Wills Eye Resident Series: Vision changes after COVID-19 infection in a 40-year-old, *p. 64*

REVIEW® of OPHTHALMOLOGY

December 2022 • reviewofophthalmology.com

Clinical advice you can trust

IOL Fixation: Pearls from the Pros

Surgeons offer strategies for locking down IOLs using suturing, gluing, the Yamane technique and other current alternatives. **P. 39**

Also inside

xiidra® (lifitegrast ophthalmic solution) 5%

When Selecting an Rx Treatment for Dry Eye Disease

DON'T MAKE HER WAIT. CHOOSE XIIDRA.

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

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

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

Indication

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

Important Safety Information

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

NOVARTIS

Novartis Pharmaceuticals Corporation
East Hanover, New Jersey 07936-1080


Not an actual patient.

Important Safety Information (cont)

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

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

†Pivotal trial data

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

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

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

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

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

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

1 INDICATIONS AND USAGE

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

4 CONTRAINDICATIONS

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

6 ADVERSE REACTIONS

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

- Hypersensitivity *[see Contraindications (4)]*

6.1 Clinical Trials Experience

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

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

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

6.2 Postmarketing Experience

The following adverse reactions have been identified during post-approval use of Xiidra. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish a causal relationship to drug exposure.

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

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Risk Summary

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

Data

Animal Data

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

8.2 Lactation

Risk Summary

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

8.4 Pediatric Use

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

8.5 Geriatric Use

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

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NEWS

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VOLUME XXIX • NO. 12

DECEMBER 2022

VA Permits "Invasive" Procedures by Community ODs

The U.S. Department of Veteran's Affairs has removed language from two Eye Comprehensive Standardized Episode of Care (SEOC) guidelines about community providers that previously ensured veterans would receive complex and surgical care only from ophthalmologists. The previous wording stated that "only ophthalmologists can perform invasive procedures, including injections, lasers and eye surgery." The new language, which was revised to reflect some states' expanded scope of practice laws for ODs, says that these services can now be provided by "an ophthalmologist or optometrist based on the state licensure of the provider."[1]

Alaska (2017), Arkansas (2019), Wyoming and Mississippi (2021), and Virginia and Colorado (2022) have added advanced procedures to their optometric scope of practice. Some of the permitted procedures are injections, excision and removal of non-cancerous lid lesions and chalazion, YAG capsulotomy and greater prescribing authority.

The VA has partnered with ophthalmology to provide care to patients and train ophthalmology residents for more than 75 years, but with these changes, many members of the ophthalmic community are upset and concerned for patient safety. As the VA is the largest integrated health system in the country, its policy changes have widespread effects.[2] Department chairs at academic medical centers with VA affiliations have sent more than 10 letters already.

"We're concerned that this revision, which is happening without the full involvement of ophthalmology, runs the risk of an expansion of scope that's not in our veterans' best interests," says American Academy of Ophthalmology CEO and former chair of ophthalmology at the UCSF Stephen D. McLeod, MD. "The scope of practice of optometrists who work within the VA hasn't changed at this point, but it could and that is a major concern."

Dr. McLeod says that at present, the policy guidance for care within VA health facilities limits complex care and surgical procedures to ophthalmology, but a language change to the VA's community care referral guideline allows VA providers to refer out surgical cases to community-based optometrists who aren't VA employees. "This revision of the community care guideline language was advanced through the VA without input from the ophthalmologists within the VA, who are primarily responsible for the surgical care of these patients," he says.

At this point in time, the referring VA provider would only have the option to refer out a case in one of the few states that have passed a law allowing optometrists to perform laser and other surgical procedures. "If the VA has declared that it's willing to consider this for its patients who are seeking care outside the VA, we're concerned that they won't appropriately consider the implications for patients within the VA," Dr. McLeod says.

The degree of skills training that VA ophthalmologists have is a "world of a difference" from the exposure skills training that an optometrist delivering the same care on the outside of the VA has, Dr. McLeod points out. "There are about 23 optometry schools in the U.S. and only a few of those schools are located in the handful of states that permit OD laser surgery. There just isn't the opportunity to learn or be exposed to the procedures. Furthermore, the criteria to become certified to perform these procedures is minimal—sometimes requiring only a didactic component or a single case.

"When you compare that with the extraordinarily structured and deliberate training that's part of medical surgical training for ophthalmology residents, there's really no comparison whatsoever," he continues. "We could end up with scenarios where if you're in the VA, you receive treatment from an ophthalmologist with a wealth of experience and rigorous training, but if you go out to the community you could be treated by someone whose first procedure is going to be on a veteran. It just defies logic."

(Continued on p. 8)

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(Continued from p. 5)

VA Procedures

This change in language is also dangerous, he says, because many patients aren't aware of the "profound distinction in the rigor of training between ophthalmologists and optometrists."

The Academy is actively reaching out to medical centers and legislators to inform them of the VA's changes and the risk to veterans' eye care.[3,4] "We hope that the VA will be willing to listen to those who have expertise in this area as they make what may seem like an administrative decision but is really a decision of patient safety and quality of care," Dr. McLeod says. "We've received universal support from ophthalmologists who are also veterans. We view this as an issue of health equity for our veterans. We want to ensure that veterans will have access to the same quality of care regardless of which states they find themselves in."

Proponents of the language change have framed this as a victory for veteran's access to care, citing a case in which the VA reportedly suggested a patient be referred to an ophthalmologist 60 miles away for an epilation.[1] According to a story on the AOA's website, the VA stated to Mississippi Congressman Trent Kelly that "providing quality care in a timely manner is of utmost importance. Utilizing community care providers to their full extent is part of the process."

Dr. McLeod says that expansion of scope for ODs is frequently advanced as an access-to-care issue. "Firstly, when you look at geographic locations and geospatial maps, there's significant overlap where optometrists and ophthalmologists reside," he says. "Generally speaking, it's not as if optometrists are living where ophthalmologists are not. Secondly, there's absolutely no evidence from the VA right now that when patients are sent out of the VA for optometric care there's been any inability to find an appropriately trained ophthalmologist for that care.

"The other thing I find disturbing is that, even if there were an access-to-care issue, that the way to solve that problem would be to dispatch our veterans to providers with a substantially lower level of training and experience than they'd receive within the VA," Dr. McLeod says.

In addition to these recent changes to the SEOC guidelines, the VA is currently developing its new national standards of practice for ODs and 50 other health-care positions within its system. The Federal Supremacy Project, as it's called, aims to develop "a standardized set of services that all health-care professionals in a given occupation can perform regardless of what is permitted by a state license, certification or registration."[5]

The VA states on their website that these national standards "are designed to increase veterans' access to safe and effective health care, thereby improving health outcomes for our nation's veterans."[5] Dr. McLeod says the Academy is working to ensure it "has a voice in informing these standards."

In response to a request for comment by *Review*, the VA replied: "… At this time, VA is still reviewing optometry rules across the United States and has not made any decisions about how we will proceed. When we decide on what we believe may be the best Standard for our Veterans, we will seek input from the public, the States, and our own employees through a transparent online process. More information about that process can be found on our website at https://www.va.gov/standardsofpractice/. We will not move forward with a final OD National Standard of Practice until we have had the benefit of these consultations, and therefore it is premature to make any official statements or predictions about the specific content of the national standard of practice at this time."

The national standards for optometry are expected to be released in early 2023. ◀

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INDUSTRY NEWS

Apellis to Submit Amendment to Data
Apellis plans to submit 24-month efficacy data from Phase III DERBY and OAKS studies as part of its New Drug Application for intravitreal pegcetacoplan for the treatment of geographic atrophy. The submission, planned for November, will be a "major amendment" to the NDA, extending the review period by three months with an expected Prescription Drug User Fee Act target action date in February 2023.

Clearside Phase I/IIa AMD Results
Clearside Biomedical announced results from its OASIS Phase I/IIa clinical trial of CLS-AX (axitinib injectable suspension) administered by suprachoroidal injection in wet AMD patients. The company says the primary safety endpoint was achieved at all timepoints and there were no serious adverse events, Clearside says.

Iveric Bio Submits Part of NDA
Iveric bio submitted to the FDA the first part of its New Drug Application for rolling review of avacincaptad pegol (ACP, also known as Zimura) a novel investigational complement C5 inhibitor for the treatment of geographic atrophy secondary to age-related macular degeneration.

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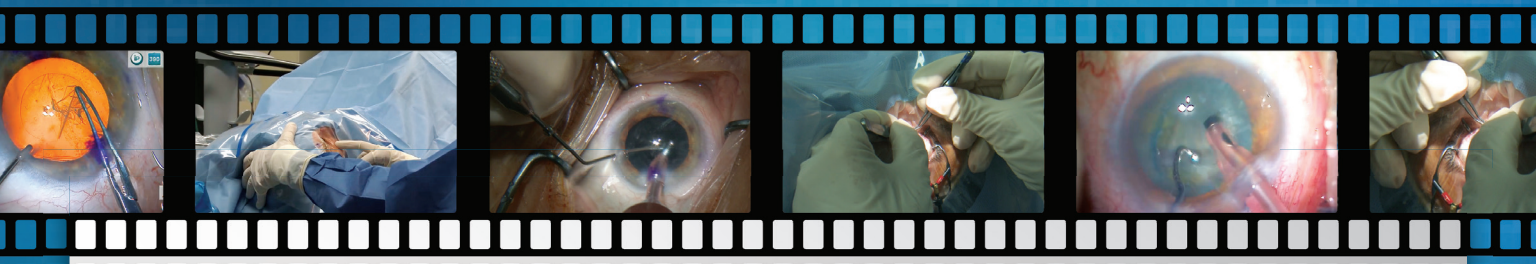

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Episode 84: "Glaucoma Microstent Implantation in a Pseudophakic Eye"

Surgical Video by: Richard J. Mackool, MD

Video Overview:

Several years after uneventful cataract-implant surgery, two glaucoma microstents are implanted in the eye of a patient with progressive glaucoma.

MackoolOnlineCME.com MONTHLY Video Series

Richard J. Mackool, MD

I am happy to announce an exciting addition as we continue into our seventh year of Mackool Online CME. This year, with the generous support of several ophthalmic companies, my son Dr. RJ Mackool and I will share the honor of presenting our surgical cases to you. Together we will continue to demonstrate the technologies and techniques that we find to be most valuable to our patients, and that we hope are helpful to many of our colleagues.

I will continue to narrate all of the cases, even as we share the surgical duties and thereby expand the variety of the cases that we bring to you. As before, one new surgical video will be released monthly, allowing our colleagues the opportunity to earn CME credits or just observe the case. New viewers are able to obtain additional CME credit by reviewing previous videos that are located in our archives.

I thank the many surgeons who have told us that they have found our CME program to be valuable and instructive; I appreciate your comments, suggestions and questions. Thanks again for joining us on Mackool Online CME.

CME Accredited Surgical Training Videos Now Available Online: www.MackoolOnlineCME.com

Richard Mackool, MD, a world renowned anterior segment ophthalmic microsurgeon, has assembled a web-based video collection of surgical cases that encompass both routine and challenging cases, demonstrating both familiar and potentially unfamiliar surgical techniques using a variety of instrumentation and settings.

This educational activity aims to present a series of Dr. Mackool's surgical videos, carefully selected to address the specific learning objectives of this activity, with the goal of making surgical training available as needed online for surgeons motivated to improve or expand their surgical repertoire.

Learning Objective

After completion of this educational activity, participants should be able to:

- demonstrate the technique of microstent implantation in a pseudophakic eye.

Satisfactory Completion - Learners must pass a post-test and complete an evaluation form to receive a certificate of completion. You must listen to/view the entire video as partial credit is not available. If you are seeking continuing education credit for a specialty not listed below, it is your responsibility to contact your licensing/certification board to determine course eligibility for your licensing/certification requirement.

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Dear Fellowship Program Director and Coordinator,

We would like to invite you to review the upcoming 2022 Glaucoma Fellowship Program and Wet Lab in Fort Worth at the Renaissance Worthington hotel. The program offers a unique educational opportunity for fellows by providing the chance to meet and exchange ideas with some of the most respected thought leaders in glaucoma. The Glaucoma Fellows Program and Wet Lab is designed to provide your fellows with a state-of-the-art didactic and wet lab experience. The program also serves as an opportunity for your fellows to network with fellows from other programs.

After reviewing the material, it is our hope that you will select and encourage your fellows to attend this educational activity which is CME accredited to ensure fair balance.

Sincerely,
Kuldev Singh, MD, MPH

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Kuldev Singh, MD, MPH

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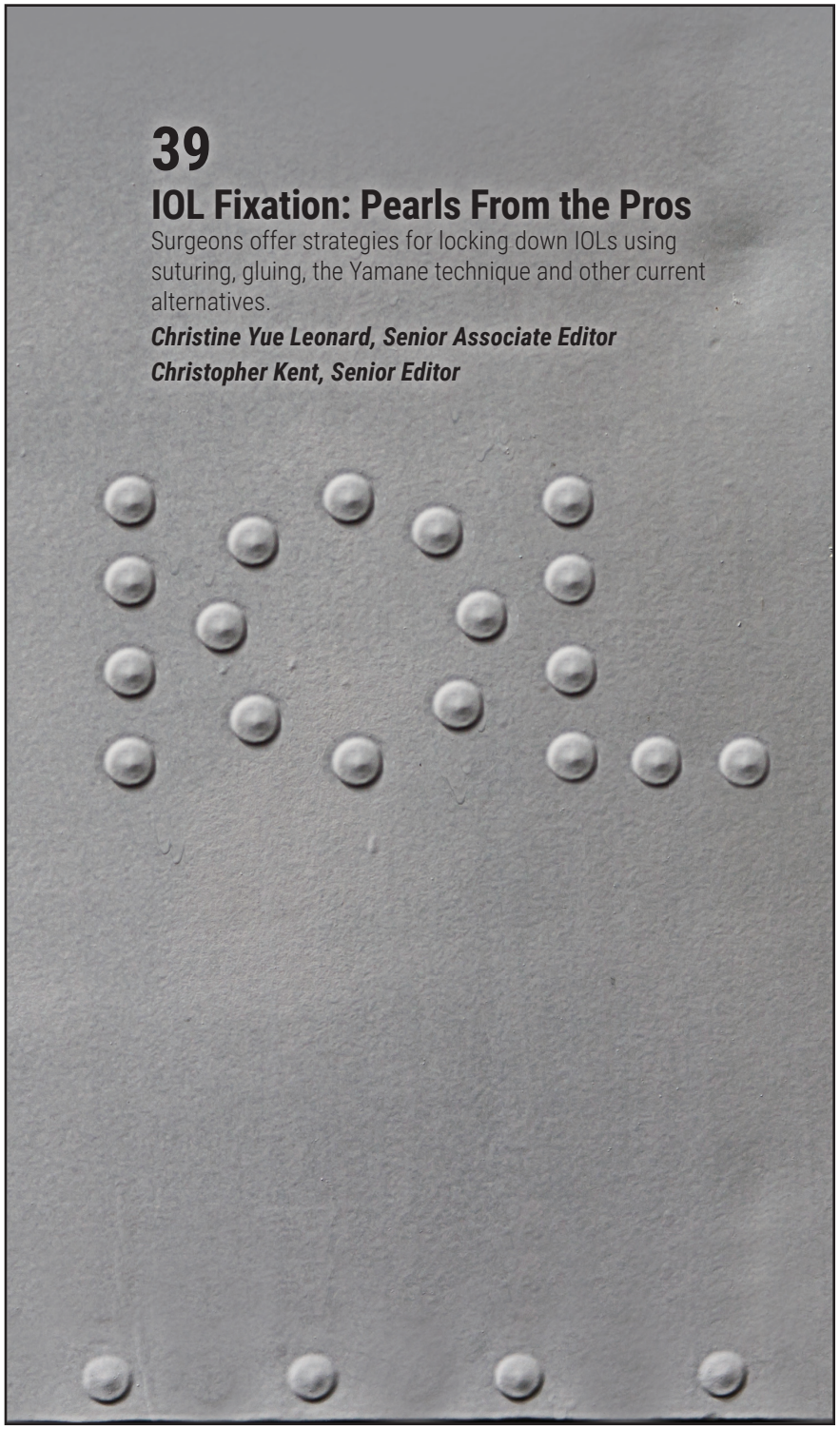

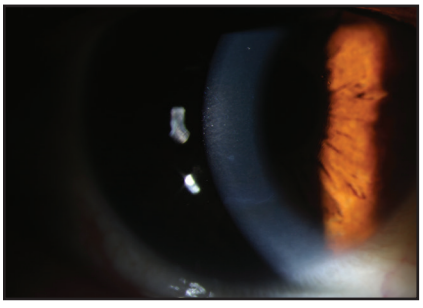

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WALTER C. BETHKE, EDITOR IN CHIEF
EDITOR'S PAGE

The Joke's On Them

Who says the universe doesn't have a sense of humor ... In mid-summer of this year, the Centers for Medicare and Medicaid Services announced the proposed rule for physician reimbursements (read: cuts) for 2023, while around the same time, the *Journal of Cataract and Refractive Surgery* published the results of the first ever survey on ophthalmologist burnout. I didn't say the universe had a GOOD sense of humor; maybe it leans a little too much toward sadistic.

In November, Medicare came out with the final rule on 2023 reimbursement, and it appears that physicians can expect as much as an 8-percent cut in payments, unfortunately. Learning this, I can't help but wonder if these constant slashes to ophthalmologists' reimbursement—how society values their services—contribute to the feelings of burnout explored in the *JCRS* survey.[1]

The survey found that one of the key factors in burnout cited by ophthalmologists was a perceived lack of control. If this is indeed the case, imagine how disruptive it can be to have a carefully laid-out plan for your practice—you know your costs, your staff, your expected procedure volumes—and then suddenly have as much as an 8-percent decrease in your revenue come down on you like a bolt from the blue. What does that do for your sense of control? Everything you just forecasted and planned has to be tossed out the window. You start to wonder how you'll be able to make up the shortfall.

Even though hospital- and academic-based ophthalmologists reported the highest feelings of burnout on the survey, this type of reimbursement decrease cuts across practice lines, inflicting a sense of loss-of-control on both institutional and private-practice ophthalmologists alike. "The lower rates of burnout among ophthalmologists in private practice suggests that physician autonomy maybe key in reducing burnout symptoms," the study authors write. However, it's hard to feel completely autonomous when you can be arbitrarily hit with an 8-percent cut in revenue.

As we've discussed before in this space, CMS has to be careful with how much they cut ophthalmologists' reimbursement, because the joke might ultimately be on them: Some physicians have expressed the potential to drop Medicare reimbursement altogether and go fee-for-service if reimbursements became untenable. In other cases, physicians might choose to transition out of medical practice and into another, more financially stable ("respected"?), line of work relatively easily. Though CMS would have achieved a large cut to its spending on physician services, it would have done so by forcing physicians out of circulation when society needs them most—as the population ages and patients with ocular issues multiply.

— Walter Bethke
Editor in Chief

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A Technique for Irregular Corneal Astigmatism

How a pinhole pupilloplasty can improve visual acuity in patients with higher-order aberrations.

LIZ HUNTER
SENIOR EDITOR

The effectiveness of small-aperture optics for patients with irregular astigmatism is well-known, leading manufacturers to develop IOLs with an integrated pinhole to improve visual acuity. However, there are still areas of the world where such devices aren't yet available or may not be viable for certain patients. Driven by their motivation to make patients happy, a group of surgeons developed and studied a new technique, dubbed the "pinhole pupilloplasty," with the goal of improving visual acuity and reducing aberrations. We spoke with one of the lead authors, Priya Narang, MD, MS, director of the Narang Eye Care and Laser Centre in Ahmedabad, India, about this technique and the outcomes she has achieved with it.

Mastering Pinhole Pupilloplasty

According to Dr. Narang, patients who specifically suffered from higher-order aberrations and corneal irregularities weren't happy with any treatment offered to them. "Any intraocular procedure that you do doesn't work well, whether it's cataract extraction with IOL implantation, or a keratoconus patient and you do cross-linking, there's some amount of fibrosis going on and these patients are never happy with their visual outcomes," she says.

This feedback led Dr. Narang and her colleagues to offer the advantage of small-aperture optics to these patients beginning approximately five years ago. They developed a pinhole pupilloplasty

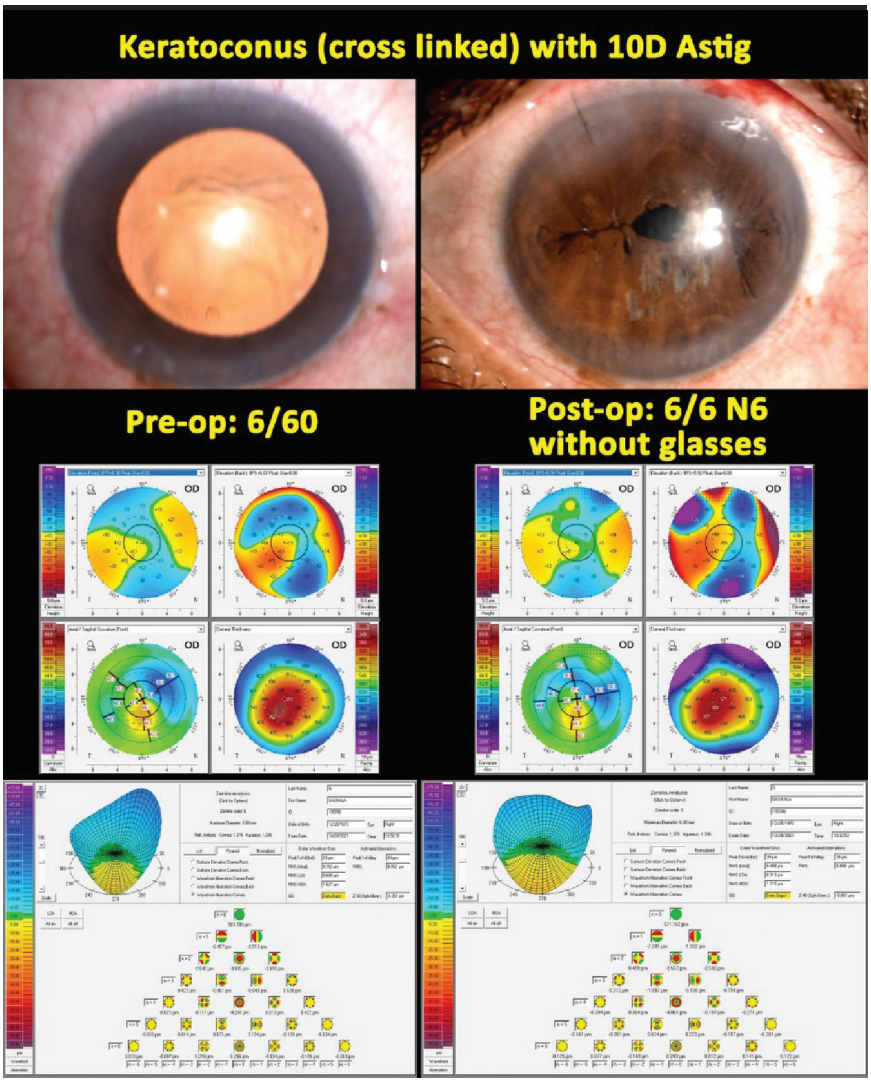

Figure 1. Pre- and postop topography of a patient with keratoconus and 10 D of astigmatism who underwent a pinhole pupilloplasty.

