office was a 30º visual field. Why did it miss a central field defect? The points in a 30º field test are six degrees apart and a small central scotoma would easily be missed on a test program like this one. The Octopus M TOP visual field test is a 10º field test in which the points tested within the central 4º of the visual field are 0.7º apart. That is why this test program was able to detect small central scotomas that explained the patient’s decreased visual acuity. BCVA was worse in the left eye (20/60) than the right eye (20/40). The Octopus M TOP visual field test confirmed that the central scotoma was greater in the left eye.

Differentiating functional from pathological vision loss can best be determined when ordering the proper tests. The referring practitioner did not order an OCT of the RNFL which would have detected thinning seen in Figure 8. In addition, the practitioner ordered a 30º visual field test but when it was found to be “full,” the practitioner should have had the patient return for a 10º visual field test. When a patient has unexplainable loss of vision in one eye, it is best to initially perform a 10º field test.

Takeaways
The cases presented in this review are but a few of the many where vision loss has been attributed to functional issues. The missed pathology can result in a delay in diagnosis which can result in vision loss that can be treatable. In other cases, the true nature of the disease is not identified, and this can affect services that could be made available to the patient, such as low vision.

In the case of unidentified inherited retinal disease, the reason for the vision loss was not accurately diagnosed, and with the development and approval of gene therapies, this could have consequences in the future. In addition, families need to be aware of the history of eye diseases for purposes of family planning. Of greatest consequence is the misdiagnosis of pathology that can result in permanent vision loss or even life because the condition was not treated in time, as in the case of visual pathway lesions that grow if undetected and untreated.

Eyecare practitioners need to rule out disease before using the catchall diagnosis of amblyopia. While a thorough eye examination is the first place to start, knowledge of amblyogenic factors and the use of current imaging technologies are extremely helpful to avoid these types of errors. In addition, the proper use of static perimetry in place of gross CVFs is essential to help detect early visual pathway disease in unexplainable acuity loss, especially in one eye in an individual over the age of eight years and where no amblyogenic factor is present. Despite this, gross CVF testing is still taught in schools today and is still used throughout the eyecare profession.

Fig. 8. OCT RNFL clock sector reveals symmetric papillomacular bundle thinning coinciding with the temporal disc pallor and central visual field defects in each eye.

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1. All the following are possible etiologies of amblyopia **EXCEPT**:  
   a. Unilateral esotropia  
   b. Anisometropia of 6.00D or more  
   c. Alternating exotropia  
   d. Uncorrected -3.00D astigmatism at oblique axes.  

2. All etiologies of amblyopia generally occur before the age of what?  
   a. Three years  
   b. Five years  
   c. Eight years  
   d. Twelve years  

3. Color vision tests in an amblyopic eye will ______.  
   a. Be normal in those with normal color vision  
   b. Demonstrate a deutan defect  
   c. Demonstrate a tritan defect  
   d. Demonstrate mixed color defects.  

4. Pupil responses in amblyopia _______.  
   a. Are usually normal  
   b. Will feature an afferent pupil defect in the amblyopic eye  
   c. Will be abnormal in both the amblyopic and non-amblyopic eye  
   d. Are normal to accommodation but not to light.  

5. Normal stereopsis in a patient with recent onset unexplained reduced vision in one eye describes which of the following?  
   a. Supports a diagnosis of amblyopia  
   b. Supports a diagnosis of pathological vision loss  
   c. Indicates that the patient is likely malingering.  
   d. Indicates that the patient developed amblyopia after eight years of age.  

6. The visual acuity of an amblyopic eye when a neutral density filter is placed in front of it will usually _______.  
   a. Remain the same  
   b. Improve significantly  
   c. Decrease significantly  
   d. Initially improve and then decline significantly over a minute.  

7. The drug of choice for controlling accommodation and determining refractive error is which of the following?  
   a. Tropicamide  
   b. Cyclopentolate  
   c. Phenylephrine  
   d. Epinephrine.  

8. Visual fields in amblyopia are usually which of the following?  
   a. Characterized by a dense central scotoma in the affected eye.  
   b. Characterized by arcuate field loss.  
   c. Characterized by an enlarged blind spot.  
   d. Full.  

