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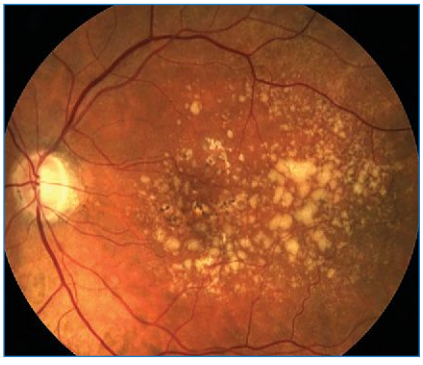
JUNE 2025

Lifestyle May Have a Bigger Impact on AMD than Fish Oil

With age-related macular degeneration a leading cause of vision loss in older adults, alternative treatments are being explored to see if they can help prevent or slow the disease, including omega-3 fatty acids found in fish oil. In a recent study presented at ARVO 2025, researchers investigated if taking fish oil supplements could help protect against new AMD in a population of U.S. veterans, but they found that it doesn't seem to lower the risk of this condition.[1]

A retrospective cohort study using ICD coding was conducted using the US Veteran Affairs Corporate Data Warehouse, including all patients aged 55 years and older who had a baseline eye exam between 2005 and 2013 without AMD recorded at or prior to baseline and a follow-up exam 10 years later. Exclusion criteria included presence of diabetic retinopathy, retinal artery/vein occlusion, retinal surgery or pentosan polysulfate sodium use. Patients receiving fish oil from the VA pharmacy at baseline were categorized into the fish oil exposure group, which was matched to a non-exposure control group without a history of fish oil prescription based on year of baseline exam, age, sex, race,



ethnicity, grouped state of residence, cardiovascular disease, hypertension, diabetes and smoking status. The primary outcome variable was AMD diagnosis at follow-up exam.

More than 64,000 US veterans aged 55 and older were followed, with most patients being male (95.7 percent) and white (79.2 percent). About half took fish oil supplements (32,499 patients) and the other half (32,318) did not. Of these, 7.3 percent of patients with fish oil exposure and 7.4 percent of patients without fish oil exposure were diagnosed with AMD. Given this lack of a meaningful difference in the number of new AMD cases between the two groups following 10 years of fish oil use, the authors concluded that taking fish oil supplements did not seem to lower the risk of developing AMD.

"Based on these findings, we recommend that preventing AMD should focus more on lifestyle changes, such as quitting smoking, which can have a bigger impact on eye health than taking fish oil supplements," the authors concluded.

1. Cao AA, Westanmo AD, Gravely AA, Armbrust KR. Omega-3 fatty acid supplementation and incident age-related macular degeneration in a US veteran population: findings from a retrospective cohort study. ARVO 2025 annual meeting.

AMD Brings Greater Dementia Risk

With age-related macular degeneration sharing several clinical and pathological features with neurological disease, one new study based out of UCLA in Los Angeles presented at ARVO has explored the former disease and dementia using the National Institutes of Health (NIH) All of Us Research Program. In this population, the presence of AMD was associated with an increased likelihood of dementia.[1]

Presented at ARVO 2025, this cross-sectional study included all research program participants from 2017 to 2022 who had electronic health record data. The primary exposure was a diagnosis of AMD. Of 287,012 overall participants included in the study, 4,732 (1.6 percent) individuals had any AMD. A secondary exposure was defined as the presence of wet vs. dry AMD. Researchers found that 19.6 percent of the participants with AMD had the wet subtype and 80.4 percent had dry AMD. The prevalence of any dementia in the overall participant population was 3,344 (1.2 percent).

Individuals with vs. without AMD had higher odds of any dementia in unadjusted (OR: 4.47) and fully adjusted models (OR: 1.46). In individuals with AMD, there were no statistically significant associations between wet vs. dry AMD and dementia in both unadjusted (OR: 1.24) and adjusted analyses (OR: 1.12).

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Those diagnosed with dementia could possibly be less likely to receive eye care, which may have implications for injury prevention, physical and cognitive function and quality of life.

The researchers concluded that, "Future studies are needed to examine the potential benefit of dementia screening in patients diagnosed with AMD and whether subjects truly have dementia since poor vision may be causing dementia-like symptoms."

1. Yun JS, Santina A, Hou KK, et al. Age-related macular degeneration and dementia: investigating associations in the NIH All of Us Research database. ARVO 2025 annual meeting.

"Frontloading" Visual Fields May Pay Dividends

In two years, three visual field tests per year are required to detect relatively fast progression (-2dB per year) in patients with average visual field variability. This proposal emphasizes the detection of relatively fast progressors, but if considering median progression rates at the cohort level, there need to be even more tests performed to identify such cases. Researchers from the University of New South Wales in Australia have continued to test their "frontloading" approach, which involves two VF tests per eye at each visit, as opposed to only at the first visit, such as to establish a baseline. In their recent study published in *Ophthalmology Glaucoma*, the team analyzed the number of VF tests attained in a clinical cohort of subjects, comparing this with evidence-based recommendations. They determined that the frontloading approach overall led to savings in time and cost in comparison to non-frontloading for achieving six reliable VFs and thus potentially provides an avenue for earlier detection of glaucomatous change.

The study used 10,010 SITA-Faster VF tests of 535 clinical subjects, of which 8,931 had a false positive rate ≤15 percent. Approximately 90 percent of subjects had early or moderate open-angle glaucoma.

When using the frontloading protocol, it took an average of 1.4 years to attain six reliable VFs for the right and left eyes, respectively. For the non-frontloaded protocol, the average times were 2.6 years and 2.5 years for right and left eyes, respectively. In the study, 82.5 percent of right eyes and 85.4 percent of left eyes achieved six reliable VFs within two years when frontloaded, but the proportion was only 15.8 percent and 18.8 percent when non-frontloaded for right and left eyes, respectively. The average total number of 24-2 tests performed per visit over the follow-up duration was 3.6, so it was uncommon for more than two tests to have been performed per eye.

The frontloading approach mitigates the issue of tailoring testing given limited information by recommending at least two tests per eye per patient unless there is a clinical decision made otherwise. This approach is helpful in the workflow, as it ensures that all testing is completed while the patient is already in the perimetry suite and while the test instructions are fresh.

"The empirical data in the present study allowed us to plot the number of cumulative tests at different time points, highlighting that the critical number of reliable visual field tests can be achieved within the first two years of follow-up for most patients using the frontloading approach," the study authors wrote in their paper.

Even accounting for a 20 percent increased patient load achievable with within-visit time savings when non-frontloading, the frontloaded approach was still monetarily less expensive, owing to the overall fewer absolute numbers of visits required to achieve visual field targets.

The researchers did note that their results were only generalizable to patients with early to moderate glaucoma. The needs of patients with more advanced stages of glaucoma may be different, but the team still believes that they may be even more likely to benefit from more visual field tests to monitor their disease trajectory.

1. Wang H, Masselos K, Tan JCK, et al. The frontloading approach to meet guideline-recommended visual field testing for glaucoma: Time and cost. Ophthalmol Glaucoma. April 11, 2025. [Epub ahead of print].

Complications in Ocular GVHD after Cataract Surgery

Cataract surgery is a common procedure required by patients suffering from ocular graft-versus-host disease, a debilitating eye condition that can result from stem cell transplantation. While topical nonsteroidal anti-inflammatory drugs are frequently prescribed to prevent cystoid macular edema—a common complication following cataract surgery—their use in ocular GVHD patients has been debated due to potential adverse effects on the cornea. In a new study whose findings were presented last month at ARVO 2025 in Salt Lake City, researchers found a significant association between the postoperative use of topical NSAIDs and an increased risk of corneal complications among ocular GVHD patients.[1]

The study was conducted at three medical sites and analyzed patients who underwent allogeneic stem cell transplantation and developed definite GVHD, as classified by the International Chronic Ocular GVHD Consensus Group. Spanning from January

(Continued on p. 12)

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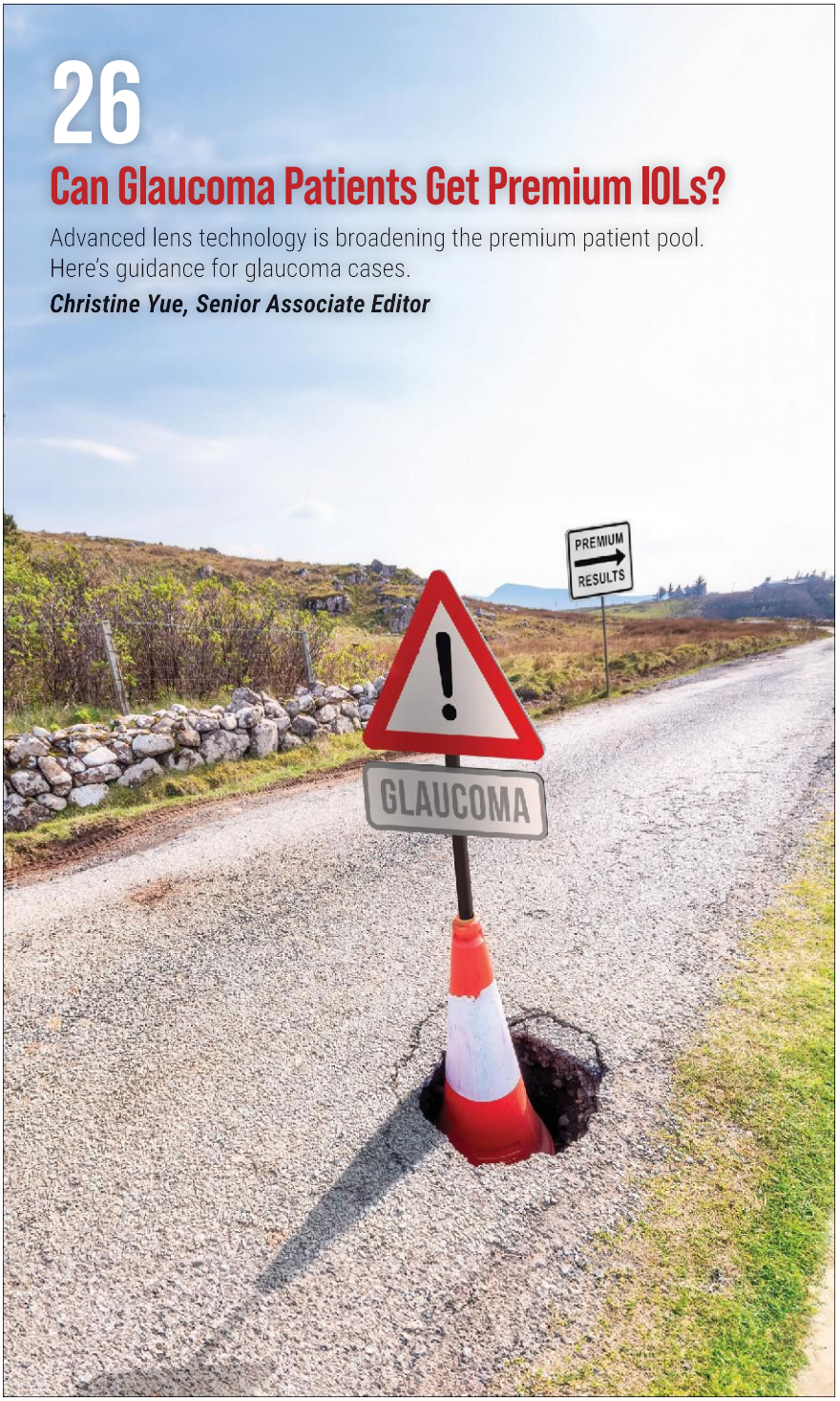

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1. iDose TR (travoprost intracameral implant) 75 mcg Prescribing Information. Glaukos Corporation. 2023.

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(Continued from p. 6)

2014 to September 2023, it used the Mayo Clinic's Ophthalmology Parametric Universal Search database to identify cases where patients showed symptoms of ocular GVHD and received topical NSAIDs within 45 days after surgery. Those lacking sufficient follow-up data were excluded. The study primarily investigated corneal complications within three months post-surgery.

Out of 80 eyes from 58 patients (43 percent female; mean age at surgery: 58), topical NSAIDs were used in 10 eyes (13 perceent) of nine patients (16 percent). Notably, there was a significantly higher occurrence of corneal complications—such as filamentary keratitis, corneal abrasions and corneal ulcers—in the group treated with topical NSAIDs (30 percent) compared to those who didn't receive the drugs (6 percent). This difference was statistically significant, with a p-value of 0.024, indicating a strong link between topical NSAID use and increased corneal complications in this particular population.

Given the retrospective nature of the study, further research is warranted to fully understand the risks and benefits of topical NSAIDs in this vulnerable group. However, the current evidence suggests that the use of these medications should be carefully considered, weighing the potential risks against the benefits to patients.

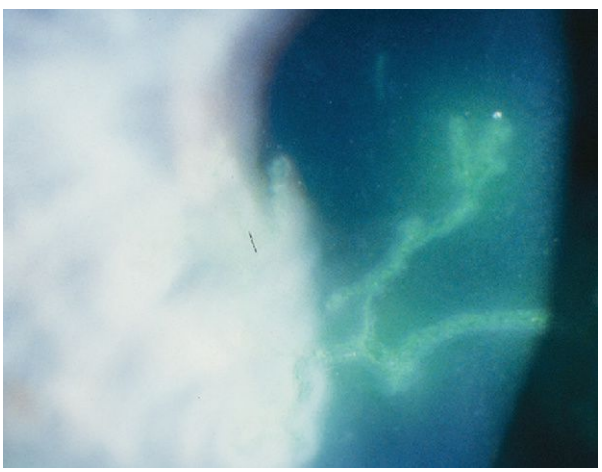
1. LSinha K, Lopez-Ruiz A, Buckner-Petty S, Shen JF. Corneal complications associated with topical nonsteroidal anti-inflammatory drug use following cataract surgery in patients with ocular graft-versus-host disease. ARVO 2025 Annual Meeting.

Treatment Regimen Impacts Chance of Herpes Flares

Repeated flare-ups of herpetic stromal keratitis, caused by the herpes virus, can damage the cornea. Early recurrence can happen within six weeks after initial improvement, which led a group of researchers from Italy to investigate what could be causing these flares. Their results were presented this past May at ARVO, identifying treatment timing and duration as primary factors.

The retrospective, case-control study sought to investigate the demographic, clinical and treatment parameters as potential predictors of early recurrence of herpetic stromal keratitis. Eligibility criteria included clinical or PCR-confirmed HSK and at least six months of follow up. Patients were stratified into two groups: cases with early recurrences (≤6 weeks) and controls with no recurrence or late recurrences (>6 weeks).

Among 111 herpes simplex keratitis episodes from 51 adult and pediatric patients, 13 adults (12 percent) were associated with early recurrences and four children (12 percent).



Extended treatment for herpes may reduce the chance of early recurrences.

Researchers showed a statistically significant association between early recurrence and shorter duration of systemic antiviral (88.3 ±169.5 vs. 309.4 ±437.1 days) and topical steroid treatment (33.4 ±23.6 vs. 199.6 ±359.2 days).

Adults differed from children in that no early recurrences were found after episodes treated with a systemic antiviral for more than 91 days and with topical steroids for more than 77 days. An increased recurrence risk was correlated with delayed treatment initiation (10.4 ±10.2 days vs. 4.4 ±5.8 days). No demographic, seasonal or clinical factor showed to be statistically relevant for the outcome.

The paper authors concluded that treatment regimen appears to be the primary predictive factor for early HSK recurrences. Although further multicentric studies should be conducted, preliminary data suggest an association between the choice of topical steroids and recurrence rates. "Our results highlight the impact of treatment timing and duration on HSK recurrence, especially in adults," wrote the study's authors in their ARVO meeting abstract. "While the data suggest that extended antiviral and steroid therapies may reduce early recurrences, these observations require confirmation through larger studies." ◀

1. Villani E, Marelli L, Ferioli E, et al. Herpetic stromal keratitis recurrence: A retrospective case-control study. ARVO 2025 annual meeting

CORRECTION

In the May installment of Technology Update, the description of the eSight Go was incorrect. It doesn't improve peripheral vision as stated in the article; rather it enhances central vision while preserving natural peripheral vision. *Review* regrets the error.

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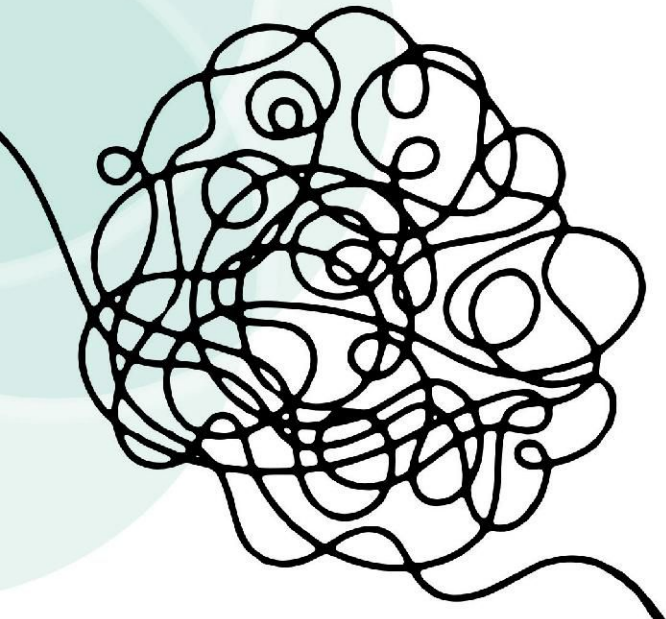

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REVIEW of OPHTHALMOLOGY

WALTER C. BETHKE, EDITOR IN CHIEF

EDITOR'S PAGE

AI Learns the Peter Principle

When I first heard about the concept of the Peter Principle, I recall being struck by how succinct, insightful and bitingly TRUE it is.

If you're not familiar with the concept, simply put, it's the idea that, in some cases, a person is "promoted to the level of their respective incompetence." So, for example, if Bob does great at a lower-level job designing and creating widgets, as a reward he gets promoted to a mid-level position. This promoting keeps happening until poor Bob is doing something on a higher level he doesn't have the aptitude for, such as managing people, and he starts doing poorly. As a result, the company as a whole then falters by keeping Bob in his position, or maybe he gets let go or quits out of frustration, yearning to get back to designing or building widgets like he used to.

If a recent *New York Times* article is any indication, it looks like everyone's darling, AI, may be learning about the Peter Principle firsthand.

According to the article, when AI maker OpenAI (of ChatGPT fame) ran its most powerful "reasoning" AI system, o3, through a benchmark test, it made errors ("hallucinated" in AI-speak) 33 percent of the time.[1] This was more than double the hallucinations of its previous system, o1. Another new system from the company, the o4-mini, hallucinated even more, at 48 percent of the time. Even more frustrating, the company can't figure out why it's happening, though they're working on it.

Out of curiosity (in a "physician, heal thyself" mood), I asked ChatGPT why newer systems seemed to be making more errors than older ones. Its response was interesting: "Newer AI models aren't necessarily 'worse'—they're being used more ambitiously, are held to higher standards and have more subtle trade-offs under the hood. Mistakes are now more visible, surprising and sometimes harder to fix."

So, AI models did well on their initial tasks so they got promoted to more complex tasks and more was expected of them—and they stumbled a bit.

The Peter Principle arrives in cyberspace.

There are a couple of takeaways for both humans and machines from this development.

For AI users in general and physicians in particular, it's a reminder to be cognizant of your AI's limitations. Don't get too relaxed. Especially if you're working with a new reasoning model of AI, be sure to check its work—maybe even check each step it takes on the way to a solution—to avoid basing a decision on hallucinatory conclusions.

For our silicon brethren, they're learning (I hope) that to be truly great in your field as all physicians know, it takes more than just being good for a year or two. Rather, you've got to be on top of your game day in and day out—for years on end—in order to produce the best outcomes for your patients (or your users).

In other words: Welcome to the real world.

— Walter Bethke
Editor in Chief

1. Metz C, Weise K. A.I. is getting more powerful, but its hallucinations are getting worse. The New York Times. May 5, 2025 [online article]. Accessed May 16, 2025.


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Seems Like Yesterday

Musings on life, medicine and the practice of ophthalmology.

MARK H. BLECHER, MD
CHIEF MEDICAL EDITOR

I've heard it said that as we get older, we keep this vision of ourselves in our head from our youth. That we don't think of ourselves as 50 or 60 but 30 or 40. Those of you 40 or younger are on your own here. No one wants to be or most certainly wants to feel old. And, if you're lucky, physically you probably don't feel what is traditionally described as "old." So, you can maintain the fantasy of a younger self. Hopefully not a younger self who is foolish and silly, since there must be some benefit of age. A fresh and vibrant version of yourself. Does anyone really want to be that grumpy old man in the corner? I was called that once by an acquaintance some 30 years younger. It hurt, and was only partially true. Then again, I had my grumpy old man moments when I was 30, so I guess it's also a state of mind and not just a physical reality. But I digress.

I was asked recently, again, when I'm going to retire. And as many of you know I did retire but came back. In a different role. And it's been great. And interesting. And I've written about it before, but perhaps an update for a future column. It's obvious when answering the question of retirement that you think back, recall all the years that have led to this point—both professional milestones and personal ones. And while I'm proud of the arc of my career over the last 40 years, I'm even prouder of my personal one. It, too, has been 40 years. This fall. Same person. I know it's not uncommon but it seems to impress when it comes up in conversation. And I stop and think, doesn't seem that strange. It didn't seem that difficult. Doesn't seem that long ago, but I guess it is. This isn't a treatise on relationships, but on the passage of time. Of time passed if not effortlessly, then smoothly. Comfortably. OK, maybe it IS about relationships, or a relationship not without its ups and downs, but one that has sailed mostly smoothly over the sea of years. In such a way that it seems impossible to have been so long, that the many memorable milestones seem like yesterday.

I'm sure we're both different people, or different versions of the people we were 40 years ago. But fortunately for us, different together as opposed to drifting apart. I was reminded of this by friends of ours who are on the verge of separating. They were together many years, and have young children. And it caused me to stop and think, why? I know there are so many reasons why. But this was a more "global" why. Why did they drift apart to get to this point? Why did it need to happen? They seemed perfect together. So it seems such a shame, such a crime and such a waste. A waste of effort but, more importantly, a waste of time. A youth squandered in a sense, in a relationship that didn't last. Hopefully lessons learned but, as I have seen so many times, lessons not applied. What percentage of broken couples make it work the second time or just continue forward by themselves? I don't like being by myself, I'm very happy as part of a couple. In my current job I'm away part of the week, but all I want to do is get back home. Because even after 40 years, and maybe because it's been 40 years, the remaining ones are even more precious. And the thought of friends who aren't going to have that hurts even more than I expected. ◀

This article has no commercial sponsorship. **Dr. Blecher** is an attending surgeon at Wills Eye Hospital.

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ABINAYA THENAPPAN, MD
CLEVELAND

Small-incision lenticule extraction is a minimally invasive alternative to LASIK, approved for the correction of myopia and astigmatism. As one of the newer corneal refractive surgery platforms, it has some significant advantages over LASIK, especially in terms of the biomechanics of the cornea and the dry-eye profile. As a flap-free procedure, SMILE's recovery is easier and less complicated, making it ideal for those with an active lifestyle who would otherwise not be candidates for LASIK, but there are challenges preventing it from being as widely adopted as LASIK.

SMILE requires precise, manual dissection of both the anterior and posterior interfaces of the lenticule, which can be challenging in the early learning phase and may increase the risk of complications such as incomplete lenticule removal.

Next, there's minimal real-time visual feedback during lenticule dissection. Surgeons rely on tactile feedback and their overall experience to navigate the different planes.

Additionally, SMILE nomograms are still evolving. Surgeons often need to adjust their own protocols based on refractive surprises. As more surgeons adopt it and we collect more data, that will become easier.

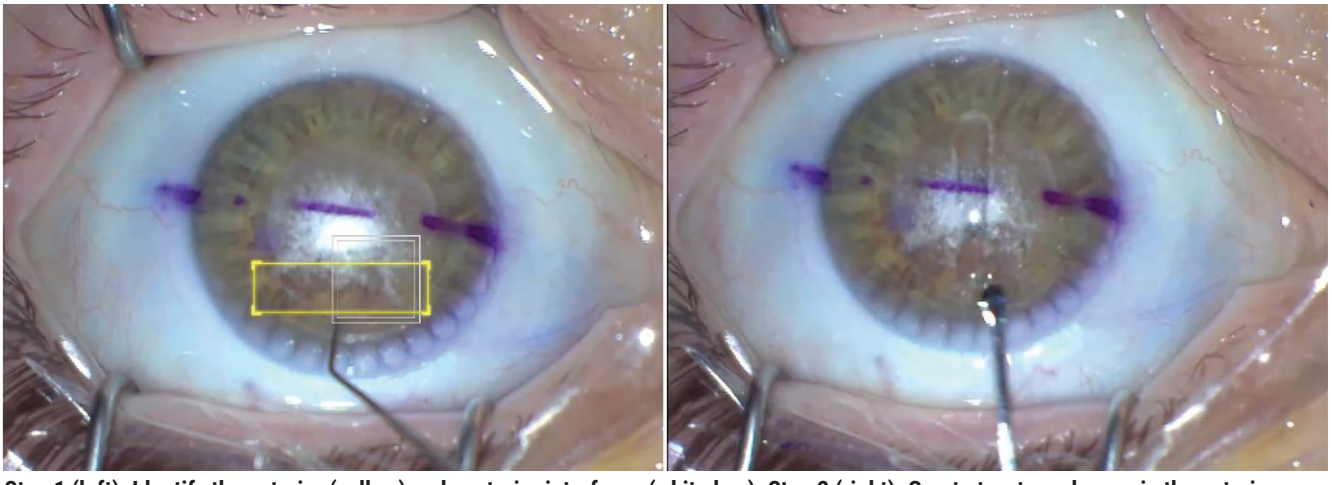
Lastly, SMILE isn't approved for hyperopia and has narrower treatment ranges than LASIK. This may cause hesitation among surgeons as they question switching to a completely new procedure with narrower treatment ranges.

To combat the learning curve involved with SMILE, in this article we'll introduce a new technique for lenticule dissection, dubbed the "double tunnel technique." Read on for this method's necessary steps and related advantages.