This article has no commercial sponsorship.

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.

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

TARPRE-DB-0042 8/22

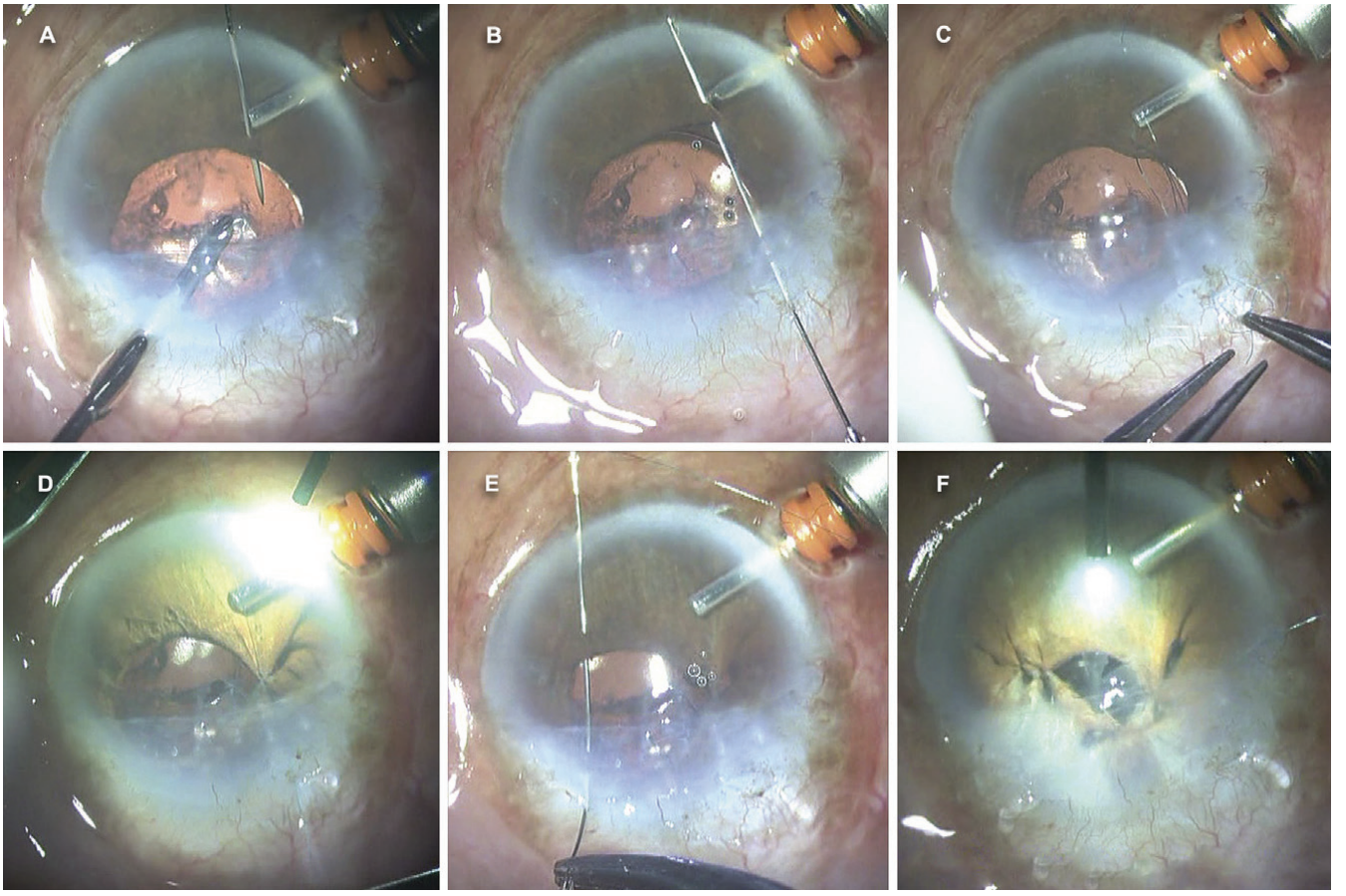

Figure 2. A pinhole pupilloplasty performed using a single-pass, four-throw method.

technique that would address patients' glare and photophobia while achieving adequate image and visual quality.[1]

Dr. Narang calls pinhole pupilloplasty a "technically demanding procedure." "A surgeon should be well-versed with doing the basic pupilloplasty procedure before attempting a pinhole pupilloplasty," she points out.

In a PPP, a surgeon performs a single-pass, four-throw pupilloplasty, an earlier technique developed by Dr. Narang and Amar Agarwal, MD, MS, in which a needle is passed through the edges of an iris defect along the margin of the pupil. The suture end is then passed through the loop with four throws in a modification to the Siepser slip-knot technique, creating a self-retaining and self-locking helical configuration.[2]

But in the instance of a PPP, Dr. Narang says a modification is made to incorporate more iris tissue into the 10-0 needle "which then is passed through the iris tissue much more centrally so that iris tissue close to the center of pupil is approximated."[1]

One prerequisite for a pinhole pupilloplasty is having a good amount of iris tissue, says Dr. Narang. "You can't do it in cases where the iris tissue is atrophic or if the eye has any other disorders, because what happens in a PPP is you bring down the pupil from all four sides, down to the center, so you need a good amount of tissue everywhere to do that," she explains.

Determining the size of the pinhole is important. "The pinhole pupil should be centered on the Purkinje image," Dr. Narang says. "In the preoperative period, you can have the patient lie down on the operating table, and with your surgical microscope light on, ask the patient to look into the light with a coaxial illumination. From there you can just put a mark on the center of the cornea because we have to do this procedure under a surgical block, and when you put a block, many times the eye can rotate. If the eye rotates, your centration won't be there."

During surgery, Dr. Narang advises that one side could be much more drawn, while the other side is a bit retracted. "You must remember that this is human tissue, it's not a mechanical thing," she says. "What happens is that wherever there's overlapping of the iris tissue in the Purkinje 1, we use the vitrector probe in the anterior chamber and we remove that iris tissue."

Patient Outcomes and Other Thoughts

Patients have been pleased with their results, Dr. Narang says, espe-

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-Alan Robin, MD, Ophthalmologist, Founding Member of the American Glaucoma Society and Advisor for Nanodropper

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TABLE 1. VISUAL ACUITY RESULTS IN FIVE PATIENTS WHO UNDERWENT PINHOLE PUPILLOPLASTY

Pupil Diameter (mm) Postop (Post Dilation)		Snellen UDVA		Snellen CDVA	Sim K Astig (D)	
Horizontal	**Vertical**	**Preop**	**Postop**	**Postop**	**Preop**	**Postop**
1.56	1.74	20/250	20/80	20/40	24.2	20.2
1.63	1.51	20/200	20/20*	20/20	4.4	2.8
1.53	2.35	20/400	20/60*	20/40	26.6	20.3
2.10	1.90	20/200	20/20*	20/20	4.2	4.0
1.80	1.60	20/400	20/120	20/120	8.2	8.0

* = partial

cially since those undergoing a PPP have never seen with any sort of clarity before.

Postop UDVA for one of the five patients in the initial study went from 20/250 to 20/80.[1]

"We take up cases with higher-order aberrations and do a Pentacam. If their RMS value is more than around 0.35 or 0.4, these are the cases that are specifically chosen for PPP," she says. "After surgery, it's not uncommon for patients to start crying. I mean, they're so happy about it and wonder why this didn't happen to them sooner."

From a technical standpoint, Dr. Narang says these patients end up with very good distance, intermediate and near vision thanks to the pinhole providing extended depth of focus. "In our studies we've measured a depth of focus that ranges from -2.5 D to +1.5-2 D; there's a depth of accommodation of about 4 to 5 diopters and that's phenomenal for these patients."

As Dr. Narang and co-authors travel and present this research, there are some common questions they hear from other surgeons.

"First and foremost, they ask about night vision for these patients, and secondly, they ask how we can see the fundus in the postop period," she notes.

> **This technique has been adopted worldwide, and I've seen even newcomers to the field learning this, so I think it's not very difficult if anyone wants to venture into it.**
>
> ***— Priya Narang, MD***

"Regarding the night vision, I've recently finished an analysis of one of our studies wherein we looked at approximately 30 cases and there were only two patients who noted that they do have slight difficulty in the evening or in dim lighting, but they were fine with it because the other benefits outweigh it," Dr. Narang explains. "These patients are not very demanding because they've never seen like this before, unlike refractive surgery patients who are more demanding."

In terms of viewing the fundus through a PPP, it could pose a challenge. Dr. Narang says that, in certain cases, "a retina surgeon might have to cut down the sutures—it can be removed at any time, you just need micro scissors and you can cut it for any posterior intervention that happens." Because of this possible difficulty, some retina specialists don't recommend this technique in patients with or at high risk for peripheral retinal pathology.

Finally, Dr. Narang emphasizes her point about familiarizing yourself with the basic pupilloplasty. "This technique has been adopted worldwide, and I've seen even newcomers to the field learning this, so I think it's not very difficult if anyone wants to venture into it," she speculates. "Even for those who do have access to the pinhole IOLs, maybe that's an easier solution, but for a PPP, there's no additional cost to the patient. Also, for other parts of the world, this is a solution for this specific set of patients." ◀

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DISCLOSURES

Dr. Narang has no disclosures to report.

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USING REMOTE IOP MONITORING TO ADVANCE CARE

Home tonometry adds real-world information for better glaucoma decision-making

Barbara M. Wirostko, MD

About three years ago, I began providing the iCare HOME tonometer to my glaucoma patients and more recently upgraded to the HOME2. Sufficient literature confirms that IOP fluctuates and elevated intraocular pressure (IOP) leads to optic nerve damage resulting in glaucoma progression.[1,2] Over the last 20 years many well-controlled, long-term randomized masked studies have indicated that IOP, a primary risk factor that we can treat, if lowered from its maximum number, can slow down progression.[3] We also know that many patients progress despite having "controlled" IOP in the office. Though other parameters beyond IOP affect glaucomatous progression, the iCare HOME2 enables me to efficiently track pressure variability and fluctuation to better assess the effectiveness of therapies and interventions in patients and determine that maximum IOP.

Knowing that glaucoma is a chronic and progressive disease characterized by fluctuating IOP, I would not be doing my best for patients by relying on one IOP measurement every 3 to 4 months to get a true picture of the disease. Outcomes of other progressive diseases such as diabetes and hypertension improve with better and tighter control, eliminating those fluctuations to slow progression and damage.[4] Toward that end, I want to use the best tools available to regularly monitor patients' IOP. My iCare HOME and now HOME2 tonometers are poised to help me achieve this.

"As I continued prescribing the iCare HOME2 tonometer, I found the ability to look at IOP response became just as important as noting spikes once I started patients on treatment or intervened with surgery or lasers."
—Barbara M. Wirostko, MD

SURPRISING BENEFITS

Initially I used home tonometry to identify IOP spikes and trends outside of the clinic as well as diurnal fluctuations. I thought this would enable me to better determine peak IOP and set a target based on those pressure swings. As hoped for, the device helped me detect very high pressures outside the clinic. It also reassured me that my ocular hypertensive patients were not spiking or fluctuating at all.

As I continued prescribing the iCare HOME2 tonometer, I found the ability to look at IOP response became just as important as noting spikes once I started patients on treatment or intervened with surgery or lasers. IOP can change over 24 hours but also over months and years, and therapies can become ineffective with long-term use.[5] Not only is the iCare HOME2 extremely valuable as an acute diagnostic device but I find it invaluable for managing the chronic—and sometimes elusive—nature of glaucoma over time especially as we turn to sustained delivery of IOP lowering agents.

ADVANCING FEATURES

As with all iCare tonometers, measuring requires no anesthetic drops, or other preparation. The HOME2 tonometer received FDA clearance in January 2022. Compared to its predecessor, the iCare HOME2 tonometer has many upgraded features, such as supine measurements, a patient mobile app and a private patient cloud account compatible with Apple, which all have been useful to me and my patients. The software can be configured to send the doctor an e-mail alert if IOP rises above a pre-set limit.

At-home measurements can be uploaded to a cloud database where they are easily accessible to me and my patients. For me, the ability to connect to the cloud-based software using my iPhone is particularly helpful. Based on IOP data I have received from home tonometry, I have changed topical therapy, and recommended surgery or lasers much earlier than in the past when I would

HOME TONOMETER CAPTURES EARLY MORNING SPIKES

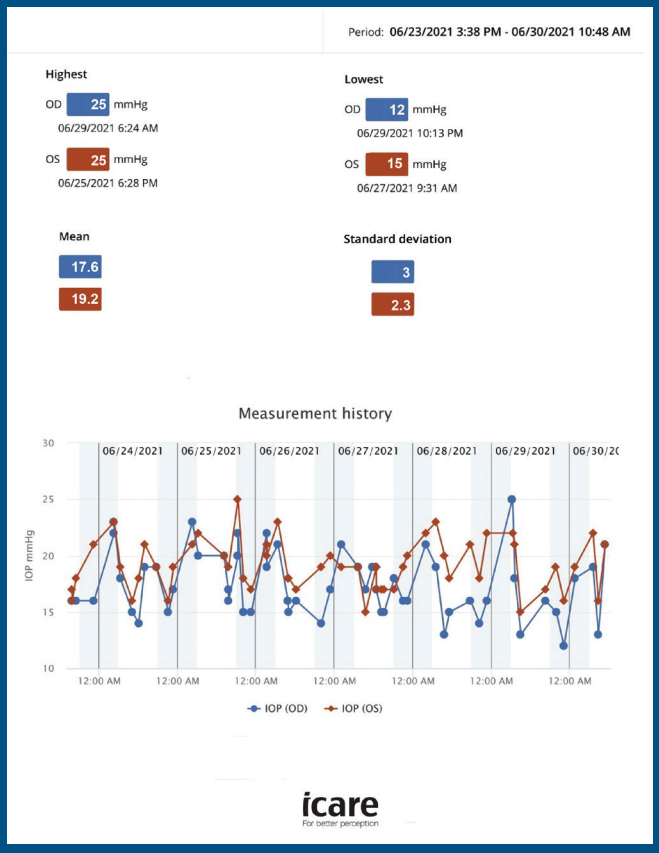
A 60-year-old male patient with advanced POAG came to see me for a second opinion in June 2021. He presented with mild transilluminations in his iris OU, so a pigmentary glaucoma diagnosis was entertained.

The patient used the iCare HOME to determine multiple occasions outside of the clinic in which his IOP was spiking as high as 26.5 mmHg OU in the early morning hours. On Simbrinza OU TID and Vyzulta OU qhs, the patient's IOPs were 14 and 15 mmHg in the clinic.

In October 2021, the patient underwent a cataract extraction and partial OMNI iTrack goniotomy OS. Two months later, in December 2021, the iCare HOME revealed spiking to 29 mmHg OD and 22 mmHg OS. Though the patient had a slight reduction of IOP in his left eye, it wasn't significant.

The decision was made for the patient to receive a XEN® Gel Stent in his right eye in January 2022, given more significant RNFL and VF loss in this eye. The iCare HOME graph in Figure 2 from March 2022 shows a marked flattening of IOP OD on follow-up.

Today, the patient's left eye is being followed closely and will receive a XEN® Gel Stent as well.



Figures 1 and 2. iCare HOME graph (left) shows the patient's IOP measurements OD and OS June 2021, revealing IOP spikes in some cases outside of normal office hours. The subsequent iCare HOME graph (right) reveals patient IOP readings OD pre-XEN® Gel Stent (blue) and post-XEN® procedure (green). The procedure's successful lowering of the patient's uncontrolled IOP emphasizes the importance of ongoing diurnal IOP monitoring for managing progressing patients. Barbara M. Wirostko, MD

have waited for changes on the visual field with evidence of progression to occur. Recently, my colleagues and I have published research showing patients are responding very differently to the same therapy,[6] meaning glaucoma management must rely on a more personalized treatment regimen. As such, patient-specific data obtained outside the office is a powerful tool for managing my glaucoma patients.

I also find the ability to measure IOP supine to be

attractive given we often see sharp IOP elevations during the early hours while people are sleeping.[7] The portable device employs a "smart light guide" to facilitate proper alignment and measurement distance. My patients can quickly center the tonometer, take a measurement, and see their IOPs using the iCare PATIENT2 app. This enables patients to follow their IOP trends using iOS or Android mobile devices. I can easily interpret the data and graphs, and the device determines the quality of the data, which gives me extra reassurance about what I am reading.

My patients love the ability to check their IOP outside the office, to track the variability and timing of that variability, as well as how it relates to exercise and daily activities. They are happy with the HOME2's user-friendly design and how the device has empowered them to better understand their disease.

"This is the future of glaucoma management—using remote patient monitoring to make real-time decisions that help glaucoma patients maintain control of their IOP and disease for better ultimate outcomes."
—Barbara M. Wirostko, MD

FAST PROGRESSORS

The iCare HOME2 tonometer is especially important for identifying rapidly progressing patients who may have reasonable IOPs at the clinic. In fact, I started MyEyes LLC to make it easier to get home tonometers into the hands of patients after one glaucoma patient was able to obtain the iCare HOME tonometer and discovered he was having pressure spikes outside of the clinic.

Though the patient's IOP readings appeared stable during office visits, we quickly realized once we had the home tonometry readings that the patient was spiking during early morning hours. My patient was already on maximum tolerated topical therapy so we no longer needed to wait for progression; we immediately discussed surgery.

At its heart, the iCare HOME2 tonometer enables me to be proactive and hopefully mitigate glaucoma damage. For this reason, many of my glaucoma colleagues have thanked me and MyEyes LLC for working with iCare to make the HOME and HOME2 tonometers more accessible to patients.

FUTURE OF GLAUCOMA MANAGEMENT

I see the iCare HOME2 tonometer playing an important role as we start to implement longer lasting drug-eluting devices and implants, as well as a more personalized glaucoma approach. One of my patients, who lives in another state, received a drug-eluting implant. Because he owns his own iCare HOME tonometer, he was able to let me know his IOP was creeping up. I promptly called in a new PGA prescription for him to start taking as the Durysta stent effect was wearing off.

This is the future of glaucoma management—using remote patient monitoring to make real-time decisions that help glaucoma patients maintain control of their IOP and disease for better ultimate outcomes. ■

Barbara M. Wirostko, MD, is the Resident Research Director and Adjunct Professor of Ophthalmology and Biomedical Engineering, John A. Moran Eye Center, University of Utah, Salt Lake City, Utah. She is the co-founder and Chief Medical Officer of Qlaris Bio and MyEyes.net.

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And to All a Good Night

Musings on life, medicine and the practice of ophthalmology.

MARK H. BLECHER
CHIEF MEDICAL EDITOR

As we get to the end of another year, and having given thanks recently for all we have, it's time to turn our thoughts to what we don't have, or perhaps to what we ought to have: Holiday wishes and New Year's resolutions. I'm not one for presents, because I hate being made the center of attention, but there is something I'd like as we end the year: A good night's sleep. Sounds easy, right? As many of you likely know, it's anything but. I seriously can't remember the last time I slept through the entire night. And I'm not counting that night my friends had me doing tequila shots. Seriously, that doesn't count. (As sleep anyway.) There's a huge industry surrounding sleep: getting to sleep; staying asleep; quality sleep. We all know how important sleep is for our physical health and mental well-being, and now, it seems, even for weight loss.

I've only got 650 words to work with here, not enough space to explore all the causes of and treatments for sleep problems. It's a complex, multivariant issue. At the risk of treading where I don't really have expertise, it can be broken down into three subtypes as alluded to earlier: Difficulty getting to sleep; difficulty staying asleep; and/or poor-quality sleep. I'll plead to two of the three. I don't really have trouble falling asleep—unless it's on an airplane. For some reason I can't sleep on a plane.

At home I wake up somewhere between 1 and 3 a.m. Sometimes I'm awake for a short time, usually for about an hour or so. And when I am asleep, I have the most complex, bizarre dreams. So, by morning I don't feel at all rested. Must be why I'm so grumpy. I'm also notorious for falling asleep at dinner parties.

Getty

Seriously though, I'm the victim of many of the typical causes of poor sleep: free-floating anxiety; the current state of the world; too much caffeine ... and martinis. For the last one, COVID made me do it. In my efforts to maintain a veneer of civility during lockdown, martinis each evening were my attempt to keep my world from descending into the "Lord of the Flies" … that, and clean underwear. And, though COVID has become a chronic condition of life, the martinis stayed. Somehow, I think they may be behind my poor sleep, since most everything I've read indicates eliminating alcohol and caffeine is a good first step. Though this might seem easy to do, I've learned that without these long-time crutches of civilization I might wind up trading a good night's sleep for a stressful day.

So, before doing something as drastic as switching to club soda, I'm trying everything else.

I'm currently working on calming my head—a chaotic place under the best of circumstances and particularly unhelpful when trying to sleep. I'm attempting to decrease the stimuli as the evening goes on, which is kind of tough to do when my job involves a fair number of after-work Zoom meetings, texts and emails. As we all know, this is when we're finally free to clear our desks.

But, this activity gets me thinking too much—that and social media. Somehow, I've gotten hooked on Twitter. Well, Twitter before Elon Musk. Maybe by the time you read this he's driven it into the ground. But before Elon, I found it the timeliest of places to find news from a variety of sources. I know there is a lot wrong with it, and to be honest, it does drive my anxiety (see the infamous "doom scrolling"). I've vowed to not look at anything potentially upsetting after dinner, and have downloaded a brown noise app. Yes, that's a thing, and it's supposed to be better than white noise. At least you don't have to clean it as often. I have also sworn to resist the urge to pour myself a nightcap, especially before surgery days. Wish me luck.

And, instead of counting sheep I think I'll try counting reindeer. It's that time of year after all. ◀

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

Weathering the Storm of Neovascular Glaucoma

By the time your patients complain of symptoms, it may be too late. An expert shares how to manage this disease.

MISHA F. SYED, MD, MEHP
GALVESTON, TEXAS

Neovascular glaucoma has a relatively low prevalence, but it contributes significantly to vision loss and visual morbidity. Unfortunately, patients often don't present with symptoms in the disease's early stages, which makes detecting and preventing neovascular glaucoma challenging. Here, I'll discuss neovascular glaucoma's risk factors, the imaging modalities best suited for early disease detection, and medical and surgical management approaches.

