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Retina Today

SEPTEMBER 2024 VOL. 19, NO. 6
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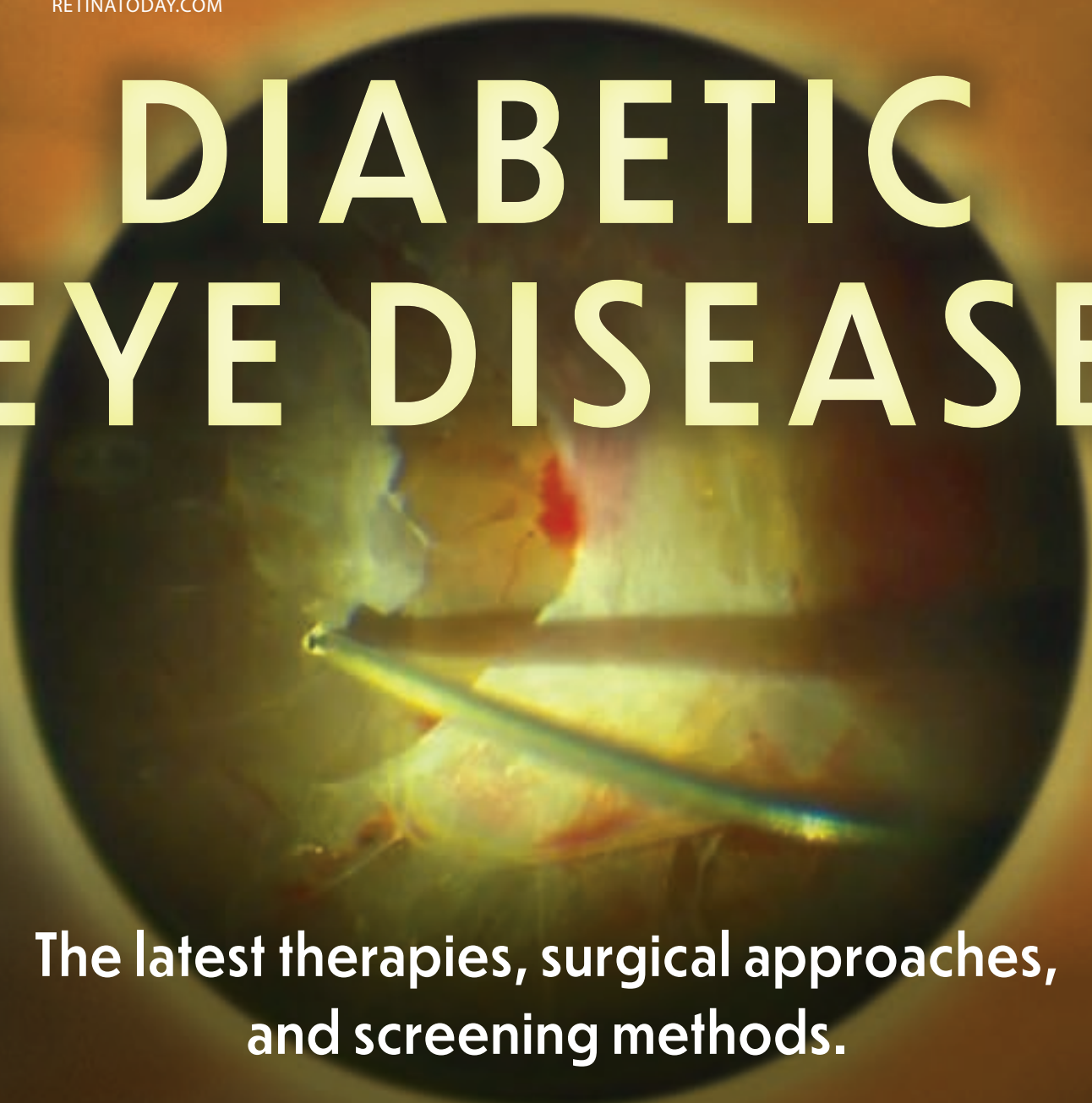
eyetube

DIABETIC EYE DISEASE



The latest therapies, surgical approaches, and screening methods.

COMPLICATED DR CASES: THE SECOND SURGERY

COMBINATION THERAPY CONSIDERATIONS FOR DME

IMPROVING ACCESS TO DR CARE

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Increased freedom
resulting from expanded extraocular working space[1-7,*]

Improved command
made possible by optimized contact[7-10,*,†]

Precision performance
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*Compared to the GRIESHABER REVOLUTION® Handle.

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GRIESHABER® DSP IMPORTANT PRODUCT INFORMATION

Caution: Federal (USA) law restricts this device to sale by, or on the order of, a physician. Indications for Use: GRIESHABER® DSP instruments are a line of single-use vitreoretinal microinstruments which are used in ophthalmic surgery, for cases either in the anterior or the posterior segment. The GRIESHABER® Advanced Backflush Handles DSP are a family of instruments for fluid and gas handling in vitreoretinal surgery. Warnings and Precautions: • Potential risk from reuse or reprocessing GRIESHABER® DSP instruments include: foreign particle introduction to the eye; reduced cutting or grasping performance; path leaks or obstruction resulting in reduced fluidics performance. • Verify correct tip attachment, function and tip actuation before placing it into the eye for surgery. • For light fiber instruments: Minimize light intensity and duration of exposure to the retina to reduce risk of retinal photic injury. The light fiber instruments are designed for use with an ALCON® illumination source. • Good clinical practice dictates the testing for adequate irrigation and aspiration flow prior to entering the eye. If stream of fluid is weak or absent, good fluidics response will be jeopardized. • Use appropriate pressure supply to ensure a stable IOP. • If unwanted tissue gets engaged to the aspiration port, it should be released by interrupting aspiration before moving the instrument. **ATTENTION:** Please refer to the product labeling for a complete listing of indications, warnings, and precautions.

References: 1. Alcon data on file, 2020. **2.** Alcon data on file, 2020. **3.** Alcon data on file, 2020. **4.** Alcon data on file, 2020. **5.** Alcon data on file, 2020. **6.** Alcon data on file, 2020. **7.** Alcon data on file, 2020. **8.** Alcon data on file, 2020. **9.** Alcon data on file, 2020. **10.** Alcon data on file, 2020.

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Laser-ablated micro-surface is designed to support atraumatic ILM peel initiation[1]

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Reference: 1. Alcon Data on FIle, 2018. **2.** Alcon Data on File, 2017.

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PERSEVERANCE IS KEY


It was an exciting summer with the 2024 Olympic Games as a backdrop to our busy clinics. We were tuning in every night after clinic, watching as world records were broken, medals were snagged by unlikely underdogs, and those labeled as the *greatest of all time* did what they do best. What struck us most this year was the admirable perseverance of many Olympic athletes who shattered the stereotypes of age, race, and gender; battled against injuries; and had the drive to become the first to accomplish what no one else could.

We could use a little of that mentality in our clinics, if we are being honest. Not because we aren't performing at the highest level possible—we are. Rather, it's because it often feels like we are fighting an uphill battle with some of the patient populations we serve. Some are losing vision no matter what we do. Some of those macular holes just refuse to close. And many patients with diabetes are *still* walking into the clinic with devastating vision loss that could have been prevented.

Annual screening for diabetic retinopathy (DR) is perhaps the easiest way to nip this problem in the bud. But these patients already have a lot on their plates with their systemic health, and ensuring they prioritize their *ocular* health can be a challenge.

A new study out of Massachusetts found that the COVID-19 pandemic set us back significantly in our efforts to increase screening rates for DR. After reviewing claims data from the UMass Memorial Managed Care Network between 2018 and 2022, the researchers noted a 12% decrease in the screening rate post-pandemic compared with pre-pandemic. What's worse, after stratifying for patient status, they found that the decreased screening rate remained significant for established patients (ie, those who *know* they are at risk), while the difference disappeared for new patients.[1]

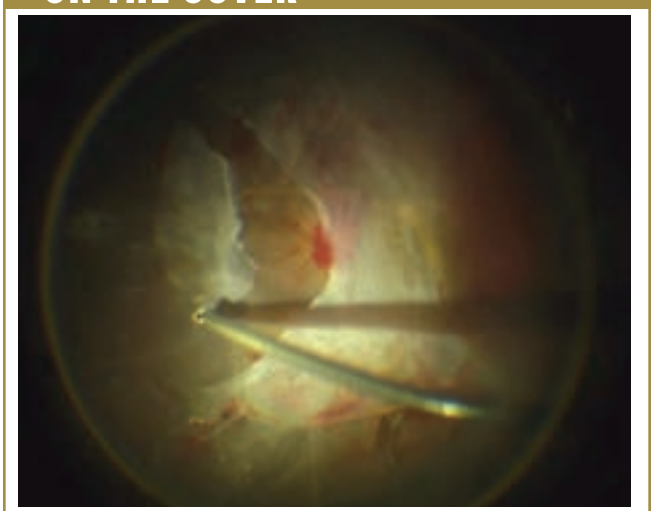
But it's worth fighting back, because blindness from diabetic eye disease simply isn't acceptable. In this issue, trainees at Wills Eye Hospital share the details of Philadelphia Diabetes Day, an annual city-wide event that provides free DR screening and access to much-needed educational and social resources. They share checklists and event flow charts in the hope that others join the cause. We also highlight new research from Wilmer Eye Institute at Johns Hopkins School of Medicine that helps us understand how a person's location affects their DR care. Not surprisingly, patients who live in more socioeconomically disadvantaged areas are more likely to experience lapses in their DR care—yet another hurdle we must overcome.[2]

Once we get patients in the clinic, we have many therapeutic and surgical approaches to address the ocular complications of diabetes. Because much has changed in our armamentarium, we asked experts to discuss the latest updates in the therapeutic space and the OR. Authors discuss caring for pregnant patients who have diabetes, combination therapy for DME, and whether we should consider intravitreal injections of anti-VEGF agents or vitrectomy for patients who present with diabetic vitreous hemorrhage. From a surgical standpoint, clinicians from the University of California, Los Angeles, outline best practices when complicated DR cases require reoperation and highlight a rare postoperative complication to keep in mind.

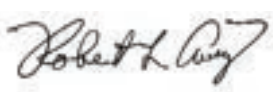
These are complicated patients, even when they don't land in the OR with hemorrhages and tractional retinal detachments—and like those Olympic athletes, we cannot give up. We must persevere and continue to care (holistically!) for our patients with diabetes, constantly looking for ways intervene sooner, improve treatment options, and save their vision whenever possible. ■

1. Bilsbury E, Mautner Wizentier M, Wood E, Doherty S, Ledwith J, Ding J. the continuing impact of the COVID-19 pandemic on diabetic retinopathy screenings [published online ahead of print July 31, 2024]. *Ophthalmic Epidemiol.*
2. Tang T, Tran D, Han D, Zeger SL, Crews DC, Cai CX. Place, race, and lapses in diabetic retinopathy care. *JAMA Ophthalmol.* 2024;142(6):581-583.

ON THE COVER



During vitrectomy in a diabetic eye, segmentation of membranes into individual islands allows dissection without undue traction, decreasing the risk of iatrogenic retinal breaks.
From: *Complicated DR Cases: The Second Surgery* by Adrian Au, MD, PhD; Blake Fortes, MD; and Pradeep Prasad, MD, MBA

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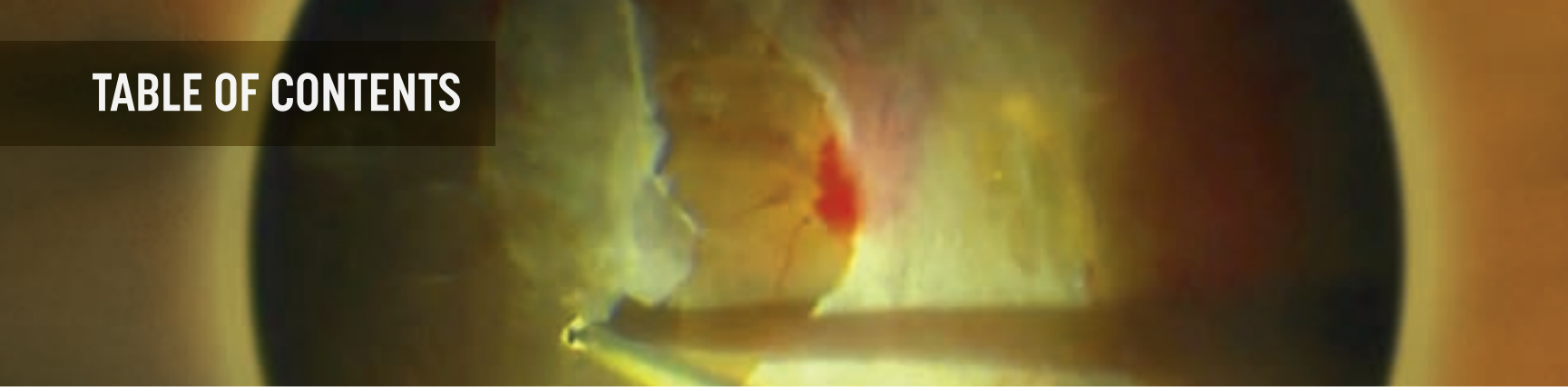

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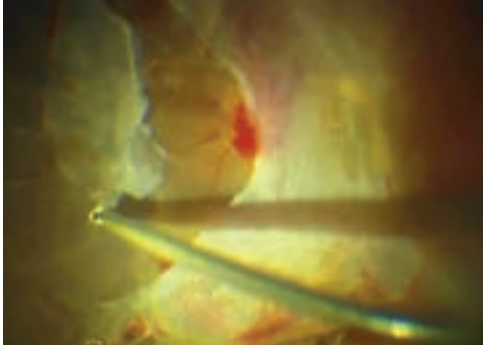


ENDOPHTHALMITIS RATES ON THE DECLINE

A recent study published in *JAMA Ophthalmology* found that the incidence of endophthalmitis following intraocular procedures has decreased substantially over the past 20 years, during which time vitrectomy was used less frequently as the primary treatment than in the past.[1]

This cohort study of 2,124,964 patients examined data from different intraocular procedures, including intravitreal injections and surgeries for cataract removal, glaucoma, retinal conditions, and corneal transplants, from 2000 to 2022.[1] Over the 22-year study period, 5,827,809 intraocular procedures were analyzed; 4,305 cases of endophthalmitis were found for an overall endophthalmitis rate of 0.07%. The yearly rate of endophthalmitis varied but generally declined from a high of seven cases per 3,502 procedures (0.20%) in 2000 to a low of 163 cases per 332,159 procedures (0.05%) in 2022. The percentage of cases treated with vitrectomy also varied but generally declined over time with a high of 17 of 35 (48.6%) in 2003 and a low of 60 of 515 (11.6%) in 2021.[1]

Multivariable analysis of the endophthalmitis incidence rate ratio showed a per-year decrease of 2.7% over the study period. A similar analysis showed that the incidence rate of prompt surgical treatment decreased by 3.8% per year throughout the study period.[1]

1. VanderBeek BL, Chen Y, Tomaiuolo, M, et al. Endophthalmitis rates and types of treatments after intraocular procedures [published online ahead of print August 1, 2024]. *JAMA Ophthalmol.*

THE PDS MAINTAINS EFFICACY IN DME AND DR OVER 2 YEARS

Genentech/Roche in July announced 2-year data from the phase 3 Pagoda and Pavilion studies evaluating the port delivery system (PDS) with ranibizumab (Susvimo) for the treatment of diabetic macular edema (DME) and diabetic retinopathy (DR), respectively.[1]

The PDS, which is being reintroduced in the United States after a voluntary recall in October 2022,[2] is a refillable eye implant that provides continuous delivery of a customized formulation of ranibizumab.[1] Following the recall, the company updated the device and refill needle to meet the necessary performance standards.[3]

In Pagoda, patients with DME receiving the PDS continued to maintain improvements in vision gains seen at 1 year (9.8 letters). Approximately 95% of patients did not need additional treatment with supplemental injections. The safety data were consistent with the known safety profile for the PDS in DME, with no new safety concerns observed.[1]

In Pavilion, patients with DR who received the PDS maintained Diabetic Retinopathy Severity Scale (DRSS) improvements seen at 1 year. Specifically, at week 100, 80% of participants achieved a two-step or greater improvement in their DRSS score from pre-implant baseline, and participants who received the PDS from week 64 either maintained or improved their DRSS score from baseline. Approximately 98% of participants did not need additional treatment with supplemental injections. Similar to Pagoda, the safety data were consistent with no new safety concerns observed.[1]

The company's supplemental biologics license application for the PDS for the treatment of DME and DR was accepted by the FDA. The filing acceptance is based on the 1-year results from these two studies, both of which met their primary endpoint.[1]

WATCH IT NOW

EyewireTV | 08.07.2024

In this episode:

- Two Phase 3 Trials for Dry and Wet AMD Drug Candidates Begin
- Wearable Aid With AI-Powered Visual Assistant is Unveiled
- ASCRS Business of Refractive Cataract Surgery Summit Launched

1. New data for Susvimo demonstrates sustained efficacy in DME and DR [press release]. Eyewire+. July 19, 2024. Accessed August 12, 2024. eyewire.news/news/new-data-for-susvimo-demonstrates-sustained-efficacy-in-dme-and-dr
2. Genentech voluntarily recalls Susvimo ocular implant for wet AMD [press release]. Eyewire+. October 20, 2022. Accessed August 13, 2024. eyewire.news/news/genentech-voluntarily-recalls-susvimo-ocular-implant-for-wet-amd
3. Genentech to reintroduce Susvimo ocular implant for wet AMD [press release]. Eyewire+. July 8, 2024. Accessed August 13, 2024. eyewire.news/news/genentech-to-reintroduce-susvimo-for-wet-amd

BUSINESS BUZZ

- EssilorLuxottica recently announced that it has reached a deal to acquire an 80% stake in Heidelberg Engineering. As part of the deal, Heidelberg will continue to serve the market under its brand.
- Opthea announced the formation of its Medical Advisory Board, which includes: Arshad M. Khanani, MD, MA, FASRS; David S. Boyer, MD; Andrew Chang, AM, MBBS (Hons), PhD FRANZCO, FRACS; Frank G. Holz, MD, FEBO, FARVO; Anat Loewenstein, MD, MHA; Dante Pieramici, MD; Carl D. Regillo, MD; Patricio G. Schlottmann, MD; Tien Y. Wong, MD, PhD; and Eric Souied, MD, PhD.
- Gene therapy company Opus Genetics has received $1.7 million in funding from the Foundation Fighting Blindness to help advance two preclinical candidate programs: a gene therapy vector designed to target rhodopsin-mediated autosomal-dominant retinitis pigmentosa and a viral vector for treating retinitis pigmentosa due to mutations in the proto-oncogene *MERTK* gene.
- Allen C. Ho, MD, was appointed to the position of chairman of the Alcon Research Institute's Executive Committee.
- Carlos Quezada Ruiz, MD, has joined 4D Molecular Therapeutics as senior vice president, clinical research and development and therapeutic area head.