The Double Tunnel Technique

In the traditional lenticule dissection technique, the surgeon creates two small pockets to access the anterior and posterior plane. Each plane is separated one at a time to loosen the lenticule before it's extracted.

In this technique, we've modified the traditional approach to minimize tissue manipulation and enhance predictability. We create two strategically placed tunnels (one in each interface) that bisect the cornea. One is slightly offset, if possible, so it can be visualized more easily with the bubble separation. This approach allows us to access both interfaces very quickly and easily. By bisecting the lenticule, you effectively have half of it as a large anchor, which stabilizes your



Step 1 (left). Identify the anterior (yellow) and posterior interfaces (white box). Step 2 (right). Create two tunnels, one in the anterior plane, and one in the posterior plane.

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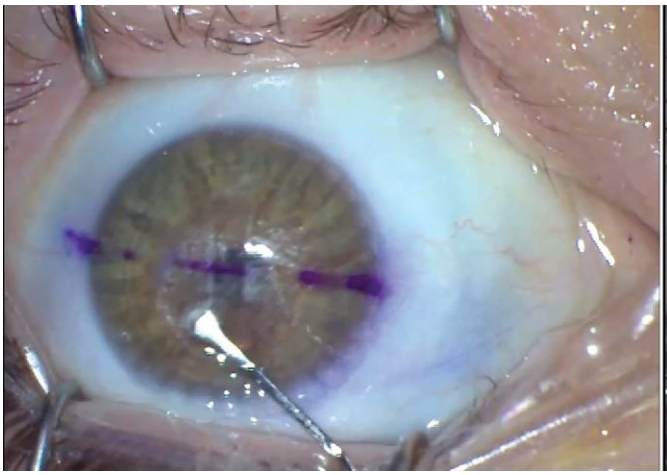
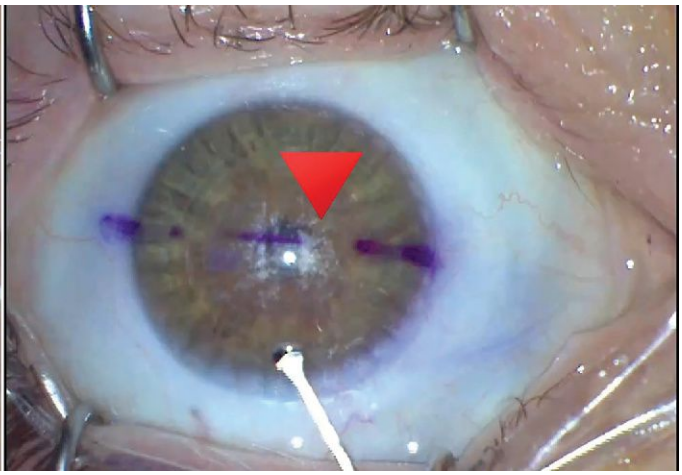
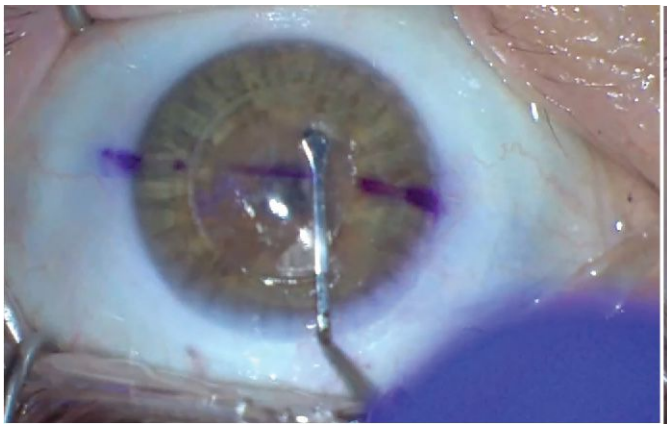
Dr. Chayet is considered a pioneer in refractive and cataract surgery, and is the medical director of the Codet Vision Institute in Tijuana, Mexico. He is a clinical investigator for RxSight, LensGen and ForSight Vision6.



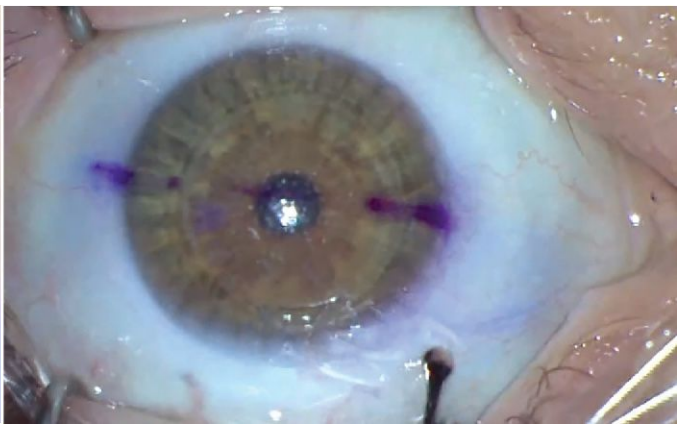
Step 3. Fully dissect the posterior plane first.



Step 4. Dissect the anterior plane next, making sure to leave at least one anchor for adequate counter traction. In this case, it happens to be at the top (red triangle).



Step 5. Release the anchor last.



Step 6. The lenticule is removed smoothly.

dissection as you move forward. This means you don't have to fixate the eye with a second instrument, which can be uncomfortable for patients and possibly lead to subconjunctival hemorrhage after the case. Each tunnel also provides a cleaner, more direct path, so you don't have to worry about plane swaps or inadvertently moving between planes and leaving part of the lenticule undissected.

This technique lends itself to improved predictability, consistency and control, especially in very thin lenticules where plane dissection or identification can be challenging. The tunnels provide a visual landmark that helps identify where each interface is.

In the double tunnel technique, we dissect the posterior plane first. It's not universally done this way in the traditional SMILE procedure, where most choose to enter the anterior plane initially. The reason we do the posterior plane first is that the most difficult-to-reach spot is directly underneath the incision in the posterior plane—those two corners are particularly hard to access. If we start with the posterior plane, we can access those difficult areas when we have the most counter-traction, which comes from the intact anterior plane.

Once we move to the anterior plane, we leave a small anchor—an undissected portion of the plane—to prevent the lenticule from floating around or becoming loose. Once we release the anchor, the lenticule is removed just as you would in any traditional SMILE procedure.

The double tunnel technique has a shallower learning curve. It allows for greater control and reduces intraoperative stress because cases can be more consistent. There's less cross-plane confusion and you have visual landmarks throughout the case. It also causes less torque on the cornea and reduces the risk of lenticule tears or incomplete dissections because you can approach each plane directly and independently.

Ultimately, it gives you more confidence in the OR and contributes to a more refined patient experience—especially since you don't need to stabilize the eye with a second instrument. ◀

ABOUT THE AUTHOR

Dr. Thenappan is a cataract and refractive surgery fellow at the Cleveland Eye Clinic. She reports no relevant financial disclosures.

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

Reference: 1. Tyrvaya. Prescribing Information. Oyster Point Pharma.

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

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

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

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

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Ocular Findings in Pediatric Nutritional Deficiencies

Why ophthalmologists should consider these in their differential diagnosis.

RACHEL DOLAN, MS4, AND TAMMY YANOVITCH, MD, MHSC
OKLAHOMA CITY

Vitamin deficiencies can significantly impact the eye health of pediatric patients, often indicating nutritional imbalances. This article explores the role of ophthalmologists in identifying and managing these deficiencies. It reviews ocular findings related to common and less common vitamin and mineral deficiencies, emphasizing their importance for visual development and overall health. We'll provide a systematic approach to diagnosis and management strategies to help clinicians effectively address these conditions.

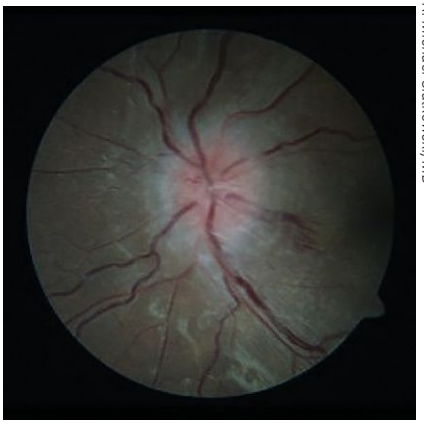
Vitamin and Mineral Deficiencies in General

Vitamin and mineral deficiencies differ significantly between the United States and other regions due to variations in dietary habits, socioeconomic factors and health-care access. In the United States, vitamin D, iron and vitamin B6 deficiencies are more common, especially among minority groups. Conversely, in developing countries, vitamin A deficiency is a significant cause of preventable blindness in children. Iron is the most widespread deficiency globally, affecting over 25 percent of the population. Other prevalent deficiencies worldwide include vitamin D, zinc and folate. In the United States, deficiencies are often related to dietary choices, medical conditions and medications, whereas globally, nutritional deficiencies are more commonly linked to poverty and food insecurity. Infants and children are at risk of deficiencies more from their increased nutritional needs and lower absorption efficiency *(Table 1)*.

In the sections below, we'll discuss some of the most common—and a few of the lesser known—nutritional deficiencies, their risk factors, ocular manifestations and treatment strategies *(Table 2)*.

Vitamin D Deficiency

Vitamin D deficiency is a relatively common condition among American children, particularly in those who are overweight or obese. The prevalence of this deficiency increases with higher body mass index, affecting 21 percent of children with a healthy weight, 26 percent of overweight children, 34 percent of obese children and 49 percent of severely obese children. Minority groups, such as African-American and Latino children, are disproportionately affected.



R. Michael Siatkowski, MD

Figure 1. Fundus photograph of optic nerve edema and retinal hemorrhage seen in a child with iron deficiency anemia and toxoplasmosis.

In its active form, 1,25-dihydroxyvitamin D [1,25(OH)2D3], vitamin D functions as a steroid hormone with roles in numerous physiological processes. Its synthesis begins in the liver as 7-dehydrocholesterol, which is then stored in the skin and converted to cholecalciferol under UV light. Cholecalciferol undergoes hydroxylation in the liver to form 25-hydroxyvitamin D [25(OH)D], the storage form, which can either be stored in adipose tissue or converted by 1α-hydroxylase to its active form.

• ***Risk factors and associations.*** VDD has been linked to malnutrition, malabsorption, exclusive breastfeeding (due to low vitamin D levels in breast milk), reduced sun exposure, dark skin pigmentation and genetic conditions such as 25-hydroxylase or 1α-hydroxylase deficiency.[1] Certain medications—including anticonvulsants, antiretroviral drugs, glucocorticoids and antifungal agents—can also exacerbate vitamin D deficiency by affecting its metabolism or absorption.[1]

• ***Ocular effects.*** VDD can have the following effects in the eye:

—VDD contributes to reduced tear production and inflammation, resulting in dryness, discomfort and an increased risk of ocular surface disease.[2]

—Deficiency may lead to conjunctival changes and delayed healing of the corneal epithelium, further compromising anterior segment integrity.[3]

This article has no commercial sponsorship.

Dr. Collinge is a pediatric ophthalmologist in West Hartford, Connecticut.

—Though less frequently studied, emerging evidence suggests links between VDD and retinal complications, particularly in pediatric patients with type 1 diabetes. These associations include potential risks of diabetic retinopathy in affected children.[4-8]

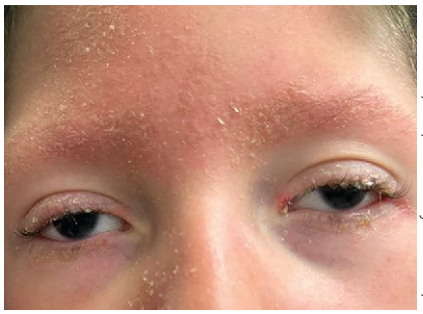
—Interestingly, studies have indicated a correlation between lower 25(OH)D levels and longer axial length, increasing the risk of myopia. While findings in children remain inconsistent, some research highlights a stronger association as patients reach adulthood.[9,10,11]

• ***Systemic symptoms.*** VDD in children can lead to a range of systemic symptoms due to its role in calcium regulation, bone health and immune function. Common symptoms include rickets, bone pain, delayed growth, muscle weakness, fatigue, frequent infections and dental issues.[1,2]

• ***Diagnosis and management.*** Diagnosing VDD requires a detailed clinical history and laboratory confirmation of serum 25(OH)D levels. Management steps include addressing the underlying causes, providing dietary supplementation and encouraging safe sun exposure.[1] Additional interventions for patients with ocular manifestations may include artificial tears for dry-eye syndrome and close monitoring of refractive status to mitigate progressive myopia.

Iron Deficiency

Iron deficiency anemia is the most common type of anemia in American children. It affects approximately 1 to 2 percent of children aged 1 to 5 years and is more prevalent in those from low-income families or with limited access to iron-rich foods.[12] Iron deficiency reduces hemoglobin production and oxygen transport and can impact cognitive development and overall health.



Rachel Dolan, MS4, and Tammy Yanovitch, MD, MHSc

Figure 2. External photograph showing severe seborrheic dermatitis in a child with a history of nutritional deficiency.

TABLE 1. NUTRITIONAL DEFICIENCIES AMONG RACIAL GROUPS IN THE UNITED STATES

Deficiency	Non-Hispanic White Americans	Non-Hispanic Black Americans	Hispanic Americans
Vitamin D	~3%	~31%	~12%
Iron	Lower prevalence	Higher prevalence	Moderate prevalence
Vitamin B6	~10%	Higher prevalence	Moderate prevalence
Vitamin A	Rare	Rare	Rare
Vitamin C	Rare	Higher prevalence	Moderate prevalence

• ***Risk factors and associations.*** Risk factors for iron deficiency anemia include dietary insufficiency related to inadequate intake of iron-rich foods such as meat, fish and fortified cereals; rapid growth, premature birth, exclusive breastfeeding beyond six months of age, chronic blood loss in conditions like gastrointestinal bleeding or heavy menstrual periods, low socioeconomic status, malabsorption disorders like celiac disease or inflammatory bowel disease, and cow's milk consumption which can interfere with iron absorption and reduce dietary diversity.

• ***Ocular effects.*** Ocular findings are relatively common in anemic children and, fortunately, are usually reversible.

—Studies have found that anemic patients frequently have conjunctival pallor, although some research has conflicted with this, with pallor being found most in severe cases.[12,13,14]

—Retinal hemorrhages and cotton wool spots have been seen in severe cases of anemia *(See Figure 1)*.[15]

• ***Systemic symptoms.*** Fatigue, pallor, shortness of breath and other systemic signs may corroborate the suspicion of anemia.

• ***Diagnosis and management.*** Laboratory testing for anemia includes a complete blood count and a peripheral blood smear to aid in identifying the anemia type (e.g., iron deficiency, megaloblastic). Iron studies measure serum iron, ferritin and transferrin saturation to assess iron status. Other suspected deficiencies associated with anemia, such as B12 or folate, also require testing. Hemolytic markers such as LDH, haptoglobin, indirect bilirubin and reticulocyte count are also needed.

Iron supplementation is the cornerstone of treatment. It's typically administered orally at a dose of 2 to 4 mg/kg of elemental iron daily, tailored to the child's age and severity of anemia.

For ocular issues such as anemic retinopathy, which may present with retinal hemorrhages, cotton wool spots or venous tortuosity, correcting the anemia often leads to the resolution of these findings.[15] Supportive care, including monitoring visual changes and managing secondary complications like retinal edema, is essential. In severe cases, where anemia is life-threatening or ocular damage is extensive, blood transfusions may be considered to restore hemoglobin levels rapidly and improve oxygen delivery to retinal tissues. Early intervention and regular follow-ups are crucial to prevent long-term visual impairment and improve overall health.

Vitamin B6 (Pyridoxine) Deficiency

Vitamin B6, pyridoxine, is a water-soluble vitamin essential for numerous enzymatic reactions, including neurotransmitter synthesis, hemoglobin production and immune function. Deficiency in vitamin B6 can lead to significant ocular and systemic manifestations, particularly in children, where growth and development are critically dependent on adequate nutrition.

• *Risk factors and associations.*

Rhea Siatkowski, MD

Figure 3. Pediatric patients with vitamin A deficiency resulting in conjunctival xerosis and corneal ulceration.

Vitamin B6 deficiency may result from poor dietary intake (lacking in bananas, potatoes and poultry), chronic conditions (i.e., malabsorption, celiac disease or kidney disease) and premature birth.[15]

• ***Ocular effects.*** Pyridoxine deficiency may result in the red, itchy, flaky eyelid rash of seborrheic dermatitis *(See Figure 2)*.[16,17] Disruption of mitochondrial oxidative phosphorylation leads to reduced ATP production and the accumulation of free radicals.[18] This disruption can damage the optic nerve and result in central visual field loss, temporal pallor of the optic disc and central scotomas. Optic neuropathy in pyridoxine deficiency is often bilateral and symmetrical.

• ***Systemic symptoms.*** Vitamin B6 deficiency has been associated with depression, confusion, irritability, nervousness, trouble concentrating and short-term memory loss, as well as seizures, anemia, immune dysfunction and growth delays.

• ***Diagnosis and management.*** Pyridoxine deficiency is determined by measuring plasma pyridoxal 5'-phosphate (PLP) levels, the active form of vitamin B6. The primary treatment is supplementation with oral vitamin B6 (0.5-1mg/day for mild deficiency; higher doses may be necessary), dietary adjustments incorporating vitamin B6-rich foods, and monitoring for resolution of symptoms and prevention of recurrence.[19]

Vitamin B6 supplementation may take up to two weeks to show an effect on seborrheic dermatitis. Optic neuropathy caused by vitamin B6 can be reversible if the deficiency is identified and treated promptly. Early intervention is crucial to prevent permanent optic nerve damage and restore vision.

Vitamin A (Retinol) Deficiency

This is a less common deficiency. Vitamin A, also known as retinol, is stored in hepatic cells and is crucial for low-light vision, gene transcription and cell differentiation. It treats conditions such as nodulocystic acne and acute promyelocytic leukemia. It's found in food such as spinach, carrots, liver, kidneys and eggs.

• ***Risk factors and associations.*** Worldwide, VAD has been most associated with inaccessibility to vitamin-rich foods, such as meats, dairy products, eggs and leafy green vegetables, especially in low-income countries.[20,21,22] It has also been found in American children with a history of autism spectrum disorder, avoidant/restrictive food intake disorder and malabsorption diseases, such as Crohn's disease, cystic fibrosis and celiac disease.[23,24] In the first six to 12 months of life, breast-fed infants are at risk if the mother is deficient, and bottle-fed infants are if given skim milk too diluted with water.[25] Certain infections, such as tuberculosis and measles, also carry a risk of VAD in children.[26,27,28]

• ***Ocular effects.*** The initial indicator of VAD is nyctalopia, or night blindness, which may go unnoticed in young children because they can't verbalize their symptoms. Conjunctival xerosis can develop, often unnoticed unless specifically examined for it. As the condition advances, Bitot's spots and corneal xerosis may appear, which are generally reversible in most cases. However, more severe manifestations such as corneal ulcers, keratomalacia and corneal scarring are permanent and can result in blindness. The other ocular effects are:

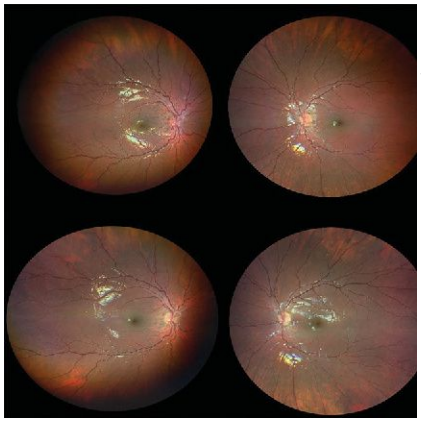
—*Conjunctival xerosis.* Patients present with dryness of the cornea and conjunctiva; the associated xerophthalmia tends to progress in stages.

—*Bitot's spots.* Keratinized, foamy,

TOP TAKEAWAYS

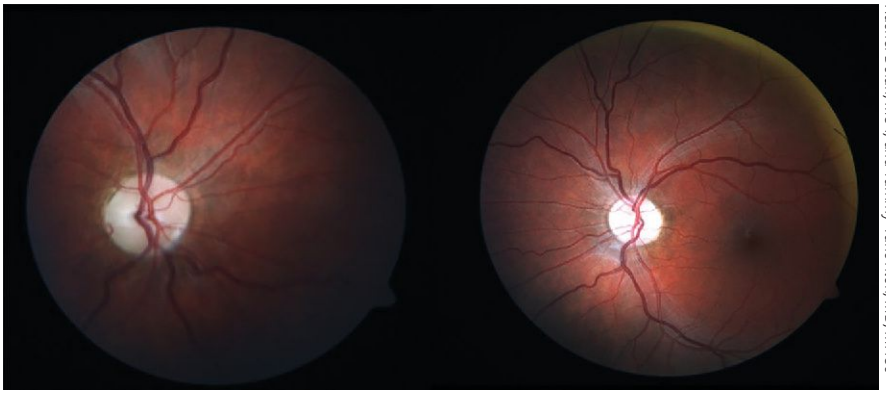
Here are the most important nutritional deficiencies for clinical ophthalmologists to consider in their differential diagnosis of pediatric ocular disease.

- **Enhanced screening for vitamin D deficiency:**
  - ***Practice change:*** Implement screening more frequently for vitamin D deficiency in high-risk populations, especially in overweight or obese pediatric patients and minority groups.
  - ***Update:*** Recognize the ocular manifestations such as dry-eye syndrome, impaired ocular surface health, and potential retinal disorders linked to vitamin D deficiency. Encourage safe sun exposure and dietary supplementation as part of management.
- **Proactive management of iron deficiency anemia:**
  - ***Practice change:*** Increase vigilance in diagnosing iron deficiency anemia in children, particularly those from low-income families or with dietary insufficiencies.
  - ***Update:*** Be aware of ocular signs like conjunctival pallor and retinal abnormalities. Ensure comprehensive laboratory testing and provide iron supplementation to address both systemic and ocular symptoms.
- **Early identification and treatment of vitamin B6 deficiency:**
  - ***Practice change:*** Incorporate screening for vitamin B6 deficiency in children with poor dietary intake or chronic conditions.
  - ***Update:*** Monitor for ocular effects such as seborrheic dermatitis and optic neuropathy. Promptly treat with vitamin B6 supplementation and dietary adjustments to prevent long-term visual impairment and systemic symptoms.



Maria Lim, MD

Figure 4. Fundus photos showing optic nerve edema and resolution in a child with vitamin A deficiency with normal opening pressures on lumbar puncture, before and after treatment. They also had a history of pseudotumor cerebri.



Rachel Dolan, MS4, and Tammy Yanovitch, MD, MHSc

Figure 5. Fundus photos showing optic nerve edema in a child with vitamin B12 deficiency.

white deposits develop on the conjunctiva, typically appearing on the temporal side.

—*Corneal xerosis.* Desiccation and thickening of the corneal epithelium occur, leading to a hazy appearance.

—*Corneal ulceration.* It appears as a grayish-white infiltrate with rolled borders and is at risk of becoming secondarily infected.

—*Corneal scar.* Scarring results in corneal opacification and irregular astigmatism, often leading to anisometropia and amblyopia in children.

—*Xerophthalmic fundus.* There can be retinal pigmentation changes and degeneration. Rods produce rhodopsin using retinol, thus allowing vision in low-lit areas. Deficiency can lead to vision problems in dim lighting, which can be challenging to detect in children, especially if they're pre- or non-verbal. At night or in a dimly lit area, this may present as less movement, difficulty finding toys or food, clumsiness or fear of the dark.[21]

—*Optic neuropathy and increased intracranial pressures.* Rarely, optic neuropathy and increased intracranial pressure can occur in severe VAD *(See Figure 4)*.[30,31,32]

Vitamin A is crucial for maintaining the health of the optic nerve. Severe deficiency can lead to optic neuropathy, which results in gradual, bilateral, painless vision loss.

Pseudotumor cerebri, diagnosed with optic neuropathy and elevated opening pressures from lumbar puncture, has also been seen in children with VAD.[23] Decreased absorption of cerebrospinal fluid by arachnoid granulation enlargement and fibrosis has been seen in calves with VAD, which could serve as a possible mechanism in humans.[30] There have also been reports of optic neuropathy in children with VAD, autism, and skull abnormalities, which were related to compression of the optic canal due to hyperostosis.[31,32]

• ***Systemic symptoms.*** Xerosis cutis, immunosuppression (including severe measles infection), stunted growth and diarrhea can be associated with decreased vitamin A levels. As measles outbreaks occur in the United States, it's crucial to recognize this highly contagious disease's connection to reduced vitamin A levels and the increased risk of severe measles infection. However, vitamin A doesn't cure or prevent measles.

• ***Diagnosis and management.*** The diagnosis of VAD requires the measurement of serum vitamin A levels. Treatment recommendations include aggressive vitamin supplementation, especially zinc, and local remedies like lubrication, retinoid acid drops and keratoplasty.[33] Adequate supplementation with vitamin A can reverse the effects if treated early. It's well-known that benign intracranial hypertension and pseudotumor cerebri have been associated with vitamin A toxicity, potentially due to toxic effects on arachnoid granules, which affect the absorption of cerebrospinal fluid. Therefore, in some instances, it's important to differentiate between optic neuropathy related to vitamin A deficiency or pseudotumor cerebri with lumbar puncture. In cases of VAD with pseudotumor cerebri, it may be beneficial to consider additional acetazolamide treatment.

For supplementation, the World Health Organization recommends immediately administering vitamin A, preferably oil-based, to treat xerophthalmia. This should be dosed at 50,000 IU, 100,000 IU, and 200,000 IU for ages less than 6 months, 6 to 12 months, and greater than 12 months, respectively.

Vitamin C Deficiency

Vitamin C, or ascorbic acid, is essential for various bodily functions, including iron absorption, synthesis of molecules like noradrenaline and collagen, and acting as an antioxidant.[34] It must be obtained from vitamin C-rich foods or supplements. It's absorbed in the distal ileum, and its concentration varies in organs, with higher amounts in the brain, liver, adrenal glands and lungs. The brain and adrenal glands maintain homeostasis effectively in guinea pigs with vitamin C deficiency.[35] It's also one of the less common deficiencies.