Pathogenesis

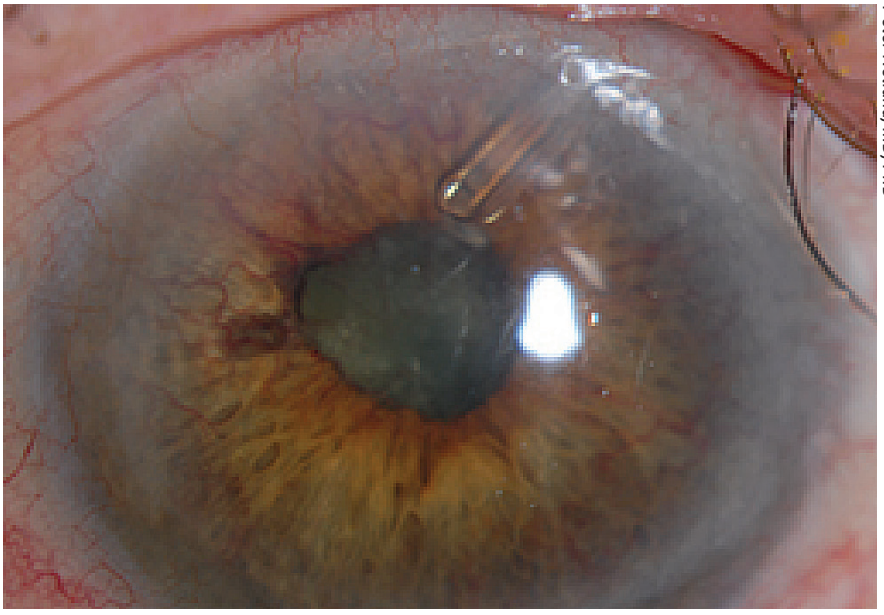
Retinal ischemia is the main driving force behind the disease. The insufficient supply of oxygen causes pathogenic and angiogenic growth factors to be released into the retinal circulation and into the anterior segment. These factors cause new vessel growth and fibroblast proliferation, increased vascular permeability and leakage, endothelial cell mitosis, and leucocyte adhesion to endothelial cells with subsequent breakdown of the blood-retina-barrier.[1]

This triggers neovascularization of the iris (NVI) and the angle (NVA) (*see Table on page 30 for classifications*). NVI and NVA are considered very early stages of neovascular glaucoma. If these conditions aren't caught and treated early on, then NVI and NVA can lead to trabecular meshwork obstruction and the open-angle stage, followed by proliferation of fibrous tissue that contracts and closes the anterior chamber angle over time. The angle can then become closed secondarily by peripheral anterior synechiae or scarring. All of this contributes to acute IOP elevation.

Until that point, patients are generally asymptomatic. Then, patients will present suddenly with eye pain, very high pressures and the classic clinical symptoms. At this point, it's too late to prevent, as pathogenesis has already occurred. It's crucial to catch the disease early and treat it before it comes to this.

Anticipate

Early detection and prevention are the best medicine when it comes to neovascular glaucoma. Common causes or medical conditions that may increase your patient's risk for developing the disease include a history of central retinal vein occlusion (especially the ischemic variant of CRVO); a history of diabetes (particularly proliferative diabetic retinopathy); and ocular ischemic



Peter Netland, MD, PhD

An 84-year-old patient with neovascular glaucoma after CRVO with an Ahmed valve. Ischemic CRVO is one of the most common predisposing conditions for neovascular glaucoma, responsible for about 33 percent of cases. The other two most common predisposing conditions are diabetic retinopathy (33 percent) and ocular ischemic syndrome (13 percent).[11]

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. **Dr. Netland** is Vernah Scott Moyston Professor and Chair at the University of Virginia in Charlottesville.

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WEISS AND GOLD CLASSIFICATION OF IRIS AND ANGLE NEOVASCULARIZATION[1,10]

	Grade 1	Grade 2	Grade 3	Grade 4
Neovascularization of the Iris (NVI)	New iris vessels at pupillary zone in <2 quadrants	New iris vessels at pupillary zone in >2 quadrants	New iris vessels at ciliary zone and/or ectropion uveae in 1-3 quadrants	New surface vessels at ciliary zone and/or ectropion uveae ≥3 quadrants
Neovascularization of the Angle (NVA)	Angle vessels cross scleral spur and ramify on trabecular meshwork in <2 quadrants	Angle vessels cross scleral spur and ramify on trabecular meshwork in >2 quadrants	Angle vessels at trabecular meshwork, and peripheral anterior synechiae in 1-3 quadrants	Peripheral anterior synechiae in ≥3 quadrants

Table adapted from Senthil et al.

syndrome. These three conditions are associated with about 75 percent of neovascular glaucoma cases. Patients who have these conditions often have a history of carotid artery occlusion, which comes from atherosclerosis, a major cause of heart disease and other cardiovascular issues in this country.

Less common causes include inflammatory conditions such as uveitis; a history of eye trauma; retinal detachment (particularly chronic retinal detachment leading to proliferative vitreoretinopathy); a history of ocular tumors such as uveal melanoma or retinoblastoma; and systemic diseases such as lupus and carotid cavernous fistula.

Prepare

If you suspect a patient may be at higher risk for neovascular glaucoma, there are a few approaches for early detection. First, conduct a thorough physical exam of the anterior chamber and its structures. Keep in mind that the angle will appear open until later stages of neovascular glaucoma, and NVA may be visible with or without NVI. Gonioscopy with a viscous coupling agent is really the only way to get a good look at the angle.

New vessels may appear as small tufts at the pupillary margin or in meandering patterns on the surface of the iris. You may see fine arborized vessels approaching the angle on gonioscopy. These will cross over, rather than behind, the scleral spur and onto the trabecular meshwork.[2]

If you don't see any abnormal vessels after performing gonioscopy, but you have a high index of suspicion for neovascular glaucoma, an iris fluorescein angiogram may help you to visualize signs of the disease. (As iris fluorescein angiography is an invasive test involving the injection of a contrast dye, you may not want to perform this on everyone, but it's an option.) Another option we have now is to use optical coherence tomography angiography to detect abnormal iris vessel growth.

For patients with cardiovascular conditions, you may also want to consider ordering a Doppler ultrasound of the carotid arteries. If your patient has significant carotid artery blockage, they may need to be treated first by a vascular surgeon who can clean out the plaque buildup. This can help prevent the potential ocular complications of neovascular glaucoma, but perhaps even more importantly, this could save the patient's life—carotid artery stenosis increases the likelihood of stroke.

Keep in mind that in these incipient stages when you're trying to catch neovascular glaucoma early, the patient's intraocular pressure often won't be elevated. You need to have a high index of suspicion, conduct a thorough exam and use some of these tests as needed to pick up early changes.

Manage the Damage

If your patient presents with high IOP and a closed angle from secondary fibrovascular membrane, the neovascular glaucoma process is in full swing. There are four key components for disease management (*see flowchart on page 32*):

1. Reduce the IOP to prevent visual loss and relieve the pain. Medical management will help lower IOP in the acute setting. When it comes to medical management of IOP for neovascular glaucoma, drug classes include beta adrenergic antagonists, alpha-2 agonists and topical and/or oral carbonic anhydrase inhibitors. Newer classes of medication include rho kinase inhibitors and nitric oxide component medication.

While prostaglandin analogues can be used, there are some data that suggest inflammation in the acute setting could be worsened by their use because they cause a breakdown of the blood-aqueous barrier. However, this isn't necessarily a fully accepted argument. So, you may find that prostaglandin analogs are a useful adjunct to your medical therapy in the acute setting.

Cholinergic agents such as pilocarpine should be avoided more often than not when treating neovascular glaucoma because they can increase inflammation. They can also worsen synechial angle closure when used chronically and decrease uveoscleral outflow, which is

PROGRESSION IN GEOGRAPHIC ATROPHY IS RELENTLESS AND IRREVERSIBLE[1-4]

While GA progression may appear to move slowly, it can affect your patients faster than you think[1,4-6]

The consequences of Geographic Atrophy (GA) are too critical to be ignored[7-9]

IN A MEDIAN OF ONLY 2.5 YEARS,
GA lesions encroached on the fovea according to a prospective AREDS study (N=3640)[2*]

2 OUT OF 3 PATIENTS
lost the ability to drive in a median time of <2 years according to a retrospective study (n=523)[10†]

GA lesions can lead to visual impairment even before they reach the fovea[1,5,6]

See the effect of GA progression on your patients

*Data sourced from the Age-related Eye Disease Study (AREDS) Report #26—a long-term, multicenter, prospective study examining progression of GA area in a cohort of 3640 patients with signs of early and more advanced forms of AMD.

†A retrospective cohort analysis (N=1901) of a multicenter electronic medical record database examining disease burden and progression in patients in the United Kingdom with bilateral GA secondary to AMD.

BCVA=best-corrected visual acuity.

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Apellis

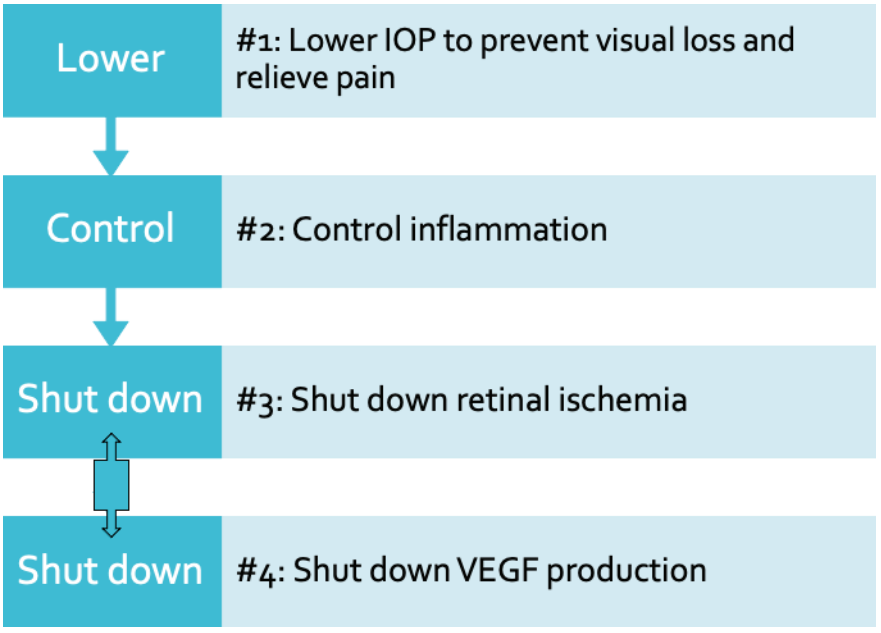
counterproductive since increasing uveoscleral outflow is the best way to lower IOP in the acute setting. For this reason, we don't tend to use cholinergic agents as first-line treatments.

2. Lower the inflammation in concert with IOP reduction. Eyes affected by neovascular glaucoma tend to become very inflamed, so as you bring the pressure down, take steps to reduce the inflammation as well. We generally use topical corticosteroids. Using a cycloplegic such as atropine can also help calm the eye and decrease inflammatory processes. This will also help to relieve the pain.

3. Shut down the inciting process. Addressing the inciting process, the retinal ischemia, and the fourth component, targeting VEGF production, should be undertaken simultaneously. With the help of our retina colleagues, we shut down the retinal ischemia by performing retinal ablation. Removing the ischemic retinal tissue will secondarily reduce the production of angiogenic factors such as VEGF.

Panretinal photocoagulation is the mainstay of therapy. It's usually performed under topical anesthesia over one to three sessions using a slit lamp or indirect laser with 1,200 to 1,600 burns using an approximately 500-µm spot size.[3] PRP isn't always possible to perform right away, however. It may be difficult to obtain good visualization of the retina in the acute setting of neovascular glaucoma because the eye is often cloudy and edematous from the high IOP. In these cases, try to lower the pressure to clear the cornea. Once you have a better view, you can reattempt PRP until the neovascularization resolves. Keep in mind that NVI and/or NVA may not regress until four to six weeks after PRP.

PRP for ocular ischemic syndrome is indicated for posterior and anterior segment neovascularization. However, PRP alone may compromise the optic nerve head blood flow. Be sure to work with your vascular surgery colleagues or cardiologists to improve retinal blood flow with carotid endarterectomy or other interventions when trying to shut down these abnormal vessels. And always keep your patient's particular medical conditions in mind when instituting these treatments.



There are four key components to managing neovascular glaucoma. The third and fourth steps, shutting down the inciting process (retinal ischemia) and VEGF production, should be undertaken simultaneously. This is typically done using PRP and anti-VEGF injections, respectively.

4. Target VEGF production as well. Anti-VEGF injections can cause regression of the abnormal blood vessels in neovascular glaucoma. However, this is a temporary regression, lasting about four to six weeks, and efficacy depends on the stage of the neovascular glaucoma you're treating.

If the disease is very advanced, studies indicate that you may not get much benefit from using anti-VEGF injections. A Cochrane systematic review of all the available data reported that long-term outcomes in neovascular glaucoma don't seem to differ with or without the use of anti-VEGF agents.[4] Notably, there were only four randomized clinical trials in the review with substantial heterogeneity of methods and analysis (in China, Brazil, Egypt and Japan). So again, these agents are more of an acute temporizing measure to attempt to shrink the blood vessels, often in preparation for a more definitive surgical management approach, which will be needed to fully control the IOP.

Surgical Management

Surgical options include trabeculectomy with mitomycin-C, glaucoma drainage devices, cyclophotocoagulation or endocyclophotocoagulation and combined procedures. There are several different glaucoma drainage device options, all of which have pros and cons. Much of the decision will be based on surgeon preference. CPC and ECP have IOP-lowering effects similar to those of a glaucoma drainage device, but there are potentially more complications with them.[5] Combining a glaucoma drainage device with a pars plana vitrectomy is another option with

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good IOP lowering potential. It may help long-term management of retinal ischemia and can be a good option if there's concomitant retinal pathology such as vitreous hemorrhage; however, there's also a potential for increased vision loss with these procedures.

There's some published data suggesting that intravitreal anti-VEGF is associated with greater overall success rates with Ahmed glaucoma valve implantation when administered preoperatively.[6] The rationale is that if you can manage the potential for bleeding intraoperatively and postoperatively that will lead to higher success rates and less chance for intra- and postoperative complications such as hyphema.

A retrospective study by Marwan Sahyoun, MD, and colleagues reported that while bevacizumab given seven days prior to surgery wasn't associated with better surgical success, BCVA or IOP control, its administration significantly decreased postoperative hyphema and the number of glaucoma medications patients used at the final visit.[7] Similarly, a prospective study in which patients were given intravitreal ranibizumab one week before trabeculectomy reported significantly decreased IOP, a significant but modest visual acuity improvement and fewer postoperative complications than Ahmed valve implantation alone.[8]

The other option is to administer anti-VEGF agents intraoperatively during glaucoma drainage device implantation, though few large studies have been conducted on this. In a randomized trial by Enyr S. Arcieri, MD, and colleagues, the treatment group received intravitreal bevacizumab injections intraoperatively as well as at four and eight weeks after Ahmed valve implantation.[9] Their two-year results suggest that adjunctive use of bevacizumab intraoperatively may lower IOP and the number of glaucoma medications needed by patients postoperatively. However, this trend doesn't appear to be statistically significant.[3]

Prognosis

Unfortunately, once neovascular glaucoma presents, it's often in the end-stages of the disease process. In general, the prognosis is guarded. Much depends on when you're able to intervene. We see more extensive damage in patients who don't come in right away, for whatever reason, and that can affect the outcome. Situations in which there's high IOP and abnormal blood vessel proliferation are very time-sensitive when it comes to avoiding permanent damage to the retina and the eye's drainage system. I tell my patients that this is a very serious condition and that there's a relatively high chance they'll lose vision permanently.

> **As our population continues to suffer from increased incidence and prevalence of diabetes and other vasculopathic conditions, we need to keep in mind that members of this ever-growing patient population could fall prey to neovascular glaucoma.**

To sum up, neovascular glaucoma is a serious, sight-threatening condition characterized by acute IOP increase and abnormal blood vessel growth in the iris and angle. Treatment consists mainly of prevention through early detection, as well as urgent management, ultimately leading to surgical intervention. Prognosis depends heavily on when intervention begins, but it remains poor.

As our population continues to suffer from increased incidence and prevalence of diabetes and other vasculopathic conditions, we need to keep in mind that members of this ever-growing patient population could fall prey to neovascular glaucoma. We should strive to gather stronger data using larger sample sizes and adopt a core outcome set so data from various studies can be combined in meta-analyses. We must also attempt to stratify randomization in trials based on etiology to help us better understand treatment effectiveness for neovascular glaucoma.

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IS MYOPIA A DISEASE OR NOT?

How myopia classification may affect decisions regarding intervention.

CHRISTINE YUE LEONARD
SENIOR ASSOCIATE EDITOR

As myopia rates rise around the world, the condition has increasingly been referred to as an epidemic, a disease and a public health crisis in the making. Myopia can lead to pathology and vision loss when it's severe, but the majority of cases don't stray into pathologic levels and can safely be addressed with corrective lenses or refractive surgery. Some ophthalmologists feel that broadly applying the term "disease" to myopia may not always be appropriate for a condition whose affected majority isn't at high risk.

On the other hand, the global prevalence of myopia is rising, and with it the proportion of individuals with high myopia who would be at risk for future retinal detachments or other conditions such as lattice degeneration and glaucoma. The COVID-19 pandemic lockdowns and stay-at-home orders have also exacerbated this rising trend,[1] with an entire generation of young children seeing more screens than trees for the past few years. Myopia, whether severe or not, also entails a heavy economic burden. Eye care services around the world will be pressed to meet this growing need.

Getty

Studies show that sunlight exposure can help slow myopia progression.[3-5]

Should myopia be referred to as a disease though? The answer is nuanced, experts say. Bioethicist and pediatric ophthalmology subspecialist Alex V. Levin, MD, MHSc, FRCSC, and the Massachusetts Eye & Ear Infirmary's Grayson W. Armstrong, MD, MPH, discuss myopia's classification and how this may drive clinicians' decisions regarding interventions.

Classifying Myopia

"I'm a bit troubled when people refer to myopia as an 'epidemic,' because I'm not sure it's always a disease," says Dr. Levin, who also holds the Adeline Lutz – Steven S. T. Ching, MD, Distinguished Professorship in Ophthalmology and is chief of pediatric ophthalmology and ocular genetics at the Flaum Eye Institute and chief of clinical genetics at the Golisano Children's Hospital at the University of Rochester Medical Center.

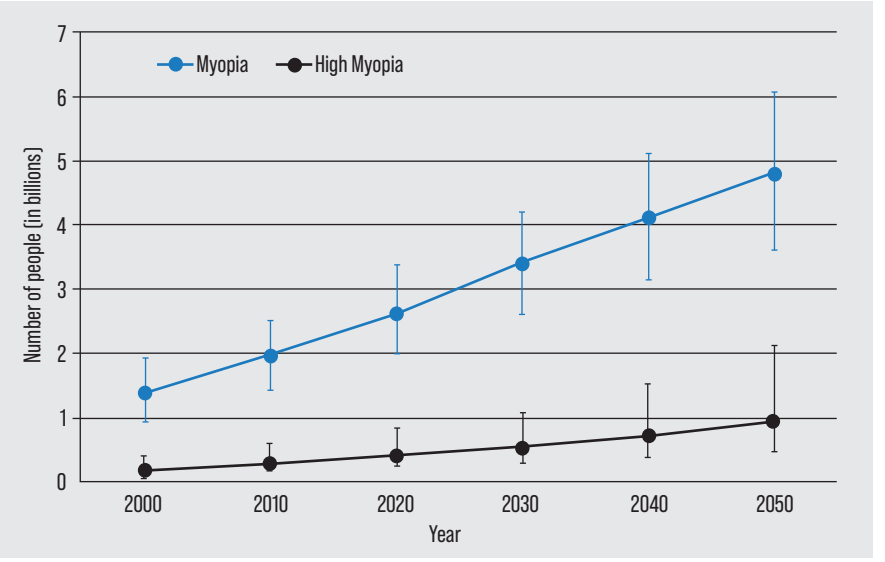
"Singapore's Ministry of Health projects that 80 to 90 percent of all Singaporean adults will be myopic by the year 2050, with 15 to 25 percent of those individuals having high myopia. When almost everyone in a population has a condition, is it still a disease?" he asks. "If there's no risk for a complication other than the fact an individual dislikes something about their uncorrected vision, can you call that a disease?

"Some people are dissatisfied by their inability to see the alarm clock in the morning. Other individuals are upset about the size of their nose," he continues. "Both could choose to have a surgical procedure to relieve this 'dis-ease.' I don't consider lower levels of myopia to be a disease category but rather a variation of normal. In medicine, we have to separate when we're treating a medical prob-

This article has no commercial sponsorship. **Dr. Armstrong** and **Dr. Levin** report no related financial disclosures.

lem that has clear, definable adverse outcomes from when we're treating the preferences of a patient."

"We know that there are genetic associations with myopia so it can be inherited like a disease, and we know that there are modifiable risk factors for it such as screen time, outdoor time and type of glasses or contacts," says Dr. Armstrong, a Harvard Medical School instructor in ophthalmology, associate director of medical student education and director of the Massachusetts Eye & Ear ophthalmology emergency services. "But most myopia isn't a disease," he agrees. "Anything that causes pathology and leads to vision loss, blindness or surgical intervention is a disease, whereas if you're correcting someone's vision with glasses and that's enough, and there are no risks of future sight-threatening complications, then that shouldn't be classified as a disease."



In 2050, an estimated five billion people (50 percent of the global population) will have myopia and one billion will have high myopia (10 percent), according to the Brien Holden Vision Institute's pre-pandemic 2016 estimate.[2] (*Adapted from Holden et al. 2016.*)

What To Do About Rising Rates?

Almost 30 percent of the global population is myopic with only about 4 percent highly myopic, but by 2050, these numbers are projected to increase to nearly 50 percent with 10 percent high myopes, according to the Brien Holden Vision Institute.[2]

Uncorrected refractive error is a major and growing cause of vision impairment around the world. As myopia rates rise, there will be more individuals seeking refractive surgical correction. Certainly, interventions such as elective refractive surgeries like LASIK and clear lens exchange can address myopia, Dr. Levin points out. "These procedures don't prevent medical problems, though," he says. "With refractive surgery, the best-corrected 20/20 patient with a healthy eye that just happens to be longer than average, is submitting that eye to the risks of refractive surgery—which could include an increased risk of retinal detachment—for the convenience (or necessity in some cases) of not wearing glasses or contact lenses.

"If there were a way to prevent people from getting into the axial length categories that put them at high risk for retinal detachment and we had a treatment that was shown to effectively reduce the rate of retinal detachment from myopia, that would be fantastic," Dr. Levin continues. "However, I'm not sure we can confidently prevent a -1 D myope from becoming a -8 D myope—yet. For pathologic myopia, which seems at least in part to be independent of axial length and likely a genetic disorder, our current therapies are likely even less effective."