9. The LEAST useful test in a 15-year-old patient who presents with an unexplained BCVA of 20/40 in one eye is ______.  
   a. OCT.  
   b. VEP.  
   c. Fundus autofluorescence.  
   d. Gross confrontation visual field.  

10. Which of the following tests should be performed to rule out structural abnormality of the macula?  
    a. OCT.  
    b. VEP.  
    c. Visual field testing.  
    d. ERG.  

11. The best test in a young patient with reduced best spectacle-corrected visual acuity in each eye with significantly increasing astigmatism in each eye is:  
    a. OCT.  
    b. VEP.  
    c. Visual field testing.  
    d. Corneal topography.  

12. An eight-year-old boy presents with decreased BCVA in both eyes. The refractive error is -2.00-1.75X 75 OD and -3.00-2.00 x 90 OS. The fundus exam is noted for attenuated arterioles. Color vision and pupils are normal. The OCT reveals cystoid macular edema. What test should the patient be referred for?  
    a. VEP.  
    b. ERG.  
    c. Corneal topography.  
    d. Neuroimaging.  

13. A 14-year-old male complained of recent onset of reduced vision in the right eye which was only correctable to 20/40. Refractive error was +0.50D sphere in each eye. The eye examination did not reveal any abnormalities in the macula or optic nerve. Gross CVF testing was full. Which test should be performed next?  
    a. Corneal topography.  
    b. Static visual field test.  
    c. ERG.  
    d. Flash VEP.  

14. A 10-year-old patient has BCVA of 20/200 in each eye. Refractive error is +3.00D sphere in each eye. The retina and optic nerve head appear normal in each eye. Visual field testing cannot be performed because the patient claims they can’t see any stimuli. The VEP is flat to both patterned and non-patterned flash stimulation. You suspect which of the following?  
    a. Inherited retinal disease.  
    b. Malingering.  
    c. Bilateral refractive amblyopia.  
    d. Visual pathway disease.  

15. All of the following types of strabismus can be associated with amblyopia **EXCEPT**:  
    a. Constant unilateral esotropia  
    b. Alternating esotropia.  
    c. Constant unilateral large angle esotropia.  
    d. Constant large angle hypertropia.  

16. All of the following conditions are often misdiagnosed as amblyopia **EXCEPT**:  
    a. Inherited retinal disease.  
    b. Coats’ disease.  
    c. Keratoconus.  
    d. Age-related macular degeneration.  

17. Pattern VEP responses in an amblyopic eye _____.  
   a. Are reduced in amplitude but not delayed.  
   b. Are reduced in amplitude and can be delayed.  
   c. Are delayed but not reduced in amplitude.  
   d. Are normal.  

18. Amblyopia causes a reduction of which of the following?  
   a. Form sense.  
   b. Light sense.  
   c. Both form and light sense.  
   d. Form sense initially but progresses to involve light sense as well.  

19. Which of the following statements is TRUE?  
   a. Visual field testing is unreliable in children less than 16 years of age.  
   b. Only gross CVF testing should be performed in children with unexplained reduced vision in one eye.  
   c. When visual acuity is reduced, and a 30º test is full, a central 10º field test should be performed.  
   d. If an OCT is normal in a patient with reduced visual acuity, a visual field test does not need to be performed.  

20. The two best functional tests to detect visual pathway disease are which of the following?  
    a. VEP and ERG.  
    b. VEP and visual fields.  
    c. ERG and visual fields.  
    d. OCT and VEP.
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Lesson 125073  RO-OSC-0724

JULY 15, 2024 | REVIEW OF OPTOMETRY 55
Adjusting Therapy When Warranted

The importance of fitting pieces together in the glaucoma puzzle.

This will be the first of two columns to explore the concept of using various pieces of information about our glaucoma patients to make educated, targeted, and personalized treatment plans. After managing patients with glaucoma for extended periods of time, it’s not unusual for progression to occur despite close surveillance and adequate patient compliance. This can happen for several reasons, including the loss of efficacy of the same medications over time, increased difficulty of stabilizing an optic nerve in an 80-year-old vs. when they initially began treatment 30 years prior, the overall health changes a patient undergoes after many years and the fact that glaucoma tends to simply become more difficult to manage over time.