• ***Risk factors and associations.*** Scurvy is linked to vulnerable populations. A review of 166 children with scurvy found 76 percent had a comorbidity, commonly neurodevelopmental disorders, anorexia and cerebral palsy.[36,37]

(Continued on p. 52)

CAN GLAUCOMA PATIENTS GET PREMIUM IOLS?

Advanced lens technology is broadening the premium patient pool. Here's guidance for glaucoma cases.

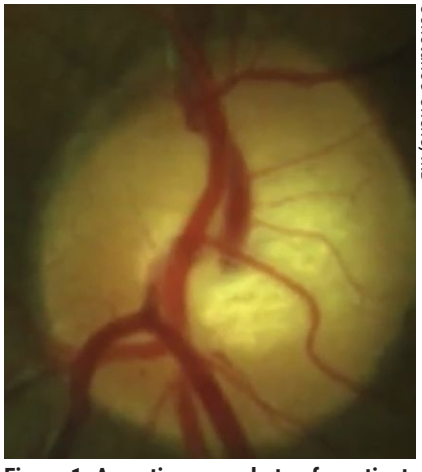
CHRISTINE YUE
SENIOR ASSOCIATE EDITOR

When considering premium intraocular lenses for glaucoma patients and suspects, the decision often hinges on disease severity. Certain premium options may exacerbate pre-existing visual symptoms. As such, ophthalmologists must determine the most suitable lens on a case-by-case basis, balancing both visual and glaucoma-related concerns. Here, experts discuss the IOL options they consider in these scenarios and how they explain glaucoma-related limitations to patients.

Clinical Factors

When evaluating whether a glaucoma suspect or glaucoma patient is an appropriate candidate for a premium intraocular lens, ophthalmologists must carefully consider a range of clinical factors that can impact both the safety and efficacy of the lens implantation.

"The primary factors I assess are glaucoma stage, visual field status and the trajectory of disease progression," says Constance Okeke, MD, MSCE, of Virginia Eye Consultants in Norfolk, and assistant professor of ophthalmology at Eastern Virginia Medical School. "Patients with mild or well-controlled moderate glaucoma, no central visual field loss and good contrast sensitivity may be considered candidates. I also evaluate the ocular surface health, pupil anatomy and whether the patient is a MIGS candidate, as combining MIGS with cataract surgery can lower IOP, reduce medication burden and improve the ocular surface, enhancing outcomes with advanced-technology IOLs.



Constance Okeke, MD

Figure 1. An optic nerve photo of a patient with mild open-angle glaucoma and near-normal visual fields. Baseline visual acuity was 20/40 OU.

"In glaucoma suspects, I assess optic nerve status, OCT findings and risk factors such as age, IOP and family history," she continues. "While I don't routinely use a specific scoring system, I do employ a comprehensive risk assessment approach. If there's no visual field loss and the risk of progression is low, I'm more open to offering multifocal, trifocal or EDOF lenses, especially when paired with proper counseling. Contrast sensitivity and night driving needs are also part of the conversation."

Certain clinical conditions preclude the use of premium IOLs in glaucoma patients. Dr. Okeke says she considers the following absolute contraindications:

—Advanced glaucoma with significant central field loss.

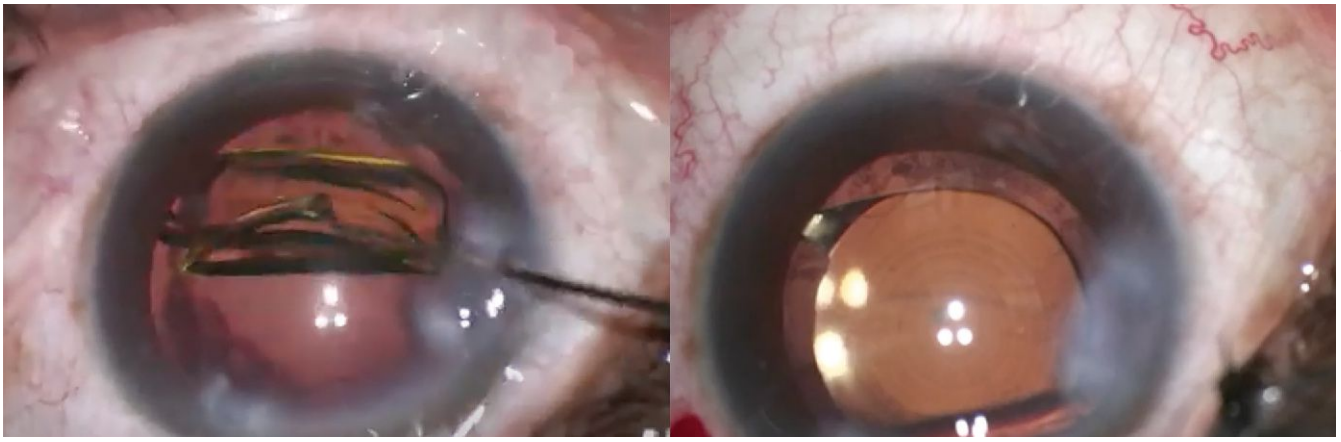
—Uncontrolled IOP or high risk of progression.

—Heavy medication burden without surgical control.

—Poor ocular surface not respon-

This article has no commercial sponsorship.

Dr. Ragusa and **Dr. Kamat** have no related financial disclosures. **Dr. Okeke** discloses financial relationships with Glaukos, New World Medical, Sight Sciences, Alcon, Bausch + Lomb, Allergan/AbbVie and Nova Eye Medical.



Constance Okeke, MD

Figure 2. The patient in Figure 1 underwent combined cataract-MIGS surgery with PanOptix implantation and Streamline goniotomy. Postop visual acuity improved to 20/20 at distance and intermediate, and to J1+ at near. IOP was 14 and 12 mmHg with a target of 15 mmHg. The drop burden was reduced from three medications to one.

sive to treatment.

—Pupil or zonular abnormalities that limit lens centration or performance.

One of the key challenges in considering premium IOL implantation for glaucoma patients is the lack of clinical tools to reliably predict which individuals will become fast progressors or develop severe disease, explains Shivani Kamat, MD, associate professor of ophthalmology and director of the glaucoma fellowship at UT Southwestern Medical Center in Dallas. "We can tell if a patient's glaucoma is progressing," she says, "but we don't yet have a consistent way to identify who may end up with more advanced disease later in life.

"I'd consider a premium lens in a glaucoma suspect or a patient with ocular hypertension—someone who doesn't have any visual field loss—but even then, I tend to be cautious," she continues. "I practice in an academic setting, and many of my patients have very severe disease. I've seen patients for second opinions who had moderate disease and received a multifocal lens, only to struggle significantly with contrast sensitivity issues. So, I tend to be more cautious even with the mild to moderate cases. I think if we had a reliable way to predict which patients are fast progressors, I'd feel more comfortable recommending premium IOLs for those with mild disease."

Recent research has explored the use of artificial intelligence to better forecast glaucoma progression, a development that could one day help identify fast progressors more reliably. Several studies show promise for future clinical translation, but now, they face key limitations including differences in datasets and methodologies and the lack of a standardized definition of progression.

Lens Options

When considering premium IOLs for glaucoma patients or suspects, ophthalmologists weigh the potential benefits of advanced lens technologies against the specific risks associated with the disease.

Nikola Ragusa, MD, of Ophthalmic Consultant of New York in Astoria, explains that "if a patient has mild disease with full fields, or if they're suspicious for glaucoma or ocular hypertension, then the IOL choice varies much more than if the patient were to have moderate to severe disease. When patients have visual field loss, their brightness, color and contrast sensitivity are all diminished, so we must be careful about the lenses we select and avoid giving them an IOL that splits light.

"For patients with moderate to severe glaucoma, multifocal lenses are generally not the best option," he continues. "They can reduce contrast sensitivity and may cause glare or halo issues, especially if the patient also has astigmatism or ocular surface problems. This is particularly problematic for glaucoma patients, who may already have diminished contrast sensitivity, brightness and color perception due to optic nerve damage.

"I wouldn't consider accommodative IOLs for these patients either," Dr. Ragusa says. "On the other hand, toric lenses are a good choice, as they help focus light more effectively onto the retina—anything that focuses the light better on the retina is a win for these patients. I also consider newer technology like extended depth of focus lenses."

"For a glaucoma suspect or a patient with ocular hypertension, I'll offer everything, including EDOFs since contrast sensitivity is less affected with those lenses," Dr. Kamat says. "I recommend a monofocal in moderate to severe glaucoma. I wouldn't put a multifocal in these patients because of the impact on contrast sensitivity.

"I consider mild disease to be a little bit of a gray zone," she continues. "I think it requires a very thorough informed consent and discussion of risks and benefits associated with the lenses. That's true in any situation, but it's especially true if you're considering a multifocal in someone who has known disease. Even in mild disease,

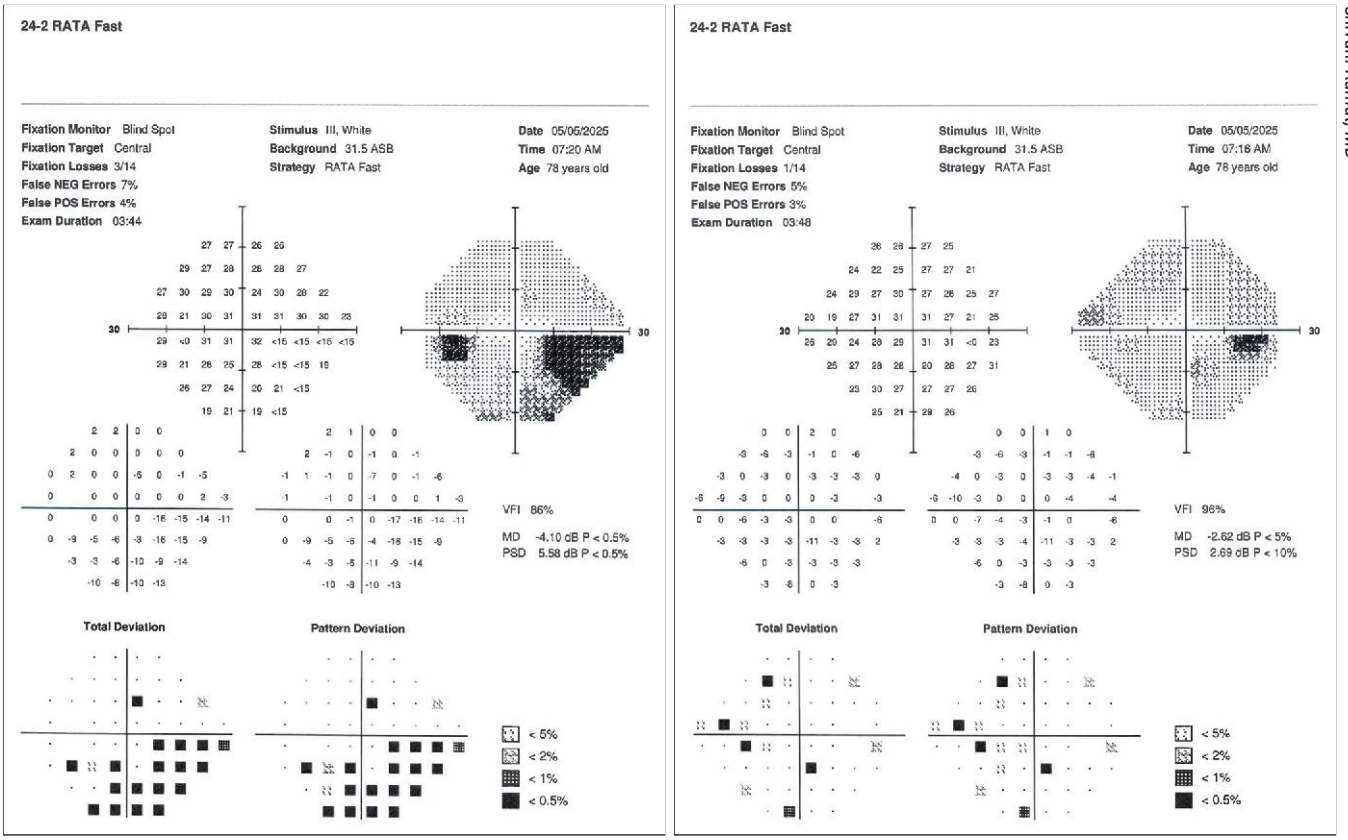
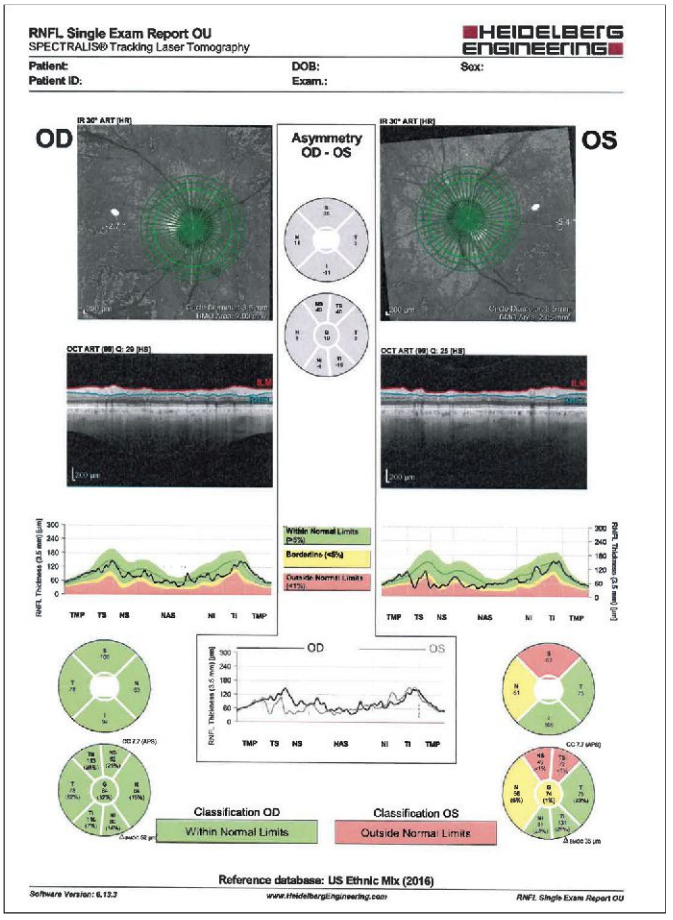


Figure 3. An example of a poor multifocal IOL candidate. The right eye of this patient is fairly healthy while the left eye has significant disease. Though the right eye is healthier without VF loss, experts say there's a concern that it would eventually end up like the other eye and have problems down the line.

we don't really know who's a fast progressor and will have moderate or severe disease within their lifetime."

Dr. Okeke says she "leans strongly toward extended depth of focus lenses, especially non-diffractive designs like the Vivity, which preserve contrast sensitivity while offering good intermediate and functional near vision. These lenses stretch and shift light instead of splitting it, which helps minimize dysphotopsias—a critical consideration in glaucoma patients, who often already have reduced contrast sensitivity. They tend to be better tolerated, even in moderate glaucoma, provided the visual fields are stable and IOP is well controlled.

"In certain patients—particularly avid readers or those desiring a greater degree of spectacle independence at near—I also offer a mini-monovision approach using Eyhance IOLs," she continues. "This lens has enhanced depth-of-focus qualities, and I typically target plano in the dominant eye and -0.50 to -0.75 D in the non-dominant eye. The contrast quality with Eyhance is excellent, and this strategy provides a smoother range of vision that often reduces or eliminates the need for reading glasses. Eyhance in mini-monovision can be a satisfying option for patients with high reading demands.



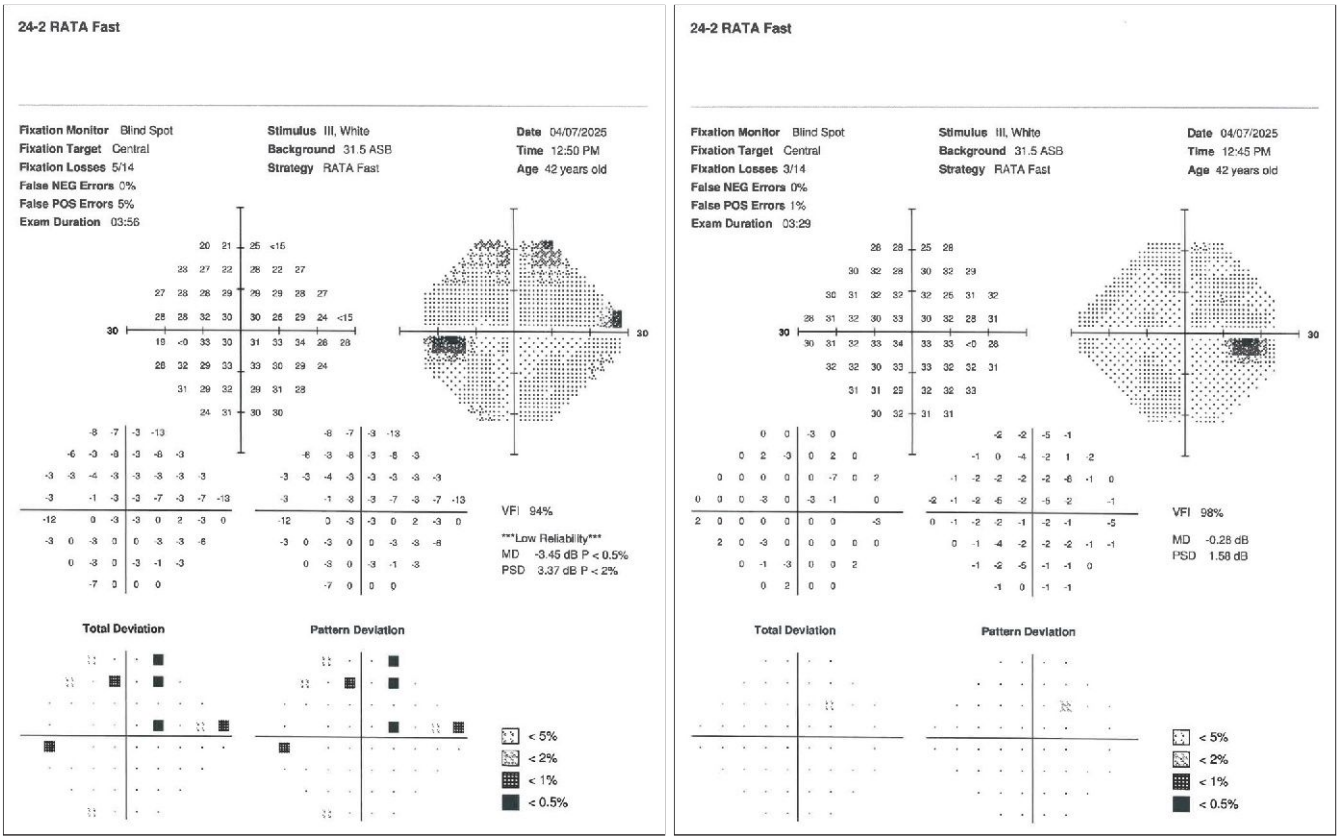
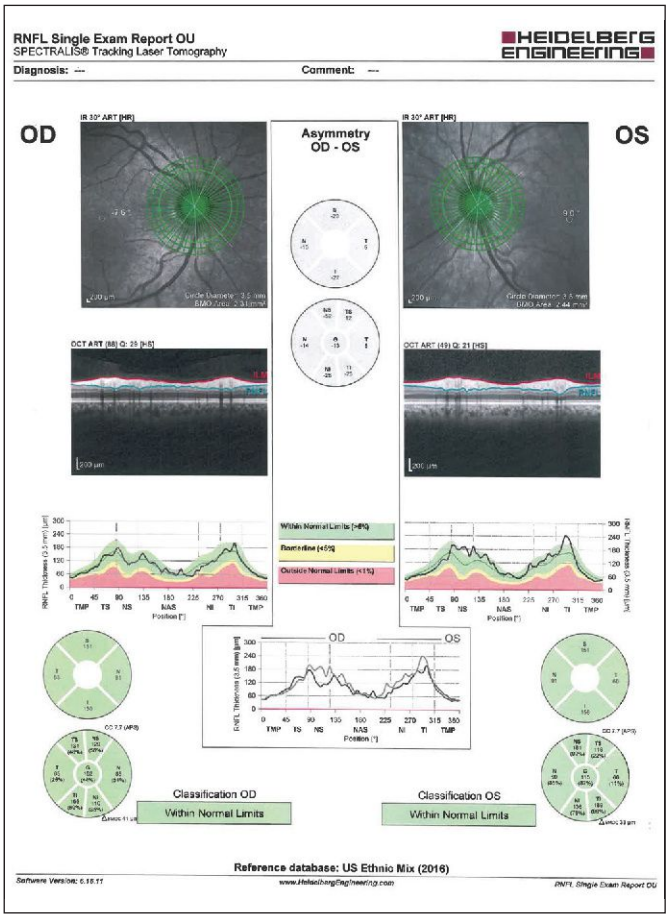


Figure 4. An ocular hypertension patient without optic nerve damage. This patient is a candidate for a multifocal IOL.



"If a patient has mild pre-perimetric glaucoma that can be easily controlled and their cornea and retinal findings are good, trifocal IOLs with PanOptix can also be a good choice for a mild glaucoma patient," she adds. "Ultimately, lens selection is highly personalized, but I favor IOLs that preserve contrast and minimize visual disturbances, especially in a glaucoma population where every bit of functional vision counts."

Dr. Okeke points out that "as long as there's good central vision, any glaucoma patient at any stage of glaucoma can be a great candidate for astigmatic correction when looking to have less spectacle dependence for distance."

Though many glaucoma patients have limited IOL options, Dr. Kamat says she discusses all IOL options with her moderate to severe glaucoma patients even though she doesn't typically recommend premium lenses. "I've learned over time that patients deserve to know all of their options, and I always want them to feel fully informed," she says. "In certain cases, I might offer options like monovision, though most patients don't take that option in my practice. If they're interested, I usually have them trial it with a contact lens first, as I've had cases where patients were unhappy and needed an exchange."

(Continued on pg. 58)

FILTERING SURGERY AT ITS FINEST

Trabeculectomy is still a safe and effective treatment option for glaucoma. Here are basic surgical pearls to help you get the best outcomes possible.

ANDREW BEERS
ASSOCIATE EDITOR

To some in medicine, the phrase, "If it ain't broke, don't fix it," rings true at their practice. The various options for glaucoma surgery exemplify this. Minimally invasive glaucoma surgery, tube shunts and laser surgery are commonly used to treat glaucoma in earlier stages, but sometimes a patient will present with high intraocular pressure and the aforementioned treatments may not be suitable options to lower pressure. So, what should be employed? Since the 1960s, trabeculectomy has been a tried-and-true method in many glaucoma surgeons' armamentariums. Although the number of trabeculectomies performed has decreased by approximately 59 percent since 2011,[1] it's still a safe and effective procedure. In fact, studies have shown that trabeculectomy with mitomycin C provides better long-term results compared to tube shunt surgery.[2-4]

It's possible that the rate at which trabeculectomy is performed will continue to decrease as other treatment options evolve, but for younger surgeons who are up to the challenge of tackling this procedure, there are specific techniques that can help improve their surgical outcomes. Here, glaucoma specialists discuss the basic strategies needed to perfect trabeculectomy.

Get Comfortable with Flap Creation

Glaucoma surgeons familiar with trabeculectomy know that the bleb is the most critical component of the procedure. This allows for filtration, which inevitably lowers IOP. But prior to creating the ostomy, flaps must be made in the conjunctiva and sclera in order to position the bleb properly in the eye. Two types of peritomies can be made—fornix- and limbal-based—and scleral flaps can come in different shapes and sizes. There are pros and cons to each method of flap creation dependent on the clinical staff available and the surgeon's comfort performing trabeculectomy.

"I'll mostly do a fornix-based flap," says Rachel G. Simpson, MD, a glaucoma specialist with the University of Utah Health System, "and that's because when the incision is anterior to the flap, I feel like you're going to get better posterior flow, which is really what we want to encourage with a trabeculectomy. It does require a little bit more meticulous closure, but that's typically not a problem. Also, you can't argue with the exposure that you get with a fornix-based flap because your visualization of the key anatomic area of where you're going to end up making your scleral flap is by far better."

"I don't see any real downside to performing fornix-based conjunctival flaps, and in fact, I believe there's some upside," adds James Tsai, MD, a glaucoma specialist and president of New York Ear and Eye Infirmary of Mount Sinai. "One benefit of a fornix-based flap is that the surgeon doesn't need a trained surgical assistant. On the other hand, with limbal-based flaps, one is dissecting so far posteriorly that one oftentimes needs a skilled surgical assistant. If a surgeon is operating at an academic medical center where residents and fellows are present, limbal-based flaps are certainly an option. However, if one is in private practice and/or operating alone, a fornix-based conjunctival flap is

This article has no commercial sponsorship.

Drs. Simpson, Tsai, Razeghinejad and **Myers** have no relevant financial interests to disclose.

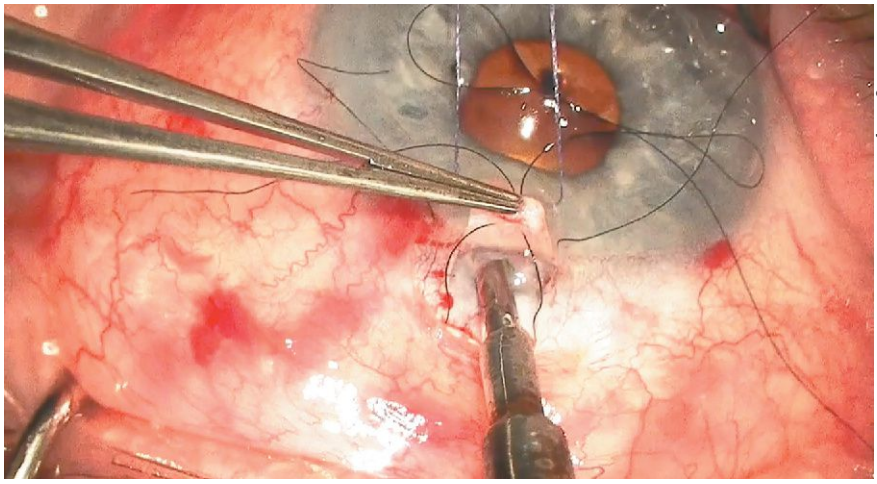
much easier to perform. I believe that another benefit of fornix-based flaps is their use when using topical subconjunctival and sub-Tenon's anesthesia. It's a lot easier getting the sub-Tenon's anesthesia to go back posteriorly when one performs a fornix-based flap; one simply dissects the flap posteriorly for the anesthesia to be directed posteriorly into the fornix."