Eyewire+ Pharma Update

- **Ocular Therapeutix** began enrollment for the phase 3 SOL-R clinical trial to evaluate repeat dosing of **Axpaxli**, a therapy in development for wet AMD. The trial will compare repeat dosing of Axpaxli every 6 months with 2 mg aflibercept (Eylea, Regeneron) dosed every 8 weeks.
- The European Trade Commission approved **faricimab (Vabysmo, Genentech/Roche)** for the treatment of macular edema secondary to retinal vein occlusion, the third indication to be approved for this drug in Europe, after wet AMD and diabetic macular edema.
- **Spryte Medical** announced that its **neuro OCT** was granted Breakthrough Device Designation by the FDA. This technology is designed to allow for detailed visualization of cerebrovascular anatomy at near-histologic levels.
- **4D Molecular Therapeutics** released positive 24-month interim data from the phase 2 PRISM trial evaluating **4D-150** for the treatment of wet AMD. The results showed good safety and tolerability with promising efficacy data; phase 3 planning is underway.
- The first patient has been dosed in the VISTA trial of **laruparetigene zovaparvovec (AGTC-501, Beacon Therapeutics)** for the treatment of x-linked retinitis pigmentosa. The study will evaluate the safety, efficacy, and tolerability of two different dose levels of the drug.
- **Sandoz** received FDA approval for its aflibercept biosimilar, **Enzeevu (aflibercept-abzv)**, for the treatment of wet AMD.
- **LumiThera's** photobiomodulation system, **Valeda**, has a new Category III CPT code—"Photobiomodulation therapy of retina, single session"—that is effective January 1, 2025.

Want more retina news from *Eyewire+*?

C1Q INHIBITOR ENTERS PHASE 3 FOR GA

Annexon recently announced new data from the phase 2 ARCHER trial investigating the efficacy of ANX007, a C1q inhibitor, for the treatment of geographic atrophy. In addition, patient dosing in the phase 3 ARCHER II clinical trial of ANX007 began in August, according to a news update from the company.[1]

In ARCHER, a new analysis of the data demonstrated a statistically significant and dose-dependent BCVA protection against ≥ 15-letter loss at month 12: 21.3% in the sham arm versus 5.6% in the monthly ANX007 arm (P = .0021). Treatment with ANX007 also resulted in greater protection of low-luminance visual acuity against ≥ 15-letter loss at month 12: 20.3% in the sham arm versus 7.6% in the monthly ANX007 arm (P = .022). Significant structural benefits from treatment with ANX007 were also noted at 12 months, including a 60% protection of photoreceptors compared with sham within the central 1.5 mm of the fovea as measured by ellipsoid zone loss (P = .0319) and a 29% protection of photoreceptors across the full retinal field (P = .017). Although not statistically significant, an 18% protection of the retinal pigment epithelium in the central foveal subfield was also observed.[1]

The primary outcome measure in ARCHER II will be BCVA protection against ≥ 15-letter loss, and data are expected in the second half of 2026.[1]

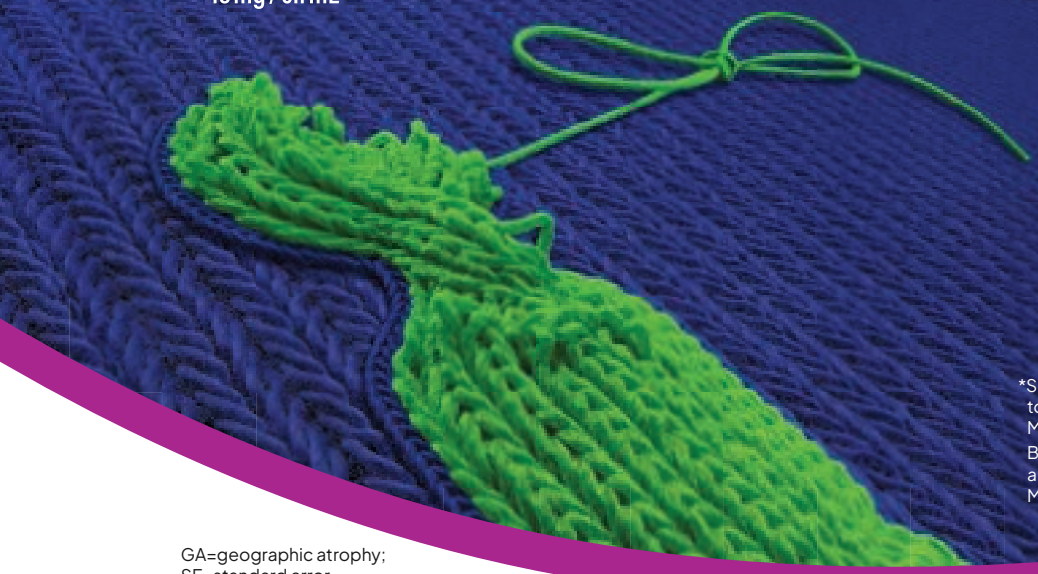
1. Annexon provides update on ARCHER II global registrational program in geographic atrophy. Eyewire+. August 5, 2024. Accessed August 8, 2024. eyewire.news/news/annexon-provides-update-on-archer-ii-global-registrational-program-in-geographic-atrophy

HEIDELBERG ENGINEERING IMPROVES OCT ANGIOGRAPHY IMAGING TIME

In July, Heidelberg Engineering received FDA clearance for its Spectralis OCT angiography (OCTA) module.[1] The preset OCTA speed of 125 kHz is designed to reduce acquisition time by 50% while maintaining image quality, according to the company. Heidelberg added that, combined with a more powerful OCT engine, updated graphics processing technology, and software optimization, the company's Shift technology delivers increased speed, maintains data integrity, and improves performance.[1] ■

1. Heidelberg Engineering introduces faster oct angiography with Spectralis Shift technology [press release]. Eyewire+. July 16, 2024. Accessed August 12, 2024. eyewire.news/news/heidelberg-engineering-introduces-faster-oct-angiography-with-spectralis-shift-technology

SYFOVRE®
(pegcetacoplan injection)
15 mg / 0.1 mL



GA unravels so much SAVE RETINAL TISSUE BY SLOWING PROGRESSION[1-3]

SYFOVRE achieved continuous reductions in mean lesion growth rate* vs sham pooled from baseline to Month 24[1,4]

Monthly	Every Other Month (EOM)
OAKS trial (mm^2): (3.11 vs 3.98) **22%**	OAKS trial (mm^2): (3.26 vs 3.98) **18%**
DERBY trial (mm^2): (3.28 vs 4.00) **18%**	DERBY trial (mm^2): (3.31 vs 4.00) **17%**

SE in trials (monthly, EOM, sham pooled): OAKS: 0.15, 0.13, 0.14; DERBY: 0.13, 0.13, 0.17.

*Slope for baseline to Month 24 is an average of slope of baseline to Month 6, Month 6 to Month 12, Month 12 to Month 18, and Month 18 to Month 24.[1]

Based on a mixed effects model for repeated measures assuming a piecewise linear trend in time with knots at Month 6, Month 12, and Month 18.[1]

GA=geographic atrophy;
SE=standard error.

Explore the long-term data

The CMS-assigned permanent J-code for SYFOVRE is J2781—effective 10/1/23[1]

INDICATION

SYFOVRE® (pegcetacoplan injection) is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- SYFOVRE is contraindicated in patients with ocular or periocular infections, and in patients with active intraocular inflammation

WARNINGS AND PRECAUTIONS

- **Endophthalmitis and Retinal Detachments**
  - Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
- **Retinal Vasculitis and/or Retinal Vascular Occlusion**
  - Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of SYFOVRE. Cases may occur with the first dose of SYFOVRE and may result in severe vision loss. Discontinue treatment with SYFOVRE in patients who develop these events. Patients should be instructed to report any change in vision without delay.
- **Neovascular AMD**
  - In clinical trials, use of SYFOVRE was associated with increased rates of neovascular (wet) AMD or choroidal neovascularization (12% when administered monthly, 7% when administered every other month and 3% in the control group) by Month 24. Patients receiving SYFOVRE should be monitored for signs of neovascular AMD. In case anti-Vascular Endothelial Growth Factor (anti-VEGF) is required, it should be given separately from SYFOVRE administration.
- **Intraocular Inflammation**
  - In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves, patients may resume treatment with SYFOVRE.
- **Increased Intraocular Pressure**
  - Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

ADVERSE REACTIONS

- Most common adverse reactions (incidence ≥5%) are ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, conjunctival hemorrhage.

Please see Brief Summary of Prescribing Information for SYFOVRE on the adjacent page.

Trial Design: SYFOVRE safety and efficacy were assessed in OAKS (N=637) and DERBY (N=621), multi-center, 24-month, Phase 3, randomized, double-masked trials. Patients with GA (atrophic nonexudative age-related macular degeneration), with or without subfoveal involvement, secondary to AMD were randomly assigned (2:2:1:1) to receive 15 mg/0.1 mL intravitreal SYFOVRE monthly, SYFOVRE EOM, sham monthly, or sham EOM for 24 months. Change from baseline in the total area of GA lesions in the study eye (mm^2) was measured by fundus autofluorescence (FAF).[1,4]

References: 1. SYFOVRE (pegcetacoplan injection) [package insert]. Waltham, MA: Apellis Pharmaceuticals, Inc.; 2023. **2.** Pfau M, von der Emde L, de Sisternes L, et al. Progression of photoreceptor degeneration in geographic atrophy secondary to age-related macular degeneration. *JAMA Ophthalmol*. 2020;138(10):1026-1034. **3.** Bird AC, Phillips RL, Hageman GS. Geographic atrophy: a histopathological assessment. *JAMA Ophthalmol*. 2014;132(3):338-345. **4.** Data on file. Apellis Pharmaceuticals, Inc.

Apellis

SYFOVRE® (pegcetacoplan injection), for intravitreal use
BRIEF SUMMARY OF PRESCRIBING INFORMATION
Please see SYFOVRE full Prescribing Information for details.

INDICATIONS AND USAGE

SYFOVRE is indicated for the treatment of geographic atrophy (GA) secondary to age-related macular degeneration (AMD).

CONTRAINDICATIONS

Ocular or Periocular Infections
SYFOVRE is contraindicated in patients with ocular or periocular infections.
Active Intraocular Inflammation
SYFOVRE is contraindicated in patients with active intraocular inflammation.

WARNINGS AND PRECAUTIONS

Endophthalmitis and Retinal Detachments
Intravitreal injections, including those with SYFOVRE, may be associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering SYFOVRE in order to minimize the risk of endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately.
Retinal Vasculitis and/or Retinal Vascular Occlusion
Retinal vasculitis and/or retinal vascular occlusion, typically in the presence of intraocular inflammation, have been reported with the use of SYFOVRE. Cases may occur with the first dose of SYFOVRE and may result in severe vision loss. Discontinue treatment with SYFOVRE in patients who develop these events. Patients should be instructed to report any change in vision without delay.
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In clinical trials, use of SYFOVRE was associated with episodes of intraocular inflammation including: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, and anterior chamber flare. After inflammation resolves patients may resume treatment with SYFOVRE.
Increased Intraocular Pressure
Acute increase in IOP may occur within minutes of any intravitreal injection, including with SYFOVRE. Perfusion of the optic nerve head should be monitored following the injection and managed as needed.

ADVERSE REACTIONS

Clinical Trials Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice.
A total of 839 patients with GA in two Phase 3 studies (OAKS and DERBY) were treated with intravitreal SYFOVRE, 15 mg (0.1 mL of 150 mg/mL solution). Four hundred nineteen (419) of these patients were treated in the affected eye monthly and 420 were treated in the affected eye every other month. Four hundred seventeen (417) patients were assigned to sham.
The most common adverse reactions (≥5%) reported in patients receiving SYFOVRE were ocular discomfort, neovascular age-related macular degeneration, vitreous floaters, and conjunctival hemorrhage.

Table 1: Adverse Reactions in Study Eye Reported in ≥2% of Patients Treated with SYFOVRE Through Month 24 in Studies OAKS and DERBY

Adverse Reactions	PM (N = 419) %	PEOM (N = 420) %	Sham Pooled (N = 417) %
Ocular discomfort*	13	10	11
Neovascular age-related macular degeneration*	12	7	3
Vitreous floaters	10	7	1
Conjunctival hemorrhage	8	8	4
Vitreous detachment	4	6	3
Retinal hemorrhage	4	5	3
Punctate keratitis*	5	3	<1
Posterior capsule opacification	4	4	3
Intraocular inflammation*	4	2	<1
Intraocular pressure increased	2	3	<1

PM: SYFOVRE monthly; PEOM: SYFOVRE every other month
*The following reported terms were combined:
Ocular discomfort included: eye pain, eye irritation, foreign body sensation in eyes, ocular discomfort, abnormal sensation in eye
Neovascular age-related macular degeneration included: exudative age-related macular degeneration, choroidal neovascularization
Punctate keratitis included: punctate keratitis, keratitis
Intraocular inflammation included: vitritis, vitreal cells, iridocyclitis, uveitis, anterior chamber cells, iritis, anterior chamber flare

Endophthalmitis, retinal detachment, hyphema and retinal tears were reported in less than 1% of patients. Optic ischemic neuropathy was reported in 1.7% of patients treated monthly, 0.2% of patients treated every other month and 0.0% of patients assigned to sham. Deaths were reported in 6.7% of patients treated monthly, 3.6% of patients treated every other month and 3.8% of patients assigned to sham. The rates and causes of death were consistent with the elderly study population.

Postmarketing Experience
The following adverse reactions have been identified during postapproval use of SYFOVRE. 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. Eye disorders: retinal vasculitis with or without retinal vascular occlusion.

USE IN SPECIFIC POPULATIONS

Pregnancy
Risk Summary
There are no adequate and well-controlled studies of SYFOVRE administration in pregnant women to inform a drug-associated risk. The use of SYFOVRE may be considered following an assessment of the risks and benefits.
Systemic exposure of SYFOVRE following ocular administration is low. Subcutaneous administration of pegcetacoplan to pregnant monkeys from the mid gestation period through birth resulted in increased incidences of abortions and stillbirths at systemic exposures 1040-fold higher than that observed in humans at the maximum recommended human ophthalmic dose (MRHOD) of SYFOVRE (based on the area under the curve (AUC) systemically measured levels). No adverse maternal or fetal effects were observed in monkeys at systemic exposures approximately 470-fold higher than that observed in humans at the MRHOD.
In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.
Lactation
Risk Summary
It is not known whether intravitreal administered pegcetacoplan is secreted in human milk or whether there is potential for absorption and harm to the infant. Animal data suggest that the risk of clinically relevant exposure to the infant following maternal intravitreal treatment is minimal. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when SYFOVRE is administered to a nursing woman.
Females and Males of Reproductive Potential
Contraception
Females: It is recommended that women of childbearing potential use effective contraception methods to prevent pregnancy during treatment with intravitreal pegcetacoplan. Advise female patients of reproductive potential to use effective contraception during treatment with SYFOVRE and for 40 days after the last dose. For women planning to become pregnant, the use of SYFOVRE may be considered following an assessment of the risks and benefits.
Pediatric Use
The safety and effectiveness of SYFOVRE in pediatric patients have not been established.
Geriatric Use
In clinical studies, approximately 97% (813/839) of patients randomized to treatment with SYFOVRE were ≥ 65 years of age and approximately 72% (607/839) were ≥ 75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies. No dosage regimen adjustment is recommended based on age.

PATIENT COUNSELING INFORMATION

Advise patients that following SYFOVRE administration, patients are at risk of developing endophthalmitis, retinal detachments, retinal vasculitis with or without retinal vascular occlusion and neovascular AMD. If the eye becomes red, sensitive to light, painful, or if a patient develops any change in vision such as flashing lights, blurred vision or metamorphopsia, instruct the patient to seek immediate care from an ophthalmologist. Patients may experience temporary visual disturbances associated either with the intravitreal injection with SYFOVRE or the eye examination. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

Manufactured for:
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MASTERING THE JOURNEY FROM MENTEE TO MENTOR

Consider these pearls from esteemed leaders in the field as you make the transition.

BY THEO BOWE, MD; YOSHIHIRO YONEKAWA, MD; AJAY E. KURIYAN, MD, MS; ALEKSANDRA RACHITSKAYA, MD; REBECCA SOARES, MD; AND JAYANTH SRIDHAR, MD

As retina fellows, we have been guided by generous and skilled mentorship along our journey through medical school and residency. Once in fellowship, we often find ourselves becoming mentors ourselves—a transition that raises many questions. Here, I (T.B.) share with you the teachings gleaned from interviews with five prolific mentors: Yoshihiro Yonekawa, MD; Ajay E. Kuriyan, MD, MS; Aleksandra Rachitskaya, MD; Rebecca Soares, MD; and Jayanth Sridhar, MD.

THEO BOWE, MD: WHAT QUALITIES DO YOU LOOK FOR IN A MENTEE?

Dr. Yonekawa: Mentorship is an integral component of academic ophthalmology and draws many of us into the field. There's nothing better than watching your trainees succeed! Mentorship is a two-way road—the best relationships are when both the mentor and mentee are genuine, committed, communicative, honest, supportive, and understanding of the bigger picture. Make sure to treasure your mentors and mentees like family. The best mentor-mentee relationships turn into friendships that last a lifetime.

Dr. Kuriyan: The best mentees have a combination of motivation and intrinsic interest in expanding their knowledge. They are organized and have excellent attention to detail. Additional skills are helpful, such as experience with statistics and scientific writing.

Dr. Rachitskaya: In medicine, we are all perpetual mentees and mentors. In my experience, a trainee should have multiple mentors. Some might be great at advising on research or surgical challenges but might not be as good at mentoring on wellbeing and work-life balance. I work with a lot of trainees, and I find it helpful when a mentee is prepared and has an idea of what they would like to discuss and focus on during meetings. Additionally, follow-up and ongoing communication is important to ensure both parties follow through on the plan.

Dr. Soares: I connect with mentees who are motivated to find a way to step beyond the bounds of what's expected. From a research perspective, I have worked with a few mentees with unique skills outside of medicine—a background in coding or statistics, for example. While their skills were not directly connected to the project at hand, they found unique ways to use their expertise to drive projects forward. From a clinical and surgical perspective, I find it rewarding to coach mentees who are responsive to feedback and request it in the first place. It shows enthusiasm for learning and malleability.

Dr. Sridhar: The best mentees are enthusiastic, humble, willing, and organized. In addition, they are flexible in their interests and schedule, understanding that even the best mentors have other time demands clinically, surgically, academically, and personally.