"I think one reason myopia is so often called an epidemic is because the number of myopes is rising," says Dr. Armstrong. "In Taiwan, close to 80 percent of children are myopic now. A large portion of these children will hopefully go on to live normal lives without a risk of retinal detachment or tears. It's perhaps worth monitoring myopia as a risk factor for disease but it's not necessarily true that all 80 percent of those Taiwanese children has a disease from an early age.

"That said, we can't always predict which of those children will go on to be highly myopic or which ones will need retinal detachment surgery or go blind from a choroidal neovascular membrane in the future, so we may want to monitor and/or treat them all as if they could be that patient," he says. "We do know that the younger a child is when they become myopic, the greater the chance they have of becoming a high myope."

This raises the question of potential intervention benefits and trade-offs. Dr. Armstrong notes that there's some evidence for increasing outdoor time and limiting screen time as a management strategy. "Though children may still progress despite increased outdoor exposure, this intervention's positive benefits extend beyond the eyes to the entire body," he says.

Findings from the Sydney Myopia Study suggest that outdoor exposure alone is enough to have an effect on myopia progression. (Indoor sports weren't associated with myopia reduction.)[3] In the study, higher levels of outdoor activity were associated with more hyperopic refractions and lower myopia prevalence in 12-year-olds; no consistent associations were noted between refraction and activity in the 6-year-old group. Light intensity, increased depth of field and decreased image blur were suggested as contributing factors. The researchers also noted that light may affect retinal

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dopamine release, an eye growth inhibitor.

Similarly, a study in which children wore wrist light sensors reported that those who experienced low amounts of daily ambient light had significantly greater eye growth than children who experienced moderate or high levels of light exposure.[4]

A study in Taiwan reported that increasing outdoor activities and sunlight exposure in school was effective at slowing myopia progression. The researchers also reported that shorter outdoor time with high bright light exposure had an effect on myopia progression comparable to longer outdoor time with moderate light exposure.[5]

"While outdoor time isn't as effective as low-dose atropine eyedrops, eyedrops also aren't 100-percent effective in preventing high myopia in all children," Dr. Armstrong notes. "There are certain risks associated with atropine eyedrops too, such as blurred vision and decrease in accommodative ability. If there's an accidental overdose, there may be systemic issues such as flushing, fever and trouble urinating."

Dr. Armstrong believes all children should be screened for glasses at a young age. "It's very important for quality of life and school success," he says. "If children can't read the board, they won't do as well in school. This is a small intervention with low risk. Defocus contact lenses and orthokeratology lenses may also potentially help with myopic progression, though these interventions aren't risk-free. Contact lenses can lead to corneal ulcers if the lenses aren't removed at night or aren't cleaned regularly."

While interventions have some associated risks and disadvantages, including cost, myopia intervention has been shown to significantly impact refraction and axial length.[6] A review of randomized clinical trials reported that a range of interventions reduced myopia when compared with placebo. The paper reported that atropine, pirenzepine and progressive-addition spectacle lenses were effective in terms of refractive correction; and atropine, orthokeratology lenses, peripheral defocus-modifying contact lenses, pirenzepine and progressive-addition spectacle lenses were effective in terms of axial length.

Overall, they concluded that pharmacologic interventions (atropine and pirenzepine) were most effective; some specially designed contact lenses (ortho-K and peripheral defocus-modifying contact lenses) had moderate effects; and specially designed spectacle lenses had a minimal effect.

The ability to retard the progression of myopia may be crucial for avoiding more serious ocular problems down the road. One study reported that a 1-D increase in myopia was associated with a 67-percent increase in the prevalence of myopic maculopathy.[7] The group reported that slowing myopia by 1 D should reduce the likelihood of developing myopic maculopathy by 40 percent, regardless of the level of myopia. Low and moderate levels of myopia, though less prone to complications than high myopia, still carry "considerable risks" for myopic macular detachment, retinal detachment, posterior subcapsular cataract, nuclear cataract and open-angle glaucoma, according to a 2020 review study.[8]

Effects of Labels

Dr. Armstrong notes that broadly classifying myopia as a disease may serve some public health aim. "Other public health experts may disagree, but it's possible that if you categorize something as a disease it could be easier to track or find funding for research, though that's a separate argument," he says. "Calling it a disease also gets people's attention, perhaps making them less likely to blow it off and assume their child only needs glasses."

On the other hand, he says it could be stigmatizing to call every single person in the world who has some level of myopia a diseased patient. "We can try to control myopia as if it's a preventable disease," he says. "But once patients get out of that risk zone—when they reach a certain age and don't have high myopia—I personally wouldn't say that person is diseased. On the other hand, someone with high myopia should perhaps be monitored as if they have a disease.

"From a clinical standpoint, if I see a patient with one diopter of myopia, I don't consider them as having a disease per se," he continues. "If that child is six months old and they're already two or three diopters myopic and I see them again and they're a four-diopter myope, then to me that rate of decline at that early age at onset is a very bad prognostic indicator that that young child is probably going to have worse outcomes and a risk of high myopia. It has to be put into context."

Looking to the Future

"We as a medical community are still learning why myopia occurs and what the best treatments are," Dr. Armstrong says. "While studies have shown that we're beginning to figure out the genetic causes, and we have found ways to start treating it, nothing's perfect and we can't always predict who will have high myopia or worse outcomes. We're not going to

(Continued on p. 60)

When It's Not Axial Lengthening

"As we discuss disease and myopia classification, it's worth mentioning that some systemic medical conditions can lead to nearsightedness," says Grayson W. Armstrong, MD, MPH, of the Massachusetts Eye & Ear Infirmary. "If an older patient who hasn't had myopia previously presents with sudden onset of new myopia, that patient may be diabetic and their blood sugar may be high, causing the lens in their eye to swell, leading to a myopic shift. Those patients will come in with acute blurring and have a lot of trouble seeing far away, but if you just prescribe them glasses, they're going to be walking around with diabetes that could be treated." He notes that acute nearsightedness may also arise from other conditions including retinitis pigmentosa, Marfan syndrome, Stickler syndrome and Ehlers Danlos syndrome.

IOL FIXATION: PEARLS FROM THE PROS

Surgeons offer strategies for completing successful fixation using suturing, gluing, the Yamane technique and other current alternatives.

CHRISTINE YUE LEONARD
SENIOR ASSOCIATE EDITOR
CHRISTOPHER KENT
SENIOR EDITOR

Although it's relatively rare, IOLs can sometimes become dislocated, usually because of the absence of zonular support. Sometimes remedying (or preventing) that requires fixating the current or replacement lens in position. The lens may be sutured to the iris, or even replaced with an anterior chamber lens, but often the lens is fixated to the sclera using one of a number of popular techniques.

Is one fixation technique better than another? Even retrospective studies have rarely compared techniques directly, but a 2020 assessment made by the American Academy of Ophthalmology reviewed 45 relevant studies and found that no technique has proven itself superior to the alternatives.[1]

Here, eight surgeons discuss the pros and cons of the most popular IOL fixation techniques, and offer pearls for making the procedures go smoothly and produce the best outcomes.

Planning Your Fixation Surgery

Surgeons suggest considering a number of factors when faced with a lens that needs fixation:

• ***In terms of timing, factor in whether the patient has had a previous vitrectomy.*** "Most of the time, you have several weeks or even months to repair a case of pseudophakodonesis with an IOL/capsular bag complex," says Richard S. Hoffman, MD, a clinical associate professor of ophthalmology at the Casey Eye Institute, Oregon Health and Science University, and a partner at Drs. Fine, Hoffman, & Sims in Eugene, Oregon. "However, if the patient has had a previous vitrectomy, the lens can drop very quickly. You should treat this as an urgent case, and make the repair within one to two days, if possible."

• ***Base your choice of approach on how much capsular support the lens has.*** Uday Devgan, MD, FACS, FRCS, in private practice at Devgan Eye Surgery in Los Angeles, points out that if the lens still has some capsular support, a relatively easy option is suturing the IOL to the back of the iris. "Those sutures are protected because they're inside the eye," he says. "They can last a long time. And because there's at least some capsular support, the lens isn't going to move around too much."

Eric D. Donnenfeld, MD, clinical professor of ophthalmology at New York University Medical Center and a partner at Ophthalmic Consultants of Long Island, agrees that if some support still exists, iris fixation is worth considering. "Suturing to the iris is very reasonable when, for example, the lens has dislocated horizontally rather than into the vitreous," he explains. "In this situation I just put a simple Siepser suture through the iris and through the IOL. That holds the lens in place very effectively."

On the other hand, Dr. Devgan notes, if there's zero or minimal capsular support, you're better off fixating the lens to the sclera. "If you're willing to use sutures in this situation," he says, "you can suture the

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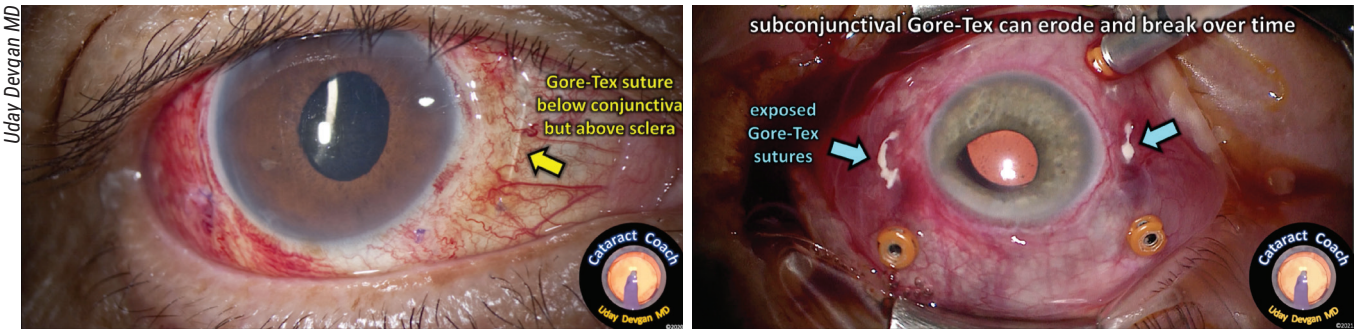
Uday Devgan MD



When suturing a lens in place, it's important to make sure that the suture material (most commonly Gore-Tex) is buried within the sclera. If it's just sitting under the conjunctiva *(above, left)*, the result can be exposure and breakage of the sutures and a dislocated IOL *(right)*.

lens to the sclera with 8-0 Gore-Tex or 6-0 prolene using what's called a belt-loop technique. If you don't want to use any sutures, you can use the Yamane technique, in which you bring the haptics of a three-piece lens outside through scleral openings, cauterize them to create a flange, and then lock the flanges in place within the sclera."

• ***Don't attempt IOL fixation without the right tools.*** "If you're going to do IOL fixation, you need to be comfortable doing pars plana vitrectomy and bimanual surgery, and you need to have the right lenses available to perform the surgery," says Dr. Donnenfeld. "If you have these skills and the right lenses, you can become pretty adept at these techniques fairly quickly."

• ***Don't expect any IOL-fixation procedure to be "one-size-fits-all."*** "The fact that there are so many options for fixating a lens tells you that there's no one ideal approach," says Kevin Rosenberg, MD, who practices at Retina Vitreous Surgeons of Central New York and is a clinical assistant professor of ophthalmology and visual sciences at SUNY Upstate Medical University, in Syracuse, New York. Dr. Rosenberg says that today he's largely transitioned to performing a modified Yamane technique using 27-ga. trocars. "I think that the Yamane technique is a really good procedure, but I'm constantly fine-tuning it. There are many ways in which it can be a little off. So the 'perfect' IOL-fixation procedure is still a work in progress."

Choosing the Right Implant

It's important to be cognizant of the limitations and advantages associated with the different lens options when the lens needs to be fixated.

Efrem Mandelcorn, BSc, MD, FRCSC, a researcher at the Krembil Research Institute, University Health Network, in Toronto, an attending surgeon at the Toronto Western Hospital and an associate professor at the University of Toronto, points out that not all lenses work equally well if you need to fixate them. "You don't want to pick a lens with flimsy haptics," he notes. "If the haptics are flimsy, there's a much greater chance that they'll bend or kink. I tend to favor Johnson & Johnson's AR40 Sensar lens; its haptics don't usually deform, helping to ensure a better outcome."

"Suture fixation comes with a number of limitations," notes Brandon D. Ayres, MD, a cornea specialist at Wills Eye Hospital and an instructor at Jefferson Medical College, Thomas Jefferson University in Philadelphia. "For one thing, you have to manage the sclerotomies and not get the sutures tangled. In addition, there are a limited number of implants that we can fixate, and those have limitations as well.

"For example, one of our favorite lenses to suture-fixate has been the Akreos AO60," he says. "This was a fairly easy technique to learn, very repeatable, and we saw very little inflammation in the eye. However, an eye that needs lens fixation tends to have more problems than an average eye, and if the patient ends up with a retinal detachment or needing a transplant, then we might have to use air or gas inside the eye. That turned out to be a problem, because we found that when we exposed that implant to air or gas, it could calcify. So we'd fix a dislocated lens; then three years later the cornea would decompensate and the patient would get an endothelial graft. Four months after that, the lens had calcium deposits that you couldn't dissolve or laser away. You had to remove the lens. So even though we had a great technique that seemed to be safe and repeatable, it came back to bite us.

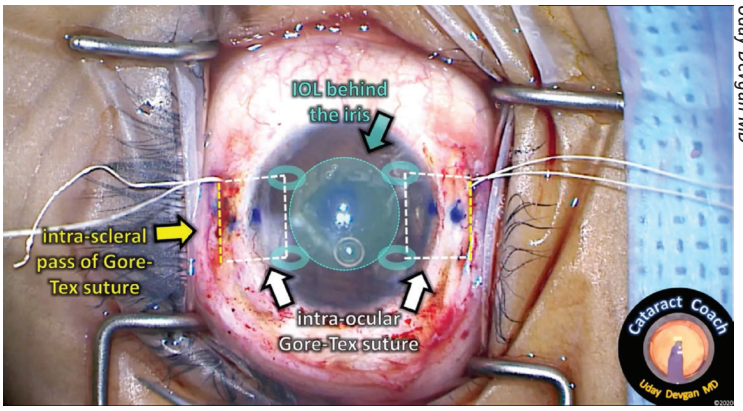
"The second lens we tried was the Bausch + Lomb MX60 implant," Dr. Ayres recalls. "The MX60 is a different shape, but we could lace a suture through what we call the haptic bridge, a little eyelet, if you will, right where the haptic inserts into the optic. Things looked pretty good and our results were nice, but we found that the haptic bridge would sometimes break, releasing the suture. So this lens didn't calcify, but if we tied the sutures too tight, the implant might dislocate again down the road.

"The third commonly sutured implant is Alcon's CZ70BD," he notes. "The CZ70 lens is a large, single-piece PMMA lens. Like the other options, it has advantages and disadvantages. It's very durable, and the haptics have little eyelets meant to help with lens positioning. We can lace a Gore-Tex suture

through those eyelets, allowing the lens to be held very securely. And because the lens is large, we don't have to worry about centration nearly as much. "The downside is that it's a 7-mm lens. That means you have to make at least a 7-mm wound, losing the advantages that come with making a small incision.

"However, if the patient has an anterior chamber lens that needs to be removed due to chronic inflammation or corneal edema, I tend to implant the CZ70," he says. "It takes a large incision to remove an AC-IOL. Since I already have to make a big wound, I might as well put a big implant back in."

Dr. Devgan adds that a lens with four haptics may achieve better fixation if fixated with sutures as opposed to the Yamane technique. "If you only have two points of fixation, one on each side, it's possible for the lens to tilt, like a hammock," he notes. "If I'm concerned about that, I'll use sutures and create four-point fixation. That will secure the lens in place, and there'll be no tilting or malpositioning of the lens. Bausch + Lomb's Akreos lens has four eyelets, making it especially good for securing in place."



Uday Devgan MD

An example of intrascleral placement of the sutures for IOL fixation. (A video of the technique shown above can be viewed at: https://cataractcoach.com/2022/10/17/1624-gore-tex-intra-scleral-iol-fixation/.)

Before Starting the Surgery

To avoid postop surprises:

• ***Warn the patient that their glasses prescription will most likely change after the surgery.*** "That's a side effect of the anterior or posterior displacement of the IOL from its original plane," Dr. Hoffman explains.

• ***Examine the patient at the slit lamp the day before surgery, or immediately before surgery.*** "I've had two patients who, for some reason, didn't appreciate that their vision had dropped to finger-counting because the lens had dropped onto the retina," Dr. Hoffman recalls. "Nothing is more frustrating than blocking a patient and then discovering in the OR that the case isn't operable from an anterior approach."

• ***Check the lens position with the patient reclining.*** "Have the patient lie back in the exam chair and look at the lens position with an indirect ophthalmoscope for illumination," advises Dr. Hoffman. "Sometimes the lens is in the proper plane when the patient is upright, but hanging by a few zonules when supine. If the lens is hanging or significantly displaced posteriorly in the supine position, you may need to coordinate the case with a retina specialist."

• ***Check the endothelial cell count.*** "The results are usually good no matter what lens you use," notes Dr. Ayres. "However, you have to watch your patient closely, and try to predict the future. Will this patient need additional retinal or corneal surgery later on? For that reason, I check the endothelial cell counts in all of these patients. You have to use that information to help you pick the implant that's going to be the best for that patient."

• ***Don't be afraid to refer these cases out.*** "These are complicated surgeries," notes Dr. Devgan. "If you know another surgeon can get a better result than you, there's no shame in referring the patient to that surgeon."

Dr. Ayres agrees. "If you don't do this procedure on a regular basis, you can quickly find yourself out of your comfort zone," he says.

• ***If you do refer out a patient, explain that you'll correct any remaining refractive error later.*** "I tell my retina colleagues which lens to implant in such a patient," notes Dr. Devgan. "I advise them to err on the side of leaving the patient a little myopic. Then, three months after the surgery, I'll do LASIK for these patients and make them '20-happy.' I tell the patient that it's like hitting the golf ball from the tee. The retina surgeon will get the ball onto the green. Once that heals in a few months, I'll do LASIK and sink the putt, so we'll get the patient to emmetropia."

Traditional Suture-fixation

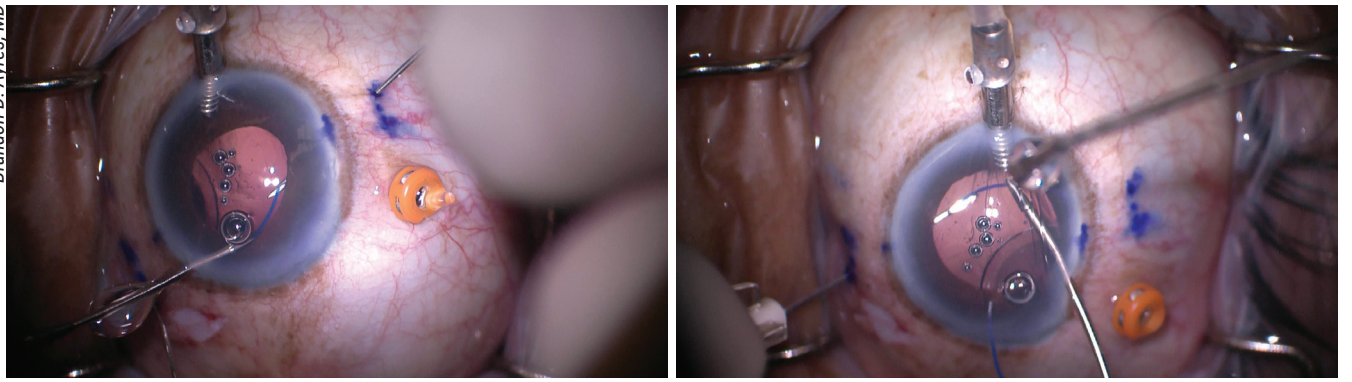
Surgeons offer these suggestions:

• ***Avoid using 10–0 Prolene in most patients.*** "We've found that 10-0 Prolene used for scleral fixation only lasts about 10 years," explains Dr. Devgan. "I wouldn't put that in a 40 or 50-year-old patient. It might be acceptable for a very elderly patient with a limited number of years left to live, but you want to make sure the sutures will last the patient's lifetime."

• ***Consider using a 27-ga. system for suturing.*** "This will have a lower risk of leakage from the sclerotomy sites," says Jason Hsu, MD, co-director of retina research at Wills Eye Hospital and an associate professor of ophthalmology at Thomas Jefferson University in Philadelphia.

• ***Consider making your clear corneal incision temporal or superotemporal.*** "I pull my Gore-Tex sutures out nasally and temporally," he explains. "If the incision is temporal or superotemporal, the IOL doesn't

Brandon D. Ayres, MD



When performing the Yamane fixation technique, the haptic is usually externalized by sliding it into the lumen of a needle, which is then used to pull it out. Surgeons note that because there's very little "wiggle room" inside the lumen, it's important to make sure that the haptic and needle are positioned so that they align properly *(above, left)*; if not, the haptic won't slide into the lumen *(above, right)*.

have to rotate as much when it's inserted. That makes it less likely to get twisted in the sutures."

• ***Be careful when threading the suture through an eyelet.*** Omesh P. Gupta, MD, MBA, who practices at The Retina Service of Wills Eye Institute and is an assistant professor of ophthalmology at Thomas Jefferson University Hospital in Philadelphia, notes that IOL breakage is a common complication when fixating an IOL. "To avoid this, pay particular attention to handling the IOL when threading the suture," he says. "Don't place an instrument into the eyelet."

• ***Make sure there's no resistance when passing through the sclerotomies.*** "Any resistance could cause eyelet fracture," Dr. Gupta points out.

• ***If you're externalizing sutures, only externalize one before inserting the IOL.*** "I recommend only externalizing the leading nasal Gore-Tex suture before inserting the IOL," says Dr. Hsu. "Externalizing all suture ends before inserting the IOL increases the risk of the IOL getting entangled in the sutures."

• ***Once you've externalized the nasal suture, keep it taut as you insert the IOL.*** "Loose sutures at this stage can cause the suture to go under the haptic of the lens, causing the IOL to tilt," Dr. Hsu explains. "You want both sutures above the plane of the haptics."

• ***Consider using the "handshake" technique to reduce the chance of sutures becoming twisted or tangled—and pass the proximal suture first.*** "In the 'handshake' technique we put the suture into the eye using microforceps, and then use forceps held in the other hand inserted through a sclerotomy to grab the suture and externalize it," explains Dr. Ayres. "When using this technique, we've found it's much easier to prevent suture twists and confusion if we pass the suture that's proximal to the surgeon first and the distal suture second."

Not every surgeon agrees that this is an ideal approach, however. "Trying to hand yourself the suture in the anterior chamber using another forceps can increase the risk of suture entanglement," says Dr. Hsu. "You may accidentally pull the suture out from under the plane of the IOL, causing it to tilt."