What are we looking for in determining stability, where do we look for it and what do we do about it? These are the questions we should be asking ourselves each time we see a glaucoma patient in follow-up.

Case
This 83-year-old Caucasian woman has been a patient of mine for many years. She was initially diagnosed with moderately advanced glaucoma when I first saw her years ago; she had the characteristic findings associated with pressure-dependent glaucoma, including elevated intraocular pressure, neuroretinal rim tissue loss and visual field defects. As is normally the case, it may take several months to stabilize the glaucoma and to be certain that the patient is not progressing—this certainty does not occur in a matter of weeks. While we may think a patient is stable after a few initial visits, we really cannot be certain of the stability of the situation until several metrics have been repeated over time which demonstrate no further progression. These metrics are centered around structural and functional stability. Essentially, this would encompass stable OCT readings and stable visual field studies over time.

Not surprisingly, when you are managing a particular patient for more than 30 years, progression can occur. When we suspect progression, especially in a patient who has been stable for an extended period, that will usually be seen as change in the OCT and/or visual field. If everything has in fact been stable, the patient is compliant with medications and scheduled follow-up visits and hasn’t suffered any significant acute systemic medical complications, we wouldn’t expect a dramatic change in disease progression from one visit to the next. Consequently, the earliest signs of progression would be subtle.

Fig. 1. Seen here is advanced glaucomatous optic neuropathy, peripapillary atrophy, retinal pigment epithelium changes in the macula and a diffuse epiretinal membrane.
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Where would we see those subtle changes indicating disease progression? Certainly a visual field defect that was present over time would enlarge should the glaucoma worsen, or other field defects associated with glaucoma would begin to show up. That is fairly straightforward, notwithstanding the increased difficulty elderly patients may have in accurately taking a visual field test.

With our OCT instruments, subtle changes can be seen before visible funduscopic changes would be appreciated \textit{in vivo}. But where should we look, especially for subtle change, in OCT analyses? As I’ve written about many times in this column, we really need to look at several areas of the posterior pole for evidence of glaucomatous progression—namely the circumpapillary retinal nerve fiber layer (RNFL), the macula and the neuroretinal rim itself. With even more advanced glaucoma analysis software, such as the GMPE software available on the Heidelberg Spectralis, we can specifically look at not just one, but three different diameter circumpapillary RNFL scans, the ganglion cell layer in the macula (as opposed to total macular thickness) and insofar as the neuroretinal rim is concerned, the minimum rim width as measured from Bruch’s membrane opening to the internal limiting membrane, which is called the Bruch’s membrane opening–minimum rim width (BMO-MRW).

Think about it for a minute: If we are looking at all these areas of the posterior pole each time we evaluate our glaucoma patients for structural stability—especially if we are looking for subtle evidence of change—would we expect \textit{all} of these areas to show signs of progression? Or would we expect, rather, subtle change to be seen in some areas and not in others? Gross change and significant progression would naturally show up eventually in all those areas where ganglionic cells are lost—but subtle change? It intuitively makes sense that subtle change may appear in some areas but not others.

In fact, that is exactly what happens. The challenge is that precisely where those subtle changes first appear can vary from patient to patient, which is what happened in this patient. In Figure 1, we see a multimodal image of the patient’s right posterior pole. Clearly visible is a thin neuroretinal rim with characteristic glaucomatous cupping, an RNFL hemorrhage at 10 o’clock on the disc and associated age-related macular changes. Figure 2 shows the progression analysis specifically of the 3.5mm RNFL circle scan. Note that there is essentially no statistical change in this area of the RNFL over a nine-year period other than expected age-related thinning. Figures 3 and 4 show essentially the same thing—no significant deterioration of the RNFL, specifically in areas further away from the optic nerve, namely at the 4.1mm and 4.7mm diameter scan locations.

Note that in all the progression analyses of the three different diameter RNFL circle scans that there is no significant evidence of progression of the glaucoma. In Figure 5, however, we can clearly see deterioration in the neuroretinal rim...
BMO-MRW scan. In fact, on close examination, we see two instances where there is progression.

Had I not been looking at the BMO-MRW scans of this patient longitudinally and instead relied solely on the RNFL circle scans, I would have missed the two instances of subtle progression. Both times when there was progression of the disease, it was identified on the BMO-MRW scan but none of the three RNFL circle scans.