DR. BOWE: HOW DO YOU LEAD A PRODUCTIVE GROUP OF TRAINEES THROUGH A PROJECT?

Dr. Yonekawa: Ensure that everyone has a solid understanding of your vision for the project. Recognize each trainee's unique strengths and assign roles accordingly;

MENTORSHIP IS A TWO-WAY ROAD—THE BEST RELATIONSHIPS ARE WHEN BOTH THE MENTOR AND MENTEE ARE GENUINE, COMMITTED, COMMUNICATIVE, HONEST, SUPPORTIVE, AND UNDERSTANDING OF THE BIGGER PICTURE.

if someone has a superpower, make sure to unleash their potential. Credit everyone for their hard work, and include everyone as coauthors; decide on the authorship order before starting the project so that everyone has the correct expectations and to avoid any hard feelings later in the process. Make sure everyone contributes to the project they are authoring. One of the reasons I love research is because it can serve as a launching pad to take trainees to new heights, whether it's in training or at the podium.

Dr. Kuriyan: As a mentor, it is helpful to spend time teaching medical students the basics of chart review and data entry. It also helps to have a clear delegation of tasks and a plan from the beginning of the project. Ideally, mentors can identify additional projects or case reports to provide all members of the research team the opportunity to lead publications or presentations and play a meaningful role in different aspects of disseminating the research, not just collecting data.

Dr. Rachitskaya: There are different demands on trainees' time during the various stages of training (eg, more and less demanding rotations, examinations, interviews). Research, though, moves along different timelines. Setting realistic expectations is key to success. Clear communication and frequent check-ins are essential to productive research.

Dr. Soares: Delegate. You cannot do everything yourself. Projects become much more thoughtful and creative when many minds are working together. Massive projects become more efficient when each person has a small role. Don't be afraid to communicate.

Dr. Sridhar: Set expectations in advance and conduct scheduled check-ins. Recognize the power difference that exists between the attending, fellow, resident, and medical student. As captain of the ship, the attending should outline everyone's responsibilities.

DR. BOWE: HOW DO YOU SUPPORT TRAINEES APPLYING TO RESIDENCY AND FELLOWSHIP?

Dr. Yonekawa: The biggest role you have is to help trainees realistically assess their chances of matching, where to apply, and how many programs they should apply for. The second biggest role you have is advocating for them during the application process.

Dr. Rachitskaya: Applying and interviewing for the next step in training is both an exciting and stressful time. The process is more complex now that some interviews are conducted virtually and some metrics historically used to differentiate candidates are changing. Be prepared—practice interviews can be quite helpful.

Dr. Soares: Honesty about the process and your own experience is important. Mentors should highlight the advantages of each program they are familiar with and be candid about the disadvantages. It is equally important to be honest with the mentee about their own abilities, needs, and weaknesses. Their success depends on finding a good fit for them.

Dr. Sridhar: Put yourself in your mentee's shoes. Think back to your time as a student applying to ophthalmology and what advice you wish you had been given. Recognize that each mentee's needs may be different. Begin the mentoring process by asking questions. This will help you be most effective as a mentor.

DR. BOWE: HOW DO YOU HANDLE LETTERS OF RECOMMENDATION?

Dr. Yonekawa: I like using personal anecdotes for letters rather than a generic template. Letters are so much more interesting and meaningful that way. Because programs see letters from us all the time, the writer's credibility can wane if they upload similar letters for every applicant.

Dr. Kuriyan: I only write a letter of recommendation if I feel I can write a strong one. I ask applicants to provide me their application materials prior to writing the letter so I can review them and incorporate their background into the letter. It is important to be honest when supporting a candidate, as you want your recommendations to be trusted and respected.

Dr. Rachitskaya: Trainees should ask people who know them well and can comment on various aspects of their application. I frequently write letters for trainees who do research with me. If there is a part of their application that I am not familiar with, for instance their surgical skills, I reach out to my colleagues who have seen the applicant operate. I also meet with the applicant before I write a letter of recommendation so that I can ask questions and learn more about them.

Dr. Soares: I strongly believe that everyone has strengths, which a good writer can elucidate. However, I also try to be honest with the candidate if I don't know enough about them. From a candidate's perspective, it is very important to know a mentor outside of just data collection and research. They can reach out to talk about the mentor's experiences and goals and ask how to get involved. When a mentor is familiar with the trainee's personality and clinical talents, it is much easier to write a vivid letter of recommendation.

Dr. Sridhar: I generally ask my students to give me at least 2 to 4 weeks to write a letter and to provide as much information as possible. I recommend that students work with me clinically and academically so that the letter of recommendation carries more weight and assesses the candidate from more than one perspective.

DR. BOWE: WHAT ADVICE CAN YOU OFFER TO FELLOWS STEPPING INTO A MENTORING ROLE?

Dr. Yonekawa: Mentoring is an integral aspect of your own training. I worked with numerous students and residents when I was a fellow, and that was such a fun and fulfilling aspect of fellowship. My happiest day during fellowship was when our students matched into residency and our work came full circle.

Dr. Kuriyan: Make sure you feel comfortable with your own clinical and surgical duties first. Then you can focus on your research efforts and figure out how to successfully incorporate other trainees into your projects. Creating a system of scheduled check-ins around your clinical schedule is very helpful for assessing the progress of your trainees. Trainees are usually eager to have more clinical exposure, so offering opportunities in the clinic and the OR will go a long way with them.

Dr. Rachitskaya: The best fellow awards usually go to fellows who take interest in junior colleagues and use every opportunity to teach and engage them. For example, I enjoy overhearing my fellow going over an OCT finding with a medical student or resident. Getting trainees involved in research projects and guiding them is another way to start building mentorships.

Dr. Soares: It is easy to be a mentor in the clinic because there is always someone below you eager to learn and get involved. The easiest way to become a mentor in the clinic is to give constant feedback. If you identify something good that a trainee has done, voice it, no matter how small. I tend to use the feedback sandwich: good feedback, constructive/negative feedback, good feedback. With continuous communication, you let trainees know that you are invested in them.

Dr. Sridhar: If you love teaching and mentoring, don't be afraid to lean into it! Students will always gravitate to a motivated mentor. Be realistic about your own training needs and avoid biting off more than you can chew. It's never too early to be a great mentor, and it'll make all the difference to a mentee! ■

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SARWAR ZAHID, MD

WHERE IT ALL BEGAN

I was born in Dhaka, Bangladesh, and my family moved to Queens, New York, when I was young. I was always drawn to biomedical science, so a career in medicine was a natural fit. If I had not pursued medicine, I would probably be in a creative field involving music or theater (I am known in the retina community as DJ Schisis).

After completing my undergraduate degree at New York University, I attended medical school at the University of Michigan (Go Blue!). I returned to New York University for residency and completed my vitreoretinal surgery fellowship at the University of Illinois at Chicago. After practicing in Chicago for 2 years, I returned to New York City to serve my hometown community.

MY PATH TO RETINA

I always knew I wanted to be a surgeon, but it was not always ophthalmology. I chose an ophthalmology elective on a whim and knew immediately that this was the field for me. I met K. Thiran Jayasundera, MD, MS, who inspired me to become a retina specialist. I worked with Dr. Jayasundera for a year of research at the Kellogg Eye Center focusing on retinal dystrophies. Thus, it was always retina from the start, and I am lucky to have found a field I love.

SUPPORT ALONG THE WAY

I am eternally grateful for the guidance of my fellowship mentors. In particular, Yannek I. Leiderman, MD, PhD, and R.V. Paul Chan, MD, MSc, MBA, shaped the way I approach preoperative surgical planning and intraoperative execution. I learned to be prepared for curveballs that can arise in both routine and complex surgeries. I still consult my mentors for advice and guidance in tough cases.

I continue to learn from my colleagues around the country during conferences and collaborative forums, such as the Young Retina Forum. These educational opportunities inspired me to start a retina surgery podcast (RetFix and Chill) with Nitish Mehta, MD, and Michael T. Andreoli, MD, where the goal is to learn from each of our unique surgical experiences.

Dr. Zahid's advice: The first year of practice is challenging, but remember that you have a community of retina friends for support. And do not be intimidated by solo practice. If and when you are ready, that same community of colleagues and friends is ready to support you.

AN EXPERIENCE TO REMEMBER

Starting Empire State Retina has been one of the most memorable and rewarding experiences. The community of solo physicians across the country has been an incredible source of education and support. This experience has allowed me to better understand every aspect of medical care, from insurance eligibility and prior authorization to medication inventory management and reimbursement.

It has also motivated me to be more involved in advocacy at the state and federal level. Reforms to prior authorization and step therapy are critical in providing timely care. It is our job to educate our legislators about these issues on behalf of our patients so that they can access safe and timely care. ■

Sarwar Zahid, MD, works in private practice in New York City, taking care of a large diabetic population. In 2022, he started Empire State Retina (**empirestateretina.com**) with Daniel Simhaee, MD. In his spare time, Dr. Zahid recently started doing stand-up comedy. Dr. Zahid is a consultant for Alcon and is on the advisory board for Abbvie. He can be reached at **sarwar@empirestateretina.com**; YouTube: **@RetFixandChill**; and Instagram: **sarwarzahidmd, empirestateretina, retfixandchill.**

PURTSCHER-LIKE RETINOPATHY: A WARNING SIGN OF LUPUS

Retinal findings in an otherwise asymptomatic patient led to a surprising diagnosis.

BY LULWA AL MATOOQ, MD; ZAINAB AL ALI, MD; AND YOUSEF AL DHAFIRI, MD

Systemic lupus erythematous (SLE) is a chronic, autoimmune connective tissue disorder affecting multiple organ systems that often follows a clinical course of relapse and remission.[1] Retinal disease occurs in 10% to 29% of patients with SLE,[2,3] with cotton-wool spots, retinal hemorrhages, and vascular tortuosity being the most common findings.[4] SLE retinopathy is usually an indication of severe, active systemic disease and poor prognosis.[5,6]

Another potential retinal manifestation of SLE is Purtscher-like retinopathy (PLR).[6] Purtscher retinopathy (PR) is a rare condition of unknown pathogenesis caused by occlusive microvasculopathy seen in patients with a history of trauma,[7] while PLR describes a heterogeneous group of diseases that have similar clinical retinal findings to PR but do not have a traumatic etiology.[8] PR/PLR is characterized by the presence of Purtscher flecken, which are seen in half of cases.[8,9] Known causes include pancreatitis, renal failure, amniotic fluid embolism, collagen-vascular disorders, and autoimmune diseases.[8,10]

Here, we report a case of an otherwise healthy patient who presented with PLR, leading to a diagnosis of SLE.

CASE PRESENTATION

A 34-year-old man presented to the hospital with painless vision loss in each eye for 3 weeks, fatigue, body ache, and generalized joint pain. His ophthalmic history included LASIK refractive surgery 1 year prior. On examination, his BCVA was 20/40 OD and 20/25 OS. External eye and anterior segment examinations were normal.

Fundus examination revealed a clear vitreous with multiple peripapillary and perimacular white indistinct polygonal lesions, cotton-wool spots, flame-shaped hemorrhages with venous congestion, sheathing, beading, and

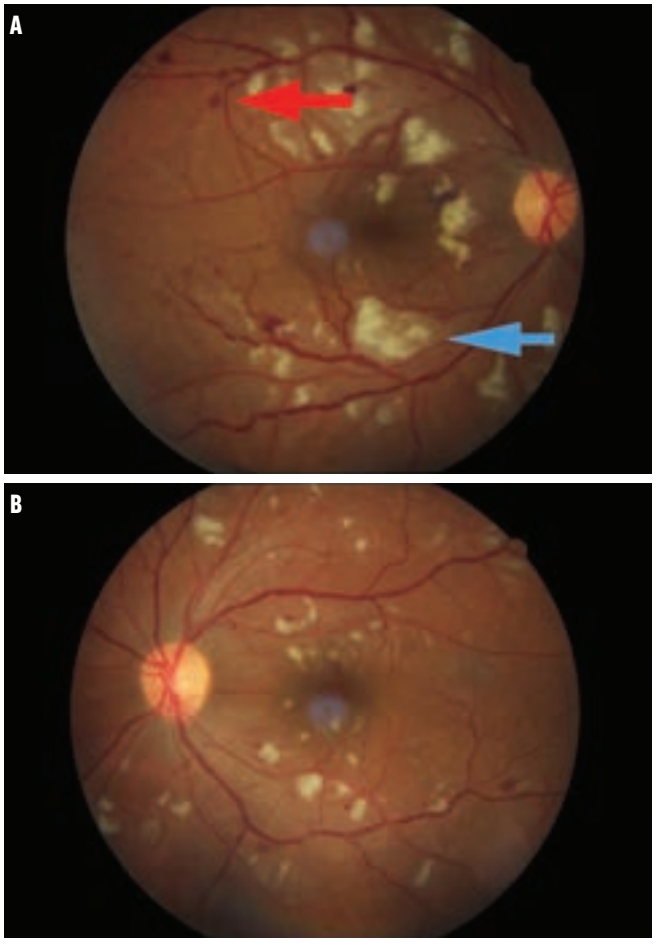

Figure 1. Fundus imaging of the right (A) and left (B) eye showed multiple diffuse cotton-wool spots/Purtscher flecken (blue arrow), intraretinal hemorrhage (red arrow), venous congestion, vascular sheathing, and beading that was more prominent in the right eye. CME was also observed in each eye.

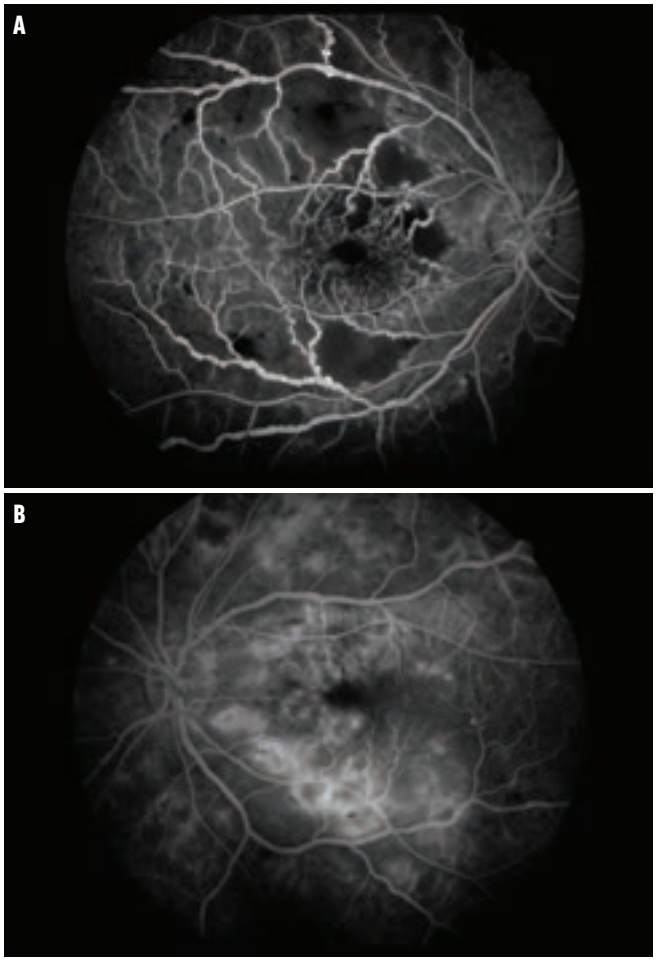

Figure 2. FA of the right (A) and left (B) eye demonstrated diffuse patchy capillary nonperfusion involving the macula and peripheral retina, vessel wall staining, and leakage.

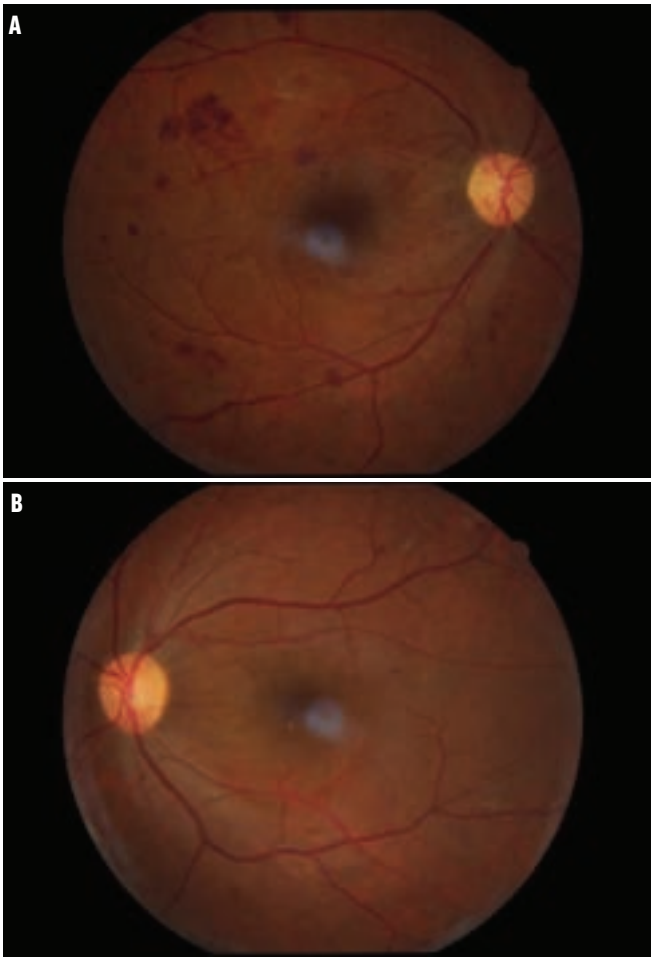

Figure 3. Follow-up imaging of the right (A) and left (B) eye revealed the development of a hyperemic optic disc.

cystoid macular edema (CME) in each eye (Figure 1). Mild disc hyperemia was also noted.

OCT of the macula showed CME with a central foveal thickness of 370 µm and 427 µm in the right and left eye, respectively. Fluorescein angiography (FA) showed multiple diffuse arteriolar occlusions and capillary nonperfusion, corresponding to the areas of Purtscher flecken, involving the macula and the peripheral retina with vascular leaking and staining (Figure 2). A diagnosis of bilateral PLR with secondary CME was made. An underlying systemic vasculitis entity was investigated with various laboratory testing, leading to a diagnosis of systemic lupus anticoagulation and antiphospholipid syndrome.

Treatment Approach and Follow-Up

The patient was managed by a multidisciplinary team that included a rheumatologist, neurologist, and hematologist and admitted to the hospital for 1 week for treatment and investigation. He was treated with 1 g/day intravenous methylprednisolone for 5 days with slow tapering over 3 months and was discharged on 1 mg/Kg/day oral prednisolone with a tapering regimen. Two weeks later, he developed deep vein thrombosis and was admitted to the hospital to receive anticoagulation treatment. The deep vein thrombosis resolved without complication.