• ***When externalizing the trailing temporal suture after the IOL has been inserted, try pushing the IOL posteriorly.*** "Doing this allows you to see the Gore-Tex strands coming out of the eyelets in the IOL," explains Dr. Hsu. "At this point I insert my forceps through the corresponding temporal sclerotomy site and grab the suture as it emerges above the plane of the IOL."

• ***If you're using a 27-ga. system, take this into consideration when tying and burying the knot.*** "When beginning the procedure, mark the four sclerotomies well with an ink pen," says Dr. Hsu. "This will facilitate visualization of the smaller 27-ga. sclerotomies.

"Later, when you're ready to create your knots," he continues, "I prefer the slip knot technique with an extra throw (1-1-1-1), as the knot will tend to be smaller and easier to bury. Grab the knot with the 27-ga. forceps—I use Alcon's MaxGrip forceps—and directly dunk it into the sclerotomy that held the 27-ga. cannula, as this one will be more dilated."

• ***Make sure the suture material (most often Gore-Tex) is buried within the sclera and not just sitting under the conjunctiva.*** Dr. Devgan notes that leaving the suture just sitting under the conjunctiva can lead to exposure and breakage of the suture and a dislocated IOL. *(See Figure, p. 40.)* "A better method is to have intra-scleral placement of the suture so that it's secure for life," he explains. (A video of this technique can be viewed at cataractcoach.com/2022/10/17/1624-gore-tex-intra-scleral-iol-fixation/.)

• ***To avoid conjunctival erosion, reapproximate the conjunctiva away from the sutured IOL.*** "One of the most common complications when fixating an IOL is conjunctival erosion," Dr. Gupta points out. "I usually drag the conjunctiva inferiorly and incorporate a scleral anchor."

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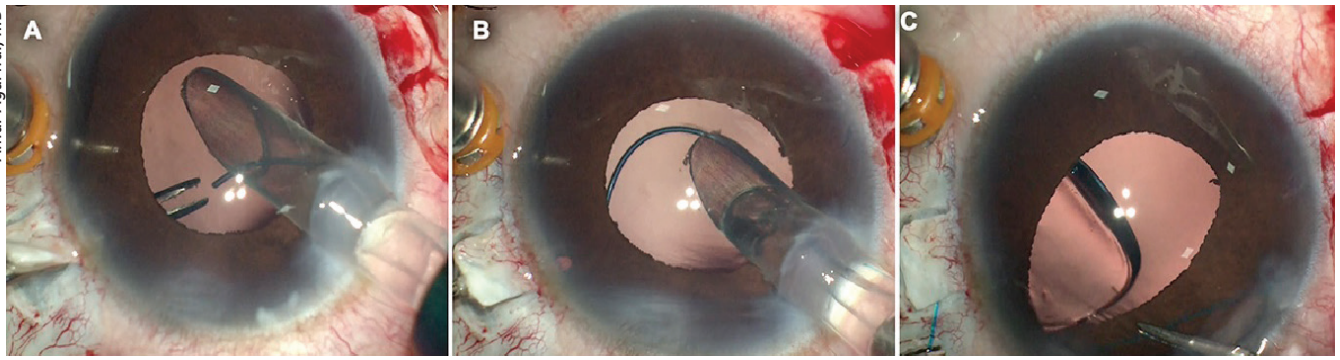


Above and facing page: The handshake technique being performed during the process of using glue to fixate an IOL. The handshake is being used to externalize the haptics for gluing. Surgeons note that the advantages of a glued IOL include stability; negligible tilt; there's no pseudophakodonesis; and there's no fear of suture erosion or irritation.

Gluing the IOL

Dr. Donnenfeld says he started out learning this technique and it's still one of his favorites. "I think this technique offers the best centration and the least rotation of the IOL," he says.

"To use this technique, you have to be comfortable creating a scleral pocket similar to what you'd create for a trabeculectomy," he explains. "You use an MVR blade to perforate through the sclera, through the pars plana to the anterior chamber, 2.5 mm posterior to the limbus. Then you perform a pars plana vitrectomy to prevent vitreous from getting entangled with the IOL.

"Next, you reach in with a microforceps and use the 'handshake technique,' where you hold the haptic of the IOL with one hand while using a microforceps held in the other hand to pull the haptic through the pars plana," he continues. "Then you perform an identical procedure on the opposite side, 180 degrees away. Finally you glue the flaps down with conjunctiva on the surface. This creates a nice planar IOL without rotation.

"There's a little bit more work involved in this technique because you have to make the scleral flaps and move the conjunctiva down, but it's a very good way to first learn to do IOL fixation," he concludes. "I think it's the least difficult technique to perform, and it's still one I like very much."

Using the Yamane Technique

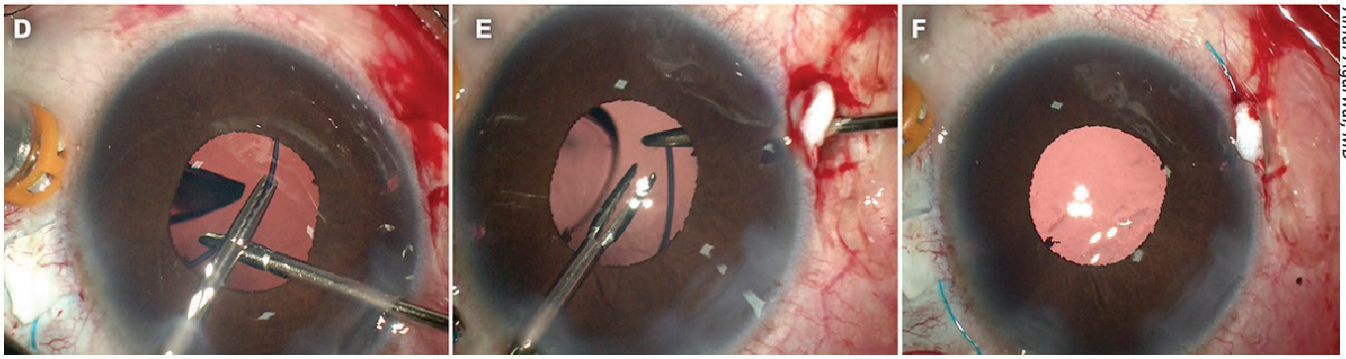
The Yamane technique, in which the haptics are externalized and cautery is used to create a flange at the tip of each haptic, has become increasingly popular in the past few years. "The Yamane technique doesn't require making a flap or gluing, although you still have to perform a thorough pars plana vitrectomy," Dr. Donnenfeld explains. "You pass a thin-walled 30-ga. needle through the sclera, 2 mm posterior to the limbus; then you extend it 2 mm into the sclera and penetrate into the anterior chamber. Next, you grab the haptic of the IOL and insert it into the 30-ga. hollow-bore needle, allowing you to withdraw the haptic. Once the haptic has been externalized, you use low-temperature cautery to create a flange that holds the lens in place so it can't fall back into the vitreous."

One advantage of Yamane noted by surgeons is the absence of suturing. "Suturing is more cumbersome for the surgeon," Dr. Mandelcorn points out. "Also, sutures can break early or late, and sometimes, suturing an in-the-bag IOL doesn't end up perfectly centered when you tighten each end. This forces you to add another suture in a third location, adding more time and uncertainty to the centration of the implant.

"It's true that all of this is less of an issue if you're using a CZ70 PMMA lens, which has eyelets in the haptics," he notes. "However, the CZ70 is a 7-mm IOL, so you have to make a large incision to use it. In contrast, if you set it up properly, a Yamane flange-fixated implant is generally well-centered at the end. After getting over the learning curve for the Yamane technique, I find that using it results in less worry about how the implant will settle at the conclusion of the case."

Dr. Ayres points out that, like the other options, the Yamane technique has advantages and disadvantages. "There's no need for multiple sclerotomies," he says. "You don't need peritomies, and it requires a smaller incision. Also, once you're good at it, it's pretty quick; you can often do a secondary IOL in 10 or 15 minutes. On the down side, it has a pretty steep learning curve. We often make it look easier in the videos than it is in real life. Also, tilt and decentration can be a challenge with the Yamane technique. Even in a carefully-measured-out surgical procedure, at the end the implant may not look right. That's really frustrating, because there may not be an easy fix.

"The best cure for a poorly centered IOL with this technique is prevention," he continues. "We do our best to make sure the lens is centered by being very careful with our measurements and making sure our sclerotomies are even on both sides of the eye. But if you do end up with the implant not properly



Amar Agarwal, MD

positioned, you might be able to pull one haptic a little further out, recut it and melt the end to create a new flange. However, this may not always fix the centration, and then you have to redo the procedure. That could mean cutting off the flange, pulling the implant back into the eye, moving the incision and externalizing the haptic again.

"Doing this is challenging and frustrating," he adds. "That's when you tend to get kinks and broken haptics. There have been times where it was so bad I just said, 'Forget it,' and we took the implant out, and tried again with a new one."

Yamane Pearls: Setting Up

Surgeons offer these suggestions to ensure the surgery goes well:

• ***Use an IOL with flexible haptics.*** "In theory, almost any three-piece IOL will work with this technique," Dr. Ayres says. "However, most three-piece implants available in the United States have haptics made of PMMA, which is a stiff plastic that can break if it's bent or kinked. So, we prefer to use Zeiss' CT Lucia 602 implant, not because the optics are necessarily better, but because its haptics are made of polyvinylidene fluoride. PVDF is very flexible, and the haptics are resistant to breaking and kinking. That makes it very durable in this situation."

• ***Do a complete vitrectomy.*** "When this technique was first described, the patients had had a full pars plana vitrectomy," Dr. Devgan points out. "Studies have shown that patients undergoing the Yamane technique have an unusually high risk of cystoid macular edema.[2,3] The Yamane technique involves twisting and turning the lens inside the eye, which can lead to strands of vitreous becoming entangled in the lens haptic or optic. That ends up putting traction on the macula, which can cause CME or even a retinal detachment.

"Today, surgeons sometimes use this technique with just a little bit of an anterior vitrectomy," he continues. "That may not be sufficient. We need to do a core vitrectomy to avoid these complications. That's why it's often better to refer a patient who needs to have a lens fixated to your vitreoretinal colleagues."

• ***Consider using a sub-Tenon's block.*** "When I'm doing a Yamane IOL I deliberately use a sharp needle block to minimize chemosis and excessive hemorrhage, as opposed to my usual scleral cut-down and peribulbar block with a blunt cannula," notes Dr. Mandelcorn. "That makes visualization of the sclera easier and helps when I'm making my scleral tunnels."

• ***Consider adding an angiocath cap to your needle instead of a syringe.*** "It's important to keep the eye pressurized with infusion to facilitate creation of scleral tunnels with the same orientation and angle on opposite sides," explains Dr. Mandelcorn. "If the needle doesn't have a cap on it, the infusion can leak out through the needle, leading to a soft eye. Putting a cap on each needle maintains a closed system and makes the technique easier."

Yamane: Performing the Surgery

During the surgery:

• ***Compare the bends in the needles outside of the eye.*** "When I'm bending the TSK needles, I compare them outside the eye before I place them, to ensure that the bend is at the same angle," says Dr. Mandelcorn. "This helps to maintain a consistent angle of the scleral tunnels on each side."

• ***Consider making peritomies before inserting the trocars.*** "In retina, we do a lot of transconjunctival insertions of ports," notes Dr. Rosenberg. "When performing Yamane, I make small local peritomies before I insert my 25-ga. trocars. That allows me easier access to closing the sclerotomies when I'm done."

• ***Make sure the haptics end up secured at the same level on both sides.*** "You don't really see where the 30-ga. needles enter the eye because you're doing it transsclerally," notes Dr. Donnenfeld. "If the needle is inserted a little bit more anterior or posterior on one side it will cause some IOL tilt. You also need to be sure the needle punctures are exactly 180 degrees apart."

• ***Consider creating a paracentesis 180 degrees from the sclerotomy.*** "This will help to optimize the direction of your 25-ga. microforceps, so the haptic can be grasped parallel to the 30-ga. needle," explains Dr. Donnenfeld.

• ***If iris capture seems possible, take steps to minimize the risk.*** "The risk of this is probably greater

if the iris has undergone trauma in the past or just seems floppy," notes Dr. Rosenberg. "If you suspect there's a risk of iris capture, you can do two things. First, you can do a peripheral iridotomy during the case, which I now do routinely. Second, you can consider placing your sclerotomies a little bit more posterior than normal. I usually place them 2 mm posterior to the limbus, but if I'm concerned about iris capture postop, I might place them 2.5 mm back. The idea is that if the lens isn't as close to the iris, there's less of a chance that iris capture will happen."

• ***Be careful during lens insertion.*** "Sometimes the inserter can damage the haptic of the lens during insertion," Dr. Rosenberg explains. "That can lead to postop lens tilt, so it's very important to make sure that the insertion is clean, and that you don't damage the haptic."

• ***Be careful if the cornea is cloudy or there's blood in the eye.*** "Inserting the haptic into the hollow-bore needle can be challenging, particularly when visualization isn't perfect," Dr. Donnenfeld points out.

• ***Be very careful about the angles at which you're holding the haptic and the needle.*** "You need to make sure that the needle and the haptic align properly so the haptic will slide easily into the lumen of the needle," explains Dr. Ayres. "The haptic is about 150 µm wide and the lumen is 200 µm. That means that there's only about 50 µm of 'wiggle room' for the haptic. If your angles aren't right, the haptic won't go into the lumen."

• ***Consider using a different-gauge needle on opposite sides of the eye.*** "I place a 27-ga. TSK thin-walled needle on one side and a 30-ga. needle on the other," says Dr. Mandelcorn. "I find that if I use a 30-ga. needle on both sides, the haptic is often very tight inside the lumen of both needles. I prefer to externalize one side at a time, although I know some surgeons pull both out simultaneously; having a little bit of movement in the needle lumen on one side avoids stretching the optic-haptic junction, which can lead to poor centration."

• ***When grabbing the haptic with your forceps, be sure to grab it at the very tip.*** "This will help prevent the haptics from kinking," explains Dr. Rosenberg.

• ***Hold onto the tip of the leading haptic (that already has a flange on it) when externalizing the trailing haptic.*** "This prevents internalizing the leading haptic back into the eye during the externalization of the trailing one," Dr. Rosenberg explains.

• ***Make sure the optic is centered before cauterizing the haptics.*** "This will allow you to adjust the centration of the IOL by positioning the haptics prior to cauterization," explains Dr. Donnenfeld.

• ***Turn off the oxygen before performing cautery.*** "There's always a risk of starting a fire in this situation," Dr. Mandelcorn points out. "There are three variables associated with intraoperative fire: high oxygen flow; any flammable substance around the site; and performing surgery above the Xiphoid bone. In this surgery, you're three for three—you have a high oxygen flow, you have flammable substances like Weck-cel sponges and the drape, and the cautery is being done on the eye. With conscious sedation you have a whole tent of oxygen right where you're administering cautery, so it's very important to make sure that the oxygen is turned off to reduce the risk of a fire. Using a low-temperature cautery also helps to mitigate this risk."

• ***Don't make the haptic flange too large.*** "If you make your flange too large, the top of it may end up externalized outside the sclera and conjunctiva," explains Dr. Rosenberg. "If that happens, you end up with a little visible nub. This may not cause any issues, but it doesn't look great and it creates the potential for endophthalmitis by opening a route into the eye. Fortunately, if this happens, the conjunctiva will eventually grow over the nub—although that can take as long as a year.

"It's best to avoid this by making sure your flange bulb isn't too big, so

THE AC-IOL OPTION

"An anterior chamber IOL can be a good alternative in these situations, especially for older patients in their 80s or 90s," says Efrem Mandelcorn, BSc, MD, FRCSC, a researcher at the Krembil Research Institute, University Health Network, in Toronto, and an associate professor at the University of Toronto. "Patients get their vision back very quickly and can often maintain good vision for the rest of their lives. Just remember a few basic pearls for AC IOL placement:

— Do things in the right order. "Remove the dislocated IOL, place Miochol, perform an iridectomy, then place the AC-IOL," he says. "An iridectomy prior to placement of the AC-IOL in the anterior chamber will prevent the iris from wrapping around the AC-IOL as a result of intraoperative pupil block. It makes things go much more smoothly."

— Be sure to place the right size IOL. "Once you've measured the white-to-white distance, add 1 mm," Dr. Mandelcorn notes. "You don't want the lens to be too big or too small."

— Place the iridectomy to the right of your corneal or scleral wound. "Haptics rotate clockwise, and you don't want to incarcerate a haptic in the iridectomy," Dr. Mandelcorn explains. "I've seen patients with chronic uveitis who have a haptic incarcerated in the iridectomy because the haptic was placed adjacent to the iridectomy. By placing the haptic to the right of your corneal wound as you rotate the AC-IOL clockwise, you minimize the risk of the haptic going through the iridectomy."

—CK

it fits within the 27-ga. sclerotomy," he concludes. "If you're not sure if this is going to happen, you can use a suture to close the conjunctiva overlying the flange tip so it's not exposed."

Yamane: Finishing Up

Last but not least:

• ***If the IOL isn't centered after using Yamane, try externalizing one haptic a little bit farther.*** Dr. Mandelcorn notes that it can be hard to grasp the haptic if it's already tucked into the scleral tunnel. "In that situation I'd use a sharp-tipped 30-ga. needle and just edge it out," he says. "Once it's out of the tunnel you trim it with scissors, and then re-melt it and create a new flange. That's probably the easiest way to deal with that situation."

• ***If the IOL tilts after Yamane, use a Prolene stitch to resolve the tilt.*** "I've had a couple of cases in which the IOL significantly tilted despite the fixation," notes Dr. Mandelcorn. "If that happens, one option is to remove the lens and start over. But another possibility is to pass a double-armed 10-0 Prolene suture through the sclera and behind the optic as a backstop to resolve the tilt. It's like a secondary pseudo-capsule that helps to keep the lens aligned. I've also adjusted significant tilt by placing a 9-0 Prolene suture through a haptic and its overlying iris to iris-fixate one end."

• ***Consider suturing any vitrectomy sclerotomies to reduce the risk of hypotony.*** Dr. Rosenberg notes that when he was first using Yamane, the eye would sometimes develop hypotony after the case. "You're putting five holes in the eye," he points out. "You're creating three holes for the vitrectomy ports and two additional sclerotomies for the 27-ga. trocars used to perform Yamane. To compensate for that, I've transitioned to suturing my three sclerotomies from the vitrectomy ports. Doing that has definitely reduced my rate of hypotony."

IOL Fixation: General Advice

These strategies apply to any fixation technique:

• ***Proceed slowly when fixating a lens.*** "When I'm teaching fellows to do this, I always tell them to slow their movements down significantly," says Dr. Mandelcorn. "If you perform a step too quickly, or don't pause to check it, you could break or bend something and your final result will be much worse."

• ***Make sure you do a careful pars plana vitrectomy.*** "This should be done under direct visualization using a 25-ga. vitrector to separate the vitreous from the IOL," says Dr. Donnenfeld. "Take care to avoid causing vitreous traction. It may help to use intracameral triamcinolone to demarcate the vitreous."

• ***Always try to fixate both haptics.*** "Fixate both haptics to the sclera if possible," says Dr. Hoffman. "If you fixate only one haptic, the other side of the IOL may eventually come loose, requiring a return to the OR."

• ***Consider learning one of the new suture-fixation variations.*** Dr. Ayres notes that the latest variations on suture fixation, in which the externalized ends of the prolene sutures are melted to create a flange that keeps them from prolapsing into the eye (instead of melting the tip of the haptic) have some advantages.

"Tying a knot with a Gore-Tex suture and burying it in the sclera is kind of a pain," he observes. "Just melting the end of a 4-0 or 5-0 Prolene suture is much easier. The Canabrava and McCabe techniques both use this idea. They're worth considering as your surgical option in these situations."

"The three major techniques used for scleral fixation are the glued IOL, popularized by Amar Agarwal, the Yamane techniques and the Canabrava technique," says Dr. Donnenfeld. "The Canabrava technique uses an IOL with eyelets. Dr. Canabrava passes a 5-0 prolene monofilament suture through the eyelets of the IOL and externalizes them; then he creates an external flange on the end of the suture using cautery, very similar to the Yamane technique. The difference is that instead of externalizing the haptic you're externalizing the 10-0 prolene which is attached to the haptic. I've noted that many retina surgeons like this technique and use it fairly often when they perform an IOL exchange."

"I'm accustomed to working with Gore-Tex sutures, so I haven't felt the need to adopt these variations," Dr. Ayres adds. "But for some surgeons who may not be as familiar with Gore-Tex suturing, or don't have access to Gore-Tex sutures, these newer techniques are very applicable. They reduce the spaghetti, meaning there's less suture to twist or tangle in the surgical field. They simplify things a little bit."

• ***Pick one technique that you're comfortable with and then get very good at it.*** "Many different IOL-fixation techniques are available today," Dr. Donnenfeld concludes. "They vary significantly in terms of surgical skill and results, but they all involve a learning curve. So it makes sense to get good at performing one technique first. Then you can try to expand your repertoire and learn other techniques as well."

Dr. Ayres agrees. "Not everybody has the kind of patient volume that makes it worth being good at three or four different techniques for suture fixation," he says. "That's why it makes sense to find one that you feel comfortable doing and stick with it."

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BEST PRACTICES FOR MANAGING EBMD

A look at the tried-and-true methods for treating this common condition, and how to handle the unexpected.

LIZ HUNTER
SENIOR EDITOR

Epithelial basement membrane dystrophy is estimated to affect approximately 2 percent of the population, establishing it as the most common corneal dystrophy.[1] Perhaps because of its high incidence rate, EBMD is relatively recognizable, and ophthalmologists have found reliable treatment methods. However, there's always the chance of something unexpected happening, so we spoke with cornea experts about the standards of care for EBMD and why you should remember to approach each case individually.

Recognizing EBMD

One of the first things to know about EBMD is that it can have more than one name, yet they all represent the same condition, says Gerami Seitzman, MD, an associate professor of ophthalmology at the University of California, San Francisco.

"In addition to those who abbreviate it as EBMD, others refer to it as corneal anterior basement membrane dystrophy, or ABMD. Often, it's referred to by its descriptive sign from the slit lamp: map-dot-fingerprint dystrophy; and if the prominent component of the examination are the dots of the map-dot-fingerprint dystrophy—it would be almost like a dot dystrophy—that's called Cogan's microcystic epithelial dystrophy. They all mean the same thing," Dr. Seitzman says.

"When we're talking about this dystrophy that has all of these names, we're talking about a disorder of the attachment of the corneal epithelium to the underlying structures," she continues.

It can occur for a number of reasons, whether idiopathic or sporadic, and occasionally there's a genetic cause, Dr. Seitzman says. "The bottom line is, we don't truly understand the mechanism of why it develops, but interestingly, the findings of EBMD are common in the general population. The estimates vary, but with careful observation at the slit lamp, it really is present in many people."