Reza Razeghinejad, MD, a glaucoma specialist at Wills Eye Hospital in Philadelphia, notes that one benefit of performing a limbal-based flap is the decreased risk of early postoperative leakage. Dr. Tsai supports this claim by stating that fornix-based blebs are commonly larger than blebs created in a limbal-based flap. This larger-sized bleb promotes desiccation and drying and leads to leaks, dysesthesia and increased risk of infection.

Once the peritomy is performed, the next step is to create a scleral flap. Physicians mention that the shape and size won't alter the outcome of the procedure as long as the surgeon performing the trabeculectomy is confident that they can suture the flap afterwards. Some shapes may be trickier to suture than others, so surgeons should focus on perfecting the flap they're most comfortable creating.

"I'd encourage surgeons to get very good with one flap shape rather than bouncing around between different approaches," says Jonathan S. Myers, MD, a glaucoma specialist and chief of Wills Eye Hospital's Glaucoma Service, who prefers a square-shaped scleral flap. "Part of the reason I like square is that for the routine cases, one can put in a suture at each of the two corners in the back, and then if you wind up doing laser suture lysis on the temporal corner, it can be a way to encourage a more posterior, temporal bleb. I try to avoid nasal blebs because of the greater risk of dysesthesia."

Similar to Dr. Myers' method, Dr. Tsai creates a rectangular flap. They both find this to be much easier to perform and suture compared to a triangular flap, which doesn't allow as much leeway when suturing due to the limited area of the shape.



Reza Razeghinejad, MD

A Kelly Descemet Punch device used to create the ostomy.

"I perform a three-millimeter by 2.5-millimeter rectangular flap at the limbus," shares Dr. Tsai. "I make my partial thickness scleral incisions perpendicular to the circumferential limbus and go back straight posteriorly approximately 2.5 millimeters—the incisions are made parallel three millimeters apart from each other. I then finish the rectangle flap by connecting the posterior edges of the flaps. If one is performing a triangular flap and using a three-millimeter base at the limbus, then one has to dissect the triangular flap precisely so that the triangular point is approximately 2.5 millimeters posterior to the limbus."

Dr. Simpson's method is slightly different, as she creates a trapezoidal shape, but her main focus when creating the scleral flap is not on the shape but rather on the precision of the dissected lines. "I'd say shape is less important than clean dissection lines," she says. "Make sure those are symmetric and smooth and you're not getting a lot of rough surfaces. The more planes of tissue you create, the more your scleral flap is going to scar down."

Standardizing the Ostomy

Drs. Myers, Razeghinejad, Simpson and Tsai have all switched from using blades in the past to now using a Kelly Descemet Punch device when creating an ostomy. Many ophthalmic companies have created their own version of this tool, but the design is simple and allows surgeons to create ostomies at a standardized size, as Dr. Simpson notes.

"You're going to get roughly the same size ostomy each time," says Dr. Simpson. "The more predictability you can build into this kind of surgery, the better off you're going to be because there are so many other things that are hard to predict."

However, a Kelly Descemet Punch device takes some practice getting used to. "For people who haven't used it a lot, sometimes when one actuates the punch, the tip can move more than anticipated," states Dr. Myers. "It's important to help control the tip as one actuates the punch so as not to disturb the iris or other structures that don't need a punch. But for people who are somewhat experienced surgeons, that can be overcome fairly easily."

Dr. Razeghinejad says he uses a really sharp blade or Vannas scissors if a Kelly Descemet Punch device isn't available. He notes, "Punching toward the sclera can increase the risk of bleeding from uveal tissue or inadvertently creating a cyclodialysis cleft. To minimize these risks, it's safer to create the ostomy at the limbus, slightly shifted into the cornea."

Suture Specifics

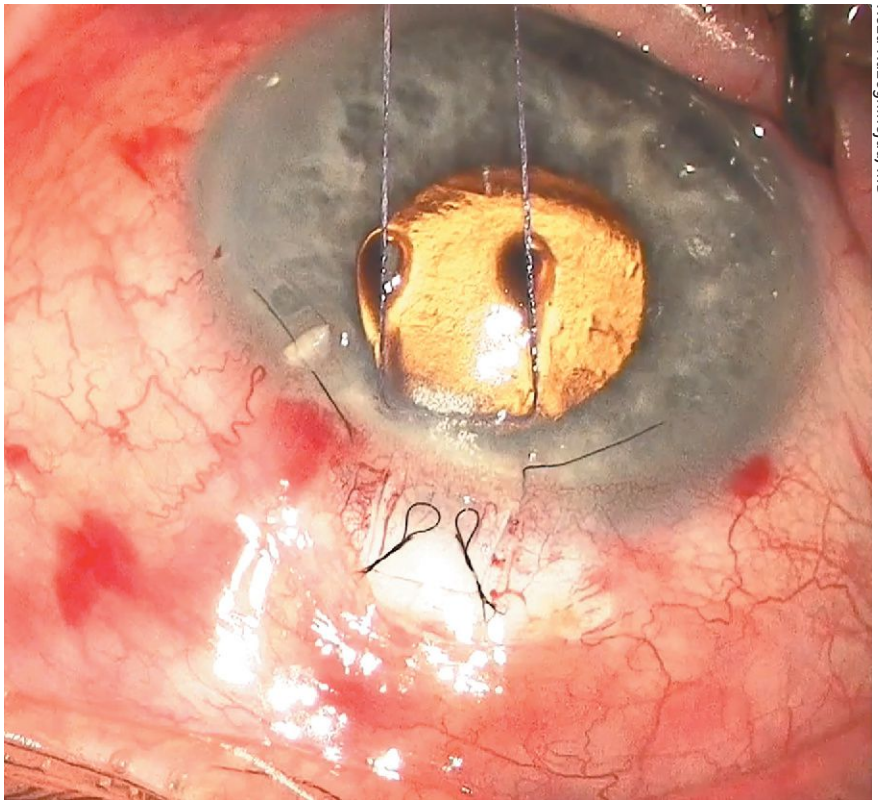
Now it's time to suture the scleral and conjunctival flaps. Usually, the sutures

used will be different for each flap, with doctors using nylon sutures for the sclera and Vicryl sutures for the conjunctiva.

"I use 10-0 nylon for the scleral flap sutures, which we can release with laser suture lysis, if needed," says Dr. Myers. "In some patients with very thick Tenon's and conjunctiva, or who might have some bleeding, and I'm concerned about the ability to do laser suture lysis, I'll do an external releasable suture with the 10-0 nylon, which is essentially a one-sided bow at the scleral side, allowing the suture to be pulled from the corneal side. It's easy to release."

Dr. Simpson has a similar approach to suturing the sclera, yet she uses a different tensile strength and diameter for her suture material. "I'll use 9-0 nylon to tie down my scleral flap and use argon suture lysis later if I'm planning on cutting my sutures," she says. "The one exception is when I'm doing this kind of surgery on patients who are either really young, have really robust Tenon's or are really apprehensive patients at the slit lamp; for those patients, I'll do releasable sutures."

Regarding closing the peritomy, Dr. Tsai uses a suture that he doesn't have to pull out so as not to disturb the wound. "The 9-0 monofilament Vicryl is an absorbable suture with a predictable absorption time," he says. "I like using the 9-0 monofilament Vicryl suture since when it fully absorbs four to six weeks later, the wound is nicely healed. I use the 9-0 Vicryl sutures for a running suture of a modified fornix-based conjunctival flap made 1.5 millimeters posterior to the surgical limbus. With a 1.5-millimeter conjunctival ledge from the limbus, the surgeon can perform a conjunctival-to-conjunctival running suture. To keep the running suture from loosening and/or unwinding, I'll interlock every other conjunctival bite. When I check the conjunctival wound at the end of the case, I'll place interrupted 9-0 Vicryl sutures if there's a potential wound leak."



Reza Razeghinejad, MD

Releasable sutures are best for patients with thick Tenon's, uncooperative patients or when laser suture lysis isn't available, surgeons say.

Perioperative Drug Management

Glaucoma patients are typically on some form of glaucoma medication prior to trabeculectomy. Sometimes it's best to get these patients to stop their regimens before performing the surgery to reduce the risk of severe inflammation and irritation.

"In patients where there's not a big risk from halting medications, I try to stop medications that may be inflammatory or irritating the conjunctiva one week before the surgery," shares Dr. Myers. "I start prednisolone four times a day, one week before the trabeculectomy. Brimonidine products are the most common medications that could irritate the conjunctiva and could possibly benefit the patient's surgical outcome by stopping them."

Other times, it may be better to create a regimen for glaucoma patients prior to surgery to ensure that their eyes are prepared for what's to come. At Dr. Simpson's practice, physicians tend to provide their patients with particular eye drops, steroids and topical therapeutics to reduce the risk of severe inflammation and irritation.

"I like to optimize the conjunctival surface and the ocular surface as much as safety will allow," says Dr. Simpson. "With my patients for whom we've got a date set for surgery that's maybe six weeks out, I'll try and optimize their ocular surface. Most often, it'll depend on the patient. A lot of times I'm trying to get them to use lots of artificial tears, do some warm compresses and make sure their ocular surface is optimized that way. I'll try and start a steroid ahead of time as well to get a head start on controlling inflammation. Oftentimes, my patients need a trabeculectomy relatively quickly, so we don't have as much time to plan strategically and get them off their drops. For those patients, I'll focus on steroid use and making sure their ocular surface is optimized with artificial tears. We don't worry as much about stopping medication."

During the surgery, antimetabolites are used to reduce the risk of bleb failure. Mitomycin C can be administered

Predicting Trabeculectomy Outcomes with AI

"There are some interesting applications for artificial intelligence in trabeculectomy," says James Tsai, MD, a glaucoma specialist and president of New York Ear and Eye Infirmary of Mount Sinai. How does artificial intelligence go hand in hand with trabeculectomy? Three studies between 2022 and 2024 explain how AI can be valuable in the prediction of trabeculectomy outcomes, ensuring that patients receive the best care.

In 2022, researchers from the West Virginia University School of Medicine created multiple machine learning models for trabeculectomy outcome prediction.[5] The team took data from 230 trabeculectomy surgeries and found that 104 cases succeeded and 126 cases failed after one year. After creating each AI model, the team took the surgical data, plugged it into each model and asked them to identify which cases succeeded and failed. The random forest model performed with the highest accuracy, recording a value of 0.68 out of 1.00.

In 2023, researchers from Italy conducted a study where they instructed AI models to predict outcomes of trabeculectomy using ocular measurements.[6] Besides collecting success and failure rates from 102 cases (60.8 percent success; 39.2 percent failure), the team collected data from OCT imaging. Conjunctival stromal thickness and reflectivity as well as patients' ages were major contributing factors that allowed for the classification tree model to "predict the filtration surgery outcomes with good accuracy."

In 2024, researchers from India created three machine learning models to assess the five-year data of trabeculectomy performed on juvenile open-angle glaucoma.[7] The models assessed multiple factors, but age at diagnosis, preoperative baseline IOP, duration of preoperative medical treatment, Tenon's thickness, scleral fistulation technique and intraoperative mitomycin C use were major contributing factors. All models presented with an accuracy of more than 86 percent when deciding whether a case would succeed or fail.

either via a sponge or through injection, and 5-fluorouracil can be injected intraoperatively or early during postop.

"Almost every case I perform, the patients receive mitomycin C," says Dr. Myers. "Typically, I do that as an injection prior to starting the incisional part of the surgery—an injection of a 30-gauge needle into the conjunctiva. Usually, the mitomycin C is mixed with lidocaine 1% non-preserved. I use 0.4 milligrams per milliliter of mitomycin C and then dilute it one to one or two to one with the lidocaine 1%."

Conversely, Drs. Simpson and Tsai use the alternative method of a sponge to employ mitomycin C. Dr. Simpson explains, "I typically use a concentration of 0.2 unless they're really young or heavily pigmented, and then I'll do a concentration of 0.4. I typically soak it in sponges. I know sometimes people will inject it, but I'll soak them in sponges and then let them sit between the conjunctiva and sclera for two minutes. Also, I'll inject a little bit of extra mitomycin C pretty far posteriorly using an angiocatheter. So, whatever little residual mitomycin that's left over after we soak the sponges, we'll drop that into an angiocatheter, inject that posteriorly first, then position the sponges and let it sit for two minutes."

Dr. Tsai recommends using 5-FU postoperatively for bleb encapsulation. "If the bleb encapsulates or is healing excessively, I'll use postoperative subconjunctival 5-FU injections," he says. "I only use the 5-FU injections weekly, and my upper limit of injection is between three to five subconjunctival injections since 5-FU has some corneal toxicity. I'll then administer the subconjunctival 5-FU injection about ninety degrees away from the filtering bleb area, and then before the next injection, I'll check to make sure there isn't any corneal epithelial toxicity because this can occur with repeated 5-FU injections."

Following trabeculectomy, surgeons stick to their favored medication regimens to help with healing and reduce the risk of complications.

"After the surgery, I'll have them hold off on their glaucoma medications, and then our pharmacy will compound a preservative-free dexamethasone," shares Dr. Simpson. "We hit them pretty hard in the first couple of weeks with preservative-free dexamethasone about every two hours, and then we'll add back medications as needed. If the pressure goes up within the first couple of weeks after surgery, then we're going to cut a suture before we restart medication. The only time I'll leave them on medication is if I know that I've tied off my flap completely watertight and I know that their pressure is going to be really high until I can open their flap. So, I might bridge them with a little bit of aqueous suppression, but typically that's not the case."

The surgeons to whom we spoke hope that these surgical pearls will help guide glaucoma specialists as they wade into trabeculectomy surgery and grow more familiar with the procedure. In the end, this traditional treatment will come in handy one time or another and may just save the day. "If you want to get better at trabeculectomy," shares Dr. Simpson, "you need to review your surgical videos, talk to your colleagues about their techniques, try to glean pearls along the way, and be a student of your technique and your outcomes so that you can constantly be improving." ◀

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IOLS FOR THE MONOCULAR CATARACT PATIENT

Surgeons weigh the risks, benefits and lens choices in high-stakes cases involving only one functional eye.

LIZ HUNTER
SENIOR EDITOR

Over the course of any cataract surgeon's career they may be presented with the occasional monocular patient. These cases require a bit of extra consideration and counseling, particularly when discussing the potential use of multifocal IOLs. Whether their situation is due to trauma or disease, the patient must be educated on how each lens will function in their individual case, and without a second eye to fall back on, surgeons must handle every aspect of the process with care.

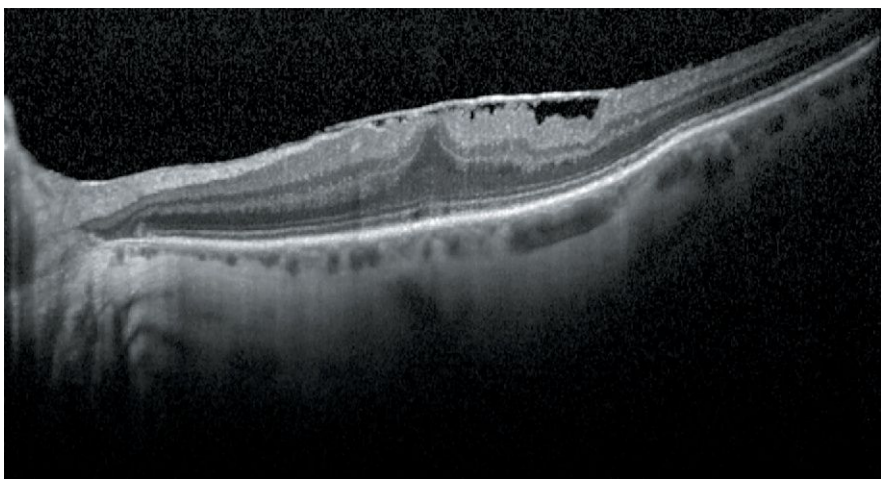
"When talking about a monocular patient, it's worthwhile first to consider what we mean by that," says John Hovanesian, MD, who practices at Harvard Eye Associates in Laguna Hills, California. "There are patients who have anywhere from just mild visual impairment in one eye to the actual physical loss of the eye. The way we manage them would be different, of course. Those who have just mild visual impairment might have different choices from those without another eye."

We spoke with several cataract surgeons about how to approach monocular patients and the strategies that are most likely to have a successful outcome. Here's their advice.

Meeting the Monocular Patient

Considering that these patients have been relying on one seeing eye either for their whole life or a number of years, it's possible they may want their cataract addressed at the earliest signs so they don't lose any vision. On the other hand, the cataract symptoms could come on slowly and may not be alarming for monocular patients. Either way, according to surgeons, the idea of surgery on their good eye is a source of anxiety.

"Most of the time, my monocular patients tend to be the last to notice complaints," says Dr. Hovanesian. "If they have a rapid-onset cataract,



Steve Safran, MD

Figure 1. An epiretinal membrane is a contraindication for a diffractive IOL but the patient would be a candidate for a monofocal or toric lens.

This article has no commercial sponsorship.

Dr. Barlow has no financial disclosures. **Dr. Hovanesian** consults for and holds equity in multiple companies in the IOL and cataract space. **Dr. Safran** has no financial disclosures.

they'll notice it, but at least in my experience, most of them seem to have a slow onset nuclear cataract that bothers them very little. Unless they're really paying attention, monocular patients with primarily nuclear cataract don't have a ton of urgent complaints because they don't have a comparison point, even though their vision is compromised."

It's not necessarily that much different than a binocular patient in terms of visual impact, according to William R. Barlow Jr., MD, a professor in the Department of Ophthalmology and Visual Sciences at John A. Moran Eye Center in Utah. "Most of these patients have adapted to their monocular status—especially those who had trauma at a young age and have been monocular for many years," he says.

"They've adapted quite nicely to that, and so it tends to be fairly typical in terms of the symptoms they might present with: increasing difficulty seeing street signs far enough away to react to them; glare or halo at night with oncoming headlights; needing more light to read; and noticing that small print is hard to see even with their correction," he continues. "So, I think the symptoms are pretty classic, and at least in my experience, they don't tend to appear earlier than the cataract would be expected to clinically present."

Addressing their fear or anxiety about the surgery is a matter of weighing the risks and benefits.

"There's this balance of wanting to be conservative in terms of the risk-benefit profile because it's their only seeing eye, but at the same time, not being too conservative to the point where surgery becomes more difficult or higher-risk, or the recovery is longer," says Dr. Barlow. "So, there's a narrower window from most surgeons' perspective in terms of when to do the surgery."

The same elements that make a typical cataract patient more complicated—white cataract, pseudoexfoliation, small pupil, Flomax—become much more frightening in a monocular patient, according to Steven Safran, MD, who's in private practice in Lawrenceville, New Jersey. "Your margin for error is gone," he says. "Every choice matters more, so I think we have to be a little more conservative. You can't afford to be cavalier."

A study published in 2012 examined the level of fear of cataract surgery among monocular vs. binocular patients.[1] Of those with monocular vision who reported feelings of fear, the most common were fear of blindness, worsening of vision, complications in the surgery, fear of the anesthesia, pain during surgery, death during surgery and pain in the postoperative period.

> **In the monocular patient, really any lens can potentially be used, but we have to consider what functionality they'll get out of it.**
>
> ***— John Hovanesian, MD***

Dr. Hovanesian says it sometimes takes an extra nudge for monocular patients to go through with the surgery. "There are risks in surgery, and we have to be very upfront about it," he says. "But sometimes for our monocular patients—if we're comfortable doing so—we have to nudge them a little bit and say, 'Look, we can't fix your other eye, but this eye—we can make it help you function better.'

"I believe most of my colleagues have good ethics and good decision-making skills for monocular patients," he continues. "We need to be as transparent as possible when counseling patients and express why—if we're suggesting surgery—we think it's in their best interest. Patients are smart. They want to follow their doctor's advice, but they also need to understand that we're really on their side."

In patients whose bad eye is legally blind or worse—20/200 for example, they may have vision for navigating around obstacles but not for discerning the details. "In that category, the first thing we always have to consider is the surgical risk in the better-seeing eye," Dr. Hovanesian says. "Do they have a cataract that necessitates surgery at all? Why expose them to any risk in their good eye if they're functioning well? We might typically be a little more conservative in recommending surgery for that eye.

"The trade-off is that, in many cases—especially as patients get older—once they've got a fairly advanced cataract it's a more risky case. So we've got one eye to work with, and it's at greater risk of complications. Usually in those cases, if the patient is beginning to experience impairment, it's better just to get it done. If the patient has a reasonable life expectancy and an active lifestyle—as so many people do—they need to see better, and they will benefit more than anyone."

Evaluating Patients' Vision Potential

A thorough screening needs to be performed before proceeding with any IOL recommendations as there are important criteria to meet and others that might disqualify them.

"For a monocular patient, you'd like to know the history of the other eye in terms of what the issue was that caused the loss of vision," says Dr. Barlow. "This is just to have a sense of whether there's anything from a prognostic standpoint that could pose a threat to vision in the other eye at some point in the future. You want to look for diseases that might present in an asymmetric fashion. It's atypical, of course, for conditions such as diabetic retinopathy, macular degeneration or glaucoma to present in a unilateral fashion, but you can certainly see significant asymmetry, which can cause significant vision

loss. In those types of circumstances, I'd be a little more reluctant to use a multifocal or trifocal lens.

"A lot of times, monocular patients have significant vision loss due to something that's truly unilateral," he continues. "Trauma, of course, isn't an uncommon cause of significant vision loss in a single eye, particularly if it's long-standing. But you're also looking at systemic diseases that could affect vision—someone with hypertension who ends up with a branch retinal vein occlusion in one eye could be at higher risk of having a similar problem in the other eye. In those cases, you may want to steer away from a diffractive optic, multifocal or trifocal type design in case something like that presents."

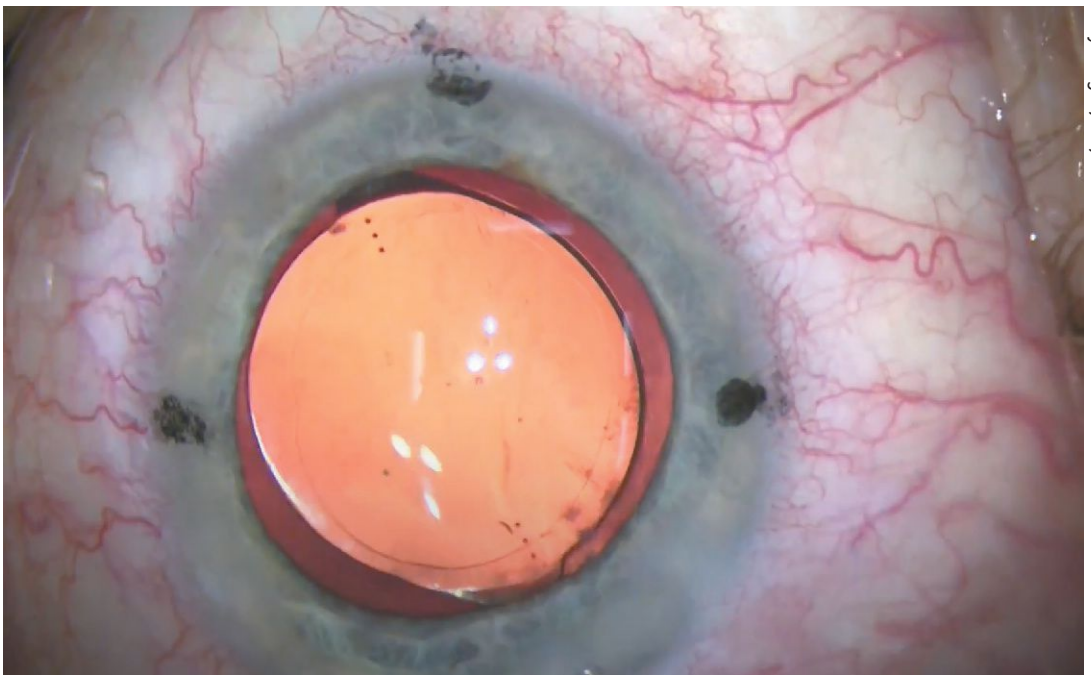
If screening confirms that the non-seeing eye was caused by a unilateral condition or event and the seeing eye is completely healthy, then advanced technology lenses would be options for these patients, Dr. Barlow says. "Obviously, there's the caveat that there may be some modest limitations to the visual functionality of a trifocal or multifocal IOL in a single eye, relative to what someone might achieve with that technology in both eyes. But certainly, it's not an absolute contraindication for a monocular patient."

Dr. Hovanesian says this is where counseling comes in. "In the monocular patient, really any lens can potentially be used, but we have to consider what functionality they'll get out of it," he says. "Just like a patient with two eyes, we need to determine what their visual needs are. Some doctors are hesitant about using a multifocal lens in patients with one eye. I've not had problems with that. Patients who are properly motivated, who understand the cautions about driving after dark and who understand the limitations of those lenses can do very well with them. There aren't any lenses that are unduly risky for one-eyed patients, we just need to have a slightly different discussion."

Dr. Barlow says these patients deserve to have all of the options presented to them despite being monocular. "As an example, if the non-seeing eye has significant trauma which wasn't due to a systemic disease or something bilateral—asymmetry like that doesn't necessarily rule out advanced lenses," he says. "I'm not necessarily pushing patients toward this technology, but I still educate them about it. I think it's unfair not to at least give the patient the chance to hear about the technology, talk about the pros and cons and then let them make a decision they're comfortable with."