The patient was then started on 400 mg oral hydroxychloroquine once daily, 1.5 g mycophenolate mofetil (Cellcept, Genentech/Roche) twice daily, and a 5 mg warfarin tablet once daily, with a plan to continue this treatment regimen for at least 24 months. One month later, OCT of the macula showed residual CME, and an off-label dexamethasone intravitreal implant (Ozurdex, Abbvie) was administered.

His VA had improved to 20/20 OU at this point, and the fundus examination showed the disappearance of Purtscher flecken, cotton-wool spots, and bland intraretinal hemorrhage. OCT confirmed the resolution of CME but showed a wide foveal contour in the right eye with mild atrophic changes in the parafoveal area, indicating ischemic insult. Five months later, he returned with severe blurred vision. Examination showed a hyperemic optic disc and

SLE RETINOPATHY DIFFERS FROM ONE PATIENT TO ANOTHER AND USUALLY INDICATES SEVERE, ACTIVE DISEASE WITH A POOR PROGNOSIS.

macular edema, and triamcinolone acetonide injectable suspension 40 mg/1 mg (Kenalog-40, Bristol Myers Squibb) was administered in each eye (Figure 3).

Fundus examination 2 months later showed neovascularization at the disc and elsewhere, for which panretinal laser photocoagulation was performed on each eye over multiple sessions. One month later, he developed vitreous hemorrhage in his right eye after an increase in his warfarin dose by his hematologist, and anti-VEGF injection was administered; it was later required to treat vitreous hemorrhage in his left eye as well. Two weeks after resolution of the bilateral vitreous hemorrhage, additional argon laser was performed in each eye. The patient was continued on 5 mg oral prednisolone, hydroxychloroquine, mycophenolate mofetil, and a warfarin tablet.

TIME TO UPDATE THE DIAGNOSTIC CRITERIA FOR SLE?

SLE usually first presents with dermatological symptoms, which include four diagnostic features: malar rash, photosensitivity, discoid lesion, and alopecia.[11] The criteria for the diagnosis of SLE includes dermatological and rheumatological signs, renal dysfunction, neurological abnormality, and hematologic and immunologic disorders.[14,15] Although retinopathy is seen in 10% to 29% of patients, it is not listed among these criteria.[3]

SLE retinopathy differs from one patient to another and usually indicates severe, active disease with a poor prognosis.[5,7,16,17] Vasculitis of retinal capillaries and local microinfarction are special features of SLE retinopathy. Patients with lupus retinopathy associated with anti-phospholipid syndrome are more prone to develop large retinal vessel occlusion.[18,19]

Visual prognosis with PLR is variable and depends on the etiology. Pancreatitis, trauma, and male sex are associated with better visual acuity, while patients who are pregnant or have been diagnosed with SLE tend to present with worse visual acuity.[7]

Our case demonstrates PLR as a first presentation of SLE. A similar case was reported by Alahmadi et al,[20] and several retrospective studies and observational case series have shown PLR occurring in patients with SLE.[6,7,9,20-23]

DIG DEEPER

SLE can have varied ocular and systemic manifestations. Although PLR is not part of the diagnostic criteria for SLE, it can be the first presentation in a patient without dermatological features or systemic disease. ■

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DIABETES DAY: IMPROVING ACCESS TO DR CARE

An annual free screening event in Philadelphia has improved patient access and reduced preventable diabetic vision loss.

BY ARI H. AUGUST, BA; CHARLOTTE N. SHIELDS, MD; JAY PENDYALA, BS; ARSLON HUMAYUN, BA; JOHN E. WILLIAMSON III, MD; JOSEPH D. DESIMONE, MD; EMILY DUFFNER, MD; SAIF A. HAMDAN, MD; JASON M. KEIL, MD, PHD; AND ALLEN C. HO, MD

Although efforts to promote public awareness and screening have successfully reduced the number of adults living with undiagnosed diabetes,[1] screening for complications, including diabetic retinopathy (DR), continues to be a challenge. Despite established recommendations, 50% of patients with diabetes do not receive annual eye examinations, a statistic that has remained stagnant for decades.[2]

Adherence to DR screening recommendations is affected by many factors that disproportionately affect marginalized racial and ethnic populations, non-English-speaking patients, and those with limited social resources, such as insurance and transportation.[2-4] Community events may simplify access to care and ultimately reduce diabetic vision loss.

After seeing patients with severe visual impairment due to delayed diagnoses of DR and lack of adherence, we established the Wills Eye on Diabetes Day in 2022 at Wills Eye Hospital. The event serves as an opportunity for patients with diabetes to receive a free DR screening and other educational and social resources. Wills Eye on Diabetes Day held its third annual event on April 20, with continued growth in patients, volunteers, and services each year.

The primary aim of Diabetes Day is to eliminate preventable diabetic vision loss. Further, we aim to reduce socioeconomic disparities in diabetic eye care in our area,

See the demographics and results of Wills Eye on Diabetes Day 2022-2024 at *retinatoday.com:*

AT A GLANCE

- An annual free diabetes screening event in Philadelphia aims to reduce socioeconomic disparities in diabetic eye care, increase community awareness of and participation in yearly diabetic eye examinations, and connect patients with services.
- During the 2024 Philadelphia Diabetes Day, 101 patients were screened, seven of whom had at least mild nonproliferative diabetic retinopathy.
- The authors hope that Diabetes Day and its missions will expand each year to improve access to screening and treatment of diabetic eye disease.

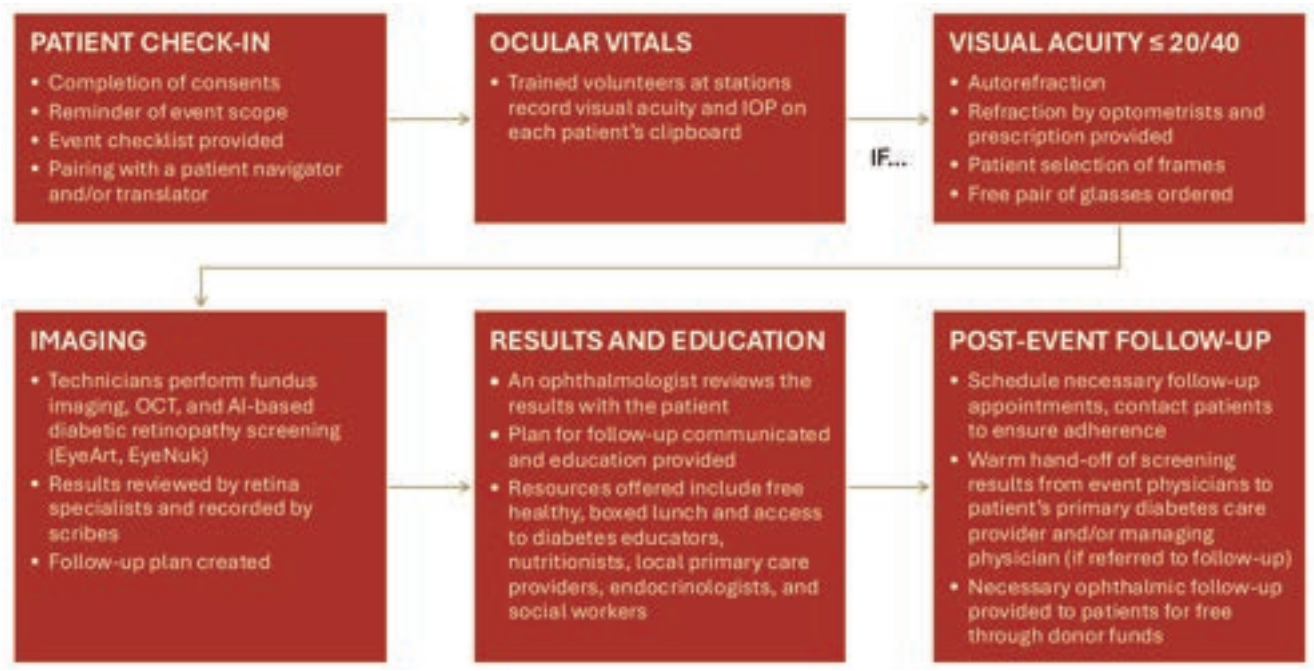

Figure. During the event, patients proceed through multiple steps to ensure that they understand and consent to the scope of the screening and its limitations, use each applicable service at the event, and receive sufficient education regarding the results, the implication of these results, and the plan for follow-up. Additional event services include a free pair of glasses (if necessary), access to a free healthy lunch, and on-site social support and educational services.

increase community awareness of and participation in yearly diabetic eye examinations, provide patients with high-quality screenings, and connect patients with services. Lastly, we hope that this program serves as a model to promote similar events on a larger scale.

EVENT PLANNING 101

Establishing a city-wide DR screening event in Philadelphia required careful planning to ensure that patients receive the standard of care in diabetes management; this is the priority, as patients participating in this event are disproportionately affected by health disparities and access to care.

Volunteers may be scheduled through an online scheduling platform (eg, SignUpGenius, Qualtrics). While skilled volunteers are necessary to provide patient care during the event, there are numerous roles for motivated community members to support these efforts. For example, community volunteers can help with scheduling and act as patient navigators and interpreters during the event. Depending on the number of volunteers, patient navigators can guide patients 1:1 through the event to ensure they receive each service necessary for a complete screening, including ocular vitals, retinal imaging, counseling on results, creation of a follow-up plan, social support services, and diabetes and nutrition education (Figure).

Interpreters/translators are particularly helpful as patient navigators. Based on patient feedback, we have learned that patient navigators significantly enhance the event experience for patients by providing conversation and companionship.

Check out an event checklist that can guide organizational efforts at *retinatoday.com:*

Scheduling patients must be done through a HIPAA-compliant platform and should include information regarding the purpose, scope, and limitations of the event. We schedule patients for an arrival time window, rather than an exact appointment time, to provide patients more flexibility and to encourage attendance, even if they are delayed by transportation or other social factors. Reminders are sent to patients via email by team leaders in the weeks leading up to the event.

Airing a televised news segment has been the most successful form of advertisement, in addition to distributing flyers through social media or posted in locations throughout the city. We strategically place these to target individuals who may have difficulty accessing care (ie, community centers, shelters, etc.). We also Involve community programs that support patients with diabetes, diabetes educators, primary care providers, and endocrinologists to help identify individuals who may benefit from the event.

The third annual event expanded into Philadelphia Diabetes Day, a one-day city-wide event with Wills Eye Hospital, Temple Ophthalmology, and Scheie Eye Institute (both of which joined in 2023). We held a live planning meeting of volunteers to generate enthusiasm and facilitate

a successful expansion. This meeting included skilled and community volunteers from each institution, allowing everyone to share ideas and hopes for future growth of the event. The meeting promoted unity and generated solutions to challenges each institution faced. Volunteers were comprised of medical students, ophthalmology trainees, clinic staff and technicians, and other interested individuals.

ONGOING CARE

Available resources vary by institution, which affects patient capacity and services. At Wills Eye Hospital, we offer refractions and a free pair of glasses to patients who have a VA worse than 20/40—helping to address another cause of visual impairment for our patients.[5] The physical token also reminds patients to continue with follow-up and encourages their return to the screening event each year.

In addition to returning to the event center at a future date for glasses pick-up, some patients are instructed to follow through with additional ophthalmic care based on their screening results. The physician and patient create a tailored care plan during the event. If there is a financial, insurance, or transportation burden, an on-site social worker steps in to assist. If patients choose to continue receiving care at our institution, treatment for conditions identified during the screening event may be provided to uninsured patients free of charge, thanks to the generous support of a donor fund and volunteer doctors.

Screening for and treatment of diabetic eye disease is only one piece of patient care; prevention of diabetic complications through proper diabetes management is crucial. Following the event, each patient's results are communicated to their identified provider (with patient consent). All patients are encouraged to follow up with their primary eye care provider, if available.

To encourage adherence, patients are followed by event staff through email and phone communications to inquire about their ability to access the recommended care.

GROW AND SAVE VISION

The expansion into Philadelphia Diabetes Day, with simultaneous events held at three separate institutions, is only the start of our plan to propagate similar diabetic eye screening events on a larger scale. Planning for the next Diabetes Day, slated for April 26, 2025, is already underway.

We have engaged with the Pennsylvania Academy of Ophthalmology and Retina Associates of Western NY, which is an auspicious sign that Diabetes Day and its missions will expand to improve screening for and treatment of diabetic eye disease and, therefore, prevention of vision loss. ■

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MANAGING DR IN PREGNANCY: A (NOT-SO) HOT TOPIC

Barriers to proper screening and care threaten the vision of this unique subset of patients with diabetes.

BY SWARA SARVEPALLI, MD, AND MAJDA HADZIAHMETOVIC, MD


Although early detection of diabetic retinopathy (DR) is crucial for effective treatment, more than 50% of patients with diabetes fail to undergo recommended retinal screenings, resulting in late-stage diagnosis and compromised visual outcomes.[1]

While there are many risk factors for the development and progression of DR, pregnancy itself is a proven independent risk factor (Figure).[2] As of 2022, the estimated rate of DR in early pregnancy was alarmingly high at 52.3% among those with preexisting diabetes.[3] DR during pregnancy can lead to severe complications for both the mother and the fetus, including eclampsia, higher rates of cesarean delivery, cardiovascular disease later in life, macrosomia, prematurity, and shoulder dystocia.[4] Despite these risks, current screening guidelines only recommend early and frequent examinations throughout pregnancy without specifying concrete guidelines or follow-up timeframes.[5]

Managing DR and its complications in patients who are pregnant requires a careful, individualized approach to balance effective treatment with the safety of the mother and developing fetus. The lack of comprehensive safety data for anti-VEGF agents during pregnancy results in hesitancy in their use.[6] The theoretical risk of systemic absorption and potential effects on fetal development, observed in some animal studies, necessitates caution.[7,8] Similar concerns apply to intravitreal steroids, where potential systemic absorption and its effect requires weighing benefits against potential risks.[9] Laser therapy remains a primary treatment option due to its safety profile.[10,11] However, its effectiveness in rapidly progressing cases of proliferative DR or diabetic macular edema during pregnancy is questionable.[10] Despite the remarkable advances in DR treatment, the need for multiple treatments and the risk of vision loss remain significant concerns in this patient population. Close collaboration between ophthalmologists, obstetricians, and endocrinologists is crucial to optimize clinical outcomes. This ensures maternal and fetal safety while effectively managing this retinal pathology.

THE LATEST DATA

Unfortunately, DR in pregnancy has not been as thoroughly studied as DR in the general diabetic patient population. A landmark study by the Diabetes Control and Complications Trial group was one of the first to provide meaningful insight on this topic. They conducted

AT A GLANCE

- Current diabetic retinopathy (DR) screening guidelines only recommend early and frequent examinations throughout pregnancy without specifying concrete guidelines or follow-up timeframes.
- A meta-analysis found that pre-pregnancy hemoglobin A1c level, disease duration, and diastolic blood pressure were significantly higher in the progression group and were independent risk factors for the development or progression of DR.
- Improving DR screening rates hinges on precise retinal imaging analysis, as well as standardized staging criteria.

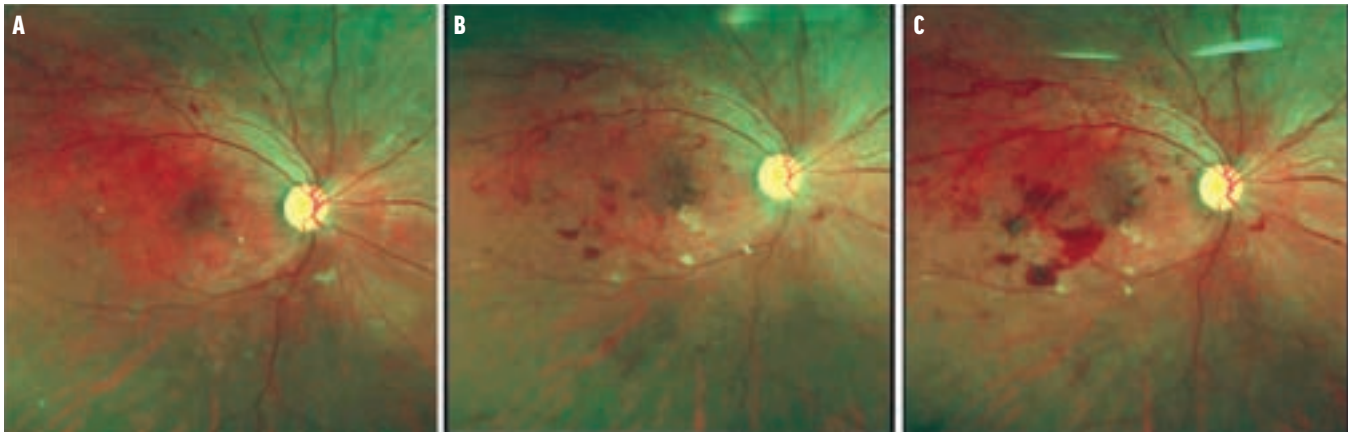

Figure. Progression of DR in pregnancy at 3 (A), 6 (B), and 8 months (C) gestation.

a large-scale study examining the effect of type 1 diabetes on DR, showing that pregnancy itself was a risk factor for progression and that the highest risk of progression was in the second trimester.[12] Chew et al conducted a similar study and reported that retinopathy of any stage and elevated hemoglobin A1c at baseline were predictive factors for the progression of DR in pregnancy.[13] They also discovered that for patients with poor pre-pregnancy glycemic control, initiating tight glycemic control during pregnancy paradoxically increased the risk of DR progression. However, tight glycemic control has been proven to decrease retinopathy rates in the long term.[13]

Our team recently conducted a meta-analysis of 27 unique studies, yielding data from 2,537 pregnant patients. We found that hemoglobin A1c level, duration of diabetes, and diastolic blood pressure at baseline (pre-pregnancy) were significantly higher in the progression group and were all independent risk factors for the development or progression of DR.[2] We also conducted a similar study at a tertiary care center examining the risk factors for DR progression in pregnancy. Similar to our meta-analysis and other published literature findings, any stage of DR at baseline was significantly related to disease progression during pregnancy. Additionally, poor blood pressure control was also associated with the progression of DR.[14]

SCREENING IMPLICATIONS

Pre-pregnancy visits should focus on obtaining tight control of glycemic levels and optimizing overall health before conception, including initiation of pregnancy-safe antihypertensive agents, if indicated. It would also be appropriate to conduct a thorough retinal examination to determine the baseline state or presence of DR, along with a thorough review of the patient's risk factors.

The quest to establish the best practices for DR screening during pregnancy remains ongoing. Numerous methods have been suggested to enhance the convenience and effectiveness of screening for expectant mothers. One study exploring obstacles to DR screening in pregnant patients revealed that many did not consider this screening essential to their pregnancy, citing inconvenience, access, and cost as significant barriers.[15] Multiple factors influence adherence to screening recommendations, making it challenging to identify a one-size-fits-all solution.