The point is that in this particular patient, subtle disease showed up in some areas (the neuroretinal rim) and not others (the RNFL). Each time that disease progression was noted, follow-up scans using the same strategy confirmed the change, therapy was subsequently adjusted and the patient was again stabilized. This is seen in Figure 5 in the first two scans as compared with scans three and four, and again in scan four, five and six as compared with scans seven and eight.

How we decide to modify therapy in the presence of disease progression is an individual clinical decision. New or different medications? Laser therapy? Surgical intervention? You must make that call depending on the specifics of the case. But if you are seeing progression without changing the treatment plan, that progression will continue to march on until all the metrics ultimately show change, at which time deterioration of the ganglion cells will no longer be subtle.

Conclusion
This 83-year-old patient still functions well in her day-to-day activities, is not encumbered visually by her advanced glaucoma and is enjoying life, albeit at a slower pace than when we first met. Isn’t that how we want these stories to go? Subtle disease is something you need to look for carefully and exhaustively, and at each follow-up visit with your glaucoma patients in particular.

![Fig. 5. The progression analysis of the BMO-MRW measurements of the same patient. Note specifically a change (thinning) of the neuroretinal rim metrics after the second scan and again after the sixth scan.](image)

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60-year-old African American woman with no past ocular history presented to the Bascom Palmer Eye Institute emergency department with blurry vision in the left eye for two weeks. The exam was notable for visual acuity of 20/20 in the right eye and counting fingers in the left. Intraocular pressures measured 13mm Hg and 15mm Hg in the right and left eyes, respectively. Slit-lamp exam was unremarkable with a clear cornea and no inflammatory cells or flare in either eye. Posterior segment exam of the left eye revealed epiretinal membrane, pseudohole and blurred inferior and superior disc margins; the posterior segment exam was unremarkable in the right eye. The pseudohole and epiretinal membrane in the left eye were not suspected to be the main cause for the severe decrease in vision due to their mild appearance and maintenance of the outer retinal anatomy. In the setting of poor vision and disc edema, an MRI of the brain and orbits with and without contrast was obtained. The MRI revealed bilateral anterior clinoidal lesions with optic nerve sheath involvement bilaterally, worse on the left side than the right (Figure 1).

Two days after initial presentation, the patient followed up in our neuro-ophthalmology clinic with a new onset intermediate uveitis in the left eye. Clinical exam showed keratic precipitates, 3+ anterior chamber reaction, 3+ vitreous cell with 1+ flare and grade one disc edema OS (Figures 2 and 3). Exam was stable in the right eye. A comprehensive review of systems revealed that the patient experienced joint pain, scattered nodular skin lesions across her body, hypoesthesia in the distal extremities and neck pain. She was transferred to an inpatient clinic for a further systemic workup given the high suspicion for sarcoidosis. We recommended an extensive lab workup including lab studies (ACE, RPR, FTA, ANCA, CBC, FTA, IgG4), chest CT with contrast and a spinal tap. The patient was advised to start prednisolone acetate 1.0% drops four times per day OS while admitted.

**The Culprit**
Sarcoidosis is a chronic multisystem disease and a common cause of ocular
inflammation. It is characterized by the formation of noncaseating granulomas in affected organs, most commonly the lungs, lymph nodes, skin, heart and eyes. Ocular sarcoidosis can be isolated to the eye or associated with other organ involvement. Ocular involvement ranges from 13% to 79% in patients with systemic sarcoidosis, and only 2% of cases have ocular complaints at initial presentation. Sarcoidosis affects all ethnic groups with the highest prevalence in northern European countries, where the condition affects 40 per 100,000 people. In the US, African Americans are 10 times more likely to develop ocular involvement compared with Caucasians. Onset occurs between the ages of 20 and 50 years with a slight female predominance.

Ocular Manifestations
Sarcoidosis can affect any ocular tissue and adnexa. Approximately 30% to 70% of cases initially present with unilateral or bilateral uveitis. Anterior uveitis manifests with mutton-fat keratic precipitates (especially in an Arlt triangle), Koepe and Busacca iris nodules and anterior and posterior synechiae. In intermediate uveitis, inflammatory aggregates organize as a clump of snowballs or in a linear strand referred to as a “string of pearls.” Posterior involvement occurs in 20% of patients with ocular sarcoidosis. Yellow or white nodular granulomatous lesions may present in the optic nerve, retina or choroid. Mid-peripheral periphlebitis is characteristic of ocular sarcoidosis. In severe cases, small, yellowish-white nodular granulomas accumulate along retinal venules, classically termed “candle-wax drippings.”