Alternatively, if there's anything abnormal with the seeing eye—issues like abnormalities in macular function, nerve function or dry eye—Dr. Barlow has a low threshold for saying the lens probably isn't appropriate. "I don't think it's an absolute contraindication," he explains. "I haven't done it a lot in my career; most of my monocular patients have had monofocal IOLs or monofocal torics. But I've had some patients who've done a lot of research and educated themselves online about lens options. They come in very motivated, and if they're a candidate for a multifocal, they'd like to do it. I haven't necessarily seen that as a reason not to go forward. You just have that conversation with the patient. In terms of functionality, assuming a normal eye, their risks of glare, halos or not feeling like they're seeing as well as they expected—the older technologies may have had that waxy description, but I think with the newer designs, we get quite good visual function with diffractive optic systems. Again, I don't think it's an absolute contraindication in a monocular patient."

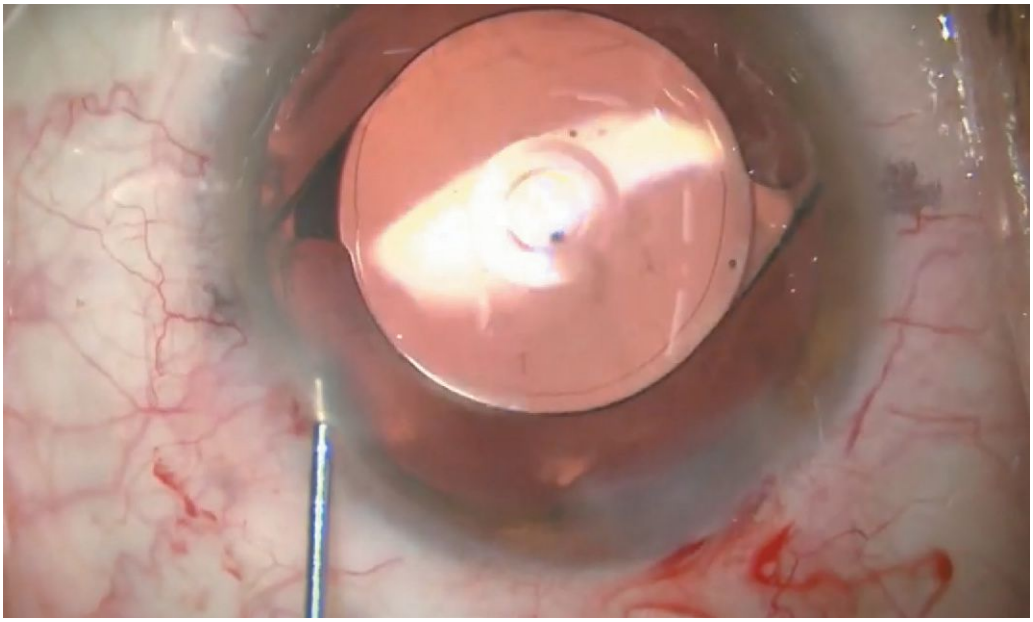
Dr. Hovanesian



Uday Devgan, MD, CataractCoach.com

Figure 2. Some surgeons prefer to use monofocal and monofocal toric IOLs in monocular patients to avoid halos, glare and reduced contrast.

says extended depth-of-focus lenses can do very well for these patients to give them a greater range of activities without corrective lenses. "In most cases, it's worthwhile—if the patient has astigmatism or is predicted to have astigmatism after surgery—that we correct that astigmatism in some manner," he says. "That could be with a lens that has toric correction—such as a monofocal toric lens—or an incisional keratotomy. Both are reasonable approaches."



Uday Devgan, MD, CataractCoach.com

Figure 3. Extended-depth-of-focus lenses may give monocular patients a better range of vision for activities without the need for glasses, say surgeons.

Astigmatism correction brings safety benefits, Dr. Hovanesian continues. "The reason I think it's worthwhile to do astigmatism correction in these patients with one eye is that, particularly as they get older, giving them at least the ability to have uncorrected distance vision without glasses allows them to ambulate without the distortion that bifocal glasses will cause," he says. "We know that about half of the falls in the older population occur in association with bifocal or progressive-add lenses. The reason is, when patients are wearing those and looking down to go downstairs or walk over uneven surfaces, there's distortion. If we can help it so that patients have uncorrected distance acuity—so they can ambulate without correction—then they're less likely to fall at night or on uneven surfaces. They'll just have better unaided acuity."

Choosing the Conservative Route

Some surgeons may opt to avoid multifocal IOLs altogether, and for good reason, they say.

"Monofocal IOLs are the lenses that provide the best quality of vision in patients, whether they're monocular or binocular," says Dr. Barlow. "Most patients choose a distance target so that their glasses are optional, and they can use reading glasses as needed. It's very simple to construct a pair of glasses for near tasks because the distance correction is minimal. But if you have a patient who does a lot of reading, especially if they're already a bit myopic, they might choose a mild near target so they can enjoy reading without glasses and use glasses for distance."

Astigmatism can be corrected with glasses or contact lenses, he continues, but there's also the opportunity during cataract surgery to use a toric lens to correct the astigmatism and reduce their dependence on glasses or contacts. "For motivated patients, that's certainly appropriate," Dr. Barlow says. "I don't think monocular status necessarily changes how people view that, though some might prefer to wear glasses for the added protection for their seeing eye, possibly with polycarbonate lenses. Depending on a patient's lifestyle, activities and occupational risks, we have that conversation and make a decision about how they want to rely on glasses after the procedure."

Dr. Safran says surgeons have to use different tools for different patients. "You have to look at the whole picture—the anatomy, the visual potential, the patient's lifestyle and their specific needs," he says. "With any monocular patient you have to treat that eye as the whole ballgame. You have to treat it with great respect, and you have to do everything you can to preserve the quality of vision and contrast."

These patients would be disqualified for premium lenses if there's any sign of macular disease, diabetic retinopathy, age-related macular degeneration, or epiretinal membranes, he explains. "If I don't think they're going to get 20/20 vision after cataract surgery, I don't think a multifocal lens is in their best interest, even if they want it. Multifocals depend on binocular summation. Patients do better when both eyes are working together. You get the benefit of depth of focus without as much perception of the downsides. But when you only have one eye, you notice all of it—the halos, the glare, the drop in contrast. If one eye has a little drop in contrast or a little glare, the other eye can help compensate."

Dr. Safran opts to implant a toric

lens in these patients. "I always use toric lenses to correct astigmatism in patients, even if they have one eye," he says. "I don't think there's any contraindication in using that, but I'm personally reluctant to use any type of diffractive lens that's going to reduce contrast. I've learned from taking lenses out and replacing them what the differences in quality of vision are in the same eye between lenses. To say to somebody, 'You're not going to need glasses if we put this in'—well, most multifocal lenses really rely on summation between two eyes to work well. I tell patients, 'It's like trying to pick up a chair. Easy with two arms. With one arm, it can be impossible.'"

There's also the fact that monocular patients should be wearing protective eyewear regularly, he adds. "While I do think there's always an advantage to correcting astigmatism—because having an implant that corrects astigmatism actually performs better than correcting it with glasses, due to how toric lenses in glasses interact with fixation shifts—having the correction built into the system is better, in my opinion," says Dr. Safran. "Very often we tell patients with only one eye that they should wear protective eyewear—polycarbonate lenses, for example—to protect the eye. So it seems kind of ridiculous to have them pay extra and reduce their contrast just so they don't have to wear glasses that they really should be wearing to protect the eye anyway."

Ultimately, it's about doing what's in the patient's best interest. "I don't personally believe that using anything that degrades contrast and quality of vision in any way to improve depth of focus is a great idea for patients with only one eye," says Dr. Safran. "I tend to avoid anything that has even the slightest chance of reducing quality of vision, clarity or contrast in patients with only one eye. Just keep it simple."

Addressing the Poor-seeing Eye

If patients present with a cataract in their seeing-eye, it's likely that a cataract is in the other eye as well, and deserves a conversation about surgery.

"A lot of eyes with poor vision actually receive a lot of benefit—in their peripheral vision, in their color perception, in their overall ability to navigate—by having binocular correction of cataract," Dr. Hovanesian says.

"Often in a monocular patient, if there's significant cataract and I think it'll benefit them, I'll suggest it," he continues. "There are two schools of thought about which eye to operate on first. Choosing first the eye with the better visual potential does give a quick and meaningful reward, but it requires a big leap of faith for the patient. I'll typically choose the worse-seeing eye first. I tell patients this: It's going to get them comfortable with the process of surgery. In a low-risk environment, they don't have as much to gain, but they also don't have as much to lose. By doing the poorer-seeing eye first, they'll say, 'Even there, in that poor eye where I understood I wouldn't see well—I do see better. And they'll say, 'Gosh, this would be good for my good eye.'"

"If there's some vision potential in that eye, then I think it's appropriate to do surgery and remove the cataract," Dr. Barlow says. "Maybe they have some peripheral visual function. I've had patients with very limited vision, but the cataract advanced enough that it impacted what limited function they did have, and in that case, it's appropriate to do the surgery. If the eye has no light perception or no projection—if they don't perceive any light or visual stimulus—I tend to be conservative and leave the cataract alone. Of course, there are debates about that, in terms of potential medical issues that can occur if the cataract becomes hypermature."

Surgery on the non-seeing eye first can also help quell some of those initial anxieties about the process, say surgeons.

"I do have some monocular patients who ask to do the non-seeing eye first so they can experience the process, see what surgery and recovery are like—a kind of dry run," says Dr. Barlow. "I don't think that's inappropriate. Depending on their motivations and the very limited visual potential in that eye, it's reasonable to try to balance the refractive error and maximize function as much as possible. If I'm doing a multifocal in the seeing eye because the patient is motivated and has educated themselves, I'll just do a monofocal in the limited eye, targeting a similar refractive outcome."

Dr. Hovanesian says he would need to see the potential for 20/25 vision in the poorly seeing eye in order to recommend a presbyopia-correcting IOL. "That's not an absolute rule," he says. "Patients who are highly motivated, who want it, who understand their limitations—I don't think it's unethical. What makes us ethical is being honest with patients, sharing with them our best judgment, the way we would treat a family member. If you do that, and still the patient can afford and really wants the fancy lens, there's nothing wrong with it. But they need to understand that they're not going to derive the value out of it that someone would with a normal eye."

Counseling and chair time will ultimately guide monocular patients on their decision to proceed with surgery and IOL selection. "The main point I focus on with these patients is gauging how much the cataract is affecting their day-to-day function," says Dr. Barlow. "I want to make sure we're not being too conservative. Most of these patients aren't rushing into surgery because of their situation, but we want to avoid a scenario where their visual function is impaired enough to raise safety concerns—for example, in driving or other important tasks—where surgery could really benefit them." ◀

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THE EVOLVING LANDSCAPE OF DRY-EYE THERAPEUTICS

A look at the current pipeline of dry-eye treatments.

CATLIN NALLEY
CONTRIBUTING EDITOR

Dry-eye disease is one of the most commonly encountered yet persistently challenging conditions in ophthalmology. Characterized by ocular surface inflammation, tear film instability, and a spectrum of often debilitating symptoms, DED affects millions worldwide. And despite a growing list of available therapies, many patients continue to struggle with incomplete or inconsistent relief.

"Dry-eye disease is inherently complex and multifactorial," says Sezen Karakus, MD, assistant professor of ophthalmology at Johns Hopkins' Wilmer Eye Institute. "While current treatments are helpful for many patients, they often fall short in those with overlapping mechanisms or underlying systemic contributors.

"One of the biggest challenges is the lack of a clear, linear relationship between pathophysiology, clinical signs and patient-reported symptoms," she continues. "Patients may present with debilitating symptoms but minimal clinical findings—or vice versa—which complicates both diagnosis and treatment decisions."

Today's therapeutic strategies often rely on broadly targeting inflammation, rather than addressing the specific root causes of disease in each patient, according to Dr. Karakus. "There's no single diagnostic test that can identify the dominant mechanism driving disease in an individual patient. Although several inflammatory cytokines and molecular pathways have been described over the years, there are currently no clinically available tests that guide mechanism-based therapy."

Furthermore, many essential structural and regenerative aspects of ocular surface health remain unaddressed in the current therapeutic arsenal. "A major gap lies in the lack of dry-eye treatments that directly support epithelial health, goblet cell restoration, corneal nerve regeneration and meibomian gland vitality," suggests Dr. Karakus. "Systemic influences—such as aging, hormonal changes, lid anatomy, neuropathies, diabetes, or medication side effects—are also commonly overlooked, despite their significant impact on disease severity and chronicity."

Another key unmet need is the absence of reliable, accessible biomarkers that can help stratify patients and personalize therapy, notes Dr. Karakus. "A precision medicine approach—where we could identify dominant mechanisms and match them to targeted therapies—would be transformative but remains out of reach in today's clinical practice."

Amid these limitations, a wave of innovation is offering new hope. "What makes the current pipeline particularly exciting is that newer agents are targeting previously untapped mechanisms—such as neuroregeneration, epithelial repair, and lipid regulation in the meibomian glands," Dr. Karakus shares with *Review*. "These innovations offer hope for broader and more sustained efficacy across the diverse and complex patient populations affected by dry-eye disease."

This article explores the evolving dry-eye treatment landscape, highlighting emerging investigational agents in the pipeline that may help fill these gaps and bring clinicians one step closer to more personalized and effective care.

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Dr. Karakus is a consultant for Dompe.

DRY-EYE DISEASE TREATMENTS IN EARLY DEVELOPMENT OR OTHER CLINICAL TRIALS

SAF-312 (Bausch + Lomb)	Phase II	Topical ocular TRPV1 agonist (libvatrep) for chronic ocular surface pain.
A197 (Aramis)	Phase II	Topical immunomodulatory agent for the treatment of dry-eye disease.
AZR-MD-001 (Azura)	Phase III	Selenium sulfide ointment for the treatment of MGD and contact lens discomfort.
TL-925 (Telios)	Phase II	Topical Bruton's tyrosine kinase inhibitor to prevent mast cell activation and degranulation for moderate to severe dry-eye disease.
OCS-02 (Oculis)	Phase II	Topical anti-TNFα therapy for dry-eye disease and uveitis.
OK-101 (OKYO Pharma)	Phase II	Using Membrane Anchored Peptide technology, this treatment consists of a 10-mer C-terminal chemerin peptide sequence, a linker component and an anchoring lipid domain, which activate immune cells to reduce inflammation.
Lacripep (Tear Solutions)	Phase II	A synthetic fragment of lacritin, a natural tear protein that's deficient in unique dry-eye cases.
GLK-301 (Glaukos)	Phase II	Also called iLution, a sterile ophthalmic topical cream applied to the lids to improve the quality of tear film and vision.
INV-102 (Invirsa)	Phase II	Indicated for the treatment of ocular conditions associated with DNA damage, this eye drop uses the p53 protein which activates the master regulator of the DNA damage response. First human trials were conducted on dry-eye patients.
CBT-006 (Cloudbreak Pharma)	Phase II	An eye-drop solution to dissolve cholesterol and other lipids in the meibomian glands.
SY-201 (Seinda)	Phase II	Ophthalmic solution for the treatment of dry-eye disease.
CSB-001 (Claris Bio)	Phase I/II	A heterodimeric molecule consisting of a 69-kD α-chain and 34-kD α-chain that binds to c-MET; a hepatocyte growth factor ophthalmic solution.
AG-80308 (Allgenesis)	Phase Ib	Eye-drop solution formed using a formyl peptide receptor agonist for the treatment of dry-eye disease.
RP501 (Redwood Pharma)	Early Development	Also called IntelliGel, this is a heat-induced hydrogel (thermalgel) that increases the amount of water delivered to the eye while reducing the amount of polymers.
Reproxalap (Aldeyra Therapeutics)	Phase III	Small-molecule inhibitor of reactive aldehyde species (RASP) developed to reduce inflammation and alleviate symptoms of dry eye.
ST-100 (Stuart Therapeutics)	Phase III	ST-100 selectively repairs disease-damaged collagen in the eye, providing restoration of the collagen matrix and structures as well as homeostatic cell signaling.
PL9643 (Palatin Tech.)	Phase III	Acts as a melanocortin receptor agonist, aiming to reduce inflammation and promote tissue repair in dry-eye disease.
AR-15512 (Alcon)	Phase III	The active ingredient in AR-15512, a proprietary small-molecule selective agonist of the transient receptor potential melastatin 8 (TRPM8) cold thermoreceptor.
IVW-1001 (iView)	Phase I/II	A novel TRPM8 agonist delivered via an eyelid wipe.

Key Pipeline Agents

The DED drug pipeline has never been more robust, with investigational therapies targeting diverse, often previously untapped mechanisms. Below is a look at several key agents under investigation, including expert insights on what makes some of these emerging therapies particularly promising.

• ***Reproxalap (Aldeyra Therapeutics)***. A first-in-class small-molecule inhibitor of reactive aldehyde species (RASP), reproxalap was developed to reduce inflammation and alleviate symptoms of dry eye. In May 2025, Aldeyra announced that their Phase III dry-eye chamber trial achieved its primary endpoint, with reproxalap significantly reducing patient-reported ocular discomfort compared to vehicle.[1] This comes after the FDA issued a Complete Response Letter in April 2025, citing insufficient evidence of efficacy in treating DED symptoms from prior data.

In response, Aldeyra plans to resubmit the New Drug Application in mid-2025, incorporating the latest trial results. "The dry-eye chamber results announced today are representative of a number of clinical trials that highlight the potential rapid clinical effect of reproxalap on reducing ocular discomfort," says Todd C. Brady, MD, PhD, president and chief executive officer of Aldeyra, in a statement.

"With no notable baseline differences across treatment arms and highly statistically significant results in favor of reproxalap over vehicle, Aldeyra believes the data potentially address the FDA feedback in the Complete Response Letter received last month and we look forward to meeting with the FDA shortly."

• ***Lacripep (TearSolutions)***. Among the dry-eye therapies currently under investigation, Dr. Karakus is particularly enthusiastic about the potential of lacripep, a first-in-class topical therapy derived from lacritin, a naturally occurring tear protein critical to ocular surface maintenance. "Lacripep stands out for its regenerative properties, particularly in patients with neurotrophic components or chronic epithelial instability," she notes. "Mechanistically, it supports both corneal nerve regeneration and goblet cell function—two key domains often unaddressed by current treatments."

Findings from a first-in-human study in patients with primary Sjögren's syndrome demonstrated that Lacripep was well-tolerated and produced clinically significant improvements in both signs and symptoms of dry eye.[2]

For Dr. Karakus, Lacripep—if validated—"could significantly alter treatment strategies by offering regenerative rather than suppressive therapy."

• ***ST-100 (Stuart Therapeutics)***. Developed to address the underlying structural damage in DED, ST-100 selectively repairs disease-damaged collagen in the eye, providing restoration of the collagen matrix and structures as well as homeostatic cell signaling by those structures, its maker says. A Phase III, randomized, double-blind, vehicle-controlled trial investigating the efficacy, safety, and tolerability of ST-100 was recently completed.[3] Results are pending and expected this year. Dr. Karakus finds this agent intriguing for its "rapid, neurosensory-modulating effects and potential to alleviate ocular surface discomfort."

• ***AZR-MD-001 (Azura Ophthalmics)***. This novel, ophthalmic ketolytic agent treats the pathophysiology of meibomian gland dysfunction, the leading cause of dry-eye disease. In June 2024, the first patient was enrolled in the Phase III ASTRO study—a multicenter, double-masked, vehicle-controlled, randomized trial assessing the efficacy, safety and tolerability of AZR-MD-001 in patients with MGD and associated symptoms of dry-eye disease. Approximately 500 patients will be dosed twice weekly at bedtime for up to 12 months.[4] The primary endpoints include changed from baseline to month three in meibomian glands yielding liquid secretion and total OSDI score. Secondary endpoints involve changes in the SPEED score and evaluation of safety and tolerability over the course of the study period.

"AZR-MD-001 has already demonstrated efficacy against a variety of clinical endpoints indicating that the product has the potential to improve the signs and symptoms of MGD for up to six months," says Francis Mah, MD, director of cornea and external disease and co-director of refractive surgery at Scripps Clinic Medical Group in La Jolla, California, in a company statement. "The ASTRO study, the second confirmatory efficacy study, will reveal important additional new findings on the use of AZR-MD-001 as a foundational treatment for MGD, and I look forward to learning more about the potential of this ophthalmic keratolytic to restore meibomian gland function in patients."

• ***PL9643 (Palatin Technologies)***. A novel ophthalmic solution, PL9643 acts as a melanocortin receptor agonist, aiming to reduce inflammation and promote tissue repair in dry-eye disease. Updated analyses from the Phase III MELODY-1 trial revealed breakthrough symptom resolution with PL9643. Data showed that six of 13 symptom endpoints had a significantly higher percentage of patients in the PL9643 group achieving complete symptom resolution compared to placebo.[5]

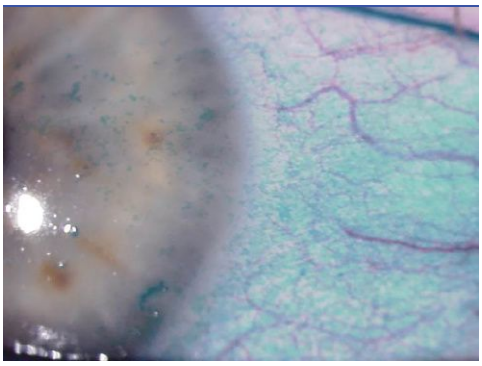
Following a Type C meeting with the FDA, Palatin received confirmation of the acceptability of the protocols and endpoints of the remaining Phase III trials—MELODY-2 and MELODY-3.[6] Should these trials meet their objectives, an NDA submission could be filed in the first half of 2026, the company says.

• ***OCS-02 (Oculis)***. OCS-02 (licaminlimab), a topical anti-TNFα biologic eye drop, demonstrated positive results in the Phase IIb RELIEF trial for dry eye. The study showed significant improvements in key efficacy endpoints, such as fluorescein staining and Schirmer's test, with the most pronounced effects observed in patients with the TNFR1 genetic biomarker. These patients saw improvements as early as Day 15, continuing through Day 43. OCS-02 was well tolerated, with mild, transient ocular adverse events.[7]

Following the success of the trial, Oculis plans to finalize Phase III development after meeting with the FDA. The company is focusing on a precision medicine approach, aiming to treat DED patients who may benefit most from the drug's dual anti-inflammatory and anti-apoptotic mechanisms.

• ***Additional agents***. Several emerging therapies are capturing attention for their novel mechanisms and regenerative potential in treating dry eye. Dr. Karakus points to INV-102 (Invirsa Therapeutics) as a promising candidate, explaining that it "modulates the DNA-damage response via p53, which may be relevant in age-related dry eye and meibomian gland dysfunction."

Therapies like TL-925 (Telios Pharma), a Bruton's tyrosine kinase inhibitor, and INV-102 represent innovative approaches by modulating mast cell signaling and DNA repair pathways—mechanisms that the company says haven't been meaningfully targeted in dry-eye treatment to date, Dr. Karakus highlights.



Developing a therapy that treats both signs (such as staining) and symptoms is challenging.

CSB-001 (Claris Bio), which uses a hepatocyte growth factor ophthalmic solution, and AG-80308 (Allgenesis Biotherapeutics), a formyl peptide receptor agonist, are also gaining attention for their regenerative potential, she adds.

Another exciting development is clusterin, a natural glycoprotein with chaperone-like properties. Preclinical models have shown that topical application of clusterin in mice with desiccating stress significantly improved ocular surface health by sealing the epithelial barrier, reducing inflammation, and promoting healing, according to Dr. Karakus. "Notably, clusterin binds selectively to damaged ocular surfaces, offering a unique mechanism of action."

From Pipeline to Practice

As new agents for dry eye move closer to potential approval, a key question emerges: What factors will influence their uptake in real-world clinical settings? For Dr. Karakus, the answer is clear. "In my opinion, the biggest practical challenges in adopting new therapies are tolerability and access, particularly when it comes to cost and insurance coverage," she explains. "Many effective treatments are limited by out-of-pocket expense or lack of reimbursement, making them inaccessible to the patients who need them most."

In a condition like DED—where long-term use is often essential for sustained benefit—comfort and convenience are paramount. "Tolerability is crucial—ocular discomfort or irritation could lead to poor adherence or even necessary discontinuation, even when the treatment is potentially effective," notes Dr. Karakus.

The challenge is heightened by the chronic nature of the disease and the often slow onset of action associated with existing therapies. "Many existing treatments require weeks to months to demonstrate noticeable improvement, which can be discouraging for patients. Therapies that offer more rapid relief without compromising safety or comfort would be welcomed in clinical practice."

Delivery method also plays a role—whether topical drops, nasal sprays or device-based systems—and will factor into patient preference and real-world compliance. For a new therapy to succeed, it must not only be effective, but also accessible, comfortable, and fast-acting enough to meet the expectations of both patients and providers.

Vision for the Future

The field of dry eye continues to evolve, and the path forward is becoming increasingly well-defined: The future lies in therapies that have deeper effects on the disease. "What's still missing are treatments that address the root causes of dry eye rather than just controlling symptoms," Dr. Karakus emphasizes. "Therapies that can rebalance the ocular surface and restore homeostasis—by promoting nerve regeneration, supporting epithelial and goblet cell function, or enhancing meibomian gland activity—would fill a critical unmet need."

If the dry eye pipeline delivers on its potential, Dr. Karakus envisions a shift toward a more personalized and mechanism-based approach. "We'll likely have a broader range of targeted therapies—but with that will come increased complexity in decision-making. Treatment algorithms will need to evolve to help clinicians determine which therapy to use, for which patient, and when."

This transformation will depend not only on new drugs, but also on new diagnostics. "As we continue to uncover new mechanisms and identify biomarkers, I believe dry eye treatment will increasingly resemble the precision-based approaches used in other areas of medicine," Dr. Karakus notes.

"Rather than relying on a one-size-fits-all strategy, we will be able to classify patients based on their dominant disease drivers and offer mechanism-specific therapies," she concludes. "This evolution holds the promise of not only improving outcomes but also reducing the trial-and-error burden that both patients and clinicians currently face." ◀

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HANDLING WHITE INTUMESCENT AND BRUNESCENT CATARACTS

Tips and techniques for dealing with these challenging varieties of cataracts, and ensuring good outcomes with minimal complications.