Recent evidence indicates that improving DR screening rates hinges on precise retinal imaging analysis and standardized staging criteria. Experts suggest that offering DR screening outside ophthalmology clinics, such as at endocrinology and primary care clinics, would improve access and adherence.[9] One Australian clinic implemented these recommendations by offering retinal imaging scans to women at their standard prenatal visits. These images were then transmitted to a virtual ophthalmology team that provided image interpretation and recommendations for the patients. With this approach, patients were better informed about the risks of DR progression in pregnancy, screening rates significantly improved, and rates of early detection of DR and treatment were much higher.[16]

Teleophthalmology could also be a viable solution for this patient population, as we often rely solely on undilated retinal imaging during pregnancy without the benefit of a complete fundus examination and other ancillary imaging modalities. This can result in questionable accuracy in disease staging, particularly when assessing peripheral retinal perfusion and making treatment recommendations.

Teleophthalmology would likely improve patient capture, especially for those who might otherwise forgo screening. Furthermore, AI-assisted image interpretation and classification of retinal pathology can also enhance accessibility to screenings and adherence to follow-up visits. With high sensitivity and specificity, results can be reported to patients and providers in a matter of seconds.[15] These solutions hold promise to make screenings more convenient and have the potential to significantly improve DR management during pregnancy.

(Continued on page 30)

COMBINATION THERAPY CONSIDERATIONS FOR DME

A summary of treatment options for patients who respond poorly to initial anti-VEGF treatment.

BY JUSTIN GRAD, MD(C); AMIN HATAMNEJAD, MD; AND NETAN CHOUDHRY, MD, FRCSC, FASRS, DABO



Although anti-VEGF agents have become the standard of care for the treatment of diabetic macular edema (DME),[1,2] approximately 30% to 40% of patients are refractive to this therapy.[3] Thus, alternative treatment approaches are necessary for some patients and can include switching to a different anti-VEGF agent, corticosteroid monotherapy, or combination therapy with anti-VEGF agents and corticosteroid. While intravitreal corticosteroid injections demonstrate similar functional and anatomical results to anti-VEGF treatment, they are associated with increased IOP and cataract development in phakic patients.[4] A review of combined anti-VEGF and corticosteroid therapy compared with anti-VEGF monotherapy did not find any significant differences in visual improvement or change in retinal thickness, but combination therapy was associated with an increased rate of IOP- and cataract-related adverse events.[5] Despite these findings, the certainty of evidence was low, and, crucially, the review did not assess treatment-refractive populations.

A FOCUS ON REFRACTIVE PATIENTS

We conducted an updated systematic review and meta-analysis to assess the efficacy and safety of combination therapy in anti-VEGF treatment-refractive populations.[6] We included randomized controlled trials or observational studies that compared anti-VEGF monotherapy with combined anti-VEGF/steroid therapy for DME refractive to initial anti-VEGF therapy. Importantly, we excluded studies involving a switch from an anti-VEGF agent to steroid monotherapy. The primary outcome was BCVA, and secondary outcomes included change in retinal thickness and adverse events.

We included a total of seven studies: four randomized controlled trials and three observational studies. In terms of

AT A GLANCE

- A systematic review and meta-analysis assessed the efficacy and safety of combination therapy in patients with diabetic macular edema who are refractory to anti-VEGF treatment.
- The meta-analysis found that combination therapy was associated with a significantly greater reduction in macular thickness; there was no significant difference in the number of injections administered between monotherapy and combination therapy.
- Faricimab (Vabysmo, Genentech/Roche), a combined anti-VEGF and angiopoietin-2 agent, is a novel treatment option for patients with DME who are refractory to anti-VEGF therapy.

visual outcomes, two of the studies found earlier visual improvement with combination therapy; however, none of them found a significant difference in visual acuity with combination therapy relative to monotherapy at the final assessment timepoint.

In addition, combination therapy was associated with significantly greater reductions in macular thickness.

Surprisingly, there was no significant difference in the number of injections administered between the two treatment groups. This is an important finding, as the treatment burden of disease is already high in DME, and this could improve patients' satisfaction with treatment.[7]

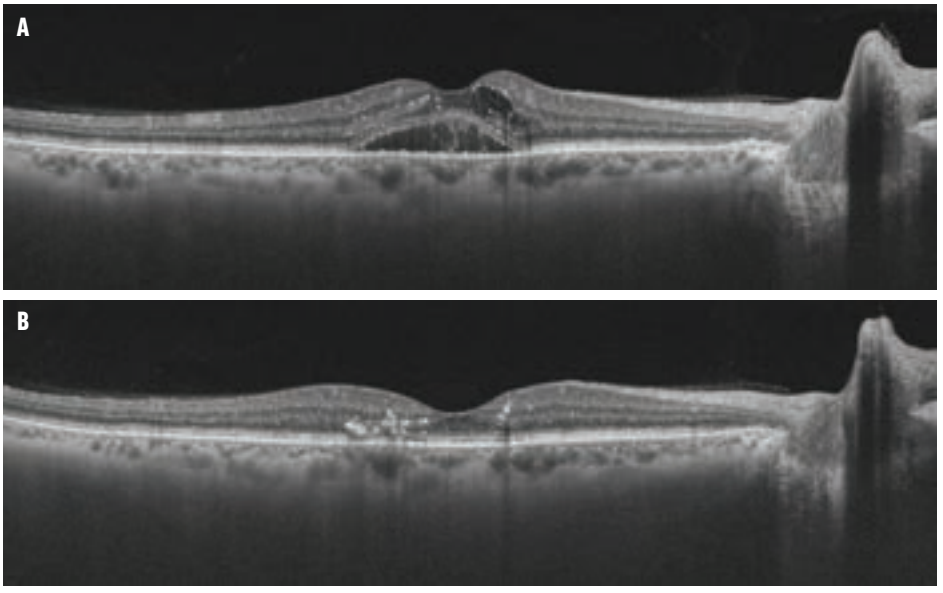

Figure. This patient with persistent DME after initial treatment with 2 mg aflibercept (A) had a dry macula OCT after receiving treatment with faricimab (B).

Not surprisingly, we noted a higher incidence of IOP-related adverse events (P = .002) and cataract-related adverse events (P = .02) with combination therapy.

We also examined the various definitions the studies used to define *treatment refractive*. There was a substantial amount of heterogeneity among the thresholds each study applied to identify when patients were switched from their initial treatment regimen. Most studies required patients to have a minimum macular thickness between 250 µm to 300 µm and six previous injections before defining them as refractive, although two studies required a minimum of only three injections. Interestingly, less than half of the studies had a visual acuity outcome as part of their criteria for defining patients as treatment refractive.

SWITCHING CONSIDERATIONS

A few key questions remain within the literature surrounding DME patients who are refractive to first-line anti-VEGF treatment, including the following:

- When should a patient be defined as treatment refractive and switched to a new treatment regimen?
- Which treatment regimen should patients be switched to after initial treatment?

Post-hoc analysis from the Diabetic Retinopathy Clinical Research (DRCR) Retina Network Protocol I randomized study found that nearly 40% of patients with DME will have fewer than five letters gained at 3 months of starting anti-VEGF treatment, and of these poor-responding eyes, only 20% to 30% of them will experience clinically significant visual recovery over the next 3 years.[3] Similarly, post-hoc analysis of the randomized DRCR Retina Network Protocol T found that, of eyes with less than a five-letter gain at 3 months, only 39% would go on to experience a gain of 10 or more letters at 2 years. The 12-week retinal thickness outcomes were not strongly associated with 2-year outcomes.[8]

Thus, early response to treatment is a strong prognostic factor for long-term treatment response. It is logical to switch the treatment paradigm immediately once a patient is identified as treatment refractive, as timely elimination of intraretinal and subretinal fluid could prevent additional damage. Retinal thickness has been widely used as a biomarker for response to treatment; however, it may be a relatively unreliable biomarker for long-term functional response. Therefore, it is likely necessary to include vision-related outcomes in definitions of treatment refractive. A recent consensus guideline recommends switching from an initial anti-VEGF treatment if the affected eye shows less than a 20% reduction in central retinal thickness and fewer than five letters gained after three to six injections.[9]

In terms of choosing the alternative treatment after a patient is deemed refractive to primary anti-VEGF therapy, switching to combination therapy should be approached with caution. Despite the significant anatomical response associated with combination therapy, patients did not see a functional benefit and often experienced the side effects of intravitreal corticosteroids.[6] In addition, the increased cost of two simultaneous treatments without strong visual acuity outcomes may be unjustified from a resource stewardship perspective.

Therefore, the chosen treatment approach should be personalized for each patient and will depend on the initial anti-VEGF agent and whether the patient has any ocular comorbidities. The NICE guidelines recommend the use of

EARLY RESPONSE TO TREATMENT IS A STRONG PROGNOSTIC FACTOR FOR LONG-TERM TREATMENT RESPONSE.

a fluocinolone acetonide implant (Iluvien, Alimera) for the treatment of chronic DME, irrespective of the phakic status of the eyes.[10] A recent meta-analysis of studies examining individuals with persistent DME after anti-VEGF injections showed that switching to a dexamethasone intravitreal implant (Ozurdex, Abbvie) resulted in significant functional and anatomical improvement.[11] However, it may be wise to avoid corticosteroids in patients with a history of glaucoma.

Another option is to switch patients to a different anti-VEGF agent, particularly if the patient was started on an older agent. For example, switching from initial bevacizumab (Avastin, Genentech/Roche) or ranibizumab (Lucentis, Genentech/Roche) to 2 mg aflibercept (Eylea, Regeneron) has been demonstrated to improve anatomical and functional responses.[12,13] Additionally, 8 mg aflibercept (Eylea HD, Regeneron) presents a promising treatment switch option. An observational study of DME patients with a suboptimal response to initial treatment found that switching from 2 mg to 4 mg aflibercept resulted in a significant reduction in retinal thickness. Thus, 8 mg aflibercept may provide an equally, if not more, efficacious treatment option.[14]

Faricimab (Vabysmo, Genentech/Roche) is a novel treatment option for patients with DME who are refractory to standard anti-VEGF therapy (Figure).[15] One meta-analysis found that faricimab was associated with improved anatomical and functional outcomes compared with bevacizumab, ranibizumab, and aflibercept.[16] Furthermore, a recent retrospective study of switching from 2 mg aflibercept to faricimab in treatment-refractive patients found that treatment with faricimab resulted in significantly improved retinal thickness and visual acuity outcomes.[17]

Although faricimab and 8 mg aflibercept are intriguing alternative treatment options, the evidence investigating their use for patients with DME who are refractive to anti-VEGF treatment is minimal, and caution should be taken to avoid overgeneralizing the results of small observational studies.

PROCEED WITH CAUTION

Clinicians may identify patients meeting refractory criteria as potential candidates for combination therapy, but they should exercise caution when applying these findings to individual cases. Future research should focus on developing standardized criteria for treatment resistance and directly compare therapeutic alternatives for patients with DME who do not respond to initial treatment. ■

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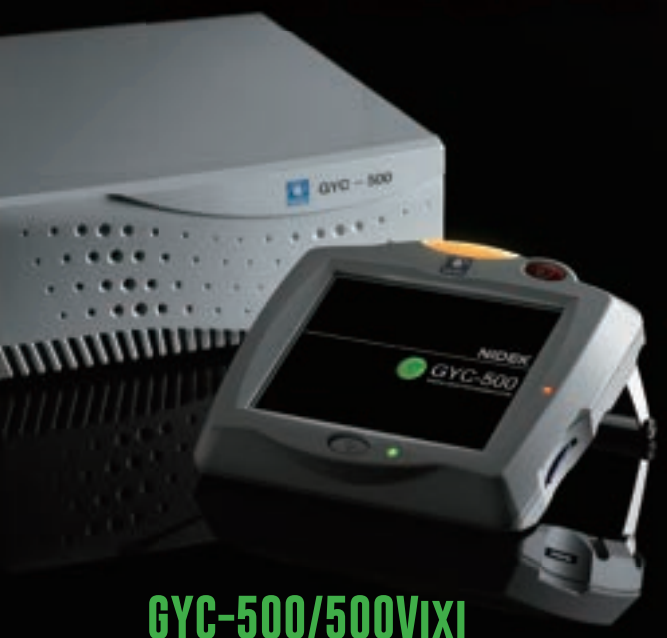

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DIABETIC VITREOUS HEMORRHAGE: INJECT OR OPERATE?

The latest DRCR Retina Network data suggest that patient selection is key to choosing the best treatment approach.

BY GEMMY CHEUNG, MBBS, FRCOPHTH, FAMS, MCI, AND DURGA S. BORKAR, MD, MMCI


Advances in our field, such as new therapeutics, smaller surgical tools, and updated techniques, have changed the way we approach myriad clinical scenarios, including vitreous hemorrhage. A relatively common complication, vitreous hemorrhage affects an estimated seven in 100,000 cases annually.[1] When it happens in a patient with proliferative diabetic retinopathy (PDR), retina specialists must decide whether they should start with an intravitreal injection of an anti-VEGF agent or head to the OR for vitrectomy. Here, two experts weigh in on this debate.

START WITH THERAPEUTICS

By Gemmy Cheung, MBBS, FRCOphth, FAMS, MCI

The Diabetic Retinopathy Clinical Research (DRCR) Retina Network's Protocol AB compared the effect of intravitreal 2 mg aflibercept (Eylea, Regeneron) versus vitrectomy with panretinal photocoagulation (PRP) for vitreous hemorrhage due to PDR.[2] The primary endpoint of the study was based on the area under the curve of BCVA up to week 24. The adjusted difference was five letters in favor of the vitrectomy arm but marginally missed statistical significance.

However, on closer examination, patients who underwent vitrectomy had better vision at postoperative week 4 compared with those receiving aflibercept (adjusted difference: 11.2 letters, $P = .003$). The mean BCVA was 35 letters at baseline in both arms and improved to 62 letters in the vitrectomy arm and 52 letters in the aflibercept arm. This difference in BCVA improvement at week 4 was most notable in the subgroup of patients with baseline VA worse than 20/800. By week 12, however, the difference in BCVA between the two arms was no longer significant. Similarly, visual acuity was comparable between the two arms for up to 2 years.[2]

Among patients in the initial aflibercept arm, about one in three eyes assigned to initial aflibercept required subsequent vitrectomy due to a lack of visual improvement or tractional retinal detachment (TRD). Similarly, one in three eyes assigned to vitrectomy required subsequent intravitreal aflibercept for the treatment of diabetic macular edema.[2]

Overall, these results suggest that both management options can improve vision effectively, but vitrectomy can achieve more rapid improvement. Other factors such as access to surgical expertise, cost, and patient needs should also be considered when selecting the most appropriate management. Patients should also be counselled regarding the possibility of requiring adjunct treatment.[2]

AT A GLANCE

- Protocol AB compared 2 mg aflibercept (Eylea, Regeneron) with vitrectomy with panretinal photocoagulation for diabetic vitreous hemorrhage.
- In Protocol AB, two-thirds of patients in the aflibercept treatment arm did equally well with medical management alone and were spared surgical intervention.
- Early vitrectomy for diabetic vitreous hemorrhage is safe and effective and can prevent associated complications when real-world patient factors are taken into consideration.

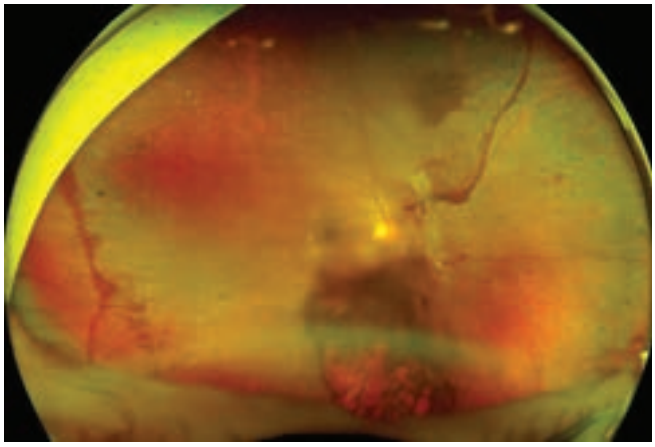

Figure 1. This patient presented with mild vitreous hemorrhage and good PRP coverage.

When managing diabetic vitreous hemorrhage in the clinic, a stepped approach could be considered. Patients can be assessed based on their response to an initial anti-VEGF injection. In a significant proportion of patients, vitrectomy may not be required with this approach. Other considerations may include patient demographics and the condition of the fellow eye. The average age of the participants in Protocol AB was 56 to 67 years of age. Generally, younger patients are at a higher risk of developing recurrent vitreous hemorrhage and TRD, as they have an attached posterior hyaloid. Thus, early vitrectomy may be a reasonable approach in younger patients. In Protocol AB, 42% to 55% of patients had received prior PRP. Patients who have not received PRP may have a higher risk of complications if managed with anti-VEGF injections alone without a fundus view. Prior PRP status is another consideration when deciding the best management option (Figure 1).[2]

THE CASE FOR EARLY VITRECTOMY

By Durga S. Borkar, MD, MMCi

Several studies have evaluated the best way to manage diabetic vitreous hemorrhage, including Protocol AB.[2] In this randomized controlled trial, the primary outcome of mean visual acuity score at 24 weeks was equivalent for both the aflibercept and early vitrectomy treatment arms.

To many, this may suggest that initial treatment for diabetic vitreous hemorrhage with intravitreal anti-VEGF therapy is equivalent to early vitrectomy. However, there are several other factors to consider. In the study, approximately one-third of patients in the aflibercept arm went on to need vitrectomy within 2 years. For many patients, particularly monocular patients, earlier surgical intervention may prevent future complications and provide quicker visual acuity improvement, which was also shown in the clinical trial.[2]

The results indicated that two-thirds of patients in the aflibercept treatment arm did equally well with medical management alone and were spared surgical intervention.[2] However, in the clinical trial setting, patients were followed regularly, and vitrectomy could be performed before further complications, such as a TRD, occurred. In fact, the follow-up rates in the clinical trial were greater than 90% in both treatment arms. Unfortunately, real-world studies of PDR suggest more than a quarter of patients are lost to follow-up for a period of time, and this is often associated with further vision-threatening complications, such as TRD and neovascular glaucoma, that can lead to irreversible vision loss (Figure 2).[3] Thus, when a patient with new-onset vitreous hemorrhage in the setting of PDR first presents, early vitrectomy may provide the most definitive treatment and minimize the risk of further complications, particularly if monthly follow-up for intravitreal anti-VEGF injections is not possible. With ongoing advances in vitreoretinal surgery, including smaller-gauge instrumentation, rates of complications have also gone down, making early surgery a more desirable option.[2]

However, there are several patient factors to take into consideration. For example, early vitrectomy may be the

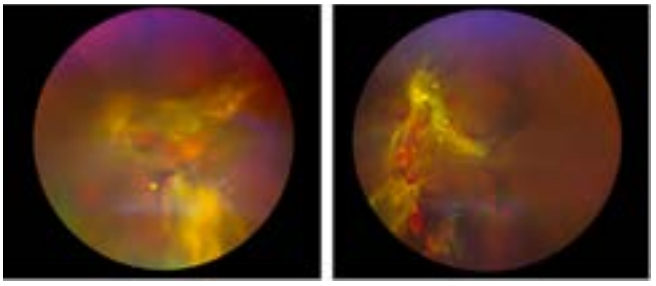

Figure 2. This patient, who initially presented with bilateral vitreous hemorrhage, had a lapse in follow-up care and returned with worsening vitreous hemorrhage, progressive fibrovascular proliferation, and traction.