Even though uveitis is predominantly associated with sarcoidosis, other ocular manifestations include scleritis, conjunctival granulomas, acute follicular conjunctivitis, orbital inflammation and lacrimal gland inflammation. Branch or central retinal vein occlusions together with peripheral retinal nonperfusion can lead to neovascularization and vitreous hemorrhages. Orbital findings include palpable masses, ptosis, ophthalmoplegia, cataracts, glaucoma, cystoid macular edema and optic nerve edema.

Diagnosis and Treatment
For suspected ocular sarcoidosis the traditional approach is to obtain serum angiotensin-converting enzyme (ACE) and lysozyme levels. Elevated serum ACE is 73% sensitive, but when used in conjunction with whole-body gallium scanning, the sensitivity increases to 100%. Serum lysozyme, on the other hand, has a 60% sensitivity for sarcoid uveitis. ACE and lysozyme levels represent the granuloma burden of the body, and if the disease is isolated to the eye, these levels might be read as normal. A chest X-ray is a great screening tool for sarcoidosis, but if the reading is normal and suspicion of sarcoidosis is high, a CT scan of the chest should be considered. While more invasive, the gold standard for diagnosis is tissue biopsy of accessible affected lesions (lung, lymph nodes, skin lesions, lacrimal gland or conjunctiva).

In 2017, uveitis specialists wrote the criteria for the diagnosis of intraocular sarcoidosis, referred to as the International Workshop on Ocular Sarcoidosis. Diagnostic criteria include seven ocular manifestations and eight systemic investigation results found in ocular sarcoidosis. The diagnostic grading ranges from “definitive” (tissue biopsy) to “presumed” (typical ocular findings with bilateral hilar adenopathy) to “possible” disease (supporting ancillary evidence).

Treatment options vary depending on the severity and chronicity of the disease. Topical, periocular or systemic corticosteroids are considered first-line treatment for ocular sarcoidosis. Topical corticosteroids paired with cycloplegics are recommended for anterior uveitic disease. Intravitreal, periportal or implanted corticosteroids are reserved for posterior segment involvement. Systemic corticosteroids are considered in chronic cases, systemic sarcoidosis or in those who respond poorly to topical or regional therapy.

Immunosuppressive therapy...
or biologics are effective steroid-sparing agents in patients who require long-term management or are intolerant to systemic steroids. Laser photocoagulation, photodynamic therapy or anti-VEGF are administered for retinal neovascularization. Treatment options to consider in advanced cases include cataract surgery, vitrectomy and/or a glaucoma device implant. Establishing care with an internist, rheumatologist or pulmonologist is essential for systemic management, as these patients often require long-term management. Visual prognosis depends on the severity and chronicity of the condition, as well as whether the patient receives appropriate treatment. Patients should be closely monitored by a uveitis specialist and, if necessary, a neuro-ophthalmologist or retina specialist.

Back to Our Patient
The patient’s chest CT showed multiple lung nodules and hilar lymphadenopathy. A lung biopsy was performed, and the pathology revealed non-caseating granulomas, confirming a diagnosis of sarcoidosis with ocular involvement. The patient started systemic therapy (mycophenolic acid and oral prednisone). The patient is currently doing well on systemic treatment, and her vision improved from counting fingers to 20/20 OS (Figure 4) while the right eye has remained stable. She established care with neurology and rheumatology.

It is important for optometrists to identify the ocular manifestations of sarcoidosis, as we might be the first to encounter its initial presentation. Timely treatment, thorough lab workup and proper referrals can help preserve vision and enhance the quality of life for these patients.

A 49-year-old Hispanic female presented for a second opinion regarding chronic floaters and photopsia OU for seven months that were previously diagnosed as a posterior vitreous detachment. Medical history included migraines and hypothyroidism that were both controlled medically. She had no personal or family history of prior ophthalmic conditions.