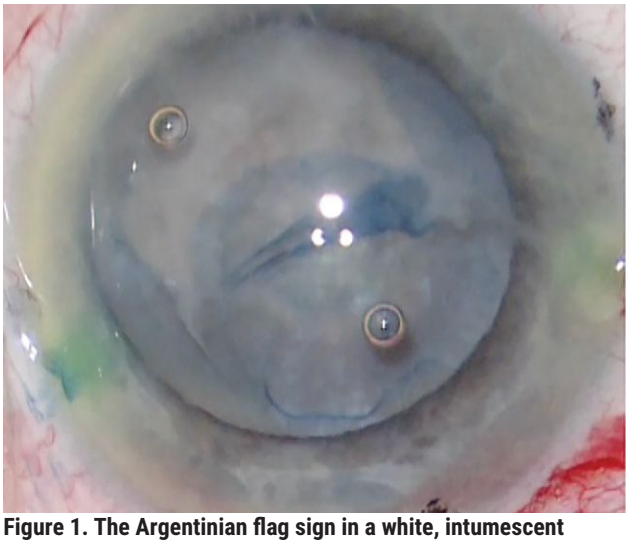
MAHSAW MANSOOR, MD
AND NICOLE FRAM, MD
LOS ANGELES

Advances in cataract surgery have transformed once nerve-wracking challenges into opportunities for precision and innovation. With new technology and refined techniques at our fingertips, tackling white intumescent and brunescent cataracts has become not only more manageable but, dare we say, even fun. Think of it as an extreme sport and be prepared for all circumstances. Despite new technologies and imaging, key concepts and strategies that giants in our field have passed down will be critical for a successful outcome.

In this article, we'll demonstrate the tried-and-true techniques enhanced by modern advancements, sharing personal anecdotes, clinical tips and the kind of hands-on advice you would offer a trusted colleague.

White Intumescent Cataract: Easing the Tension

White intumescent cataracts are notorious for their pressurized, swollen nature—a situation that can quickly escalate into a capsular catastrophe such as the Argentinian flag sign if not managed properly (*See Figure 1*). Fortunately, advances in techniques and surgical tools now provide us with more ways than ever to approach these cases with confidence.



Nicole Fram, MD

Figure 1. The Argentinian flag sign in a white, intumescent cataract.

• ***Staining with trypan blue.*** Visualization is everything. You'll inevitably lose the game if you can't visualize the capsule. Using trypan blue to stain the anterior capsule provides a stark contrast against the white lens material, giving you enhanced clarity as you proceed with the capsulorhexis.[1] This step might seem simple, but it's absolutely essential.

This can be accomplished in one of two ways: at the onset of the case prior to placement of an ophthalmic viscoelastic device or after an OVD has been placed (Osher technique).[2] After the injection of a OVD which fills the anterior chamber, balanced salt solution is gently injected onto the anterior capsule, fluid-filled space beneath the OVD. The dye is slowly injected through a 27-gauge cannula mixing with the BSS, allowing you to

This article has no commercial sponsorship.

Dr. Mansoor is the incoming Masket Foundation Fellow at Advanced Vision Care in Los Angeles. **Dr. Fram** is an adjunct assistant professor at the John A. Moran Eye Institute at the University of Utah, and co-director of the Masket Foundation Fellowship.

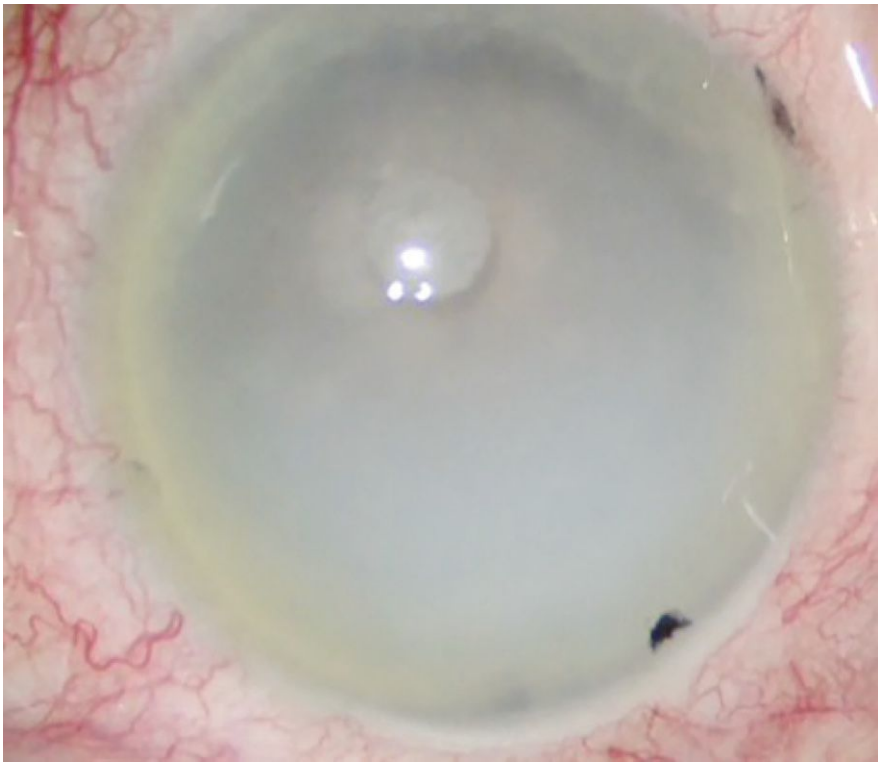


Figure 2. A flat dock and fast capsulotomy can prevent lens cortical "milk" from blocking the femtosecond laser.

"paint" the anterior capsule.

• ***FLACS or no FLACS, decompression is key.*** Before any maneuver, the initial step is to gently decompress the intumescent contents trapped within the capsular bag. Precision instruments, from ultra-fine needles to phaco tips with enhanced fluidics, help us achieve a controlled release of pressure.

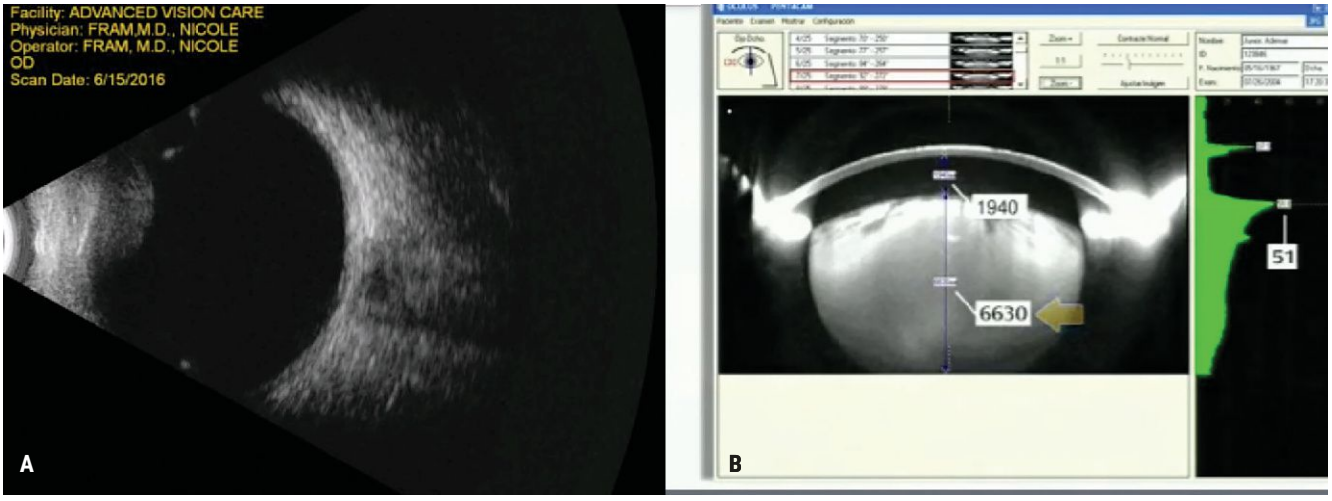
There are several manual techniques available. The most familiar is simple decompression with a 27-gauge needle, which pierces the anterior capsule and, when attached to a syringe, provides active suction to decompress the milky cortical material. Variations include using an air bubble to flatten the anterior capsule[3] or using an insulin needle attached to phaco aspiration tubing.[4] Be sure to do this through a paracentesis to avoid collapsing the anterior chamber.

For those feeling more adventurous, you might opt for the phaco capsulotomy.[5] In this technique, the phaco handpiece (either in a bevel-up or bevel-down position) is used directly to break through the anterior capsule into the lens. Using low-flow settings and a brief pulse of ultrasonic energy allows you to pierce the capsule and then remove liquified lens material with vacuum.

In contrast to these manual approaches, the femtosecond laser,[6] automated precision pulse capsulotomy,[7] or selective laser capsulotomy[8] can be extremely helpful in creating a reliable capsulotomy. Even with these automated methods, the Argentinian flag has been reported in some cases,[9,10] so you should be ready to pivot your technique if necessary.

In femtosecond laser assisted cases, liberated lens material can interfere with the laser's path, causing incomplete capsulotomies or capsular tags.[11] The key to success is ensuring a flat dock and time-efficient fast capsulotomy creation to prevent lens cortical "milk" from blocking the femtosecond laser *(See Figure 2)*.

Caution is also advised when using the femtosecond laser if the lens is spherical and intumescent, as radial rupture can occur *(See Figures 3A and B)*.



Virgilio Centurion, MD; Juan Carlos Caballero, MD

Figure 3. A) B scan to evaluate posterior segment when there is a limited view and to evaluate spherical lens. B) Pentacam demonstrated an intumescent and spheroidal lens.

Another helpful adjuvant technique is the "spiral out" or double-rhexis method.[12] With this method, you start small and gradually spiral out the capsulorhexis until you achieve adequate size. This gradual, systematic approach provides an element of predictability when managing unpredictable intralenticular pressure. Using 23 ga microforceps such as the Seibel Forceps (MST) or Guell Forceps (MST) allow for control without decompressing the anterior chamber.

Whether you prefer a manual needle approach, a femto capsulotomy, or a phaco tip, the goal remains the same: gradually release the built-up pressure to prevent sudden, uncontrolled capsular tears.

• ***The rocking technique.*** Once decompression is underway, a gentle rocking motion can further encourage the release of any remaining intralenticular pressure. This involves controlled, back-and-forth movement with your instrument and coaxing the lens to "breathe out" the built-up pressure. This technique helps maintain the integrity of the capsule throughout the process.

• ***Understand pressure differences.*** The term "intumescent" implies that the pressure within the lens and capsule is higher than that in the anterior chamber.[13] To tip the scales in your favor, generously use OVDs to maintain a relatively higher pressure in the anterior chamber. However, once you start your capsulorhexis, be careful not to over pressurize the chamber. I recall a recent case during my fellowship in a unicameral eye—the type that seemingly never can fill with OVD—by the time I reached for the Utrata forceps, the entire rhexis had radialized because I had put far too much OVD in the anterior chamber after I decompressed the lens. Even if you achieve successful initial decompression, the vector forces remain abnormal, and over pressurizing the AC can also lead to a radialized capsulorhexis.

• ***Nucleus disassembly.*** In white intumescent cases, the most challenging step is often creating a safe capsulotomy. Once the lens milk and cortical material are liberated, you may find extra space in the eye, which can be an advantage for instrument maneuverability. However, exercise caution as there is little protection for the posterior capsule once the endonucleus is removed. Many of these lenses are brittle and respond well to a quick vertical chop. Whatever your preferred method, ensure you maintain control and protect the capsule throughout the process.

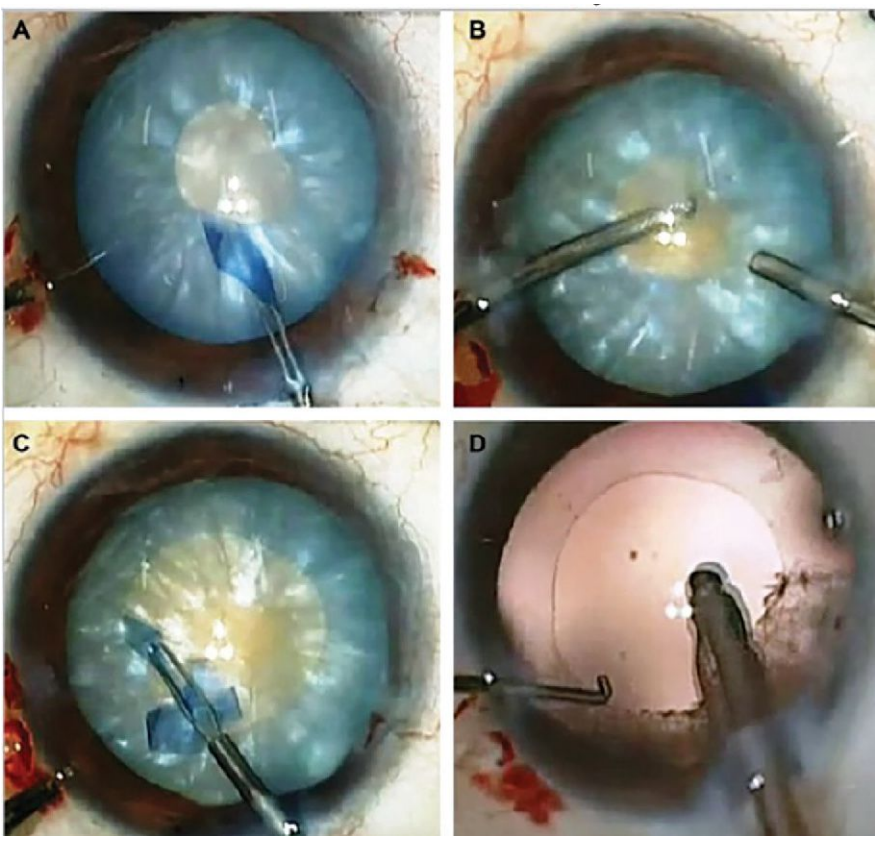


Figure 4. With the spiral-out capsulorhexis technique, start small and gradually spiral out the capsulorhexis until you achieve an adequate size.

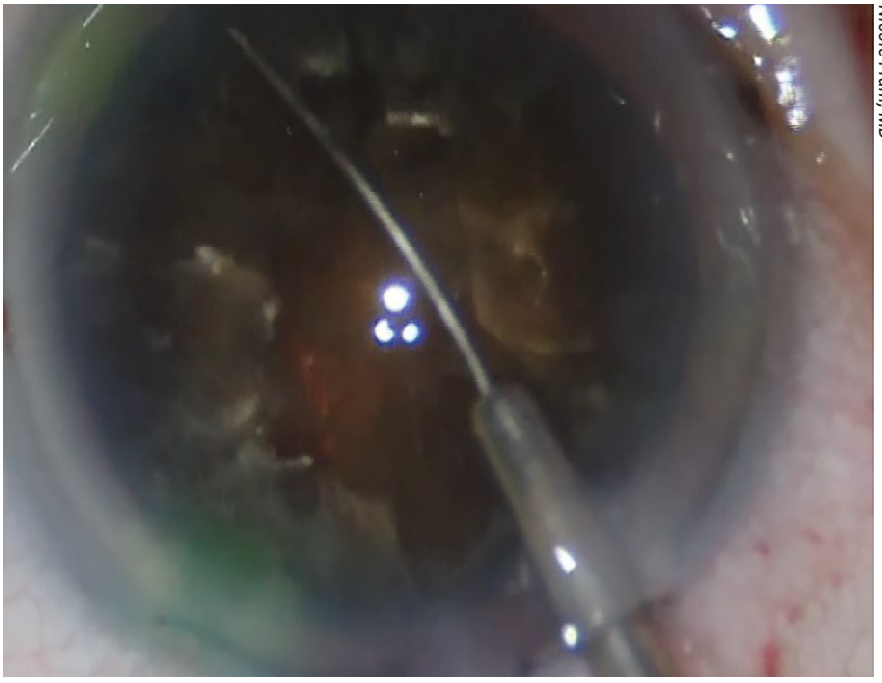
The Brunescent Cataract: The Dense, Leathery Challenge

Brunescent cataracts bring an entirely different set of challenges. Their dense, often leathery nature demands a strategic approach and readiness to adapt on the fly. As the nucleus gets denser, so do the challenges of surgery.

• ***Bring your accessories.*** These cases are associated with higher rates of complications such as corneal endothelial damage, posterior capsular rupture, zonular instability and vitreous loss. Always have a clear plan A, B and C. Ensure you have all necessary accessories—trypan blue, iris hooks, capsule hooks, capsular tension rings, lens snare devices such as miLoop (Zeiss), etc.—on standby. If you think you might need it, have it ready.

• ***Debulk the center.*** For brunescent cataracts, our first step is to debulk the central nucleus. Modern phaco technology allows for efficient central debulking, reducing the lens density and creating more working room in the anterior chamber. A softer, debulked center makes subsequent fragmentation more manageable. Every surgeon has a "dense lens" setting on their phaco machine, and this is the perfect time to use it!

• ***Femtosecond finesse.*** Femtosecond laser technology can be particularly helpful in segmenting brunescent



Nicole Fram, MD

Figure 5. The use of a miLoop to help bisect the leathery plate of a brunescent lens.

cataracts. It enables a predictable capsulotomy and facilitates lens segmentation, creating manageable fragments that can be emulsified more easily with the phaco handpiece. While femto laser can soften moderate nuclear sclerosis, it does little for mature brunescent lenses, especially when a thick posterior plate is present.

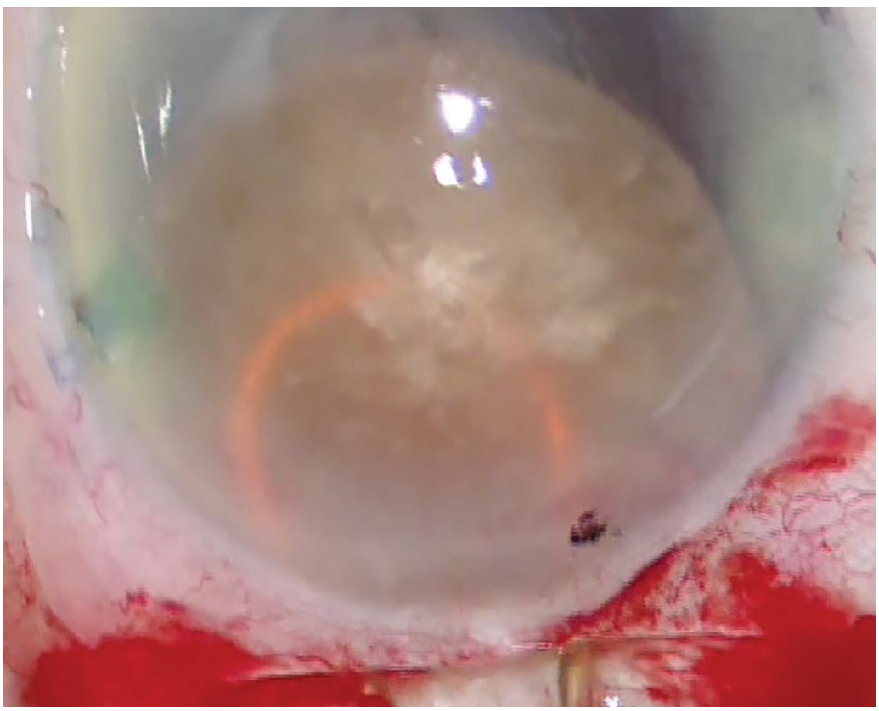
• ***Mastering OVDs.*** Maintaining a stable anterior chamber is critical in cases with dense cataracts. Dispersive OVDs are your best friend here. In dense brunescent cases, we make it a point to refill with OVD once about half the lens material has been removed. This proactive measure ensures continuous protection and optimal working space, making the procedure smoother and more controlled. OVDs are also excellent for exploiting potential space; I use them liberally to create room between the anterior capsule and the lens before placing capsule retractor hooks or using the miLoop. In challenging cases, OVD can also substitute for BSS during lens dissection.

• ***Leather plate management: MiLoop to the rescue.*** Breaking the posterior leather plate is one of the trickiest aspects of brunescent cataract surgery. Advanced lens snare devices like the miLoop allow for precise engagement and fracturing of the leathery plate without expending phaco energy or undue traction on the zonules. The miLoop has become a go-to in my practice, helping me manage these stubborn leathery plates with confidence. I find that counterbalancing the nucleus with a lens manipulator in tandem with the miLoop snare helps create even-sized nuclear fragments and breaks the leathery plate.

• ***Floppy bag management.*** With dense brunescent lenses, the capsular bag becomes stretched and taut. After nucleus removal, the posterior capsule often moves in an anteroposterior direction and can be quite delicate.

Even with a mastery of fluidics and stability of the newest phaco machines, you can "bite" the capsule at the eleventh hour once the final piece is removed. There may also be a recalcitrant plaque on the posterior capsule in these cases. When confronted with this, every young cataract surgeon should heed Dr. Osher's advice: Resist heroics and consider opening the capsule with a YAG laser at a later date.[14]

• ***Be ready to transition.*** Despite the power of phacoemulsification, there are times when the brunescent cataract simply won't yield. When the lens won't mobilize or the miLoop isn't performing as expected,



Nicole Fram, MD

Figure 6. Conversion to manual small incision cataract surgery (MSICS).

pivot! Having a backup plan is not a sign of defeat, but of preparedness. If the density proves too challenging, be ready to switch to manual small-incision cataract surgery or extracapsular cataract extraction. These techniques are as effective as phacoemulsification in brunescent lenses.[15]

Wrapping It Up: Embracing the Challenges with Confidence

Every cataract surgery presents its own set of challenges and opportunities. White intumescent and brunescent cataracts, though demanding, push us to refine our techniques and embrace the latest surgical innovations. The key is to blend the timeless principles of cataract surgery with modern technology, an approach that not only improves outcomes but also makes the process more enjoyable.

Success in the OR is not solely about mastering techniques; it's about being adaptable, staying curious and continuously learning. As I look forward to joining Dr. Fram and Sam Masket, MD, as a fellow next year, I'm reminded that the journey is as rewarding as the destination. With every case, we refine our skills, share our experiences and, ultimately, provide the best possible care for our patients. ◀

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Laser-based Glaucoma Treatments

As data matures, these innovations in treating outflow may redefine first-line and adjunctive glaucoma therapy in the clinic.

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ITHACA, N.Y.

In recent years, glaucoma management has entered a transformative era, marked by the emergence of minimally invasive glaucoma surgeries as well as selective laser trabeculoplasty as a first-line treatment. But as with any field, the technology continues to evolve. Three new technologies aimed at treating aqueous outflow—direct selective laser trabeculoplasty, femtosecond laser image-guided high-precision trabeculotomy and excimer laser trabeculostomy—have garnered growing interest. Here, I'll provide an overview of these novel laser-based approaches.

Direct SLT

The Alcon Voyager technology, originally developed by Belkin Vision under the name Eagle, is based on the concept first described in *Journal of Glaucoma* in 2017 as "transscleral selective laser trabeculoplasty without a gonioscopy lens." Rather than relying on direct visualization of the trabecular meshwork using a gonioscopy prism, this non-contact approach delivers laser energy over the limbal tissue—essentially through the corneoscleral region above the trabecular meshwork. Despite the absence of direct targeting with a gonio lens, the laser appears to penetrate effectively to reach the intended tissue and thus exert its therapeutic effect.

The Alcon Voyager's operation is fully automated. The system uses imaging software to identify and select appropriate treatment zones, after which the physician confirms the targeting. This approach is ergonomic for the treating physician, eliminating the need to use the oculars of a traditional laser system. Additionally, there's no need for a gonio prism or coupling agent required during standard SLT procedures.

In terms of clinical validation, the GLAUrious Trial (NCT03750201), sponsored by Belkin Vision, provided robust data on the safety and efficacy of this direct SLT approach. The randomized controlled trial directly compared the system with conventional SLT. The primary endpoint was non-inferiority at six months, and the trial met that benchmark.

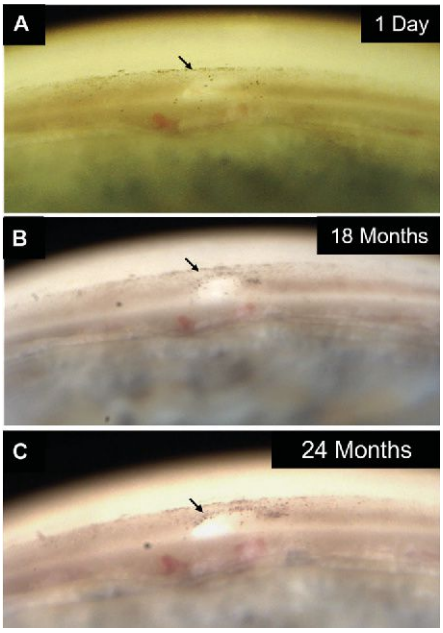
In the study, 84 patients were randomized to DSLT and 77 patients to SLT.[1] At the baseline, IOPs were similar in both groups. At the six-month washout, IOPs were approximately 20 mmHg in the direct SLT group and 19 mmHg in the conventional SLT group. Both groups exhibited a similar mean reduction of unmedicated IOP at six months (DSLT: 5.46 ±0.51 mmHg; SLT: 6.16 ±0.53 mmHg). Statistical analysis confirmed non-inferiority. Furthermore, 12-month safety data showed similarly favorable results, with comparable non-washed out IOP outcomes between the two

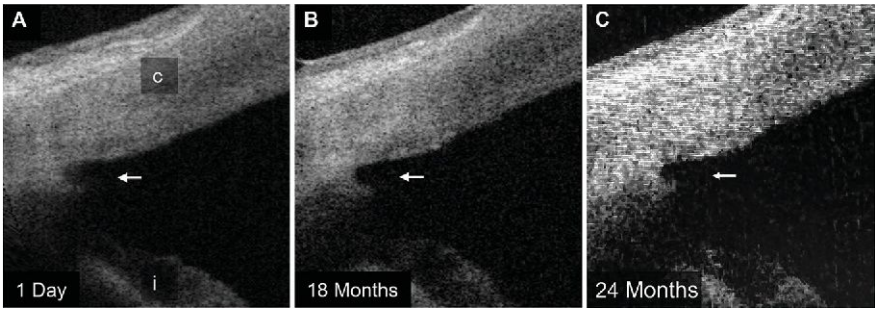
Gus Gazzard, MD

Gus Gazzard, MD, performs direct selective laser trabeculoplasty with the Belkin Vision Eagle, now Alcon Voyager.