ABOUT ONE IN THREE EYES ASSIGNED TO INITIAL AFLIBERCEPT REQUIRED SUBSEQUENT VITRECTOMY DUE TO A LACK OF VISUAL IMPROVEMENT OR TRACTIONAL RETINAL DETACHMENT.

best and most definitive treatment for patients with no prior treatment for their retinopathy and a delayed presentation. Reasons for delayed presentation could be multifactorial, but if the initial presentation to an ophthalmologist is for vitreous hemorrhage, this may suggest that, in some cases, there has not been screening at recommended intervals in the past. Additionally, monocular patients may not be able to wait for the delayed visual acuity improvement associated with medical management alone.

In some cases, patients may present with preexisting PRP, and medical management could be sufficient to prevent other vision-threatening complications.

Some patients with PDR may have associated end-organ complications of their diabetes that are being actively managed and, thus, are not good candidates for anesthesia and the OR. In these cases, medical management may be the best option. Aside from these situations, early vitrectomy for diabetic vitreous hemorrhage is safe and effective and can prevent associated complications, such as TRD, when real-world patient factors, such as the risk of becoming lost to follow-up, are taken into consideration. ■

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(Continued from page 23)

PRIORITIZING VISION DURING PREGNANCY

Pregnancy is a known risk factor for the development and progression of DR, requiring careful assessment. Despite the high risks of vision loss associated with DR in pregnancy, only a small fraction of research focuses on this vulnerable population. This issue is further complicated by the potential adverse effects of poor glycemic control on the newborn.

The limited interest in this topic highlights the lack of expert consensus on screening guidelines and patient compliance with retinal examinations during pregnancy. As clinicians, we should prioritize improving patient education, pre-conception counseling, and management of lifestyle risk factors. Further research is essential to establish optimal screening practices and improve clinical outcomes. ■

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COMPLICATED DR CASES: THE SECOND SURGERY

Taking patients with diabetes to the OR requires careful planning and expert execution, particularly when it's a reoperation.

BY ADRIAN AU, MD, PHD; BLAKE FORTES, MD; AND PRADEEP PRASAD, MD, MBA



Managing complex cases of diabetic retinopathy (DR) in the OR can pose significant challenges. The primary goals of surgical treatment include removal of vitreous hemorrhage (VH), relief of vitreoretinal traction, and application of laser to achieve quiescence, restoring visual function and mitigating the need for subsequent surgical interventions. However, when a second surgery becomes necessary, understanding the failures from the initial surgery and strategically planning for reoperation are critical for improving patient outcomes.

GETTING IT RIGHT THE FIRST TIME

The initial surgical approach for advanced DR prioritizes techniques that achieve surgical goals while minimizing risks that can lead to reoperation. Success begins with the management of preoperative and systemic risk factors. Collaboration with the patient's primary care physician and endocrinologist to optimize blood pressure control and discuss anticoagulation medications in the perioperative period can decrease the risk of intraoperative and postoperative VH. Surgical scheduling should consider hemodialysis schedules and time for medical clearance, which, when not coordinated, can result in delays in surgical care. This is particularly important for patients receiving preoperative anti-VEGF injections, as surgical delays put the patient at risk for retinal detachment (RD) if surgery is unexpectedly canceled. Lastly, administering panretinal photocoagulation prior to surgery in areas of the retina not obscured by VH and away from areas of vitreoretinal traction can stabilize the retina and decrease the risk of complications during fibrovascular membrane dissection.

Beware of Hemorrhage

Early postoperative VH following diabetic vitrectomy can delay visual recovery, negatively affect a patient's perception of surgical success, and increase the risk of postoperative complications. Mild postoperative VH can often be observed, but severe and persistent cases may require additional surgery. Several factors contribute to early postoperative VH: blood in the residual anterior vitreous, inadequate diathermy, relative hypotony after surgery, and residual traction on fibrovascular membranes. To reduce the risk of postoperative VH, surgeons can employ several measures, including lowering the infusion pressure to physiologic levels to identify sources of bleeding and removing as much anterior VH as possible, which is easier in pseudophakic eyes and with scleral depression. Surgeons can also perform a complete fluid-air exchange to remove residual VH and

AT A GLANCE

- The initial surgical approach for advanced diabetic retinopathy (DR) prioritizes techniques that achieve surgical goals while minimizing risks of reoperation.
- Indications for reoperation include recurrent vitreous hemorrhage, epiretinal membranes, residual vitreous traction, subretinal fluid, redetachment, and proliferative vitreoretinopathy.
- When reoperating on a challenging DR case, ensure all new retinal breaks are cleared of traction from residual vitreous and adjacent preretinal membranes.

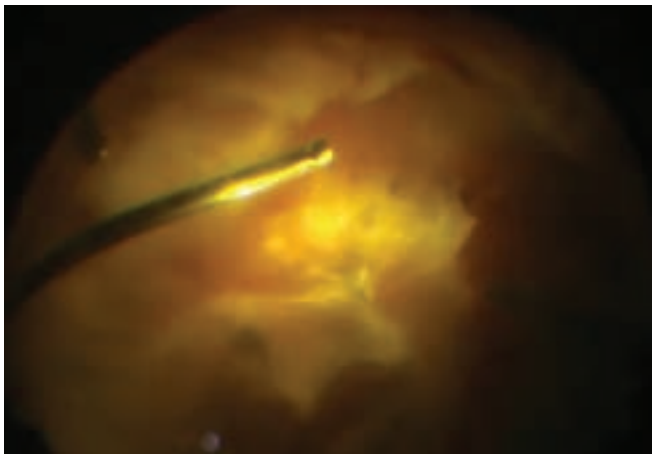

Figure 1. During diabetic vitrectomy, releasing anterior-posterior traction helps to prevent the development of vitreous base tears when dissecting tractional RDs.

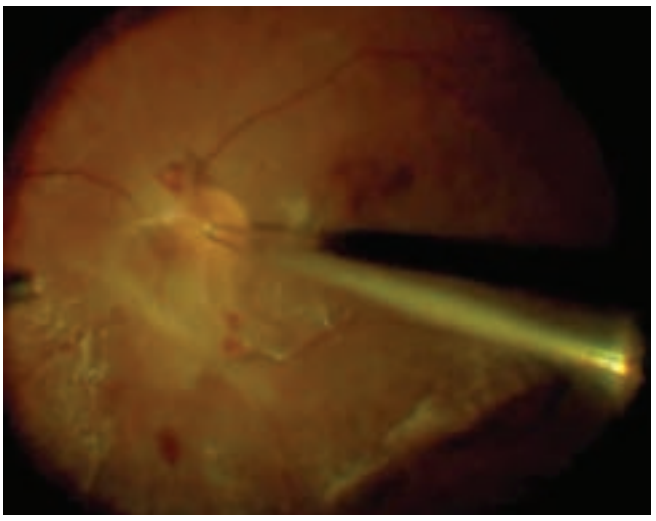

Figure 2. Surgeons can use ILM forceps to induce a PVD over the nerve. This is a safe location to enter the correct surgical plane in the setting of vitreous schisis.

minimize oozing in the early postoperative period, confirm that sclerotomies are sealed (and, when necessary, suture wounds to prevent hypotony), and thoroughly segment and/or delaminate fibrovascular membranes. Triamcinolone staining can be useful to confirm the absence of residual vitreous adhesions. Additionally, preoperative and intraoperative anti-VEGF injections may be beneficial.[1]

Reduce Traction

Residual vitreoretinal adhesions and traction can lead to a series of complications, including recurrent VH, epiretinal membrane formation, and tractional RD that can progress to combined rhegmatogenous and tractional RD.

Successful relief of vitreoretinal traction begins with accurate identification of the posterior hyaloid face. Induction of a posterior vitreous detachment (PVD) in diabetic eyes can be challenging due to the presence of vitreous schisis and tight adhesions of the vitreous to the retinal surface.[2] Triamcinolone acetonide staining can aid in the identification of the posterior hyaloid face. In some cases, a partial vitreous detachment may be present in the midperiphery.

A useful first step is to segment the posterior vitreous 360° from the vitreous base (Figure 1). Partial midperipheral vitreous detachments can often be identified and propagated circumferentially. Furthermore, segmentation of the anterior and posterior vitreous can minimize the risk of anterior breaks during membrane dissection.

When a midperipheral vitreous detachment is not present, it may be necessary to induce a PVD by aspirating or peeling the vitreous anteriorly from the optic nerve (Figure 2). When tackling broad fibrovascular membranes, segmentation into smaller, more manageable foci alone may be sufficient to achieve surgical goals (Figure 3). Segmentation can also minimize the risk of unwanted traction on adjacent areas of fibrosis when delamination is necessary.

Many approaches to segmentation and delamination have been described in the literature, including the use of a combination of the vitreous cutter, horizontal and vertical scissors, viscodissection, and bimanual techniques using chandelier illumination (Figure 4). We find that tractional membrane delamination over bullous RDs is more efficiently removed with bimanual techniques, whereas membrane delamination over non-bullous RDs can be achieved with the vitreous cutter alone. Furthermore, the vitreous cutter can be used as a multipurpose tool, functioning as a hook or pick to elevate membranes that can be cut to relieve traction.

INDICATIONS FOR REOPERATION

Despite optimal management during initial diabetic vitrectomy, some patients may require additional surgery. Indications for reoperation include:

- **Recurrent VH.** This refers to early postoperative or recurrent VH that does not clear after a period of observation with or without the use of anti-VEGF injections.
- **Secondary glaucoma.** Persistent VH may lead to ghost cell glaucoma, where red blood cells obstruct aqueous outflow through the trabecular meshwork. This may occur in phakic, pseudophakic, or aphakic patients when the anterior hyaloid face is disrupted.
- **Epiretinal membranes or residual vitreous traction.** Epiretinal membranes or residual cortical vitreous over the macula may contract, resulting in blurred vision or visually significant metamorphopsia.
- **Subretinal fluid.** Persistent subretinal fluid may be slow to resorb even after successful release of traction. Monitoring with serial OCTs can help to confirm stable or improving subretinal fluid. When subretinal fluid is increasing in size or extent, reoperation should be considered for a likely rhegmatogenous etiology.
- **Redetachment from new retinal breaks.** Entry site breaks, stretch breaks from residual vitreoretinal traction, and microbreaks not identified during the

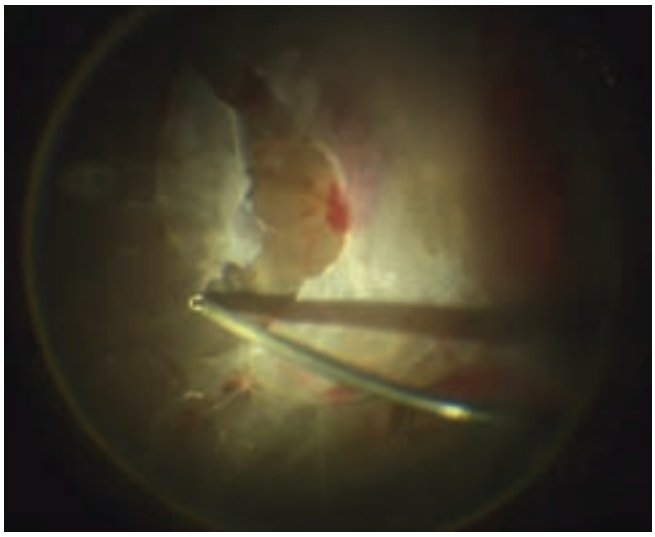

Figure 3. Segmentation of membranes into individual islands allows dissection of membranes without undue traction, decreasing the risk of iatrogenic retinal breaks.

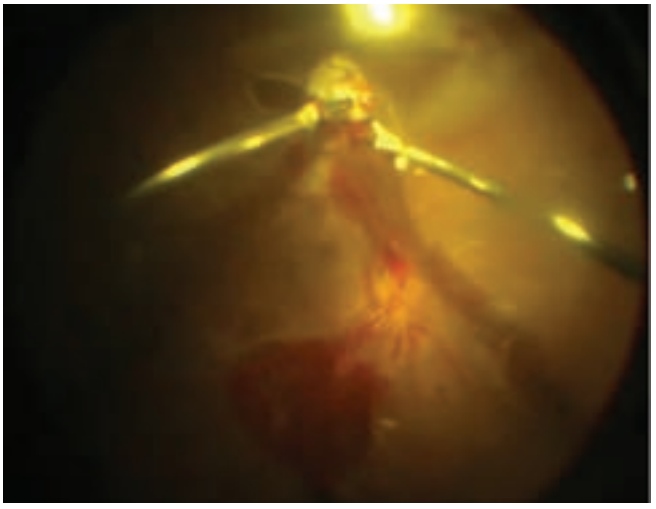

Figure 4. With a bimanual technique, surgeons can use end-grasping forceps and horizontal scissors to dissect a tractional membrane from a detached retina, where the lack of counter-tractional forces can make delamination more challenging.

primary vitrectomy may lead to postoperative RD.

- **Proliferative vitreoretinopathy (PVR).** Patients with combined rhegmatogenous and tractional RD or iatrogenic breaks at the time of initial surgery may be at risk for recurrent RD secondary to PVR.

APPROACH TO REOPERATION

When reoperation is indicated, the surgical plan should be tailored to address the reason for primary surgery failure. Additionally, the patient's visual prognosis should be assessed to determine if reoperation is warranted. If a second surgery is performed, the same principles for primary surgery apply with some additional considerations:

- Consider phacoemulsification in phakic patients to allow for adequate visualization and more thorough anterior vitreous shaving.
- Confirm the presence of a complete PVD with the use of triamcinolone staining.
- Determine if complete segmentation/delamination of fibrovascular membranes is contributing to recurrent VH.
- Examine with scleral depression to help identify new retinal breaks, especially around prior sclerotomy sites.
- Ensure all new retinal breaks are cleared of traction from residual vitreous and adjacent preretinal membranes. We recommend delamination of all preretinal membranes within one to two disc areas from a retinal break.
- Consider adding a scleral buckle to support the vitreous base if anterior retinal breaks are present.
- For patients with secondary glaucoma or rubeosis iridis, comanage the case with a glaucoma specialist and consider tube shunt implantation and/or cyclophotocoagulation to normalize IOP.
- In patients with PVR or when residual traction cannot be easily removed, removal of preretinal membranes, focal or extended retinectomy, anterior vitreous base dissection, and long-acting tamponade (eg, silicone oil) may be necessary.

TRY AGAIN

Surgery for advanced DR requires careful planning and expert execution. Despite best practices during primary diabetic vitrectomy, patients may require reoperation for a variety of indications. When a second surgery is required, it is important to understand and address the failures of the primary surgery to achieve surgical success. ■

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TRANSVITREAL FIBRINOID REACTION: A RARE COMPLICATION

Be prepared to handle this adverse event following vitrectomy in patients with diabetic retinopathy.

BY YAQOOB QASEEM, MD, AND JAYANTH SRIDHAR, MD


Pars plana vitrectomy (PPV) is often indicated to improve the vision of patients with proliferative diabetic retinopathy (PDR) complicated by diagnoses such as non-clearing vitreous hemorrhage or tractional retinal detachment (TRD).[1] One rare and early postoperative complication in this setting is the formation of transvitreal webs of fibrin, which requires prompt management to prevent subsequent complications, such as TRD.[2-5] Here, we present a characteristic example of a fibrinoid reaction following PPV in a patient with diabetes who achieved resolution over the course of 2 weeks with topical steroids.

CASE PRESENTATION

A 57-year-old man with type 2 diabetes complicated by diabetic foot infection, resulting in below-the-knee amputation, and PDR in each eye presented to the retina clinic for surgical evaluation. His VA was counting fingers OD and no light perception OS. IOP was 15 mm Hg OD and 70 mm Hg OS. Anterior segment examination showed no active neovascularization of the iris in either eye. Posterior segment examination of the right eye showed neovascularization of the disc, with fibrotic membranes emanating from the nerve superiorly and inferiorly alongside vitreomacular traction causing macular edema. OCT of the macula showed tractional membranes and vitreomacular traction with severe cystoid macular edema (CME) and subretinal fluid with an impending macular hole (Figure 1). The left eye was noted to have neovascular glaucoma with absolute cupping of the optic nerve.

The patient underwent preoperative intravitreal bevacizumab (Avastin, Genentech/Roche) injection in the right eye followed by PPV with membrane peel, endolaser (360° panretinal photocoagulation), fluid-air exchange, and intraoperative intravitreal bevacizumab. On postoperative day 1, the patient was noted to have a 60% to 70% air fill, with some mild intravitreal membranes below the level of the air bubble without significant anterior chamber reaction. He was started on 1% prednisolone acetate and 0.3% ciprofloxacin drops four times daily and 1% atropine twice daily.

One week later, his posterior segment examination was notable for a 30% air fill with significantly increased inferior membranes, consistent with a fibrinoid reaction (Figure 2). Again, there was no significant anterior chamber reaction or conjunctival injection, and the patient denied any pain. Topical 1% prednisolone acetate was increased to every 2 hours while awake. The patient was also maintained on 1% atropine twice daily, and ciprofloxacin was discontinued.

At postoperative week 2, the inferior vitreous webs had

AT A GLANCE

- The formation of transvitreal webs of fibrin is a rare postoperative complication after vitrectomy for proliferative diabetic retinopathy.
- Although the cause of transvitreal fibrinoid reaction is not always clear, clinicans must always rule out endophthalmitis.
- The fibrinoid reaction often resolves rapidly with topical steroids alone, although other management options exist for refractory cases.