In fact, a thorough slit lamp exam is one of the most valuable steps in identifying EBMD. "A lot of people sort of rush at the slit lamp. They don't take the time to see it, because there are some little special tricks of lighting, such as indirect illumination, that often highlight the epithelial abnormality best," continues Dr. Seitzman.

The good news is that the vast majority of people are totally asymptomatic, and no treatment is needed, she says. But this can be tricky when it comes to cataract or refractive candidates.

Angela Zhu, MD, who practices at the Bascom Palmer Eye Institute in Miami, says screening for EBMD is important for anyone undergoing refractive surgery. "Patients are going in expecting perfect visual outcomes, but because the pathology in this disease is that the epithelium doesn't attach as well in the areas that are affected, or to the basement membrane, a procedure such as LASIK can actually worsen the condition," she says. "We see patients come in after LASIK surgery with previously undiagnosed EBMD who are now experiencing severe recurrent corneal erosions, severe

This article has no commercial sponsorship. **Dr. Seitzman** is a consultant for Dompé Pharmaceuticals. **Dr. Zhu** is a consultant for Santen Therapeutics and an advisor for Eliksa Therapeutics.

pain, and ongoing symptoms which can obviously affect their vision and become a problem."

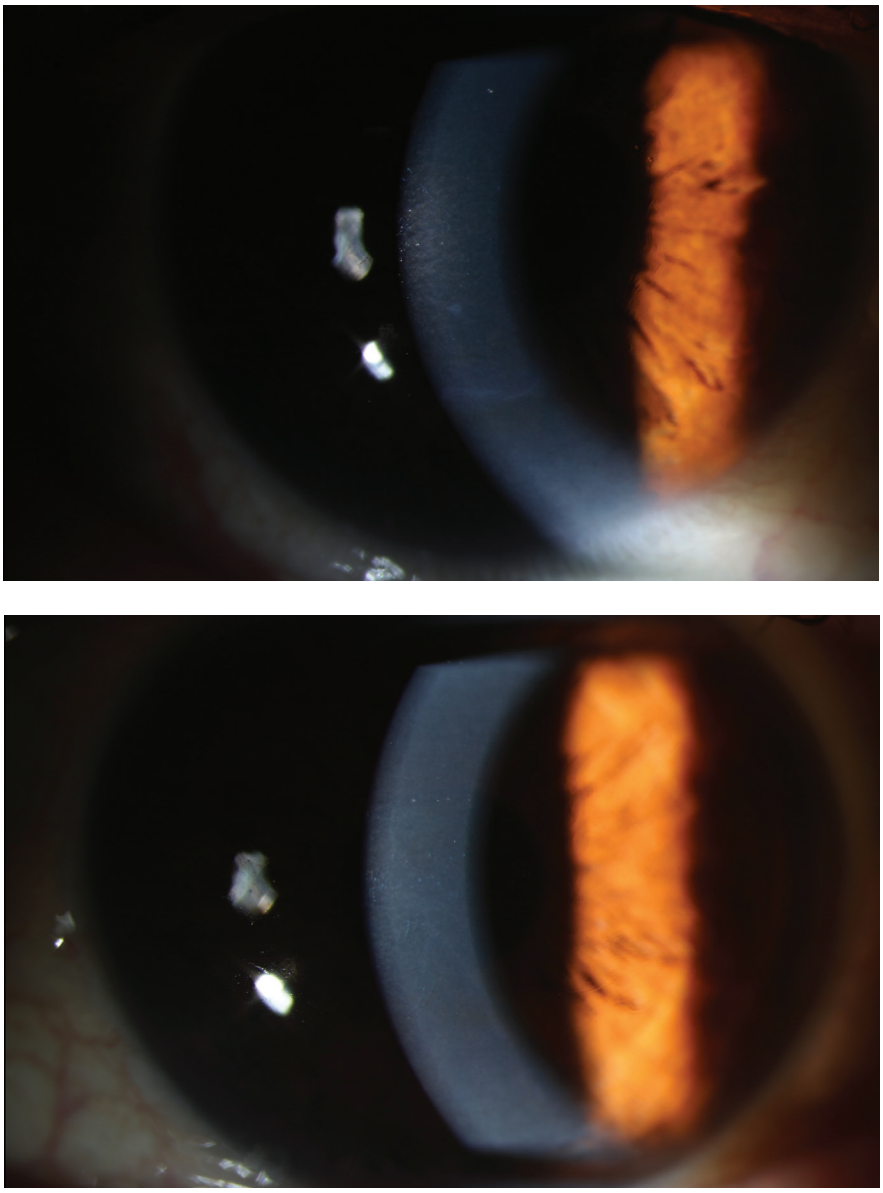
Calculations for cataract surgery may also be affected, Dr. Zhu continues. "EBMD can affect the regularity of the surface of the cornea, so the power calculations for the IOL implants may not be as accurate. Or, patients may still have other distortions in their vision afterwards, and they're unhappy after surgery."

For those who do experience symptoms, decreased vision isn't the most common problem. Instead, the most common and most painful symptom of EBMD is recurrent corneal erosions.

"This happens because the eyelids get hold of these tiny irregular ridges from the irregular attachment of the epithelium to the underlying cornea. The eyelid can hook onto these areas of corneal epithelial irregularity and scratch the cornea," says Dr. Seitzman. "Any defect in its outer layer causes a tremendous amount of pain and tearing. Classically, recurrent erosion syndrome occurs in the morning. Though it can occur at any time of the day, typically, when your eyelids have been closed for the whole night, that leads to more opportunity for the eyelid to stick to these ridges. So, the classic symptom is that the patient says: 'When I wake up in the morning, it feels like my eyelids are stuck to my eyeballs, and when I force them open I feel terrible pain and have a ton of tearing.' "

Dr. Seitzman notes that these open defects can put patients at risk for corneal ulcers if the tear is infected.

"[In patients with vision complaints] there are ridges and whorls and dots over the patient's pupil. They don't have pain at all, but they have blurred vision because, instead of light coming into the pupil in a perfect straight line to the back of the eye to be registered as sight, these little ridges and dots can induce irregular astigmatism," says Dr. Seitzman. "These irregular areas of epithelial attachment over their pupil can register as blurry vision or shadow vision or little halos when they're looking straight ahead at an object."



Angela Zhu, MD

Under slit lamp examination, the textbook presentation of EBMD is the descriptive map-dot-fingerprint dystrophy. Here, you can see a central "dot" (top) with an inferior "map line," and central "map/fingerprint lines" (bottom).

Other subtle early signs may be similar to dry eye, meibomian gland dysfunction or blepharitis, Dr. Zhu adds.

How to Treat EBMD

According to Dr. Zhu, EBMD is one disease where there haven't been too many notable advances in treatment, for good reason. "The treatments that have been established actually work very well," she says.

She says EBMD treatment is a stepwise approach. "If the patient is rarely symptomatic, maybe one or two episodes a year or just a very rare kind of symptomatology in terms of the recurrent dry eye, then we may just treat it with recurrent lubrication and preventative measures," she says.

Dr. Seitzman says patients can

use a thick ointment on the inside of their eyelids before bed at night, which forms a mechanical barrier between the corneal epithelial layer and the eyelid. "Some patients use this ointment for the rest of their lives or for a prolonged period of time and they're fine," she says.

There's some debate whether the ointment or similar lubricating drops should have salt in them, Dr. Seitzman continues. "The most common over-the-counter ointment is Muro, which is 5% sodium chloride. Some people think using this dehydrates the skin, allowing it to adhere better to the cornea," she says. "However, we don't have definitive large, randomized, control trials to show that any recurrent erosion treatment is better than another. Often what happens is the treatment has to be tailored to the individual patient and their unique presentation."

It may also be wise to include a steroid and oral doxycycline, Dr. Seitzman says. "When you have recurrent erosion on the cornea, the ocular surface becomes quite inflamed. That becomes a cycle of further erosion, meaning when you have high levels of inflammatory proteins and cytokines in the tear film, that further disrupts the attachment of the epithelium to the underlying corneal tissue," she says. "So not only do the corneal erosions themselves become inflammatory, but if you have other external disease conditions, commonly blepharitis or allergic conjunctivitis, and you already have an inflammatory ocular surface, the combination of all of this inflammation really inhibits epithelial adhesion."

A retrospective single-observer case study published in 2008 looked at 21 patients with recurrent corneal erosion syndrome who were treated with 50 mg oral doxycycline twice a day, and topical fluorometholone 0.1% three times daily for a minimum of four weeks. At eight weeks, 15 were symptom free and all but one patient reported improvement in symptoms.[2]

"It's very common as a medical therapy that we place patients on a steroid drop and oral doxycycline," says Dr. Seitzman. "That combination is quite anti-inflammatory for the ocular surface. With medical therapy alone, many patients can have improved comfort without needing surgery."

If topical treatments aren't successful, it's time to explore surgical treatment, of which there are various options.

> **"It's very common as a medical therapy that we place patients on a steroid drop and oral doxycycline. That combination is quite anti-inflammatory for the ocular surface. With medical therapy alone, many patients can have improved comfort without needing surgery."**
>
> ***— Gerami Seitzman, MD***

"In general, a surgical treatment requires removal of the loose corneal epithelium and some procedure where the underlying tissue is roughened a bit," Dr. Setizman says. "This roughening can cause micro scar tissues, and scarring promotes adhesion."

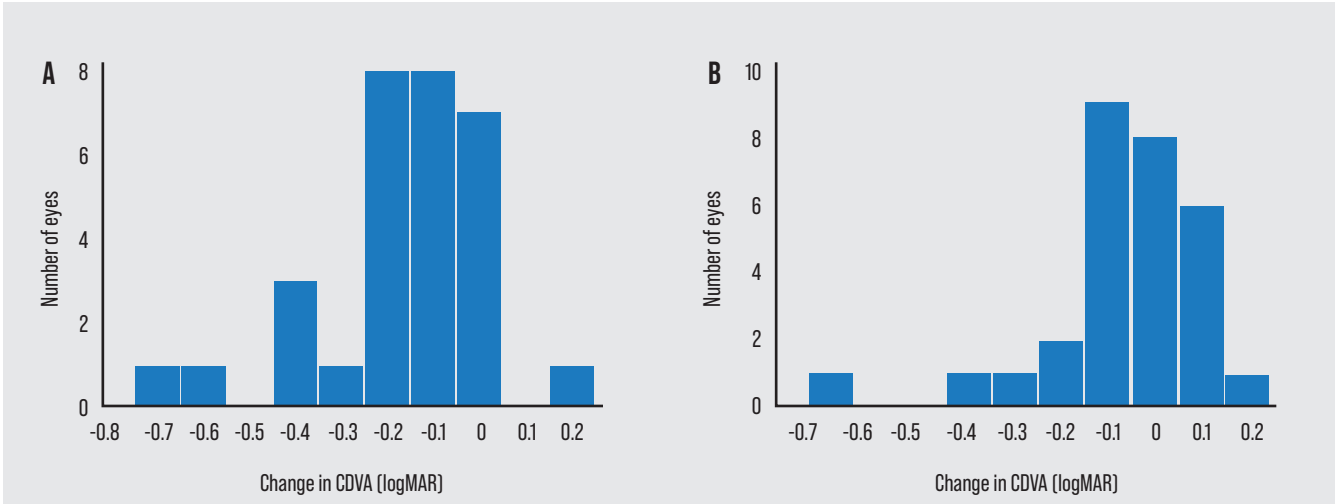
There are two routes to go: either superficial keratectomy or phototherapeutic keratectomy. Both have been shown to have similar outcomes, perhaps making the decision a matter of personal surgeon preference. A 2002 study comparing PTK to SK with a diamond burr showed no statistically significant difference in symptoms returning or BCVA. However, the study authors hypothesized that diamond burr treatment may have an advantage, due to it being simpler and less expensive.[3]

Dr. Zhu says it can often come down to ease of scheduling. "I think it can depend on your practice, where you're located in the United States, and what's covered by insurance," she says. "So the ability to send patients to a minor procedure room in your office where you essentially scrape the epithelium or go an extra step and do an anterior stromal puncture or diamond burr polish to roughen it up a bit may be preferable." After the procedure, a bandage contact lens is placed over the eye to promote adherence of the cornea without the lid disrupting the growth of the new corneal epithelium.

"The last type of surgical treatment is PTK, which is a very superficial excimer ablation of the top layer of the cornea, which promotes these micro scars from the laser essentially, and roughens up that area," Dr. Seitzman says. "It can only be done in the central cornea, usually within the central 8 or 9 mm of the cornea."

"Again, this is a little bit surgeon-preference and insurance dependent," emphasizes Dr. Zhu. "Each approach has its own individual risks, but I think in general, most of us prefer starting with epithelial debridement and anterior stromal puncture and diamond burr polish. Then, if there are recurrent cases, we move to PTK. Sometimes, if it's in the very central visual axis, or if we're already planning another refractive surgery procedure, or if there's also prolonged haze in that area that's already causing scarring, that's when I would jump to PTK first."

As previously mentioned, undiagnosed EBMD could pose a challenge for cataract and refractive surgery. If a LASIK candidate is found to have asymptomatic EBMD, Dr. Zhu recommends considering PRK instead. "With PRK,



Notes: The x-axis represents the change in CDVA in logMAR (0.1 logMAR =1 Snellen acuity line) between preperative and postoperative measurements, with negative values cor-responding to improved CDVA.

Figure 1. Patients treated with PTK for visual disturbances (Graph A), had a mean final postop CDVA of ~20/25, with 14 eyes gaining ≥2 lines of visual acuity. Those who underwent PTK for painful recurrent erosions (Graph B) had a mean final postop CDVA of ~20/20.[1]

you debride the epithelium, which is one of the fundamentals of treating this disease, so it offers a better alternative," she says. "If surgeons just consider a slight change in their planning, it can essentially still lead to good outcomes and simultaneously treat this disease."

Both Dr. Seitzman and Dr. Zhu say it's important to address each case individually. "Even though the literature shows good efficacy for these treatments, there are also cases where it doesn't work for some patients, and it's hard to say which ones it will or won't work for," says Dr. Zhu.

"Some patients do really well with just one of the treatments that we discussed, while some patients actually have to cycle through more than one," Dr. Seitzman says. "As with many eye conditions, it's really hard to create a general rule for patients who have other diseases. For example, in ocular rosacea or atopic eye disease where there's a lot of inflammation, that inflammatory ocular surface can promote more erosion. If one treatment doesn't work, we can use another, and many times we use many at the same time. So, if it's a very severe case, we may be talking about a surgical procedure but, at the same time, we're also treating it with steroids and doxycycline, and all of these procedures can be repeated."

Final Considerations

Dr. Zhu thinks general practitioners should keep EBMD on their differential.

"If patients say they're always waking up feeling like their eyes are more dry, or every once in a while they wake up with significant pain, or they still feel like their vision isn't quite that sharp all the time after refractive or cataract surgery, it's worth taking another look and seeing if this underlying condition is actually causing their problems," says Dr. Zhu. "Sometimes it's easy to forget about EBMD because the signs can be very subtle, especially in the setting of the more common day-to-day dry eye, meibomian gland dysfunction and blepharitis type of issues."

It's also important not to confuse EBMD with other disorders or diseases, says Dr. Seitzman.

"The corneal epithelium can only heal properly if there's adequate corneal sensation," she says. "Sometimes, a non-healing corneal defect can be misattributed to EBMD when the underlying disorder is actually neurotrophic keratopathy. EBMD often occurs with neurotrophic keratopathy, and that gets a little trickier to heal because you really do need corneal sensation to promote adequate corneal healing."

The pattern of healing could even be mistaken for herpes keratitis, continues Dr. Seitzman. "When you have an erosion in a patient with EBMD and the skin is healing, it heals in a funny/irregular pattern that can sometimes appear linear, and can also sometimes be misdiagnosed as herpes, because we associate herpes infections with linear shapes on the cornea. Sometimes, however, a healing EBMD erosion can heal in a linear pattern and mimic HSV keratitis." ◀

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Worms in the Eye: DUSN

A discussion of the etiology of this disease, and how to diagnose and treat the rare patient that might present with it.

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Though diffuse unilateral subacute neuroretinitis is a rare condition, it has a long history in the medical literature. Since 1952, multiple cases of unilateral vision loss with subretinal roundworm have been reported. Diagnosing DUSN can be a challenge, since patients can be asymptomatic in the early stages and the worm is visible in less than half of all cases. Here, we'll break down the etiology of DUSN, how it causes vision loss and the ways you can confidently diagnose and treat it if one of your patients presents with it.

Etiology

In a 1978 paper, J. Donald M. Gass, MD, and Ronald Scelfo, MD, proposed the term DUSN, instead of "unilateral wipe-out syndrome" for patients with evidence of severe central and peripheral vision loss, associated with retina and optic nerve inflammation.[1]

The primary cause of DUSN remained unclear until motile subretinal nematodes were found in two patients in 1978.[2] In 1983, Dr. Gass and Robert Braunstein, MD, presented further evidence proving that different species of nematodes play roles in the pathogenesis of DUSN.[3] Research has since been done to identify the nematodes involved. In one study, Eduardo Cunha De Souza, MD, and Yasuyuki Nakashima, MD, recovered the nematode through aspiration of subretinal material. However, the material subsequently deteriorated, making a confirmatory histopathologic investigation impossible.[4] Newer techniques such as polymerase chain reaction amplification and sequencing analysis can be used to identify the nematode if the worm can be recovered from the eye.[5]

Due to the lack of specific serologic testing or stool examination, diagnosis of the etiologic agent of DUSN is mostly based on a combination of clinical, morphological and epidemiological information. Most of the reported cases are infected by two different sizes of worms: small worms (400 to 700 µm), including *Toxocara Canis* and *Ancylostoma Caninum*; and larger worms (1,000 to 2,000 µm), including *Baylisascaris Procyonis*. Larger nematodes (4,500 to 17,000 µm) have rarely been reported in the literature.[6,7] Smaller worms are more commonly seen in the southeastern United States, Caribbean Islands, Latin America and South America. Larger nematodes are endemic in the northeastern and midwestern United States.[8] However, nematode species are not restricted to endemic areas and occasional cases have been reported worldwide.

Pathogenesis

DUSN mostly affects healthy children and young adults with no past ocular problems. It usually involves one eye, though reports of bilateral cases are found in the literature.[9] Infection is usually through the fecal-oral pathway. After entering the body, larvae migrate to the subretinal space, where they may spend months or years without changing size or shape. The worm's migration through the retina, coupled with released toxins and subsequent inflammatory reaction, is thought to play role in the pathogenesis of DUSN and cause damage to the inner and outer retina.[8]

Clinical Manifestation

In the early stage, most patients are asymptomatic with or without central or paracentral scotoma. Acute unilateral visual loss may occur due to vitritis and optic disc edema. Recurrent multifocal regions of white-yellowish evanescent lesions in the outer retina and choroid are common at this stage and are attributed to reactions to the presence of nematode in the subretinal space. These lesions are typically concentrated in one segment but can migrate to other areas based on the worm's location and movement. Lesions usually disappear within a few weeks and can leave persistent scarring and retinal pigment

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mottling.[10] Longer worms are more likely to leave tracts of RPE clumping, whereas shorter worms cause atrophic chorioretinal scars.[11] Less common abnormalities in the acute phase include ocular discomfort, congestion, iridocyclitis, subretinal hemorrhage, serous exudation, macular cysts, perivenous exudation, local retinal detachments and choroidal neovascularization.[12,13]

In the late stage of DUSN, patients may present with degenerative changes in the retina, particularly in the retinal pigment epithelium. As the disease progresses, retinal vessels become narrow and progressive ganglion cell loss occurs, leading to optic atrophy and profound vision loss. Additional signs of DUSN include an afferent pupillary defect, mild to moderate form of vitritis, increased internal limiting membrane reflex (Oréfice's sign), multiple choroidal lesions and subretinal tunnels (Garcia's sign).[8,14,15]

Diagnosis

A definitive diagnosis of DUSN is, of course, seeing the worm in the eye. However, patients with clinical and diagnostic features of the disease without visualization of the worm are also classified as presumed DUSN. The worm is visible during eye examinations in only 25 to 40 percent of cases as a motile, white, glistening nematode that tapers at both ends. The examination light may cause the worm to coil and uncoil slowly or, less frequently, it may slither snake-like in the subretinal space, making it more visible. The most common location for finding the worm is the posterior pole, near the edge of the gray-white lesions. There's also a higher chance of identifying the nematode in younger individuals.[8] In cases with unilateral chorioretinitis, specialists need to maintain a high level of suspicion and perform meticulous serial exams to detect the worm in this rare condition. Scanning laser ophthalmoscopy with high-contrast images and ultra-widefield photos could also be helpful in identifying the worms.[16] Moreover, a recent study by the U.K.'s Simrat K. Sodhi, MD, and co-workers suggested that using a blue-light laser would cause the worm to move around, helping the clinician detect its location.[17]

The following tests are helpful when faced with a possible DUSN patient:

The examination light may cause the worm to coil and uncoil slowly or, less frequently, it may slither, snake-like, in the subretinal space, making it more visible.

• ***Fluorescein angiography.*** Focal white-gray lesions demonstrate an early hypofluorescence followed by late staining. This might be accompanied by dye leakage around the optic disc or in a perivenous pattern. As the disease progresses and RPE loss becomes worse, fluorescein angiography manifests increased background choroidal fluorescence and a window defect.[11]

• ***Indocyanine green angiography.*** Early-stage DUSN is characterized by hypofluorescent dark spots, some of which are persistent, and others that become isofluorescent in the advanced stage. Persistent dots are most likely caused by full-thickness choroidal infiltration preventing ICG diffusion, whereas isofluorescent areas are partial-thickness lesions that gradually get encircled by the dye of surrounding tissues.[18]

• ***Electrophysiologic testing:*** Autoimmune, inflammatory, and/or toxic insult to the retinal bipolar cells can cause a mild to moderate decrease in rod and cone function, with the b-wave being more affected than the a-wave. Patients with DUSN exhibit a negative electroretinogram, which is evidenced by a flat, below-normal response of the b-wave and a decline in the b-wave to a-wave ratio.[18]

• ***Visual field studies.*** Various patterns of visual field loss have been reported, which correspond to the areas of chorioretinal lesions.

• ***OCT.*** All retinal layers can be impacted in DUSN. Neuroretinal atrophy, loss of the inner retinal layers, and hyperreflectivity of the regions affected by the worms have been reported.[11] Some studies have demonstrated progressive atrophy in retinal nerve fiber layers associated with poor visual outcomes in the affected eye.[19] En face OCT scans may provide clear visualization of the worm and highlight hyporeflective, well-delineated sections, representing vitreous lacunae created by the worm movement.[17] OCT angiography can also be used in the diagnosis of DUSN by detecting the worm's movement. Because nematodes lack blood vessels, however, they can't be identified while they're motionless.[20]

• ***Blood and stool test.*** Mild eosinophilia can be seen in patients. However, no specific change in the serologic, peripheral blood smear and stool examinations is seen and these tests have little diagnostic value in DUSN.