This article has no commercial sponsorship.

Dr. Singh is a professor of ophthalmology and chief of the Glaucoma Division at Stanford University School of Medicine. He is a consultant to Alcon, Allergan, Santen, Sight Sciences, Glaukos and Ivantis. **Dr. Netland** is Vernah Scott Moyston Professor and Chair at the University of Virginia in Charlottesville.





Visual patency of a FLigHT treatment over two years visualized using a handheld gonio camera (left) and AS-OCT (above).[2] (*Used with permission under the CC BY-NC-ND license http://creativecommons.org/licenses/by-nc-nd/4.0*)

methods (DSLT: -3.2 ±0.38 mmHg; SLT: -3.28 ±0.4 mmHg.)

In the DSLT group, the mean number of medications was reduced by about half, from 1.19 medications to 0.63 medications at one year. Similarly, the SLT group's mean medication burden decreased from 1.22 to 0.68 at one year. More than half of patients were medication-free at one year in both groups. The study reported no safety concerns.

The Alcon Voyager DSLT device received FDA clearance in December 2023, based on the GLAUrious trial data.

The FLigHT Procedure

ViaLase's FLigHT procedure, which stands for femtosecond laser image-guided high-precision trabeculotomy, is a non-incisional approach to lowering intraocular pressure by facilitating aqueous outflow through Schlemm's canal. Like other emerging therapies aimed at restoring physiological outflow, the core concept involves creating a conduit through the trabecular meshwork to improve outflow. ViaLase's procedure uses a femtosecond laser guided by optical coherence tomography to create a drainage channel without making incisions in the eye.

The docking portion of the ViaLase procedure is similar to that used in femtosecond laser-assisted cataract surgery. A gonioprism is placed directly on the eye, providing treatment access to all four quadrants of the angle. The combination of treatment software and OCT imaging offers a highly detailed, real-time view of the trabecular meshwork, allowing for precise targeting and treatment planning.

Because the procedure is non-incisional, the expected risk of infection is essentially zero, marking a significant safety advantage over intraocular glaucoma surgeries.

In terms of durability, the ViaLase procedure offers encouraging early evidence. Using its proprietary gonio camera and anterior segment OCT, researchers have demonstrated visual patency of the laser-created pores out to 24 months post-treatment in a non-washout group (n=18).[2] In the company's first-in-human safety study, a single laser conduit measuring 500 µm x 200 µm was created in each treated eye. A total of 88 percent of eyes achieved an IOP below 18 mmHg, representing a mean reduction of 34.6 percent (22.3 ±5.5 to 14.5 ±2.6 mmHg, p<5e-5). The average number of glaucoma medications decreased from 2.2 ±1.1 at baseline to 2 ±1.2 at 24 months (p=0.22). A total of 82 percent of eyes achieved an IOP reduction ≥20 percent. Importantly, no serious adverse events were reported throughout the 24-month follow-up period.

ViaLase's FLigHT procedure is CE-marked and available in Europe, but it isn't FDA approved in the United States.

Excimer Laser Trabeculostomy

The Elios laser is an excimer laser-based addition to the minimally invasive glaucoma surgery pipeline, continuing the trend of implant-free procedures that aim to improve aqueous outflow. Excimer laser trabeculostomy uses an intraocular approach with a specialized probe to create 210-µm microchannels in the trabecular meshwork to connect the anterior chamber and Schlemm's canal, promoting aqueous outflow.

In terms of the procedure, the Elios device is similar to approaches currently used in other MIGS procedures. Intraoperative visualization tends to be best in the nasal quadrant, and the safety profile is expected to mirror that of cataract surgery combined with MIGS procedures. Given its similarity to other MIGS in terms of technique and execution, the learning curve for this procedure is anticipated to be relatively straightforward for surgeons familiar with these minimally invasive techniques.

The Elios device has a long track record outside the United States, with multiple peer-reviewed publications supporting its safety and efficacy in both combined cataract

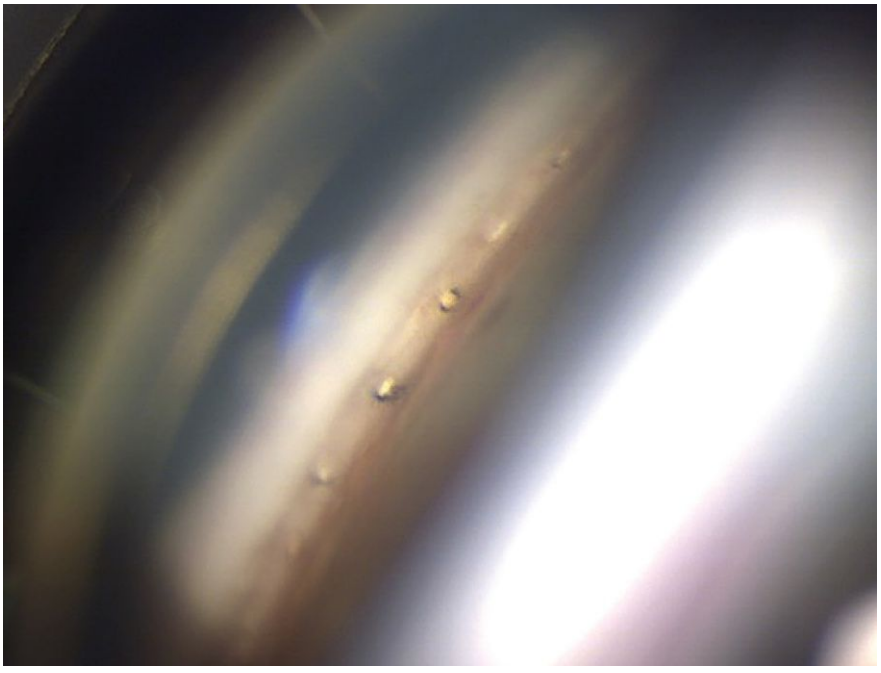
surgery and standalone procedures.[3] The IOP reduction from baseline without washout is about 20 to 40 percent. Additionally, patients typically experience a reduction in medication burden, making it a promising alternative for long-term glaucoma management.

In the company's eight-year follow-up study of the Elios laser combined with cataract surgery, patients experienced a significant mean IOP reduction from 19.3 mmHg at baseline to 15.4 mmHg at eight years (p=0.004). Additionally, only 3.7 percent of the 128 patients required a secondary surgical glaucoma intervention during the study period. No serious adverse events were observed.[4]

Another study demonstrated positive phaco-Elios laser outcomes with good safety, a 14.3-percent IOP reduction and a reduction of glaucoma medications by one active ingredient in patients with low initial pressures at one year.[5]

Similarly, yet another study reported significant decreases in mean IOP at one year, from 20.9 ±2.6 mmHg on medication preoperatively to 16.3 ±1.9 mmHg after phaco-Elios laser (p<0.0001), and a medication burden reduction from 1.7 ±0.7 to 0.3 ±0.8 medications (p<0.0001).[6] At one year, 81 percent of eyes were medication-free. Adverse events included postoperative hyphema (two eyes), transient IOP spikes (three eyes) and subsequent filtering surgery at three months (one eye).

The Elios excimer laser system isn't approved in the United States. The company is currently engaged in a major U.S. interventional trial (NCT04899063), which has completed outcome measure data collection and anticipates study completion in July 2025. The U.S. trial will evaluate the safety and efficacy of the Elios system for pressure reduction in adults with mild to moderate primary open-angle glaucoma undergoing cataract surgery.



Elios

Microchannels created by the Elios excimer laser were visually patent at 31 months.

The COAST Trial

One of the key studies in the field of glaucoma treatment right now is the Clarifying Optimal Application of SLT Therapy (COAST) trial, led by Tony Realini, MD, at West Virginia University. The COAST trial aims to answer two critical questions: 1) Can we achieve similar clinical outcomes to standard SLT by reducing the laser energy? 2) Can we extend medication-free IOP control with annual low-energy SLT compared to as-needed (PRN) standard SLT?

The trial is structured as two consecutive randomized trials. Initially, subjects with newly diagnosed, treatment-naive, or briefly treated mild to moderate primary open-angle glaucoma or high-risk ocular hypertension were randomized to either standard energy SLT (i.e., "champagne bubbles" technique) or low-energy SLT (0.4 millijoules per spot for 360 degrees). The primary outcome for the first year was medication-free IOP control, without requiring repeat SLT at the 12-month mark.

At 12 months, a second randomization occurred. Patients received either annual low-energy SLT, regardless of their IOP levels, or as-needed standard SLT at the initial randomized energy. Both groups were slated for follow-up out to 48 months.

However, the interim analysis showed that patients who initially received low-energy SLT were more likely to require retreatment within the first 12 months. As a result, enrollment in the initial low-energy SLT group was halted, and now all patients are receiving standard SLT as the initial treatment. At the one-year mark, patients are either given annual low-energy SLT or as-needed standard SLT.

While the first question—whether low-energy SLT can achieve similar outcomes to standard SLT—was answered early with a "no," at least at the initial treatment, the second question remains relevant. Reasonable, non-randomized, controlled evidence suggests that follow-up low-energy SLT treatments on a scheduled basis (as opposed to PRN) can still maintain reasonable IOP control. This model mirrors what's commonly done in retinal treatments, like anti-VEGF injections,

where a loading dose is followed by a treat-and-extend approach to maintain control over time.

At this point, the COAST trial is still actively enrolling participants. Clinicians are encouraged to learn about the eligibility criteria and consider referring suitable patients if they're located near a participating site.

The Takeaway

A robust pipeline is emerging for IOP reduction via laser-targeted outflow enhancement. As ongoing research continues to refine best practices, power and frequency settings for SLT are likely to evolve. Consider referring patients to COAST study sites. ◀

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(Continued from p. 25)

Other associations include enteral feeding, iron overload from multiple transfusions and gastrointestinal malabsorption.

• ***Ocular effects.*** These consist of subperiosteal orbital hemorrhage and proptosis due to fragile capillaries,[38,39,40] severe, bilateral dry eyes and/or retinal hemorrhages from broken capillaries.

• ***Systemic symptoms.*** Scurvy manifests as coiled hair, gingivitis, easy bruising, loose teeth, arthralgia, anemia and impaired immune response. Musculoskeletal pain is common in children, especially in the lower extremities.[41]

• ***Diagnosis and management.*** Scurvy can be diagnosed clinically through history and physical exam. Lab values show decreased plasma or leukocyte vitamin C levels and anemia. Treatment involves oral supplementation.

Vitamin K Deficiency

Another less common deficiency, Vitamin K is crucial for newborns, with a single injection recommended at birth.[42] It acts as a cofactor for coagulation and bone formation. Deficiency in vitamin K is associated with malabsorption, malnutrition, warfarin use and prolonged antibiotic therapy. Neonates experience deficiency due to intestinal sterility, inability to cross the placenta and neonatal liver's inability to produce vitamin K.

• ***Risk factors and associations.*** VKD in newborns can be exacerbated by exclusive breastfeeding, maternal deficiency, prematurity, biliary atresia, chronic diarrhea and refusal of prophylactic vitamin K injection. Parental refusal of vitamin K injection has risen in recent years.[43]

• ***Ocular effects.*** These include proptosis from intraorbital/retrobulbar hemorrhage,[44] hyphema from bleeding[45] and/or retinal hemorrhages due to fragile capillaries. Since retinal hemorrhages can be seen in shaken baby syndrome and VKD, it's important to perform a thorough history and workup.[47]

TABLE 2. OCULAR FINDINGS AND SYSTEMIC SYMPTOMS OF NUTRITIONAL DEFICIENCIES

Deficiency	Ocular Findings	Systemic Symptoms
Vitamin D	- Dry-eye syndrome - Ocular surface disease - Retinopathy	Rickets Bone pain Delayed growth Muscle weakness Fatigue Frequent infections Dental issues
Iron	-Conjunctival pallor -Retinal hemorrhages, cotton-wool spots	Anemia Fatigue Pallor Shortness of breath
Vitamin B6	-Seborrheic dermatitis -Bilateral optic neuropathy -Central visual field loss	CNS symptoms Depression Confusion Irritability Nervousness Trouble concentrating Short-term memory loss Seizures Anemia Immune dysfunction Growth delays
Vitamin A	-Xerophthalmia -Night blindness -Conjunctival xerosis -Bitot's spots -Corneal xerosis -Corneal ulcer -Keratomalacia -Corneal scarring -Xerophthalmus fundus	Xerosis cutis Immunosuppression Severe measles infection Stunted growth Diarrhea
Vitamin C	-Subperiosteal hemorrhage -Proptosis -Retinal hemorrhages	Musculoskeletal pain – most common Subperiosteal hemorrhage Weakness Bone pain Arthralgia Limping/refusal to walk Disrupted collagen synthesis Coiled "corkscrew" hair Gingivitis Easy bruising Loose teeth Anemia Fatigue Paleness Impaired immune response
Vitamin K	-Retinal, subconjunctival hemorrhaging (retinal hemorrhages may mimic shaken baby syndrome) -Proptosis -Hyphema	Hemorrhagic disease of the newborn Oozing from the umbilicus Bloody stool Epistaxis Cephalohematoma Intracranial bleeding Jaundice Easy bleeding Bruising Anemia
Vitamin B1	-Pediatric Wernicke Encephalopathy -Nausea, vomiting, loss of appetite -Classic triad of confusion, abnormal eye movements, and ataxia -Biotin-thiamine-responsive basal ganglia disease -Abnormal eye movement -Ophthalmoplegia -Nystagmus	Wet Beriberi Dry Beriberi Infantile thiamine deficiency Cyanosis, cardiomegaly, lethargy, seizures, aseptic meningitis
Vitamin B12	-Optic nerve abnormalities -Commonly optic atrophy -Sometimes optic neuritis	Pernicious anemia Anemia Fatigue Failure to thrive Hearing loss Peripheral neuropathy Hypotonia Glossitis Diarrhea

• ***Neonatal deficiency.*** Hemorrhagic disease of the newborn can be prevented by vitamin K injection at birth. Symptoms include easy bruising, bleeding, blood in urine or stool and intracranial bleeding.[46] Signs include oozing from the umbilicus, bloody stool, epistaxis, cephalohematoma, easy bruising, intracranial bleeding and jaundice, among other manifestations, signifying poor coagulation.

• ***Systemic symptoms.*** VKD in children correlates with vitamin K's role in clotting and bone formation.

• ***Diagnosis and management.*** VKD can be diagnosed through clinical history and lab values showing increased prothrombin time, typically increased activated partial thromboplastin time, normal bleeding time and decreased coagulation factors. Treatment involves vitamin K administration.

Vitamin B1 (Thiamine) Deficiency

Vitamin B1, or thiamine, is essential for carbohydrate and amino acid metabolism. Deficiency in children, though less common than other deficiencies, is linked to maternal deficiency, genetic abnormalities and underconsumption.

• ***Risk factors and associations.*** B1 deficiency is associated with cancer, gastrointestinal disease, malnutrition, psychiatric or neurodevelopmental disorders, kidney disorders and obesity surgery.[48,50] Excessive intake of soft drinks may also be linked to deficiency.[49]

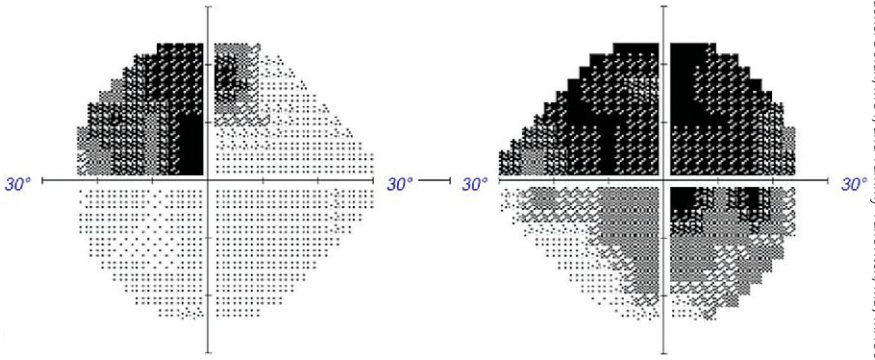
In addition, biotin-thiamine-responsive basal ganglia disease (BTBGD) results in thiamine deficiency caused by mutations in the SLC19A3 gene. Children with BTBGD typically present with intermittent subacute encephalopathy, movement disorders, cognitive deficits, seizures, ataxia and external ophthalmoplegia. Acute episodes of encephalopathy often follow febrile illness or significant stress. This genetically induced neurometabolic syndrome often responds to high doses of biotin and thiamine.[53,57]

• ***Ocular effects.*** These consist of abnormal eye movements, including nystagmus, oscillopsia and oculomotor nerve palsy.[52-56] In the posterior segment, you may observe optic neuropathy, including optic disc edema and peripapillary hemorrhages.[57]

• ***Systemic symptoms.*** Thiamine deficiency can cause dry beriberi (peripheral neuropathy, paralysis, muscle weakness, confusion) and wet beriberi (cardiac failure, dilated cardiomyopathy, edema). Infants may present with cyanosis, cardiomegaly, tachycardia and aseptic meningitis.[58-61]

In severe cases of thiamine deficiency, Wernicke encephalopathy is evident by confusion, gaze-induced nystagmus, diplopia, conjugate gaze palsy, and a wide-based gait. The most common prodromal symptoms included nausea, vomiting and loss of appetite. Delayed treatment can lead to Korsakoff syndrome, which is chronic and irreversible, although this is extremely rare in children if given prompt treatment.

• ***Diagnosis and management.*** Prompt supplementation with thiamine followed by glucose is recommended. Labs can be obtained for confirmation, including blood thiamine, lactate, pyruvate and alpha-ketoglutarate. In addition, it's important to measure serum thyroid-stimulating hormone and get an electrocardiogram if cardiomyopathy is evident on exam.



Rachel Dolan, MS4, and Tammy Yanovitch, MD, MHSc

Figure 6. Humphrey visual field 24-2 SITA fast demonstrating bitemporal hemianopsia due to optic neuropathy secondary to vitamin B12 deficiency.

Vitamin B12 Deficiency

Vitamin B12, or cobalamin, deficiency is rare due to high liver storage. It's essential for enzyme functions, including methionine synthase and methylmalonyl-CoA mutase.

• ***Risk factors and associations.*** Deficiency is associated with inadequate dietary intake, malabsorptive disorders, pregnancy, maternal deficiency, inherited disorders and certain medications.

• ***Ocular effects.*** There can be optic nerve effects, including optic atrophy and optic neuritis *(See Figures 5 and 6)*.

• ***Systemic symptoms.*** Deficiency can cause anemia, fatigue, developmental delay, failure to thrive, irritability, hypotonia, inflamed tongue, diarrhea and neuropathy.

• ***Diagnosis and management.*** Screening involves measuring serum vitamin B12 levels, complete blood cell count and folate levels. Treatment involves vitamin B12 supplementation.

In conclusion, recognizing and managing ocular signs of pediatric nutritional deficiencies is crucial for better patient outcomes. Early identification and treatment lead to healthier eyes and overall health for children. ◀

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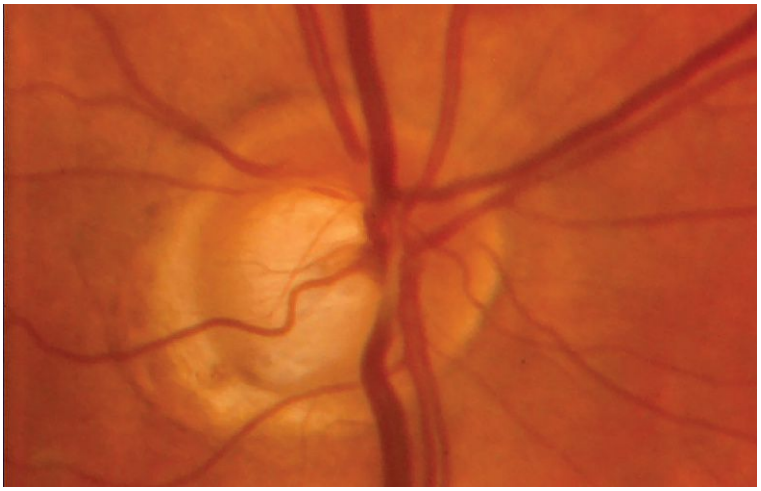
Gum Disease/Glaucoma Connection Investigated

Inflammation plays a major role in periodontitis, and recent findings have suggested that patients with this gum disease may also be at higher risk of glaucoma development and progression. Researchers sought to investigate this matter in a recent study for *Journal of Glaucoma* and indeed found a strong association between both conditions, especially in patients aged 40 and older, men and those with diabetes.

The study included 3,681 individuals in the Korea National Health and Nutrition Examination Survey aged 19 years or older who underwent both dental and ophthalmological examinations that met International Society of Geographical and Epidemiological Ophthalmology criteria. Exclusions included patients with history of ocular surgery (e.g., refractive, cataract, retina) or age-related macular degeneration, as well as those who were pregnant, undergoing orthodontic treatment or missing data.

Of all individuals included, 197 (4.6 percent) had glaucoma and 3,484 (95.4 percent) did not. Among the glaucoma patients, 80 (39.5 percent) had periodontitis compared with 892 (22.2 percent) of those without glaucoma.

The authors hypothesized that the correlation between periodontitis and glaucoma, which is consistent with previous studies, could be due to inflammation from periodontitis causing damage to the retinal ganglion cells and optic nerve, eventually leading to glaucomatous change.



Inflammation from periodontitis could damage retinal ganglion cells and the optic nerve, researchers say.

The advanced glycation end products (AGEs) in diabetic patients may cause toxic effects on neurons by excessively activating microglia of the central nervous system. AGEs also interact with AGE surface receptors to impair the structural and functional activities of lipids and proteins, causing inflammation, the authors explained in their article.

"This series of events is associated with inflammation of the central nervous system, inducing a neurodegenerative response in the optic nerve," the authors write in their paper. "Moreover, insulin resistance induced by factors such as decreased blood-brain barrier permeability in diabetic patients can exacerbate neuroinflammation and neurodegeneration in the central nervous system."

Given the impact of periodontitis on the central nervous system in relation to the inflammatory response, it's plausible that periodontitis patients with diabetes may be at elevated risk of glaucoma, which the present and several prior analyses have demonstrated.

Aging on its own may also cause an inflammatory cascade, the authors explained. Factors such as TNF-α or oxidative stress, which increase in old age, induce necroptosis—a process distinct from apoptosis due to its induction of inflammatory responses—leading to neurodegenerative diseases.

"Also, as the retina ages, oxidative stress and lipid peroxidation cause para-inflammation, which can accelerate neurodegenerative changes in the optic nerve and act as a risk factor for glaucoma," the authors note in their article. "In periodontitis, initial neutrophil infiltration occurs due to pathogens, and then reactive oxygen species are released as antimicrobials. Excessive action of free radicals provokes reactions including lipid peroxidation, which damages proteins and DNA in the host cell."

Periodontitis can regulate proinflammatory cytokines such as TNF-α, IL-1β and IL-6, and these molecules induce systemic inflammation in the central nervous system. "This is expected to have a synergistic effect with aging, which can elevate risk of glaucoma," the authors write.

While it's not clear why periodontitis had a greater impact on glaucoma

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in males, in this study, males had a higher smoking prevalence than females, and previous studies have showed a high association between smoking and primary open-angle glaucoma, as well as increased intraocular pressure among make smokers and an association between smoking and early-onset open-angle glaucoma.

No relationship with glaucoma was found for other oral health factors, such as tooth loss, brushing frequency, use of oral health products or self-awareness of oral health status. This could be because individuals with poorer oral health may engage in more rigorous oral hygiene practices, potentially masking the expected association between oral health behaviors and periodontal disease, and the oral health behaviors may not accurately reflect an individual's actual oral health status.

"This discrepancy between actual oral health status and oral health behaviors could influence the observed lack of association with glaucoma," the authors write in their paper. "Moreover, complex factors, such as genetic factors or unmeasured variables not included in the survey, may further complicate this relationship."

The authors conclude that because it was difficult to clearly identify the mechanisms underlying the correlation between periodontitis and glaucoma, further studies are required.

J Glaucoma 2025; Feb 1. [Epub ahead of print].
Noh JH, Lee MY, Yoo C, et al.

Comparison of Two Side-port Incisions in Phaco

Scientists compared the accuracy, safety and consistency of near-square and asymmetric trapezoid side-port incisions in cataract surgery, as part of a prospective pilot study at Aier Eye Hospital of Wuhan University, Wuhan Hubei Province, China.

Patients were divided into Groups A and B using the random number table method. Group A received a near-square side-port incision with a 22G needle, and Group B received an asymmetric trapezoid SPI with a 15-degree blade. Scientists contrasted the differences in incision length, width and shape; surgical time; and postoperative intraocular pressure between the two groups.

Eighty eyes from 80 patients were included. Here are some of the findings:

- The mean external width of the incision in Group A was much smaller than that in Group B (p<0.01), while the internal width in Group A was significantly larger (p<0.01).
- In Group A, no statistically significant difference was found between the external and internal incision diameters (p=0.081).
- In Group B, the external diameter was obviously larger than the internal diameter (p<0.01).
- The incision diameter consistency in Group A was higher than that in Group B.
- No statistically significant difference in incision length between the two groups was found (p=0.67).
- One day after surgery, no significant differences were found in incision morphology (p=1.0; 0.723) or operating time between the two groups (p=0.89).
- No obvious incision leakage was reported in either group after surgery (p=0.337).

The authors say that a near-square side-port with a 22G needle was smaller and resulted in better incision consistency. Moreover, they noted, the 22G needle was inexpensive and could be easily obtained.

J Cataract Refract Surg 2025. Mar 31. [Epub ahead of print].
Guo H, Peng T, Luo W, et al.

Nerve Abnormalities and Dry Eye After Refractive Surgery

Scientists wrote that chronic neuropathic ocular pain (NOP) can develop alongside chronic dry eye post-laser-assisted in-situ keratomileusis, although its specific characteristics remain poorly understood. This study aimed to compare the clinical characteristics of patients who developed DE and NOP after LASIK to those with only DE, and to asymptomatic LASIK patients, to facilitate the diagnosis of NOP.