Her entering VA was 20/20 OU, IOP was 12mm Hg OU, confrontation visual fields and extraocular motilities were full and pupils were equally round without a relative afferent pupillary defect. Slit lamp exam revealed a 1+ anterior and posterior subcapsular cataract OS and 1+ anterior and posterior vitreous cell OU.

**Take the Retina Quiz**
1. Which is true regarding the imaging?
   a. There is retinal vasculitis on the fluorescein angiogram.
   b. There is diffuse choroidal infiltration on the indocyanine green angiogram.
   c. There are fine vitreous opacities though no cystoid macular edema on the OCT.
   d. All of the above are true.

2. What is the most likely diagnosis?
   a. Behçet disease.
   b. Birdshot chorioretinitis.
   c. Primary vitreoretinal lymphoma.

3. Which is a known human leukocyte antigen associated with this condition?
   a. HLA-A29.
   b. HLA-B27.
   c. HLA-B51.
   d. HLA-DR4.

4. Which of the following is not a typical etiology for decreased vision in this disease?
   a. Cataract.
   b. Cystoid macular edema.
   c. Exudative retinal detachment.
   d. Retinal damage and photoreceptor loss.

5. What is the appropriate treatment?
   a. Medrol Dosepak.
   b. Pars plana vitrectomy.
   c. Topical prednisolone acetate one drop four times daily tapered weekly.
   d. Oral prednisone with early immunomodulatory therapy induction.

*For answers to the quiz, see page 82.*
Discussion

Birdshot chorioretinitis is a chronic, bilateral, non-infectious posterior uveitis with a typical phenotype of diffuse creamy choroidal lesions that are classically most prominent inferonasally. It was first described as “birdshot” in 1980 based on the distinct appearance and distribution of the lesions; the following year, the term “vitiliginous chorioretinitis” described the resemblance of the choroidal depigmentation to that of vitiligo. Birdshot chorioretinitis has an estimated prevalence of less than one in 100,000 and accounts for 1% of all uveitides and 7% of all posterior uveitides.

Diagnostic Criteria

Ones from the Standardization of Uveitis Nomenclature working group include: 1) characteristic bilateral multifocal choroiditis (“birdshot spots”) on ophthalmoscopy, 2) mild to no anterior chamber cell in the absence of keratic precipitates and posterior synechiae, 3) moderate to no vitritis or 4) +HLA-A29 in the setting of either characteristic “birdshot” lesions or characteristic hypocyanescent lesions on ICGA. The presence of criteria one through three or four alone are sufficient to make a diagnosis. Exclusions include positive serologies for syphilis, evidence of sarcoidosis (radiographic or tissue biopsy) or intraocular lymphoma. HLA-A29 positivity is nearly diagnostic in the appropriate clinical setting as it is present in nearly all patients with birdshot chorioretinitis. The association is so strong that authors have regarded HLA-A29 positivity as a “sine qua non” (i.e., without which, not) criterion for the diagnosis of birdshot chorioretinitis; thus, in patients with a negative HLA-A29, alternative diagnoses (including malignancy) must be thoroughly excluded. HLA-A29 is present in approximately two to three in 10,000 of the general population, 7% to 9% in all Caucasians and >95% of all birdshot chorioretinitis patients. Approximately 97.5% of patients are symptomatic to floaters, photopsia, blurry central vision, loss of peripheral vision, impaired contrast sensitivity or nyctalopia at time of diagnosis.

Vision loss is usually due to cystoid macular edema (CME) or retinal damage with photoreceptor damage. Clinical exam shows creamy ovoid lesions disbursed throughout the fundus with inferonasal predominance.

Multimodal Imaging

OCT is useful for the diagnosis and monitoring of CME as well as photoreceptor integrity. FAF is of little value in the diagnosis of early disease state, but can help monitor the status of the retinal pigment epithelium (RPE) (which portends photoreceptor health) in the later stages of disease. FA is useful in the diagnosis and monitoring of retinal vasculitis but is of little utility in the assessment of the choroidal lesions.

ICGA is perhaps the most helpful imaging modality to demonstrate the presence of choroidal lesions as diffuse multifocal hypocyanescence, especially in early presentations where the lesions may be difficult to discern ophthalmoscopically due to subtlety or pigmentary fundus alterations (blonde fundus, chronic inflammation, etc.).