Treatment

When the worm is localized, laser photocoagulation can be used to kill, barricade or stop it from moving and causing further damage. To avoid a central scotoma and visual field defect, laser treatment should be administered distant from the fovea. To achieve this, a very low laser intensity or light application can cause the worm to flee to the periphery and be eliminated with minimal collateral harm.[12] In cases with no detectable worm, patients are best treated by a combination

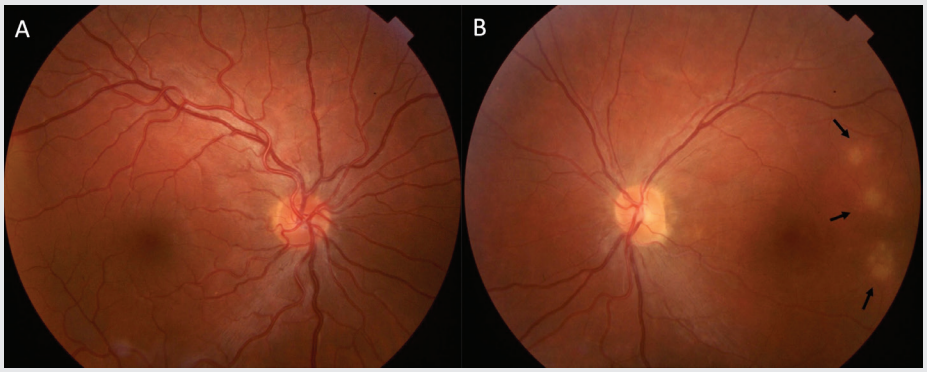

Figure 1. Fundus images of the right (A) and left (B) eyes. Multiple hypopigmented chorioretinal lesions were noted temporal to the fovea in the left eye (arrows).

CASE REPORT

A 23-year-old man from Uruguay presented to the clinic with progressively worsening white cloud in vision in the left eye (OS) starting two years prior. Patient denied eye pain or redness. On examination, the best-corrected visual acuity was 20/20 in the right eye and counting fingers in the left. Intraocular pressure was normal. There was a left relative afferent pupillary defect. Retinal exam of the right eye was unremarkable and in the left eye multiple hypopigmented chorioretinal lesions were noted temporal to the macula (Figure 1). Further investigations revealed significant

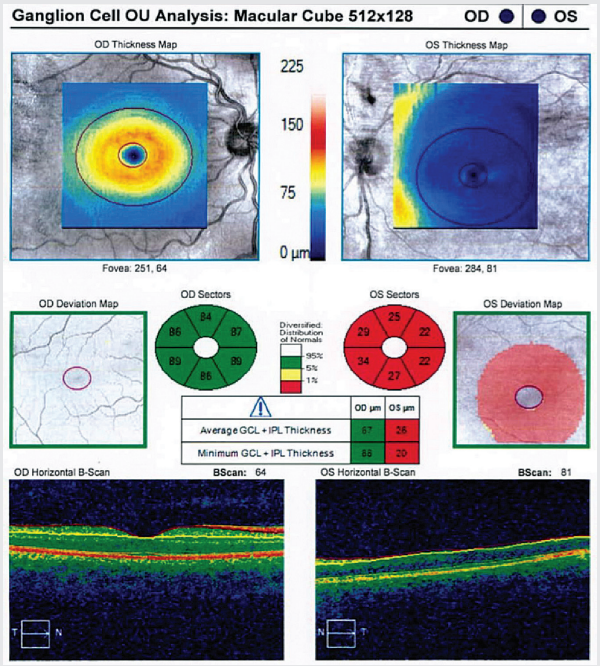

Figure 2. OCT scan shows significant thinning of the retina and loss of macular ganglion cells.

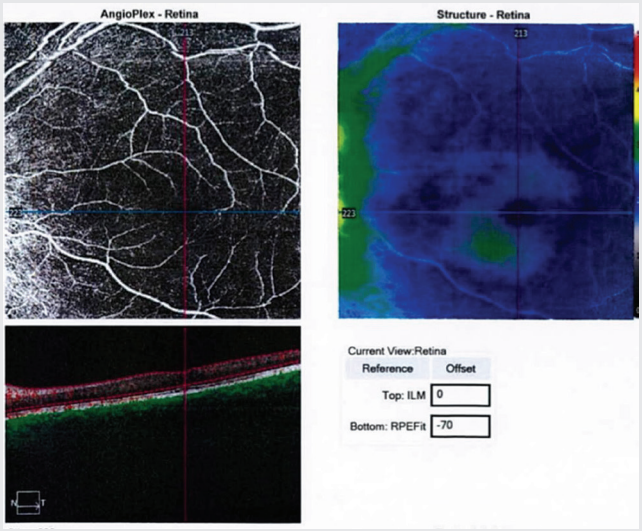

Figure 3. OCT angiography of the left eye shows retinal thinning and mild decrease in retinal vascularity.

of oral anthelmintic drugs, corticosteroids and scattered laser photocoagulation. The oral anthelmintic albendazole crosses the blood-retinal barrier more efficiently than thiabendazole and demonstrated remarkable results in DUSN patients. In one study, after receiving albendazole for one month, patient's visual acuity improved from counting fingers to 20/30.[21] Corticosteroids may also be used to reduce inflammation, particularly following the nematode death. The dosage and duration of treatment with anthelmintic drugs remain unclear. Most studies have suggested 400 mg/d oral albendazoles for 30 days. However, short-term albendazole combined with steroid therapy has also been proposed.[22]

Prognosis

If the patient is diagnosed and treated at the early stages, visual acuity might be preserved. However, diagnosis is delayed in most cases, which can result in permanent visual field loss. It's important for ophthalmologists to keep DUSN in mind as a differential diagnosis of unilateral (or bilateral) vision loss and chorioretinitis in young patients from endemic areas. Serial examinations along with other diagnostic methods are helpful for early diagnosis and the prevention of poor outcomes.◀

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thinning of the retina OS on optical coherence tomography and mildly decreased flow on OCT angiography (Figures 2 and 3). Systemic work-up was performed which revealed a negative venereal disease research laboratory (VDRL) test and interferon-gamma release assay for tuberculosis. With the working diagnosis of diffuse unilateral subacute neuroretinitis, the patient received 400 mg/d of oral albendazoles. Fundus examination performed a month later clearly localized the worm, which was then barricaded with laser photocoagulation (Figures 4 and 5).

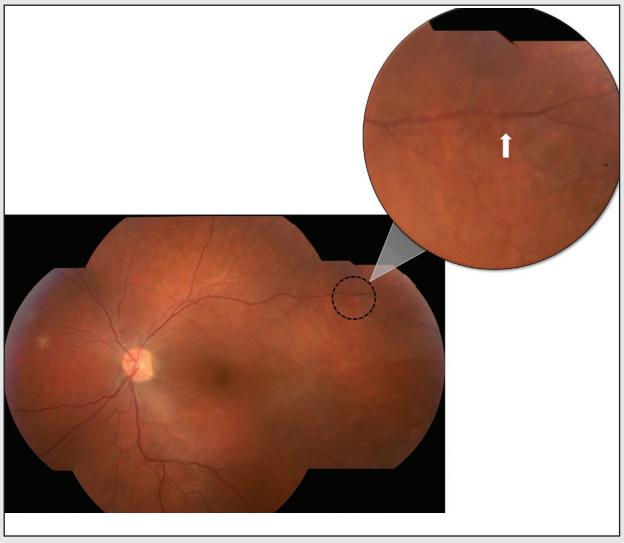

Figure 4. One month after treatment with systemic antihelmintic medication, examination of the left eye reveals the worm's location adjacent to a blood vessel (arrow).

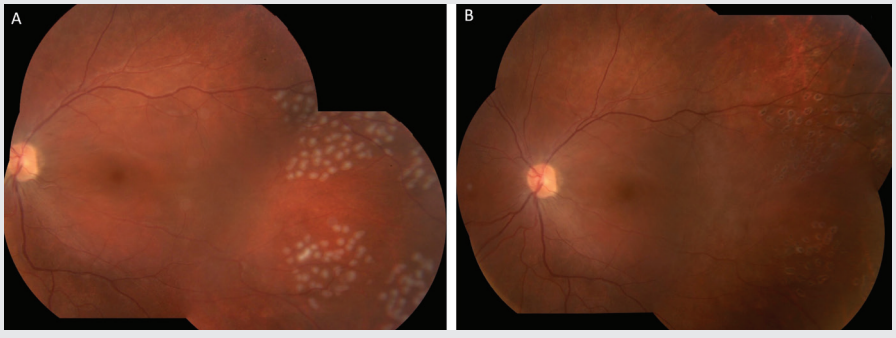

Figure 5. Laser photocoagulation was applied to barricade the worm (A), retinal exam one-month after laser application shows stable disease without further dissemination of chorioretinal lesions (B).

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PRODUCT NEWS

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

GLAUCOMA MEDICATION

A Generic Version of Zioptan Now Available

If you or your patients have been looking for a new generic glaucoma option, Prasco, through its partnership with Thea Pharmaceuticals, recently began marketing tafluprost ophthalmic solution 0.0015%, which the company says is therapeutically equivalent to Merck's Zioptan.

Like similar drugs, the companies note that tafluprost 0.0015% can cause increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes, as well as an increase in the length, thickness and number of lashes. Other prescribing information on the new generic, including possible adverse events, can be found at theapharmainc.com.

DRY EYE

Take on MGD Singlehandedly

When evaluating patients with symptoms that suggest possible meibomian gland dysfunction, a thorough examination of both the upper and lower eyelids is crucial to detect and assess the condition. A new eyelid eversion tool called the Meivertor aims to help clinicians obtain high-quality images of the meibomian glands. The tool can be used with a single hand, freeing up the second hand to control the meibographer, the company says.

The Meivertor's stainless-steel handle features grips with etched surfaces to optimize its rotation and silicone tips designed to securely and evenly grip across the eyelashes, the company notes on its website. The device's maker adds that the tips are sold in a pack of 100 and are single-use disposable to ensure patient hygiene.

The Meivertor instrument can be used with just one hand, allowing clinicians to control other devices during an examination.

For more information on the instrument, visit meivertor.com.

LOW VISION

Smart Glasses Get Smarter

Following the release of Eye4 smart glasses last fall, the company Eyedaptic recently introduced its latest version of the low-vision aid, duly named Eye5.

Similar to the previous model, the augmented reality glasses are tethered to a handheld cell phone—which is provided by the company—allowing users to take advantage of two cameras—one in the smartphone and one in the glasses—to help deal with central vision loss from retinal conditions such as age-related macular degeneration and diabetic retinopathy and to better see and navigate their environment.

The new facial detection capability using artificial intelligence software is the main feature that sets Eye5 glasses apart from previous models, the company explains in a press release. As with the Eye4 model, Eye5 features an all-in-one custom user interface, auto zoom mode, image stabilization and contrast enhancement. The embedded camera in the new device also functions the same as in the previous model: It automatically enhances visual images by capturing the wearer's environment and manipulating the pixels, re-displaying the image in higher resolution.

Eye5 smart glasses are designed with the same lightweight material as Eye4, weighing in at only three ounces to enhance comfort and discreetness of wear, the company says.

For more information on the new Eye5 and how it differs from the previous model of the device, visit eyedaptic.com. ◀

I was only seeing light flashes early on, but light

FLASHES

when you've not seen anything for so many years—it was wonderful

—Keith H, retinal prosthesis recipient

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

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FOUNDATION FIGHTING BLINDNESS

FightingBlindness.org

IOL Calculations in Keratoconus

Scientists compared the prediction accuracy of the Barrett True-K for keratoconus with standard formulas (SRK/T, Barrett Universal II and Kane) and the Kane keratoconus formula.

The multicenter retrospective case series took place at the Shaare Zedek Medical Center, Jerusalem, Israel; and University Eye Clinic, Maastricht, the Netherlands.

Eyes with stable keratoconus undergoing cataract surgery were included. Predicted refractions were calculated for SRK/T, Barrett Universal II, Barrett True-K for keratoconus (predicted and measured), Kane and Kane adjusted for keratoconus formulas. Primary outcomes were prediction error (PE), absolute error (AE), and percentage of eyes with PE ±0.25 D, ±0.50 D and ±1 D. Subgroup analyses were performed based on the severity of the keratoconus.

Fifty-seven eyes were included in the study. Here are some of the findings:

- PE wasn't significantly different from zero for SRK/T, Barrett True-K (predicted and measured) and Kane keratoconus formulas (range: 0.09 to 0.22 D; $p>0.05$).
- The AE of Barrett True-K predicted (median: 0.14 D) and Barrett True-K measured (median: 0.10 D) were significantly lower than the Barrett Universal II (median: 0.47 D) and Kane (median: 0.50 D); $p<0.001$.

Scientists concluded that the Barrett True-K formulas for keratoconus had higher prediction accuracy than new-generation formulas and a prediction accuracy similar to the Kane keratoconus formula.

J Cataract Refract Surg 2022; Oct 28. [Epub ahead of print].
Vandevenne M, Webers V, Segers M, et al.

Prevalence of AMD in the U.S.

Researchers aimed to produce estimates of early- and late-stage age-related macular degeneration prevalence overall and by age, gender, race and ethnicity, county and state.

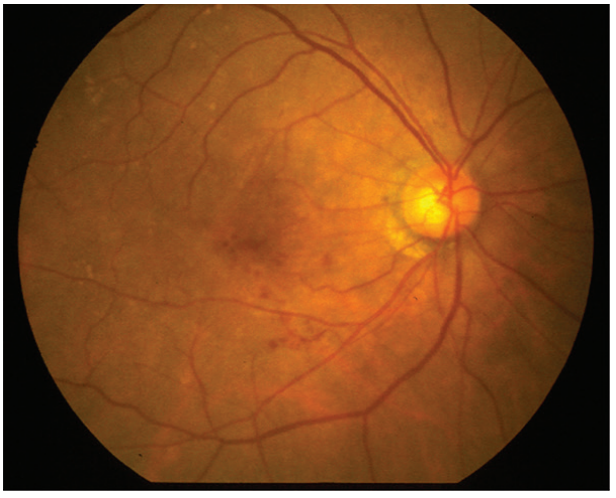
The study team conducted a Bayesian meta-regression analysis of relevant data sources containing information on the prevalence of AMD among different population groups in the United States.

Researchers included data from the American Community Survey (2019), the National Health and Nutrition Examination Survey (2005 to 2008), U.S. Centers for Medicare & Medicaid Services claims for fee-for-service beneficiaries (2018) and population-based studies (2004 to 2016). They included all relevant data from the U.S. Centers for Disease Control and Prevention's Vision and Eye Health Surveillance System.

Researchers estimated the prevalence of early-stage (defined as retinal pigment epithelium abnormalities or the presence of drusen 125 or more microns in diameter in either eye) and late-stage AMD (defined as choroidal neovascularization and/or geographic atrophy in either eye) and stratified it, when possible, by the factors listed earlier. Data analysis occurred from June 2021 to April 2022.

Here are some of the findings:

- In 2019, approximately 18.34 million people ages 40 years and older (95 percent uncertainty interval [UI], 15.30 to 22.03) living with early-stage AMD, corresponding to a crude prevalence rate of 11.64 percent (UI, 9.71 to 13.98).
- Approximately 1.49 million people 40 years and older (UI, 0.97 to 2.15) living with late-stage AMD, corresponding to a crude prevalence rate of 0.94 percent (UI, 0.62 to 1.36).

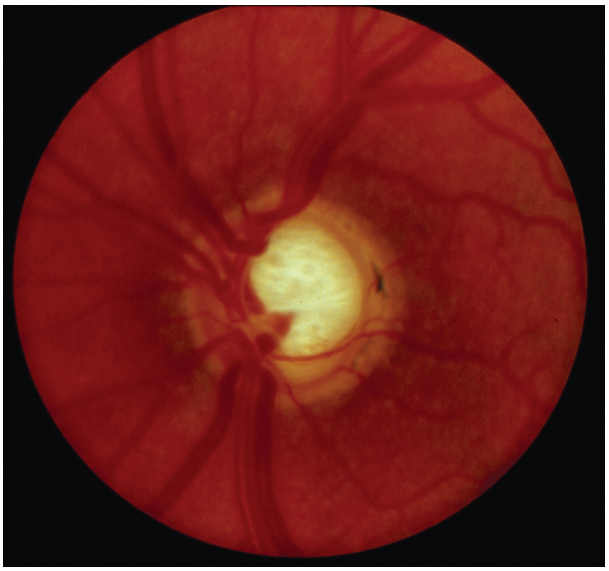


- Prevalence rates of early- and late-stage AMD varied by demographic characteristics and geography.

Researchers estimated a higher prevalence of early-stage AMD and a similar prevalence of late-stage AMD compared with earlier studies. They suggested that state-level and county-level AMD estimates may help guide public health practice.

JAMA Ophthalmol 2022. Nov 3. [Epub ahead of print].
Rein DB, Wittenborn JS, Burke-Conte Z.

Microvascular Abnormalities and OAG



Researchers evaluated peripheral microvascular abnormalities associated with open angle glaucoma patients, as part of a cross-sectional study.

Patients with OAG and controls underwent a detailed ophthalmic evaluation, including Humphrey visual field tests and swept-source optical coherence tomography. Researchers performed nailfold capillaroscopy (NFC) and laser Doppler imaging (LDI) to evaluate peripheral microvascular abnormalities. Using NFC, they recorded the presence of microhemorrhages, tortuous capillaries, dilated capillaries, avascular areas and the capillary density, among other characteristics. Fingertip blood flow (FBF) was measured using LDI at different time points, before and one, 10 and 20 minutes after exposure to a cold stimulus. In addition, venous blood samples were collected to measure serum endothelin-1 (ET-1) concentrations as well as serum auto-antibodies.

Main outcome measures included presence of microhemorrhages, tortuous capillaries and dilated capillaries; FBF, ET-1 and auto-antibodies.

Here are some of the findings:

• Sixty-eight subjects (43 patients with OAG and 25 controls) were enrolled.

• Microhemorrhages were found in the nail bed of 65.1 percent of OAG patients compared to 25 percent of the controls (p=0.003).

• A significant difference was found in the mean FBF at baseline in OAG patients (293.6 ±100.2 perfusion units) vs. controls (388.8 ±52 perfusion units) (p<0.001), together with a significant decrease in the mean FBF 10 and 20 minutes after cold stimulus in OAG patients in comparison to controls (p<0.001 for all comparisons).

• A positive correlation was found between mean baseline FBF and HVF MD (r=0.27, p=0.03), and between mean baseline FBF and average retina nerve fiber layer thickness (r=0.44, p=0.001).

• Neither the analysis of ET-1 concentrations (p>0.71) nor the auto-antibodies measurements (p>0.05, for all) showed any difference between the two groups.

Researchers reported significant peripheral microvascular abnormalities were found in open-angle glaucoma patients compared to controls, suggesting that microvascular changes might play a role in the pathogenesis of the disease. In addition, they wrote, some of the abnormalities seemed to correlate with functional and structural glaucomatous damage.

Ophthalmol Glaucoma 2022. Oct 25. [Epub ahead of print].
Taniguchi EV, Almeida INF, Gracitelli CBP, et al.

A.I. and Diabetic Retinopathy

This study investigated the feasibility of using deep learning (DL) models to automatically segment retinal capillary non-perfusion and neovascularization on ultra-widefield fluorescein angiography images from patients with diabetic retinopathy.

This retrospective, cross-sectional chart review study included 951 UWFA images collected from patients with severe nonproliferative DR or proliferative DR. Each image was segmented and labeled for NP, NV, disc, background and outside areas. Using the labeled images, DL models were trained and validated (80 percent) using convolutional neural networks (CNNs) for automated segmentation and tested (20 percent) on test sets. The accuracy of each model and each label was assessed.

Here are some of the findings:

• The best accuracy from CNN models for each label was:
— 0.8208 for NP;
— 0.8338 for NV;
— 0.9801 for disc;
— 0.9253 for background; and
— 0.9766 for outside areas.

• The best intersection over union for each label was:
— 0.6806 for NP;
— 0.5675 for NV;
— 0.7107 for disc;
— 0.8551 for background; and
— 0.924 for outside areas.

• The mean boundary F1 score (BF score) was:
— 0.6702 for NP;
— 0.8742 for NV;
— 0.9092 for disc;
— 0.8103 for background; and
— 0.9006 for outside areas.

Researchers determined that DL models could detect neovascularization and non-perfusion as well as disc and outer margins on UWFA with good performance. They added that automated segmentation of important UWFA features will aid physicians in DR clinics and in overcoming grader subjectivity.

Br J Ophthalmol 2022. Oct 14. [Epub ahead of print].
Lee PK, Ra H, Baek J.

Hypertensive Drugs and Cataract

Researchers say that hypertension medications don't increase the risk

of lens opacity.

A recent study looking into the association between antihypertensive use clinically and cataract risk found that this class of drugs wasn't associated with an increased prevalence of this ocular occurrence. Previous research was inconsistent on the matter.

The case-controlled study evaluated the Korean National Health Insurance Service-Health Screening Cohort database from a time period spanning 2002 to 2013. Cases were defined as patients prescribed antihypertensives who underwent cataract surgery between 2010 and 2013. Controls were patients prescribed antihypertensives with no history of cataract diagnosis or surgery between 2002 and 2013. Four controls were matched to each case, and adjusted odds ratios and 95% confidence intervals were estimated for cataract risk using a conditional logistic regression model after adjustment.

The analysis included 12,166 cases and 48,664 controls. The adjusted ORs for cataract were 1.18 with thiazide diuretics, 1.12 with beta-blockers, 0.94 with calcium channel blockers, 1.22 with angiotensin-converting enzyme inhibitors and 0.97 with angiotensin II receptor blockers compared with non-use of each antihypertensive.

The researchers say that given the benefits of treating hypertension, such as the reduction in further complications, they suggest it's not necessary to change current clinical practice for antihypertensives. They add that, however, in a few sections of drug exposure, the risk of cataract increases with the duration of the use of some antihypertensives, clinicians should take into account that hypertension itself may increase the risk of cataracts rather than the use of antihypertensive drugs.

Ophthalmic Epidemiol 2022. Nov 11. [Epub ahead of print].

Yang HL, Byun SJ, Park S, et al.

Post Hoc Analysis of VISTA And VIVID Studies

In a post hoc analysis of the Regeneron-sponsored VISTA and VIVID studies of aflibercept (Eylea), investigators characterized diabetic macular edema incidence in the fellow eyes of patients treated for DME in the study eye.