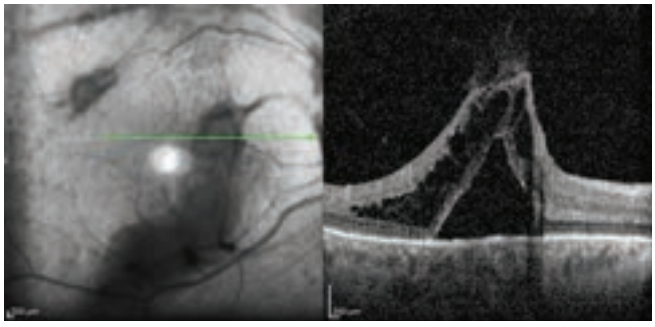

Figure 1. The patient's OCT revealed fibrotic membranes and vitreomacular traction causing CME with subretinal fluid.

improved but were not fully resolved (Figure 3). The same treatment was maintained with resolution of the fibrinoid reaction 1 week later, at which point the prednisolone acetate was tapered to four times daily.

The patient also had relieved macular traction and an improvement in subretinal fluid. The patient will be considered for intravitreal bevacizumab or a dexamethasone implant (Ozurdex, Abbvie) at future visits, depending on the persistence of subretinal fluid.

UNDERSTANDING THE COMPLICATION

In a 1982 retrospective review of 280 diabetic vitrectomies,[5] 15 eyes developed strands of fibrin on the surface of the retina and behind the iris between postoperative days 2 and 14. This was followed 1 to 2 days later by a "gelatinous mass" in the vitreous that resulted in TRD and neovascular glaucoma. This clinical course was reversed by systemic and topical corticosteroids in only six of 15 eyes. Additionally, the complication was found to occur more commonly with concurrent lens surgery or scleral buckling, and it was proposed that these combined surgeries may result in increased vascular permeability with resultant fibrin deposition.[5]

More recently, Luo et al described a series of eight eyes of seven patients, all of whom underwent PPV with endolaser and fluid-air exchange.[3] All patients exhibited the fibrinoid bands on postoperative day 1.[3] While one patient was given oral moxifloxacin due to slow resolution of fibrin, all other patients achieved resolution of the fibrinoid reaction on standard postoperative drops (atropine, antibiotic, and prednisolone acetate from four times daily to every 2 to 3 hours). Mean time to resolution of fibrin was 8.75 days.[3]

Nelson et al described a case of submacular fibrinoid material noted on postoperative day 4 after cataract extraction with IOL insertion, PPV, endolaser, partial fluid-air exchange, intravitreal bevacizumab, and sub-Tenon triamcinolone acetonide.[4] This resolved in 2 weeks following repeat treatment with sub-Tenon triamcinolone. The patient's other eye underwent a similar surgery without sub-Tenon triamcinolone and subsequently developed transvitreal and submacular fibrinoid material

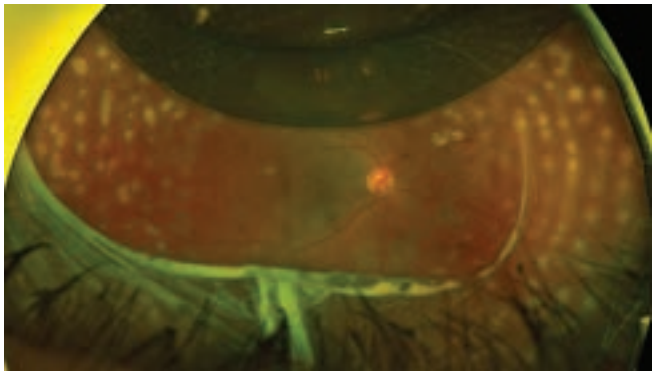

Figure 2. One week postoperatively, the patient presented with inferior vitreous membranes consistent with a fibrinoid reaction.

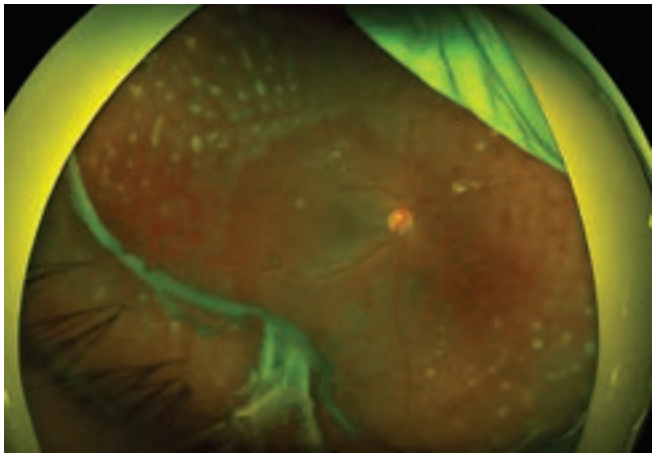

Figure 3. At postoperative week 2, the patient showed improvement but not resolution of the fibrinoid reaction after treatment with 1% prednisolone acetate every 2 hours.

on postoperative day 4, which again achieved near resolution 2 weeks following sub-Tenon triamcinolone.[4]

Sinha et al described a case of dense transvitreal bands appearing on postoperative day 1 after PPV with endolaser that improved with systemic and topical steroids; however, the patient experienced worsening vision due to progressive traction requiring reoperation.[2]

Of note, because the cause of a transvitreal fibrinoid reaction is not always clear, clinicans must always rule out endophthalmitis. Unlike endophthalmitis, the postoperative sterile fibrinoid reaction has minimal or no pain, anterior chamber reaction, vitreous cell, and conjunctival injection, and the retina is typically visible through the bands.[2,3,6]

Even once endophthalmitis is ruled out, the differential diagnosis could include sterile intraocular inflammation resulting from the use of intraocular agents, such as triamcinolone acetonide and bevacizumab.[6]

Several contributory mechanisms for the fibrinoid reaction observed after PPV in diabetic patients have been posited.[5] The diabetic vitreous has some inherently proinflammatory characteristics, which may be exacerbated by operative interventions, such as PPV and endolaser.[2,3]

(Continued on page 44)

CAN'T-MISS LECTURES FROM ARDS 2024

This year's meeting included three named lectures covering everything from rare conditions to the latest imaging tools.

BY MAHMOOD KHAN, MD

Ongoing research and innovations have led to significant progress in our imaging and understanding of many retinal diseases. During the 52nd Annual Aspen Retinal Detachment Society (ARDS) Meeting, held from March 2-6, 2024, in Snowmass Village, Colorado, the esteemed named lectures focused on new findings in pseudoxanthoma elasticum (PXE; presented by K. Bailey Freund, MD), high-resolution OCT imaging (presented by Giovanni Staurenghi, MD), and central serous retinopathy (CSR; presented by David S. Boyer, MD). Here are some key pearls from their talks (Figure).

FOUNDERS LECTURE: PSEUDOXANTHOMA ELASTICUM

PXE is a rare genetic disorder, caused by mutations in the *ABCC6* gene, that affects multiple systems, including the cardiovascular, gastrointestinal, and skin systems. The 13th Annual Founders Lecture by Dr. Freund highlighted the extensive retinal manifestations of PXE, which he noted go beyond the classic angioid streaks to include optic disc drusen, comet lesions, pattern dystrophy, and macular neovascularization. Dr. Freund shared several cases of PXE to highlight the varied presentations on fundus photography, fundus autofluorescence images, high-resolution OCT, and ICG angiography (particularly if hemorrhage is impeding the view). While detailing imaging findings in angioid streaks, he commented that, because of the fragility of the Bruch membrane, eyes with PXE are very susceptible to blunt trauma and can present with significant hemorrhages—something clinicians should discuss with the patient.

Dr. Freund also emphasized the significant effect anti-VEGF therapy has had on managing neovascularization in PXE patients, although many still experience vision loss due to macular atrophy. Fortunately, most patients with neovascularization secondary to PXE respond well to anti-VEGF therapy, he said.

A notable new finding discussed was the occurrence of acute inflammatory retinopathy in PXE patients, resembling conditions such as punctate inner choroidopathy and multiple evanescent white-dot syndrome. This inflammatory retinopathy can lead to vision loss if not properly identified and treated, according to Dr. Freund.

ABOUT THE SPEAKERS

K. Bailey Freund, MD
- Clinical Professor of Ophthalmology, New York University Grossman School of Medicine, New York
- Senior Partner, Vitreous Retina Macula Consultants of New York, New York

Giovanni Staurenghi, MD
- Professor of Ophthalmology; Chairman, University Eye Clinic; Director, University Eye Clinic Department of Biomedical and Clinical Science, all at the Luigi Sacco Hospital, Milan, Italy

David S. Boyer, MD
- Senior Partner, Retina-Vitreous Associates Medical Group, Los Angeles
- Adjunct Clinical Professor of Ophthalmology, University of Southern California Keck School of Medicine, Los Angeles

TAYLOR SMITH & VICTOR CURTIN LECTURE: HIGH-RESOLUTION OCT

During the 41st Taylor Smith & Victor Curtin Lecture, Dr. Staurenghi discussed the potential clinical utility of high-resolution OCT. He first summarized the evolution of OCT technology, highlighting the improvements in axial resolution from 10 µm to nearly 2 µm. These advancements allow for better visualization of retinal layers and structures. For example, high-resolution OCT provides an excellent view of the choriocapillaris, and clinicians can differentiate the outer deep capillary plexus, inner deep capillary plexus, and superficial capillary plexus, he explained.

Dr. Staurenghi provided examples of high-resolution OCT images, which reveal details not visible with standard commercial devices. He pointed out various retinal layers, as seen on high-resolution OCT, which allow for the identification of early signs of geographic atrophy, reticular drusen, and basal laminar deposits, to name a few. He showed several cases to highlight the value of these new OCT images in the setting of wet AMD, geographic

Images courtesy of Kevin Caldwell Photography

Figure. The 52nd Annual Aspen Retinal Detachment Society Meeting boasted three named lectures, led by (from left to right) Drs. Freund, Staurenghi, and Boyer.

atrophy, CSR, choroidal folds, and even PXE. Dr. Staurenghi also emphasized the importance of combining fundus autofluorescence imaging with OCT to identify areas of photoreceptor loss.

To conclude, Dr. Staurenghi discussed the future of OCT technology, including its application in visualizing retinal vessels and its role in early disease detection and clinical trials. The lecture emphasized the importance of combining scientific rigor with practical application in clinical settings and ended with a look at the future directions of OCT technology in retinal imaging and disease management.

TAYLOR SMITH & VICTOR CURTIN LECTURE: CENTRAL SEROUS RETINOPATHY

For the 42nd Taylor Smith & Victor Curtin Lecture, Dr. Boyer focused on CSR, a condition first described in 1866 by Von Graefe as "relapsing central luetic retinitis."[1] It primarily affects men from 40 to 50 years of age, with a higher incidence in Asian populations.[2]

According to Dr. Boyer, CSR manifests in acute and chronic forms, with acute CSR often resolving spontaneously and chronic CSR potentially leading to severe vision loss. Risk factors include hypertension, *helicobacter pylori* infection, steroid use, erectile dysfunction medication, and sleep apnea. Multimodal imaging with OCT and ICG is crucial for early and accurate diagnosis, Dr. Boyer emphasized, although differentiating CSR from other retinal conditions can be challenging.

Dr. Boyer noted that treatment options for CSR have expanded over the years to include observation, micropulse laser, photodynamic therapy (PDT), and mineralocorticoid receptor antagonists. PDT is considered the standard, while other treatments such as anti-VEGF medications, mifepristone, propranolol, and rifampicin show varying degrees of efficacy. He pointed out that research on scleral thickness, mitochondrial DNA levels, and genetic factors is providing new insights into CSR. He also mentioned that the use of AI in the diagnosis and prediction of therapeutic outcomes is an emerging area of research.

APPLYING WHAT YOU LEARNED

ARDS attendees walked away from these three named lectures with a number of clinically relevant pearls, including the following:

- Retinal manifestations of PXE extend beyond angioid streaks to include optic disc drusen, comet lesions, and macular neovascularization. Acute inflammatory retinopathy, which can resemble conditions like punctate inner choroidopathy and multiple evanescent white-dot syndrome, is a significant finding in patients with PXE and requires proper identification and treatment.
- Advancements in high-resolution OCT technology have improved our visualization of retinal layers and may aid in early disease detection. Although widespread use of this technology is currently limited, clinicians must remember to combine scientific rigor with practical application.
- Diagnostic techniques such as OCT and ICG help in the early and accurate diagnosis of CSR, although differentiation from other retinal conditions can be challenging. Treatment options include observation, micropulse laser, PDT, and mineralocorticoid receptor antagonists, with ongoing research exploring personalized strategies and emerging therapies. ■

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2. Gäckle HC, Lang GE, Freissler KA, et al. Central serous chorioretinopathy. Clinical, fluorescein angiography and demographic aspects. *Ophthalmologe.* 1998;95:529-533.

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SAVE THE DATE
53rd Annual Aspen Retinal Detachment Society
March 1-5, 2025
The Viceroy, Snowmass, Colorado

WHAT MAKES VBS UNIQUE: 2024 HIGHLIGHTS

Trainee-focused programming, awards, and a new mid- to late-career session set this meeting apart.

BY MATTHEW JOHNSON, MD; OGUL E. UNER, MD; GEETA A. LALWANI, MD; HARRY LEVINE, MD; JORGE ANDRADE ROMO, MD; MELISSA YUAN, MD; LOUIS Z. CAI, MD; JIA XU, MD; AND LINDSAY KOZEK, MD, PHD

There were many demogorgons and strange things afoot at the 12th Annual Vit-Buckle Society (VBS) meeting, held in Miami, April 4-6, 2024. And while the theme of this year's meeting was inspired by the popular Netflix TV show *Stranger Things*, no one was a stranger to the VBS trainee-focused programs, Lifetime Achievement Award, and Mentorship Award. New this year was the VBS Silver program.

FELLOWS AND FOCUS

The Fellows Program and the FOstering Careers for Underrepresented Stars (FOCUS) Program are designed to provide tips and tricks to trainees who attend the Thursday lineup of sessions and events.

Student Loans and Financial Considerations

Jayanth Sridhar, MD, and Nikisha Kothari, MD, started the day by discussing the necessity of disability insurance to protect a trainee's sizable educational and time investment. Dr. Sridhar recommended trainees obtain disability insurance as early as possible to lock in a lower rate.

They also discussed weekly or monthly automatic investments, periodic lump-sum investing, index funds, and other stock investment strategies.

As for student loans, they explored consolidation, private refinancing, public service loan forgiveness, repayment programs, and repayment clauses in job contracts.

Practice Settings

During a panel on navigating different practice settings, Gordon Crabtree, MD, discussed the pros and cons of private equity (PE) and how to protect yourself when negotiating your first job contract. Including a "fractional buy-in" allows for a guarantee of some financial benefit if your practice sells to PE, he said.

Brandon Johnson, MD, urged attendees to recognize red flags in contracts, such as the absence of a definitive partnership guarantee. He also noted that opening his own solo practice took about 6 months.

Alex L. Ringeisen, MD, explained that multispecialty group practices have built-in referral bases that minimize the time demand of networking with local eye care specialists and hospital systems.

Regardless of practice type, fellows should consider enlisting a lawyer to assist with contract negotiations, the panelists agreed. Doing so can increase earnings, address loan forgiveness, avoid noncompete clauses, include fractional buy-ins, protect research time, secure research support, and guarantee teaching engagements.

Burnout

During the next session, Laurel S. Mayer, MD, a psychiatrist at Columbia University, discussed burnout in ophthalmology, noting that more than half of PGY-2 ophthalmology residents reported burnout, compared with less than one-third of ophthalmology attendings.

Burnout was more prevalent among women, those who are underrepresented in medicine, and those who identify as LGBTQIA+. She also noted that 71% of trainees with low well-being scores significantly overestimated their well-being score, suggesting severe distress tends to be normalized.

Dr. Mayer then touched on the concept of physician self-sacrifice but emphasized that altruism should not come at the expense of a trainee's physical or mental well-being.

Ergonomics

The last session of the morning focused on ergonomics by Joshua Curie, DPT, a physical therapist at the University of Miami. While treating a retina specialist, he became interested in the many postural challenges in ophthalmology. He cited a study that found that the prevalence of neck and back pain was 68% after specializing in vitreoretinal surgery, compared with 34% prior. Attendees voiced obstacles to maintaining good posture at the slit lamp, operating with attendings with significant height differences, using indirect ophthalmoscopes, and multitasking in clinic. Core exercises, yoga, strength training, and even putting an ice pack on the neck after laser treatments are a few strategies to combat occupational musculoskeletal pain and morbidity, he said.

Dr. Curie noted that even a few seconds of rest between extreme postures is helpful in preventing neck and back pain. He provided practical advice on good posture in and out of the OR before leading a group exercise.

Research Options During Training

The first afternoon session focused on incorporating research into training and a career. Matthew A. Cunningham, MD, who started a clinical research program at the Florida Retina Institute, discussed obstacles during his journey, including increasing office space, arranging finances, and forming new relationships with industry.

Tina Felfeli, MD, PhD, a prior FOCUS participant, shared her experience performing research as a trainee. She touched on the need for selectivity and recommended only saying "yes" to projects you are passionate about.

Kristen Nwanyanwu, MD, MBA, MHS, shared her inspirational journey to becoming a health equity researcher and forming the community-based Sight-Saving Engagement and Evaluation in New Haven (SEEN) research program at Yale University. She encouraged trainees to ask questions that haven't been asked before and relentlessly pursue their answers, as patients depend on scientific research.

VBS SILVER

The inaugural VBS Silver meeting convened to address the challenges that mid- to late-career retina specialists face, with a focus on navigating issues like PE in the retina space and transitioning into industry roles. The event provided a platform for experienced professionals to share insights, strategies, and best practices to effectively manage these unique challenges.

Attendees engaged in robust discussions regarding the evolving landscape of retina practices, beginning with PE-backed acquisitions and consolidation; many of these discussions emphasized the importance of preserving the quality of patient care and professional autonomy.

The highlight of the meeting was the keynote lecture by Jerry Bovino, MD, one of the founding members of the Vitreous Society (which would later become the American Society of Retina Specialists), who recounted his colorful, bold, and inspiring path since retiring from clinical practice.

Image courtesy of Kevin Caldwell Photography

Figure 1. Dr. Thanos (left) and Dr. Runner (right) interviewed Dr. Hassan (center), the 2024 VBS Lifetime Achievement Award honoree.

Through collaborative dialogue and open exchanges, the VBS Silver meeting empowered attendees with the knowledge and resources necessary to navigate mid- to late-career challenges and thrive.

VBS plans to continue conversations at future Silver meetings regarding the intimate challenges all retina specialists face with family, aging, and the search for meaning in our lives.

LIFETIME ACHIEVEMENT AWARD – TAREK S. HASSAN, MD

This year's Lifetime Achievement Award was presented by Aristomenis Thanos, MD, and Margaret M. Runner, MD, who provided a deeper look into the impressive life and career of Tarek S. Hassan, MD (Figure 1).