A prospective, cross-sectional case-control comparison study of 89 subjects post-LASIK was conducted in three groups:

- 34 patients developing NOP and DE (NOP-DE group);
- 25 patients developing only DE (DE group); and
- 30 asymptomatic subjects (control group).

Assessments included clinical history and symptom questionnaires (OSDI, mSIDEQ, NRS, WFPRS), anxiety and depression evaluation (HADS), tear film stability (osmolarity and TBUT) and production (Schirmer's), and ocular surface integrity. Corneal mechanical and thermal sensitivity thresholds were measured using Belmonte's non-contact esthesiometer, while tactile sensitivity threshold was assessed pre/post-topical anesthesia using the Cochet-Bonnet esthesiometer. *In vivo* confocal microscopy (IVCM) was used to evaluate the sub-basal nerve plexus characteristics and dendritic cell density in the central cornea. Group comparisons and correlations were conducted.

Here are some of the findings:

- Compared with DE group, patients in the NOP-DE group exhibited:
  — significantly more DE symptoms with mSIDEQ (p=0.019);
  — a higher level of pain with NRS and WFPRS;
  — increased use of ocular lubrication (p=0.003);
  — greater frequency of pathological results on anxiety and depression questionnaires (p<0.001);
  — a higher prevalence of central sensitization syndromes (p<0.001); and
  — higher tactile corneal sensitivity post-topical anesthesia (p=0.002).

• IVCM revealed lower nerve density (p=0.049) and higher microneuroma density (p=0.008) in the sub-basal nerve plexus of NOP-DE patients compared to DE patients without NOP (p=0.008).

• Most nerve metrics correlated moderately to strongly with clinical parameters.

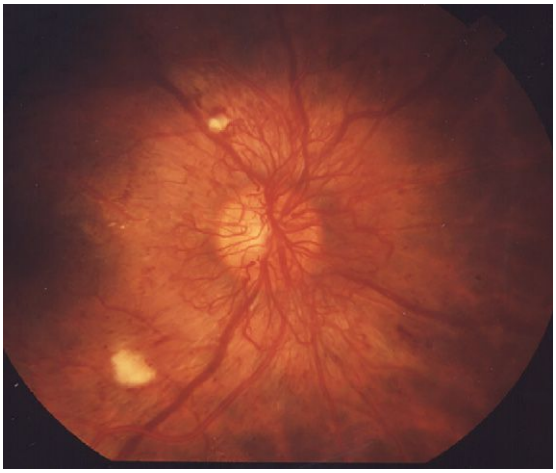
Scientists say that persistent high corneal tactile sensitivity post-anesthesia, reduced nerve density and increased microneuroma density in the central cornea, and may serve as diagnostic indicators for confirming neuropathic ocular pain in patients experiencing chronic dry eye post-laser-assisted in-situ keratomileusis. The authors suggest that the findings underscore the potential utility of incorporating these measures into clinical assessments to improve diagnostic accuracy and guide management strategies in this patient population.

Amer J Ophthalmol 2025; Apr 17.[Epub ahead of print.]
Vázquez A, Blanco-Vázquez M, Martínez-Plaza E, et al.

GLP-1 Drugs' Link to Ocular Issues

Given the recent influx of evidence suggesting a connection between the popular diabetes and weight loss drug, glucagon-like peptide-1 receptor agonists (GLP-1 RAs), and various ocular adverse events, a new study aimed to investigate this potential association on a global scale. Its findings, published recently in the *American Journal of Ophthalmology*, revealed a notable correlation between semaglutide, the most commonly prescribed GLP-1 RA, and increased incidents of ischemic optic neuropathy, diabetic retinopathy and several other retinal and vitreous issues.

The study drew data from two major sources: the US FDA Adverse Event Reporting System (FAERS) and WHO's VigiBase. It encompassed reports filed from December 2017 to September 2024, marking the respective approval dates of two GLP-1 RAs, semaglutide and tirzepatide. Both drugs were evaluated for their association with optic nerve and retinal adverse events and compared with metformin, empagliflozin, dulaglutide and insulin.



Use of semaglutide is associated with a high risk of diabetic retinopathy.

Findings showed that within the 12,936,341 cases reported in FAERS, semaglutide and tirzepatide contributed to 76,444 cases (0.59 percent). In WHO's VigiBase, which documented over 35 million cases, these drugs accounted for 118,639 instances (0.34 percent). Semaglutide was notably associated with high risks of ischemic optic neuropathy and diabetic retinopathy; in FAERS, the reporting odds ratio for ischemic optic neuropathy was 11.12; for diabetic retinopathy, it was 17.28. In VigiBase, these ratios were 68.58 and 7.81, respectively. The drug was also linked with significant increases in retinal/vitreous detachment, retinal/vitreous hemorrhage and retinal tears. Moreover, while exclusive to VigiBase, semaglutide users also demonstrated a higher risk of macular edema, macular hole and papilledema.

In contrast with semaglutide, tirzepatide showed limited associations with ocular adverse events. In FAERS, this GLP-1 RA showed a notable connection with diabetic retinopathy, but its effect was not as prominent in other conditions when compared to other drugs like insulin.

"This discrepancy may arise from tirzepatide's unique dual GLP-1 and GIP receptor agonist mechanism and lower GLP-1 receptor affinity, affecting ocular vascular and metabolic responses differently than semaglutide," the authors explain in their *AJO* report. "Differences in receptor binding and pharmacodynamics could explain this observation, but further investigation is needed to determine whether the differences stem from drug properties, population characteristics or both."

The authors also disclose their inability to establish causality for the association between semaglutide and ocular AEs, noting that the biological mechanisms remain unclear. "Although GLP-1 receptors in the retina, ganglion cells and central nervous system play a neuroprotective role by suppressing neuroinflammation—suggesting no direct causality—the rapid normalization of glycemic control and weight loss may disrupt pre-existing vascular stability, potentially increasing the risk of NAION," they write. "Our sensitivity analysis with exenatide suggests that NAION may be unique to semaglutide, indicating a mechanism beyond transient glucose reductions associated with GLP-1 receptor agonists."

The growing compendium of research exposing the ocular risks associated with GLP-1 RAs is concerning as the popularity of these drugs continues to rise, though more prospective studies are still needed to clarify the mechanisms behind these associations.

The study authors conclude by advising, "Until further evidence emerges, health-care providers should be mindful of potential ocular risks in GLP-1 RA users." ◀

Am J Ophthalmol 2025; May 8. [Epub ahead of print.]
Lakhani M, Kwan ATH, Mihalache A, et al.

Key Considerations for Implanting Premium IOLs in Glaucoma Patients

When considering premium intraocular lenses for glaucoma patients, it's crucial to balance vision enhancement with careful management of ocular health. The following guidelines from Constance Okeke, MD, MSCE, of Virginia Eye Consultants in Norfolk, outline essential dos and don'ts to ensure the best outcomes.

Do

- Thoroughly assess visual fields and optic nerve health.
- Set realistic expectations regarding spectacle independence.
- Optimize the ocular surface preoperatively (e.g., treat MGD).
- Consider combining with MIGS for better IOP control and fewer drops.

Don't

- Implant multifocal IOLs in patients with central visual field loss, poor contrast sensitivity or advanced glaucoma.
- Forget to assess for anatomical issues (e.g., zonular instability, small pupils).
- Overpromise outcomes in patients with unpredictable disease progression.

(Continued from pg. 29)

Setting Expectations

When discussing lens options with glaucoma patients, experts say it's crucial to set realistic expectations about the limitations and potential outcomes of available lenses, given the nature of glaucomatous disease. "It's especially important to explain everything upfront with glaucoma patients, even more so than with typical cataract cases," Dr. Ragusa says. "They need to know the severity of their glaucoma, how it's affecting their vision and the purpose of the surgery. Making sure the patient's expectations align with what we're trying to accomplish is key to a successful outcome."

Visually walking patients through their disease status can aid the discussion about lens choices. Dr. Okeke uses visual field reports and OCT imaging to do this. "I stress that visual field loss can't be corrected by any IOL and that premium lenses enhance the quality of vision, not the health of the optic nerve. For suspects, I explain the potential for progression and the need for continued monitoring, while offering more flexible lens options with appropriate caution."

Depending on the severity of the glaucoma, there's a limit to how much a patient's vision can improve. "Some of my severe glaucoma patients have noticed their glaucoma-related defects more clearly after cataract surgery, which can be disconcerting and upsetting for the patient, so I always have a conversation about this beforehand," Dr. Kamat notes. "I emphasize that we'll do our best to improve their vision, but I never promise 20/20, especially in severe cases. I make sure to set realistic expectations, because I believe that clear communication upfront makes the postoperative period much smoother."

Postop Pitfalls

A common concern for glaucoma patients after cataract surgery is the development of visual disturbances, which can be more pronounced depending on the type of lens implanted. "Visual complaints can include glare or halos, especially with multifocal lenses, though much less so with EDOF IOLs," Dr. Okeke says.

Managing glaucoma patients postoperatively also requires careful attention to potential complications that may arise more frequently in this population. "Some patients tend to be more sensitive to postoperative steroids and require closer monitoring," says Dr. Ragusa. "Pressure fluctuations can be more unpredictable, especially when combining angle surgery with premium lenses. I recently had a patient who had well-controlled pressures at 8 mmHg off drops for two months, only to come back with pressures in the 40s, seemingly overnight. It may have been that scar tissue from the angle surgery developed. Now we have to manage his pressure again with topical medications. These patients simply need more sensitive, frequent follow-up."

"In my experience, combining ATIOLs with MIGS procedures helps to mitigate pressure spikes by lowering IOP and reducing reliance on medications that can exacerbate ocular surface disease, which in turn improves visual comfort and outcomes," says Dr. Okeke.

Dr. Ragusa adds that "patients with pseudoexfoliation, which is common in my glaucoma patient population, can experience lens subluxation over time, which can severely affect vision—even if the lens is just slightly decentered. This is another reason why, for most of these patients, monofocal or toric lenses are usually the best option."

Looking Ahead

As technology and research continue to advance, glaucoma patients may gain access to a broader selection of premium lens options. Ongoing research under Dr. Okeke's AGE (Advocates for Glaucoma Education) Initiative, which aims to raise awareness about glaucoma and promote early detection and treatment, is evaluating visual and IOP outcomes in glaucoma patients undergoing ATIOL implantation, both with and without concurrent MIGS.

"Early data show that EDOF lenses, particularly non-diffractive designs, offer favorable visual outcomes with fewer dysphotopsias and preserve contrast better than multifocal options," says Dr. Okeke. "As we gather more long-term data, particularly in moderate glaucoma patients, we may see broader acceptance and refined guidelines for use of ATIOLs in this population." ◀

PRODUCT NEWS

New items on the market to improve clinical care and strengthen your practice.

SURGICAL SYSTEMS

Retina and Cataract Come Together in Unity

Alcon recently launched the Unity Vitreoretinal Cataract System and Unity Cataract System. The new platform offers two configurations, a combined console (VCS) and a standalone cataract system (CS).

Alcon says the system's features include Hypervit 30K, which can execute 30,000 cuts per minute, Unity 4D Phaco that the company says delivers extremely fast nucleus removal during cataract procedures and 41 percent less energy into the eye.

With Unity VCS/CS, the company says surgeons can operate at more physiologic conditions without compromising efficiency.

For more information, visit alcon.com.

GLAUCOMA TREATMENTS

New Leos System from BVI

If you're in the market for a minimally invasive way to reduce patients' intraocular pressures, the new Leos laser endoscopy system from BVI Medical may be worth a look.

The company says Leos uses a novel, intuitive laser ECP procedure that can integrates seamlessly into the surgical workflow. It lowers intraocular pressure by addressing aqueous humor production in a minimally invasive ab interno procedure, BVI says. The company says it incorporates unique endoscopic capabilities to provide superior visualization of the eye anatomy in a way not seen in the past, or with the latest in imaging systems.

For information, visit bvimedical.com/us/.

Alcon Voyager DSLT Debuts

Alcon recently announced the full U.S. commercial availability of Voyager DSLT, which it says is the first and only Direct Selective Laser Trabeculoplasty device.

Alcon says the device is fully automated—efficiently delivering 120 laser pulses without the need for a gonio lens as with manual SLT.

Voyager DSLT is controlled through a touchscreen, taking the slit lamp and manual gonio lens aiming out of the equation, and reduces the specialized training required with manual SLT, according to Alcon. The laser delivery is powered by Alcon's SureTrac eye-tracking technology, to accurately and safely deliver laser pulses through the limbus to the trabecular meshwork, stimulating the eye's natural healing response to improve aqueous outflow.

For more information on the Voyager DSLT system, visit alcon.com.

INTRAOCULAR LENSES

PanOptix Turns Pro

Alcon recently announced the U.S. introduction of the Clareon PanOptix Pro intraocular lens.

The company says PanOptix Pro uses the company's Enlighten NXT Optical technology that it says delivers the highest reported light utilization of any trifocal IOL—and the lowest light scatter. Alcon says these enhancements also provide more uninterrupted light distribution from distance to near, and a 16-percent increase in optical image contrast between distance and intermediate. The company adds that PanOptix Pro builds on the clinically proven low visual disturbance profile, high spectacle independence and high patient satisfaction of PanOptix.

PanOptix Pro comes in powers ranging from +6 through +30 D (in 0.5-D increments), +31 through +34 D (in 1-D increments), with a +2.17 D intermediate and a +3.25 D near add power. Like all Alcon IOLs, PanOptix Pro will be available with blue light and ultraviolet filtering.

For more information, visit alcon.com.

REFRACTIVE SURGERY

Ride the Wave

Alcon also recently introduced the new WaveLight Plus refractive procedure.

The company says one of the unique features of the system is Sightmap, which measures the patient's optical system using biometry, tomography and wavefront. Innovative ray-tracing methods create a personalized 3D model of the eye, used to plan a truly unique treatment with the goal being excellent visual outcomes, Alcon says.

For more information, visit alcon.com.

OFFICE DESIGN

New Clinic Design Catalog Released

If you're thinking about refreshing your office's style, Eye Designs recently announced the release of its latest Orvos Exam Room Catalog and Resource Guide.

The catalog features more than 100 pages of products designed for the exam lane, including clinic configurations and smart office wall organization systems, as well as items that may minimize doctor fatigue, such as standing desks and scribe integrations. For eye-care providers considering adding a med spa or other specialty room, the catalog also offers display solutions for nutraceuticals and dry-eye treatments.

To browse the catalog online, visit eyedesigns.com/exam-guide.com. ◀

EDITED BY ERIK MASSENZIO, MD

WILLS EYE RESIDENT CASE REPORT

A 42-year-old presents to Wills Eye's Emergency Department with acute-onset, unilateral vision loss to no light perception.

HENRY BAIR, MD, MBA, SARAH THORNTON, MD
PHILADELPHIA

Presentation

A 42-year-old male presented to the Wills Eye Emergency Department for acute vision loss in the right eye that occurred two days prior. This was preceded by three days of an opaque "gray dot" appearing in the central vision of the same eye. The patient also reported mild discomfort with movement of the right eye in all gazes, as well as a right-sided, pressure-like headache. He denied any prior episodes, constitutional symptoms or neurological deficits.

History

The patient had no known ocular history. Past medical history was notable for Chiari malformation type 1, for which he underwent decompressive suboccipital craniectomy approximately 20 years ago without issue; Hashimoto's thyroiditis with resulting hypothyroidism; and gout. There was no family history of hereditary diseases, and social history was unremarkable, including for use of tobacco. At the time of presentation, the patient did not have any home medications.

Examination

On ocular examination, best-corrected visual acuity was no light perception in the right eye and 20/20 in the left eye. The right pupil had a relative afferent pupillary defect. Intraocular pressure was 9 and 11 mmHg in the right and left eye, respectively. Confrontation visual field and color plates were unable to be performed for the right eye and full for the left eye. Extraocular movements were intact for both eyes, with the patient noting a "tugging" sensation behind the right eye when gazing in all directions. On slit lamp examination, the adnexa, lids, conjunctiva and anterior segment were unremarkable in both eyes. Fundus exam of the right eye, however, was notable for optic disc elevation with blurring of the margins especially in the nasal quadrant. In addition, the retinal veins appeared tortuous and enlarged, and there were scattered dot-blot hemorrhages noted in all quadrants, involving the macula but without macular edema. Fundus exam of the left eye revealed trace blurring of the superior optic disc margin but was otherwise unremarkable. Figure 1 shows fundus photos of the right and left eyes obtained at bedside.

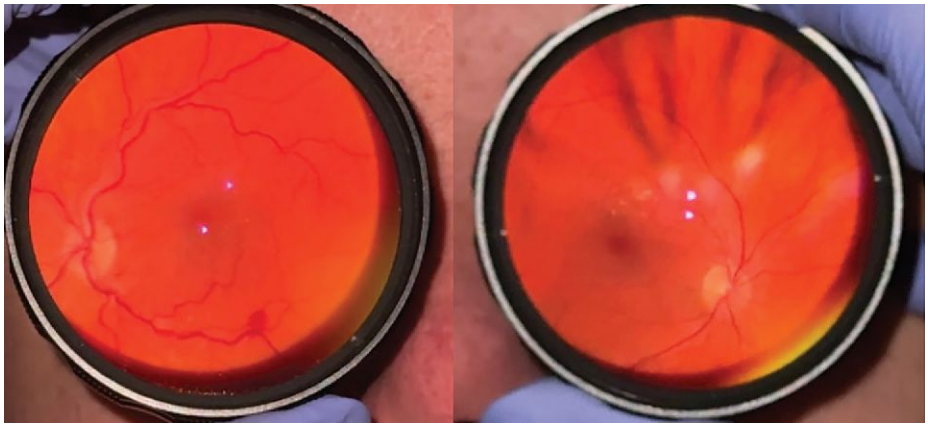


Figure 1. Bedside fundus photographs of the right eye (left) and left eye (right). In the right eye, there's blurring of the optic disc margins, vascular tortuosity and enlargement, and dot-blot hemorrhages. In the left eye, there's trace optic disc margin blurring but vascular caliber is normal and there are no retinal hemorrhages.

What's your diagnosis? What management would you pursue? The case continues on the next page.

Workup, Diagnosis and Treatment

The patient has a complicated presentation including painful extraocular movements, bilateral disc edema and venous tortuosity with retinal hemorrhages in the right eye. The differential diagnosis is broad and includes inflammatory, infectious, compressive and vascular etiologies. The finding of NLP vision in the right eye helps narrow the differential diagnosis, as vision loss to this degree is seen with specific conditions including inflammatory optic neuritis, infiltrative optic neuropathy, ischemic optic neuropathy in the setting of vasculitis or severe nonarteritic anterior ischemic optic neuropathy and compressive or infectious optic neuropathy. The patient's symptom of painful extraocular movements may suggest an inflammatory process such as retrobulbar optic neuritis, though the presence of venous tortuosity and retinal hemorrhage in the right eye would be atypical. Compressive optic neuropathy from a mass lesion causing elevated intracranial pressure and subsequent nerve swelling in the left eye could also be considered.

Magnetic resonance imaging of the brain and orbits with and without gadolinium contrast revealed T2 hyperintensity and postcontrast enhancement in the bilateral intraorbital optic nerves, with more extensive enhancement in the right optic nerve, consistent with bilateral optic neuritis *(Figure 2)*. MRI of the brain was unremarkable with no evidence of demyelinating lesions. Magnetic resonance angiography of head and neck vasculature didn't reveal significant arterial stenosis or dilation.

The patient was admitted for treatment with intravenous methylprednisolone at a dose of 250 mg every six hours for five days. Over the course of five days, visual acuity in the right eye significantly improved and discomfort with eye movement resolved. On day six, visual acuity was 20/20 in both eyes and the patient was discharged on an oral prednisone taper. Extensive laboratory testing was notable for an elevated myelin oligodendrocyte glycoprotein (MOG) antibody titer (1:160), and serologies for Bartonella, toxoplasmosis, Lyme, tuberculosis and syphilis were negative. The patient was instructed to follow up with the neuro-ophthalmology service.

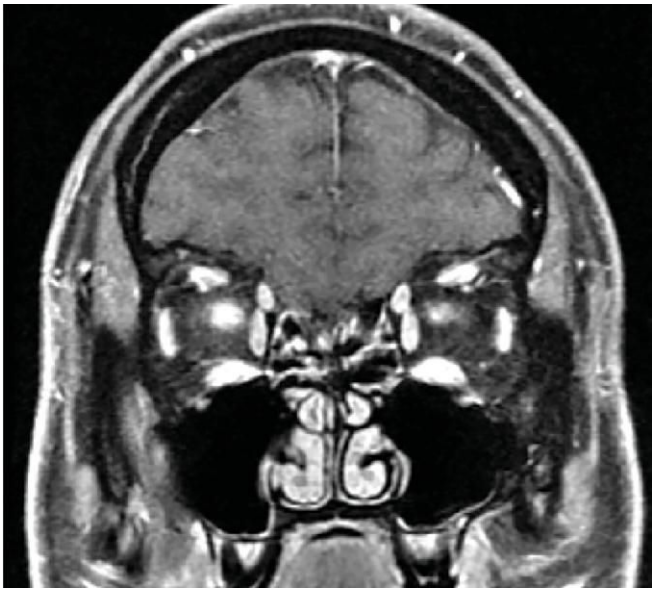


Figure 2. Coronal T1-weighted postcontrast MRI of the orbits showing abnormal enhancement involving bilateral intraorbital optic nerves.

Discussion

Myelin oligodendrocyte glycoprotein antibody-associated disease (MOGAD) is a recently recognized central nervous system demyelinating disorder distinct from multiple sclerosis and neuromyelitis optica spectrum disorder, characterized by autoantibodies against MOG, a protein on central nervous system myelin and oligodendrocytes. MOGAD has a global incidence of 1.6 to 4.8 per million and a prevalence of 1.3 to 2.5 per 100,000, with peaks in children aged 5 to 10 and adults aged 20 to 45.[1,2] In children under 11, it accounts for nearly half of acute demyelinating syndromes.[3,4,5] Optic neuritis is a common presentation especially in adults (30 to 60 percent) and is often bilateral (50 to 60 percent). Notably, severe vision loss, including NLP, occurs in 15 to 20 percent of cases, which is significantly more common than in MS-associated optic neuritis.[6,7,8] Moreover, MOGAD-ON, in contrast to both MS-ON and NMO-ON, frequently presents (in up to 86 percent of patients) with anterior optic nerve inflammation, manifesting as optic disc swelling.[9]

An unusual feature in our patient was the fundus finding of venous tortuosity with scattered intraretinal hemorrhages extending far beyond the peripapillary region, suggestive of venous stasis. While this finding can be seen with optic neuritis,[10] our literature review revealed only two previously reported cases of venous stasis associated with MOGAD.[11,12] The pathophysiology of venous stasis in MOGAD-ON is likely multifactorial. Severe anterior optic nerve inflammation can compress, obstruct or damage the retinal venous vasculature, impairing venous outflow. This leads to venous dilation, tortuosity and diffuse retinal hemorrhages.

Acute MOGAD-ON management relies on high-dose intravenous methylprednisolone administered for three to five days, followed by a slow oral taper over one to three months. Second-line treatments, such as plasma exchange (PLEX) or intravenous immunoglobulin, are used for steroid-refractory cases. Long-term therapies, including rituximab or mycophenolate mofetil, are frequently needed to prevent relapses, with newer treatments like complement inhibitor eculizumab and interleukin-6 receptor blocker satralizumab showing promise for severe or refractory cases. Diagnosis hinges on detecting MOG antibodies via cell-based assays and excluding alternative causes.[1]

While high-dose steroid treatment often leads to visual

improvement, outcomes can be variable. Most MOGAD patients (85 to 95 percent) recover to a visual acuity of 20/40 or better with timely treatment, but 5 to 10 percent experience vision worse than 20/200.[13] The presence of venous stasis is of unclear significance regarding visual prognosis. In the two previously reported cases of venous stasis in MOGAD optic neuritis, both patients initially had vision worse than 20/800 in the affected eye. In one case, vision recovered to 20/20 within five days (similar to our patient),[12] while in the other, recovery to 20/20 took more than four months, with persistent visual field deficits remaining.[11] Despite positive initial response to corticosteroids, relapses occur in 50 to 60 percent of MOGAD-ON cases, particularly with rapid corticosteroid tapering. Poor outcomes are more likely with delays in treatment, recurrent attacks, or severe optic disc swelling.[14,15]

In summation, this case adds to our understanding of vascular complications in MOGAD-ON by demonstrating venous stasis as a rare but increasingly recognized associated finding. Clinicians should be aware of this atypical presentation to ensure appropriate diagnosis and intervention. Aggressive and early treatment are crucial to improve visual outcomes and minimize relapses. ◀

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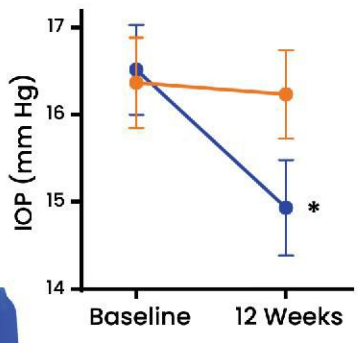
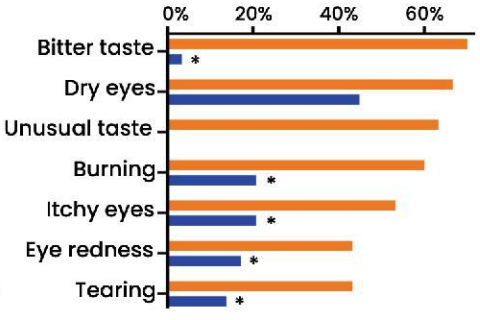


Reduced prevalence of adverse side effects



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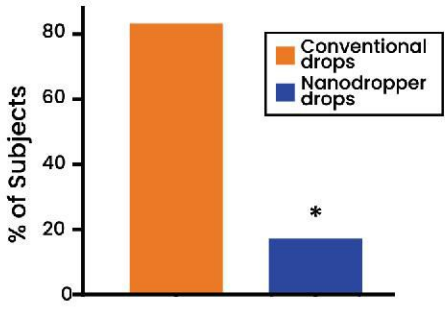

n = 30 in conventional drop group, 29 in Nanodropper group; Error bars: Mean ± SEM; * p<0.05.

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