The analysis evaluated the data on fellow eyes without diabetic macular edema at baseline through week 100. The presence of diabetic macular edema in the fellow eye was inferred by investigator-reported DME adverse events and use of interventions to treat the diabetic macular edema.

Here are some of the findings:

• Over 100 weeks, the following groups of fellow eyes developed DME:

— intravitreal aflibercept injection (IAI) 2 mg q4 weeks (n=245): 44.9 percent;

— IAI 2 mg q8 weeks (n=258): 44.2 percent; and

— laser control (n=252): 42.9 percent.

• Mean time to DME development in combined treatment groups was about six months.

• Multivariable regression analysis confirmed patients with shorter diabetes duration (HR per 10-year decrease: 1.16; 95 percent CI, 1.03 to 1.30; p=0.0160) and thicker baseline study eye central subfield thickness HR per 10-µm increase, 1.01; CI, 1.01 to 1.02; p=0.0002) were at higher risk of developing DME in the fellow eye.

Investigators found, among patients with diabetic macular edema in one eye at baseline, almost half developed DME in the fellow eye over two years. They added shorter duration of diabetes and thicker central subfield thickness in the study eye were predictors of diabetic macular edema development in the fellow eye.

Retina 2022. Oct 17. [Epub ahead of print].

Dhoot DS, Moini H, Reed K, et al.

(Continued from p. 38)

Myopia Classification

be able to treat everyone and prevent high myopia with the tools we have today.

"Researchers in the myopia space will need to focus on myopia as if all of it were a disease and treat the patients at the highest risk of developing high myopia and related complications, as well as find ways to treat it before it reaches that point," he continues. "These future treatments won't apply to a patient who's, say, a half-diopter myope at age 12 but they may be appropriate for children with four or five diopters of myopia who are really at risk of developing complications later in life.

"Ultimately, we have to take each case very seriously and focus on the disease aspects of myopia," he says. "If we can pinpoint ways to curb the rates of myopia in those countries, then hopefully we can lower the rates of high myopia and associated vision-threatening conditions that come down the road. Myopia can have incredibly devastating consequences for people's vision, quality of life, economic productivity and family. There are serious potential outcomes, so we should take the condition seriously and treat it with what we can."

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Time for An Upgrade?

A look at the latest smartphones and how their features could benefit you.

LIZ HUNTER
SENIOR EDITOR

Few announcements in the tech industry are as highly anticipated as those pertaining to smartphones. Die-hards from each camp—Apple or Android—never fail to upgrade, no matter how small the difference in features; it's all about having the latest and greatest. However, for the average person, upgrading annually isn't realistic or even necessary, but if some features might make their life easier or better, they're more apt to consider it.

Here, we've compiled several highlights of the latest smartphones, including the iPhone 14 Pro and Max, the Samsung Galaxy S22 Ultra and the Google Pixel 7 Pro. We also spoke with doctors to hear their thoughts on the technology. Whether you rely on your phone simply for capturing family memories or use it as an integral tool in your practice, these models are likely to offer some level of enhancement.

Features at a Glance

Manufacturers have focused their energy on some key elements in the recent releases, including speed, security and cameras.

The iPhone 14 Pro/Max is powered by an A16 Bionic chip, which Apple says is the fastest chip ever used in a smartphone; it's designed to speed up performance while using multiple apps. The Samsung Galaxy S22 Ultra uses a Snapdragon 8 Gen 1, claiming a 10-percent increase in graphics processing unit clock speeds and improved power efficiency. In the Pixel 7 Pro, Google has installed its second-generation Tensor G2 processor, designed to enhance the AI experience on the phone.

All of these phones have 5G capabilities, and all say their batteries can last approximately one day under regular use, although each manufacturer has its own way of wording it, such as "all-day battery life" (Apple) and "24-plus hour battery life" (Google). These claims become strained depending on use, especially for the camera.

The camera specs continue to impress, giving users the ability to capture moments like a professional.

The iPhone 14 Pro/Max has a 48-MP main camera with sensor-shift optical image stabilization and enhanced low-light capture. Apple says that the 12-MP ultra-wide camera delivers detailed macro photography, and there's a telephoto camera with 3x optical zoom. Users can also record video in 4K at 24 fps, and enable Action mode for smooth filming even if experiencing motion or vibration.

The Samsung Galaxy S22 Ultra has improved graphics.

The Samsung Galaxy S22 Ultra has a 108-MP main camera and a 40-MP front-facing (selfie) camera. It also has improved its image quality in low-light conditions with its "Super Clear Glass Lens" over the camera to help reduce reflections.

The Pixel 7 Pro's rear camera is a 50-MP Octa PD Quad Bayer wide camera with Macro Focus, and up to 30x Super Res Zoom. It also comes with Photo Unblur that can improve blurry pictures with a few taps. Its front camera is 10.8 MP and has a feature called Guided Frame that assists those who are blind or visually impaired with capturing selfies using audio guidance and haptic feedback.

From here, the features begin to differentiate more clearly. The iPhone in particular highlights its new "Always-On" display that keeps certain apps and widgets open on the screen, and Crash Detection with Emergency SOS that enables the phone to detect a car crash through motion algorithms; it will call for help, even if there's no cell or WiFi coverage available.

However, one change not seen in the newest iPhone is in the charging port. This model still features the proprietary lightning port, as opposed to USB-C, which has become the new standard in tech devices and allows for faster data transfer and charging speeds. Apple has until 2023 to make this change

This article has no commercial sponsorship.

Dr. Colvard is a surgeon at the Colvard-Kandavel Eye Center in Los Angeles and a clinical professor of ophthalmology at the Keck School of Medicine of the University of Southern California. **Dr. Charles** is the founder of the Charles Retina Institute in Germantown, Tennessee.

to meet EU regulations, so it's expected we'll see this on the next iPhone model.

The Galaxy S22 Ultra includes the fan-favorite feature of the Samsung Note: the S-pen. Embedded in the device, the S-pen allows the user to quickly mark up documents, sketch or turn a handwritten note into text.

The Pixel 7 Pro comes with five years of security updates, anti-phishing and anti-malware protection and end-to-end security designed by Google, and it will soon have a built-in VPN to encrypt your online activity.

Tommy Korn, MD

Enhanced macro photography capabilities on smartphones can help patients update physicians with their progress. However, some in the field would like to see better front-facing camera technology.

Are They Worth the Hype?

To evaluate whether it's time to invest in an upgrade, we asked a couple of tech-savvy ophthalmologists to weigh in. First, it's important to think about the things an ophthalmologist would rely on their phone to do, says Tommy Korn, MD, who practices in San Diego.

He says his top three uses for his smartphone are communication, medical data access and photography.

"My iPhone keeps me in contact with patients, care team members and other doctors," he says regarding communication. "This is via voice, text or video apps. There are numerous communication apps and it's all a balance between ease of use and HIPAA compliance/privacy.

"The second job I need my smartphone for is to access patient data in the EMR," Dr. Korn continues. "I can access any EMR from a slow enterprise desktop/laptop PC. I can also access the EMR via fast mobile EMR apps on my iPad or iPhone."

The iPhone 14 Pro

In these EMRs, Dr. Korn is often storing ophthalmic photos he took with his own smartphone. "I take pictures of people's eyes so I can document their disease and its progression," he says. "Patients also take pictures of their own eyes and send them to their eye doctors when they're distressed. These images (either doctor- or patient-captured) are often stored in an EMR. The innovative way is to share these eye photos directly with the patient's secured smartphone. I often send the eye photos I take to their iPhones via Airdrop, which doesn't allow my personal phone number to be compromised. This is a novel way that allows the patient data to travel with them on their personal smartphone, not a siloed EMR. Siloed EMRs are a major source of burnout and frustration for doctors and the health industry. Sharing the patient's eye photo is an innovative way of enhancing patient care. Patients can take their stored smartphone eye photos to any ophthalmologist or optometrist in the world and get continuity of care.

"In my opinion, the camera technologies for all high-end smartphones—iPhone Pro, Google Pixel, Samsung Galaxy—are all amazing," Dr. Korn adds. "It's a matter of personal preference based on camera tech specs, photo editing features, image quality and ecosystem."

The macro photography capabilities of these new phones are of particular importance, Dr. Korn continues. "Most smartphones now have macro camera photography capabilities," he says. "What this means is, you no longer need a special lens to take photos of things up close (flowers, insects, or in our case, eyeballs). Most ophthalmic photographers use Digital SLR cameras, pocket cameras, or even smartphones that are attached to a $15,000-plus slit lamp. But now you're starting to see patients take amazing photos of their own eyes with smartphone macro photography. They'll send these photos to their eye doctors, and this becomes a novel way to deliver remote telehealth eye care. That's the power of having amazing camera technology in the hands of consumers, not just doctors or professional photographers."

Even with this technology at their fingertips, it's not going to replace traditional ophthalmic imaging, opines Ken Lord, MD, a vitreoreti-

nal specialist in St. George, Utah, and a co-developer of the Eye Handbook mobile app.

"The pictures you're able to take with these cameras are incredible," Dr. Lord says. "You've got as powerful a camera in a half-inch thick phone as you do in some of the most expensive cameras on the market, but the practicality of using your phone to take images of your patient is still not there. I know there's a market for people selling adapters and devices, but it's not something I personally feel I have time to fiddle with when I have patients to get to."

Dr. Lord also feels that the phones themselves haven't gone through enough of an evolution. "I think the cameras, memory, security and usability of the phones are unsurpassed, but we're kind of at a plateau right now," he says. "I'm just not convinced that some of the technology has been as impactful as other [updates] in the past five years. There hasn't really been a 'wow' in these devices, but I'm still looking forward to all the new features that these designers come up with."

So, what would ophthalmologists want to see in future updates?

Dr. Korn would like to see improved front-facing cameras, for one. "All the rear cameras have multiple lenses, but the front camera has a single lens," he says. "It turns out that most patients can't take a picture of their own eye with the rear camera and without another person helping them. The front camera technology is nascent right now. When it improves, you'll see telehealth in ophthalmology take off."

Cellular connectivity and access to fast 5G mobile networks are also lacking in many areas, he continues. "Metropolitan cities have fast internet access, but many rural areas don't," he says. "Patients can have the most advanced smartphone, but it's useless if fast internet connectivity is limited."

Dr. Lord says he'd like to see how phones are adapted for augmented reality. "Virtual and augmented reality are being heavily targeted with companies investing billions of dollars—maybe over-investing. I'm not convinced that headsets make sense," he says. "It's essentially disconnecting you from the world around you, so I'd like to see how that virtual experience comes from your phone in a seamless way."

Whatever the future holds for the next generation of smartphones, Dr. Korn believes the keys to success are integration, simplicity and privacy. "If medical apps and smartphones work seamlessly, both doctors and patients will have delightful user experiences," he says. ◀

DISCLOSURES

Dr. Korn is a consultant for Doximity. **Dr. Lord** is a co-founder of Eye Handbook and Eye Patient.

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EDITED BY BONNIE SKLAR, MD
WILLS EYE RESIDENT CASE REPORT

Vision changes after COVID-19 infection in a man in his 40s.

SAIF A. HAMDAN, MD, WILLIAM E. BENSON, MD
PHILADELPHIA

Presentation

A 41-year-old man presented for decreased central vision in both eyes of approximately one week's duration. He described sudden symptom onset, characterized as bilateral central scotomas that persisted with cross-covering. Review of systems was notable for upper respiratory symptoms starting two weeks ago and a positive COVID-19 PCR test one week prior to presentation. He denied any recent trauma or changes to medications. He reported normal vision at baseline in both eyes prior to the viral infection. He denied any additional sequelae of recent infection.

Medical History

Prior ocular history included cataract extraction with intraocular lens placement in both eyes. Otherwise, the patient denied any additional medical history or current medications. Prior surgeries included an appendectomy, cholecystectomy and hip surgery. Family history was notable for multiple relatives with development of cataracts at young ages.

Examination

The patient's vital signs were stable and within normal limits. Visual acuity was 20/70 in the right eye and 20/40-2 in the left. Confrontational visual fields revealed a small central scotoma in both eyes. The patient didn't demonstrate a relative afferent pupillary defect in either eye. Anterior slit lamp examination was unremarkable. On fundus examination, the only abnormalities seen were a cotton wool spot (CWS) and an adjacent flame hemorrhage along the inferior arcade of the left eye (*Figure 1*). Otherwise, posterior exam of each eye revealed clear vitreous and flat optic nerves with sharp borders and healthy rim tissue with cup-to-disc ratios of 0.3. The vessels were normal in caliber and contour, and the macula was flat without any evidence of exudates or pigmentary changes. There were no retinal detachments or breaks in the peripheral retina.

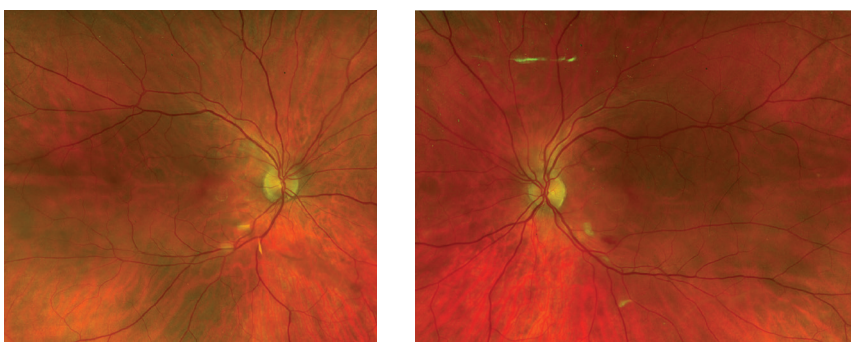

Figure 1. Fundus photo of each eye without clear visible macular changes. A cotton wool spot and flame hemorrhage along the inferior arcade of the left eye are apparent.

What's your diagnosis? What further work-up would you pursue? The diagnosis appears on the next page.

Work-up, Diagnosis and Treatment

Given the patient's clinical exam findings, further diagnostic testing and imaging was performed. Initial hematologic work-up included: non-reactive HIV antigen/antibody; normal complete blood count and comprehensive metabolic panel; and normal lipid panel. Advanced diagnostic imaging included normal carotid and orbital doppler ultrasonography and unremarkable MRI/MRA of the orbit and neck. Near-infrared imaging revealed petaloid-shaped, well-demarcated darkening in the macula of both eyes (*Figure 2*). Optical coherence tomography of the macula of the right and left eye revealed outer retinal irregularities with disruption of the ellipsoid zone. A prominent hyper-reflective plaque extending from the outer plexiform layer to the outer nuclear layer was also noted in the left eye (Figure 2).

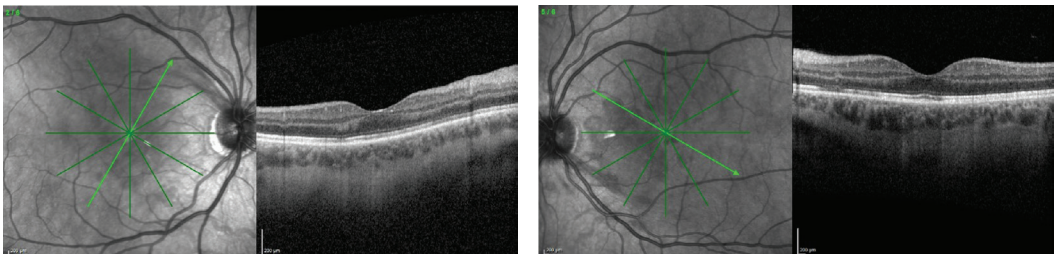

Figure 2. Near-infrared reflectance of each eye demonstrates a dark, well-demarcated lesion in the macula. OCT shows outer retinal irregularities with ellipsoid zone disruption in each eye. A hyper-reflective band extending from the outer plexiform layer to the outer nuclear layer was identified in the left eye.

The differential for this presentation was limited in scope, however it included acute macular neuroretinopathy (AMN), Krill's disease, traumatic or whiplash retinopathy, and old retinal infarcts. However, the classic imaging patterns helped narrow down the diagnosis to acute macular neuroretinopathy.

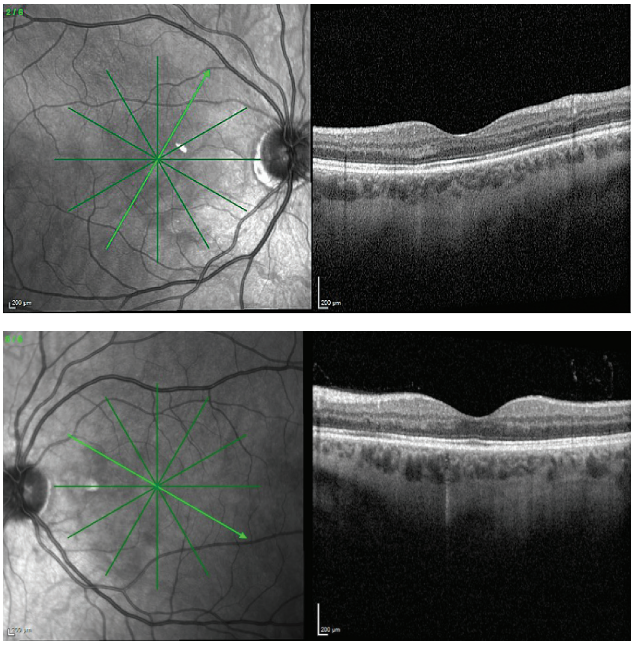

Figure 3. Repeat OCT of both eyes at the six month follow-up visit reveals regression of outer retinal changes at previous areas of involvement.

At this time, further serologic work-up including hypercoagulable investigation revealed a positive Factor V Leiden genetic analysis (heterozygous trait). Observation was advised as no treatment has been established for AMN. He was recommended to follow up with a primary care provider regarding his hypercoagulable work-up. On repeat examination at four weeks and six months, the patient was noted to have stable visual acuity and resolution of the previously noted CWS and hemorrhage in the fundus of the left eye. He continued to complain of a persistent paracentral scotoma in both eyes. Repeat OCT at six months revealed regression of the outer retinal changes of both eyes and improvement of the hyper-reflective plaque noted in the left eye (*Figure 3*). Per patient request for work clearance, 10-2 Humphrey visual fields were performed and revealed paracentral depressions in both eyes, though with limited reliability of the right eye (*Figure 4*).

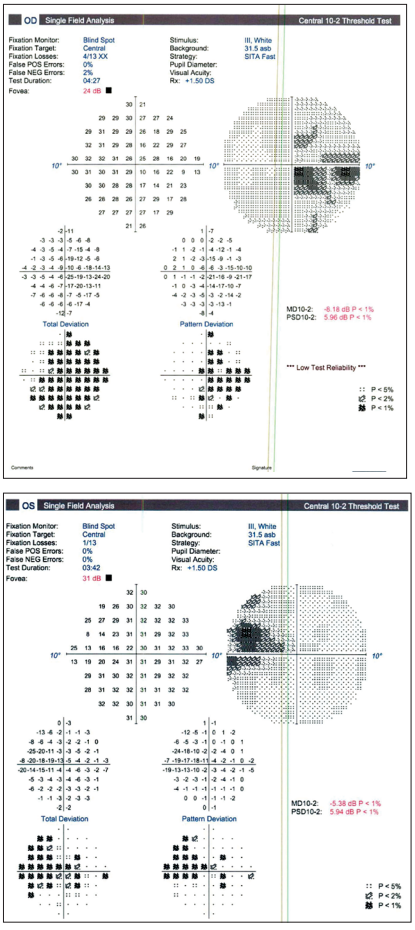

Figure 4. 10-2 Humphrey visual field of each eye with paracentral changes.

Discussion

First described in 1975, AMN is believed to be a multifactorial disease, with a unifying vascular etiology, affecting the outer retina secondary to compromise of the deep capillary plexus resulting in visual field deficits.[1-3] It generally affects younger patients and has been found to be more prevalent in females.[2] Symptoms often follow different triggering events. The most commonly known trigger for AMN is a non-specific flu-like illness or fever with approximately half of patients reporting such symptoms prior to their disease.[2] Other causes include the use of vasoconstrictors, hypotension/systemic shock, use of oral contraceptive pills and trauma.[2] More recently, there have been several standalone case reports linking AMN with either acute infection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) or COVID-19 vaccinations. While the pathophysiology of such associations is yet to be delineated, it's hypothesized to be precipitated by the hyperinflammatory and hypercoagulable state of COVID-19.[4] This dysregulated state superimposed on the underlying thrombophilia from Factor V Leiden was presumed to be the trigger in our patient. To our knowledge, there are no previously published case reports of AMN in patients with a hereditary thrombophilia, and the pathophysiologic role of Factor V heterozygous trait remains unclear.

> **In summary, AMN should be suspected in patients with central visual field deficits that have known risk factors.**

Most patients with AMN present with scotomas (estimated around 70 percent).2 The scotomas appeared to resolve in approximately half of the patients on long-term follow-up.[2] Decreased vision is less commonly encountered, with more than 80 percent of patients presenting with visual acuity greater than 20/40 in the affected eye. Common findings on clinical exam include a wedge-shaped coloured macular lesion with the apex directed toward the macula.[2] There are, however, patients who don't demonstrate any appreciable changes on fundus exam and further imaging is required to identify the disease.[2] More than half of patients with AMN present with bilateral disease.[2]

The most useful diagnostic tests in AMN are OCT and near-infrared reflectance. OCT findings in AMN include hyper-reflectivity of the outer retinal layers, ellipsoid zone changes, and outer nuclear layer thinning.[2,5] These changes may be persistent on follow-up testing, with studies demonstrating persistent outer nuclear layer thinning in approximately 19 percent of affected eyes and ellipsoid zone disruption in approximately 9 percent.[2]

Near-infrared imaging, which is obtained in conjunction with OCT, is also an important diagnostic test that helps visualize subclinical disease. These images demonstrate a dark well-demarcated lesion proximal to the macula and often correspond to the areas of OCT changes and visual field defects.[2] Fluorescein angiography has low utility in AMN with the majority of eyes (approximately 75 percent) demonstrating normal angiograms. However, hypofluorescence of the affected area has been described in approximately 20 percent of patients.[2]

Visual field testing can help delineate the scotoma and monitor for its improvement or resolution. These scotomas appear to follow the shape of the lesion visualized clinically, and persistent scotomas have been previously documented in nearly half of patients with AMN on long-term follow-up.[2] Most reports of fundus autofluorescence in AMN show no abnormalities; however, hypofluorescence corresponding to the area of the lesion has been noted.[2,6] Optical coherence tomography angiography has also been used in AMN. Findings include reduced deep capillary flow signal with evidence of flow recovery on follow-up.[7] There is also evidence to suggest that the choriocapillaris may be involved in certain cases.[8]

In summary, AMN should be suspected in patients with central visual field deficits that have known risk factors. Although clinical examination can raise the suspicion for the disease, unique findings on multimodal imaging, including a well-demarcated darkening on near-infrared, outer retinal changes on OCT and central visual field defects on HVF, can help establish the diagnosis. ◀

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