Treatment

Initial management consists of systemic (with or without local) corticosteroids and early induction of corticosteroid-sparing immunomodulatory therapy (IMT) due to the incomplete response of birdshot chorioretinitis to corticosteroid monotherapy.
Birdshot chorioretinitis generally requires long-term extended IMT to maintain suppression of intraocular inflammation and therefore preservation of vision. Similar to the general uveitis population, 4% in the general uveitis population. Biologic agents such as adalimumab have a more favorable side effect profile than conventional immunosuppression and have demonstrated efficacy at controlling disease activity in both primary and refractory cases. Local therapies (sub-Tenon triamcinolone acetonide, intravitreal dexamethasone implant, intravitreal fluocinolone acetonide implant) are used in patients where systemic treatment is either intolerable or insufficient, though they carry a higher risk of cataract and glaucoma.

**Prognosis**
Preservation of the choroidal pigment is necessary to maintain normal function of the overlying RPE and photoreceptors. Long-term visual prognosis depends on extent of choroidal infiltration; literature reports that 14% to 16% and 20% to 22% of patients will be legally blind (20/200 or worse in both eyes) at five- and 10-year follow-ups, respectively, as compared with 4% in the general uveitis population. Furthermore, 57% of patients achieve VA of 20/60 or worse, compared with 35% in the general uveitis population; the leading cause of vision loss in these patients is CME which is seen in 50% to 84%, compared with 30% in the general uveitis population.

Once serologies ruled out infectious etiologies, our patient was started on oral prednisone 60mg daily and recommended early induction of IMT. She was resistant to initiating IMT due to concern for side effects and frequently self-discontinued her methotrexate initially and adalimumab later. Ultimately, adequate disease control was obtained with a combination of oral steroids, temporary use of IMT and local therapy with sub-Tenon triamcinolone acetonide. Her cataract OS eventually worsened and she underwent surgery. Her BCVA remains 20/20 OU, and she is being followed closely for any sign of disease reactivation with multimodal imaging.

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A 68-year-old African American male presented to the clinic for a routine eye examination with a chief complaint of blurred vision OS of many months’ duration. His ocular history was remarkable for cataracts and blunt trauma OU. His systemic history was remarkable for appropriately treated hypertension and diabetes. He denied allergies to medications. His best-corrected entering visual acuities were 20/20 OD and 20/30 OS at distance and near, with no improvement upon pinhole or refraction. His external examination was normal with the exception of the facial Amsler grid OS. There was no afferent defect.

Biomicroscopic exam demonstrated normal anterior segment tissues with grade II nuclear sclerotic cataracts, present in both eyes. His intraocular pressures measured 16mm Hg by Goldmann applanation tonometry. The pertinent posterior segment findings are demonstrated in the photographs and OCT scans shown here.

**Additional Testing**
A traditional Amsler grid revealed some relative scotomata and metamorphopsia centrally OS; this was substantiated upon formal automated perimetry. Additional funduscopic examination was completed with a 90-diopter lens; there was no Watske-Allen sign (vertical strip of light perceived by the patient as “broken” or distorted). OCT testing was completed, uncovering the clear diagnosis. A laser interferometer could also have been used to assess best acuity under the current conditions, showing little improvement. Color photography was also completed for the purposes of documentation.

**Your Diagnosis**
What would be your diagnosis in this case based on the presentation? What is the likely prognosis? To find out, read the online version at www.reviewofoptometry.com.

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**Fundus examination revealed the following presentations. Does this match the case history?**

**Do the OCT scans seen here give you more information about the patient’s ocular status? Which findings are most pertinent to the case?**

---

**Dr. Gurwood thanks Megan Cruce, OD, for her contributions to this case.**

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**Retina Quiz Answers (from page 78)—Q1: d, Q2: b, Q3: a, Q4: c, Q5: d**

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**About Dr. Gurwood**
Dr. Gurwood is a professor of clinical sciences at The Eye Institute of the Pennsylvania College of Optometry at Salus University. He is a co-chief of Primary Care Suite 3. He is attending medical staff in the department of ophthalmology at Albert Einstein Medical Center, Philadelphia. He has no financial interests to disclose.
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