Although Dr. Hassan began medical school at the University of Michigan leaning toward a career in cardiothoracic surgery, he realized that path would clash with his desire to be active in his children's lives. Once he chose ophthalmology, he knew retina was right for him.

Dr. Hassan spoke fondly of his fellowship mentors at Associated Retina Consultants/Beaumont, remembering being "taught by giants in the field with a desire to contribute at a higher level."

As a mentor, Dr. Hassan has trained 60 clinical fellows (and counting), and he shared his three most important tips on mentoring: 1) Don't treat everyone the same, 2) provide specific instructions, and 3) practice like you play.

Dr. Hassan founded Club Vit in 1996 and the Retina Fellows Forum in 2001 and has served as president of the American Society of Retina Specialists (2016 – 2018), Retina World Congress (2019 – 2022), and Retina Hall of Fame (2020 – 2024). When asked about his motivation for participating in these societies, he reflected that "there is so much potential to be great, but the opportunity to access

Image courtesy of Kevin Caldwell Photography

Figure 2. The 2024 Mentorship Award honoree, Dr. Vajzovic (second from left), is joined on stage by Dr. Thomas (left), Dr. Lalwani (second from right) and Dr. Finn (right).

information and collaborate was weak when I was finishing fellowship." He wanted to fill that unmet need by gathering people together to learn from each other.

Dr. Hassan is now the chief development officer at Aviceda Therapeutics. He took this role because he no longer felt challenged in his day-to-day work and wanted to keep growing; the new career trajectory has been refreshing, he said, noting that he enjoys seeing patients now more than ever. This role has given Dr. Hassan an opportunity to "help people in a bigger way and on a larger scale," he emphasized.

MENTORSHIP AWARD – LEJLA VAJZOVIC, MD

The VBS Mentorship Award was presented to Lejla Vajzovic, MD. Interviewed by her former fellows Avni P. Finn, MD, MBA, and Akshay S. Thomas, MD, MS, Dr. Vajzovic shared her inspiring journey from her early life in Bosnia to her esteemed career in the United States (Figure 2).

Dr. Vajzovic's path to excellence in vitreoretinal surgery was paved with both challenges and triumphs. As a teenager, Dr. Vajzovic left Bosnia to join her brother in the United States as a refugee. Despite the culture shock, she graduated summa cum laude from the Honors College at the University of Missouri, with a full scholarship to the Mayo Clinic School of Medicine. Dr. Vajzovic attributes much of her success to the unconditional support from her brother, American family, and parents in Bosnia.

Dr. Vajzovic completed an ophthalmic pathology fellowship and her residency at the Bascom Palmer Eye Institute, followed by a vitreoretinal surgery fellowship at the Duke Eye Center. The mentorship of retina luminaries such as Sander R. Dubovy, MD, and Cynthia A. Toth, MD, set Dr. Vajzovic on a career path toward pediatric retina.

Dr. Vajzovic expressed her passion for learning new surgical techniques and nurturing the next generation of vitreoretinal surgeons, remarking, "I am excited by new advancements [...] they keep [surgery] entertaining."

Throughout her journey, Dr. Vajzovic has been supported by her husband Edin and daughters Lamia and Alma, who joined her at VBS this year to celebrate the award.

Dr. Vajzovic concluded her interview by imparting the following wisdom: "There's really no balance [...] there are just priorities." For her, family, work, mentees, and patients top the list of priorities. The Mentorship Award is a recognition of Dr. Vajzovic's professional excellence and a testament to the effect of mentorship, family support, and resilience in achieving greatness in the field of vitreoretinal surgery. ■

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RISING STARS IN RETINA

Get to know outstanding retina fellows from the class of 2024.

Farzad Jamshidi, MD, PhD

***Retina Today:* When did you first know that you wanted to become a retina specialist?**

Before residency, I did research in ocular genomics with Eric Pierce, MD, PhD, in Boston—that showed me the fascinating world of retinal biology. During my first retina rotation in residency at Dean McGee Eye Institute, I was in awe that findings that were a matter of microns in size could have such specific implications for a patient's ocular and systemic health. Finally, the cool gadgets and exceptional skills of retina surgeons like my attending Vinay Shah, MD, won me over. By the time I was a second-year resident, I knew this was what I loved to do.

***RT:* Who do you look to as mentors in the field?**

Drs. Pierce and Shah are incredible ophthalmologists and role models. My program director, Michael Siatkowski, MD, was a paragon of ethical patient care and pushed us to be the best versions of ourselves. During my fellowship at the University of Iowa, I was fortunate to work with amazing mentors and role models. Elaine Binkley, MD, and H. Culver Boldt, MD, sacrifice so much for trainee education, and they go above and beyond for their patients; it is incredible to see them at work. Ian Han, MD, teaches surgery in a way that I wouldn't have ever imagined before experiencing it for myself. He also spends his Saturdays teaching fellows and guiding us through our careers. We are indebted to him. Edwin Stone, MD, PhD, is a brilliant clinician-scientist whom I have been fortunate to learn from. I could name many mentors to whom I am immensely grateful.

***RT:* What has been one of the most memorable experiences of your fellowship thus far?**

Several instances of grateful patients come to mind right away. While on call, we diagnosed a patient with a systemic infection based on her retinal presentation, and her thank-you card was particularly kind and thoughtful. Interactions with many incredibly kind and grateful retinal detachment patients have also been memorable. I feel so blessed to do what we do.

***RT:* What are you hoping to accomplish once you are in practice?**

First and foremost, I hope to continue to grow and become the best practitioner and surgeon I can be and never become complacent. I also hope to get involved in meaningful research and play a part in improving our capabilities in treating patients.

FIRST CAREER MILESTONE

Dr. Jamshidi will join the faculty at the University of Pittsburgh Department of Ophthalmology.

***RT:* What advice can you offer to residents who are considering retina?**

Don't forget the importance of each patient encounter. We have this amazing capability to see inside a human organ, identify pathology at a cellular level, and confidently make diagnoses that may be peculiar to other specialties. Retina can be challenging, and it is not for the faint of heart. Remember the positive impacts we make every day, and you will be reminded that our profession is a wonderful gift. ■

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THE VALUE OF MULTIMODAL IMAGING IN THE RETINA CLINIC

The utility of simultaneous multimodal image capture illustrated in various disease conditions.

BY PAULO EDUARDO STANGA, MD

Although OCT has become an integral part of clinical practice, other noninvasive imaging modalities have also become staples, such as widefield (WF) imaging, ultra-widefield multiwavelength (UWF-MW) fundus imaging, and color fundus photography (CFP). Many imaging techniques require multi-capture frames, or they can be invasive and require dye, such as fluorescein angiography (FA) and ICG angiography (ICGA).

While somewhat uncomfortable and invasive, these tests are, in many cases, essential. In addition, many modalities complement each other, and the findings of an ICGA test may confirm the FA results, or anatomic anomalies missed on OCT may be picked up on UWF-MW imaging.

Innovation has led to multimodal platforms that allow simultaneous capture of several modalities in one imaging session, streamlining the process and improving clinic flow.

MY EXPERIENCE

I have used multimodal imaging in my practice, The Retina Clinic London, for years. The platforms in my clinic include, but are not limited to, the Silverstone (Optos), the Spectralis (Heidelberg), and the Triton (Topcon). The Silverstone provides UWF-MW imaging with central and navigated peripheral swept-source OCT (SS-OCT), UWF FA, ICGA, green-light fundus autofluorescence (FAF), and multiwavelength modalities (up to 200°). The Spectralis includes OCT, OCT angiography (OCTA), and WF and UWF fundus photography (up to 150° with use of a Staurenghi contact lens). The Triton offers CFP, FAF, OCT, OCTA, and FA.

Recently, my team and I investigated the utility of simultaneous capture of multiple modalities and found that multimodal imaging allows more precise characterization of retinal diseases in some patients, helping the retina specialist provide treatment tailored to specific anatomic findings, diagnose and treat conditions earlier, and monitor patients more precisely and accurately over time.[1]

Here, I share our findings with respect to the utility of multimodal imaging in certain retinal pathologies.

THE ADOPTION OF MULTIMODAL IMAGING COULD IMPROVE ACCESS TO EARLIER CARE FOR PATIENTS THROUGH TELEMEDICINE AND LEAD OUR FIELD TO THE MORE OBJECTIVE AND PRECISE PATIENT-TAILORED MEDICINE WE STRIVE TO PRACTICE.

AMD

OCT imaging is essential for the diagnosis and accurate and objective monitoring of both wet and dry AMD. However, to characterize a patient's specific type of neovascularization, OCTA and FA/ICGA may be necessary. As our understanding of peripheral findings (eg, drusen) in AMD evolves, UWF images will help us better classify the disease. We routinely image AMD patients using UWF technology.

Now that there are two approved drugs for the treatment of geographic atrophy (GA), we must determine the most relevant imaging platform for the diagnosis and longitudinal tracking of GA. Multimodal imaging will allow providers

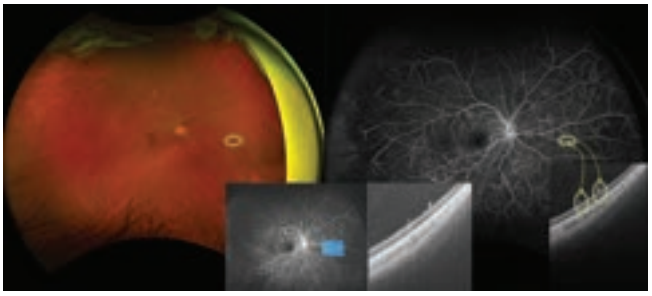

Figure 1. Navigated midperipheral SS-OCT over FA imaging shows two buds of incipient neovascularization elsewhere, providing complementary anatomical information of the neovascularization.

to more effectively track GA progression and response to therapy on multiple validated modalities. The clinical utility of platform- and wavelength-specific modalities will more clearly emerge as real-world applications are published.

Proliferative Diabetic Retinopathy

Navigated midperipheral and peripheral SS-OCT is a useful tool for assessing proliferative diabetic retinopathy (PDR). UWF FA is necessary to rule out peripheral retinopathy. In patients with DR, risk of progression is higher with concomitant peripheral lesions, and the early and accurate detection of these lesions can better inform treatment.[2]

In our study, we found that UWF FA alone sufficiently depicted ischemia and neovascularization to diagnose active PDR.[1] Further, the use of navigated peripheral SS-OCT over the FA image detected previously unseen neovascularization and provided complementary anatomical information of the neovascularization (Figure 1). We often determine whether and how to use targeted retinal photocoagulation based on peripheral retinal findings on UWF-MW fundus imaging, FA, and navigated OCT. By combining all three modalities, we can examine patients thoroughly, diagnose earlier, personalize treatment, and monitor objectively, all while reducing the likelihood that pathology goes undetected.

When using FA in patients with diabetes, an UWF perspective allows providers to capture the entirety of a particular phase of the angiogram. Thus, rather than taking several snapshots and montaging them to describe a particular phase of FA, technicians capturing UWF FA images can capture the widest possible image depicting a singular moment in any given phase without registration errors.

Sickle Cell Disease

Patients with sickle cell disease (SCD) may be asymptomatic but still present with peripheral retinal changes that are easy to miss during routine examinations.[3] In patients with suspected or diagnosed SCD, multimodal imaging of the retinal anatomy may reveal undetected retinal abnormalities.

In our study, we concluded that examination of patients with SCD using both UWF-MW imaging and navigated peripheral SS-OCT reduced the likelihood of misdiagnosis.[1] We also found that the combination of UWF FA and navigated peripheral SS-OCT highlighted vitreoretinal traction, retinal schitic changes, and intraretinal fluid secondary to SCD with ischemia and neovascularization (Figure 2). Further study is needed to elucidate these findings.

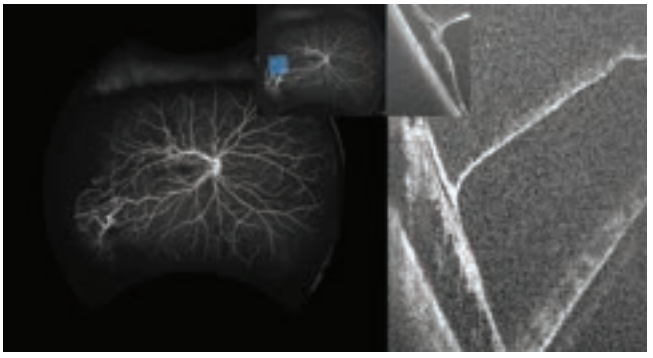

Figure 2. Simultaneous UWF FA and navigated SS-OCT show vitreoretinal traction, epiretinal fibrosis, retinal schitic changes, intraretinal fluid adjacent to peripheral retinal ischemia, and sea fan-shaped neovascularization secondary to SCD.

Vogt-Koyanagi-Harada Disease

In Vogt-Koyanagi-Harada (VKH) disease, UWF FA, UWF ICGA, and central and navigated peripheral SS-OCT are essential tests, and all patients with VKH disease who present to our clinic are imaged with these modalities so that we can characterize baseline retinal and choroidal changes. Navigated peripheral SS-OCT also assists in objectively and accurately assessing response to treatment over time.

STANDARDIZATION OF THE NOMENCLATURE

Although researchers generally understand the terms *widefield* and *ultra-widefield*, no strict definition had been established prior to a 2019 consensus meeting. That meeting, organized by the International Widefield Imaging Study Group, proposed clarification on these terms.1 After determining that no uniform terminology existed in the literature and that device-specific terminology leads to potential confusion, the consensus group suggested the following definitions:

Widefield images include "images depicting retinal anatomic features beyond the posterior pole, but posterior to the vortex vein ampulla, in all four quadrants."[1]

Ultra-widefield images depict "retinal anatomic features anterior to the vortex vein ampullae in all four quadrants."[1]

1. Choudhry N, Duker JS, Freund KB, et al. Classification and guidelines for widefield imaging: recommendations from the international widefield imaging study group. *Ophthalmol Retina*. 2019;3(10):843-849.

In our report, we described the case of a 55-year-old patient who was diagnosed with VKH disease by simultaneous navigated peripheral SS-OCT over UWF FA/ICGA imaging. Findings revealed multiple areas of serous retinal detachment outside the macula.[1] Navigated peripheral SS-OCT also found evidence of vasculitis, characterized by intraretinal perivascular high reflectivity.

CHALLENGES OF MULTIMODAL IMAGING

Multimodal imaging does have its challenges. For one, a standardized lexicon has not been adopted by all stakeholders. Reliance on manufacturer-specific terms leads to confusion when discussing inter-platform findings, impeding research to better understand these innovations. The International Widefield Imaging Study Group is working to reconcile nomenclature (see *Standardization of the Nomenclature*). In addition, patient compliance with a technician's instructions can be a barrier to capturing high-quality images. The invasive nature of some imaging modalities remains a significant challenge in our clinics. Finally, the capital expense to acquire new equipment must also be considered.

THE WAY OF THE FUTURE

The benefits of using multimodal imaging in retina care outweigh the potential challenges. Cutting-edge clinics aiming to maximize the potential and efficiency of their imaging suite should assess whether multimodal platforms are a good fit and can be integrated into their workflow.

In a wider sense, the adoption of multimodal imaging could improve access to earlier care for patients through telemedicine and lead our field to the more objective and precise patient-tailored medicine we strive to practice.[4] Multimodal imaging is here to stay—it's just a matter of how you will embrace it. ■

1. Valentin Bravo FJ, Ayliffe W, Stanga SFE, et al. New imaging technology for simultaneous multiwavelength-UWF fundus fluorescein angiography and indocyanine green angiography with navigated central and peripheral SS-OCT. *Ophthalmic Surg Lasers Imaging Retina*. 2023;54(7):401-410.
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(Continued from page 35)

Endolaser may also compromise the blood-retina barrier, particularly in patients with diabetes who already have preexisting vasculopathy.[2-4] Furthermore, the use of air may result in the fluid-air meniscus serving as an inflammatory interface for the deposition of fibrin.[3]

However, the inflammatory nature of the fibrinoid reaction is somewhat challenged by accounts of fibrinoid reactions occurring despite the use of intraoperative corticosteroids.[3,4] Additionally, it is unclear why the fibrin would be confined to the posterior segment and have minimal anterior chamber reaction or vitreous cell.[3] Other theories include the idea that the fibrinoid response may represent a posterior segment equivalent of toxic anterior segment syndrome, resulting from a particular substance, possibly a contaminant, triggering a brisk immunologic response.[2,3,6]

While corticosteroids are generally considered the mainstay of treatment, tissue plasminogen activator has also been used to rapidly and successfully resolve post-PPV fibrin in both the anterior chamber and vitreous cavity.[7]

BE ON THE LOOKOUT

The rare complication of transvitreal fibrinoid reaction following PPV in diabetic eyes may be more common in the setting of concurrent endolaser, fluid-air exchange, and other combined procedures such as cataract extraction. The fibrinoid reaction often resolves rapidly with topical steroids alone, although other management options exist for refractory cases. Clinicians should be aware of this rare entity to avoid confusion with endophthalmitis and to guide proper management. ■

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COMBINATION THERAPY FOR METASTATIC UVEAL MELANOMA


A look at the response of large choroidal metastatic melanoma to treatment with darovasertib and crizotinib.

BY LAUREN B. YEAGER, MD, AND BRIAN P. MARR, MD

Uveal melanoma (UM) is the most common intraocular tumor in adults. Plaque brachytherapy has been the mainstay of treatment for UM tumors since the pivotal COMS trial, which proved the noninferiority of brachytherapy compared with enucleation for the treatment of medium-sized tumors. While brachytherapy offers a globe-salvaging treatment with more than 95% effectiveness, significant visual impairments occur in more than half of patients, mainly due to radiation-related complications.[1,2] Current research focuses on enhancing brachytherapy by reducing complications, improving visual outcomes, and expanding indications for use. Enucleation remains necessary for large tumors that exceed 11 mm in thickness and/or those that cannot be adequately covered by the plaque.

Metastatic UM (MUM) develops in up to 50% of patients diagnosed with UM.[3] The prognosis is historically poor in cases of MUM, and treatment options remain limited, although clinical trials on targeted therapies are making slow and steady progress. Nearly 90% of UM cases are associated with *GNAQ*/*GNA11* mutations, which lead to consistent activation of the protein kinase C (PKC) and the mitogen-activated protein kinase pathway, driving tumor progression.[4] Studies have shown that PKC inhibition slows the growth of *GNAQ*/*GNA11*-mutated melanomas[5]; however, the results of PKC inhibitors when used alone are suboptimal.[6] This may be due, in part, to hepatocyte growth factors (HGF) binding to c-Met, a receptor tyrosine kinase, leading to cell proliferation,[7] and evidence suggests c-Met inhibition combined with PKC inhibition may have a synergistic effect.[8] This has led to ongoing clinical trials evaluating darovasertib, a small-molecule PKC inhibitor for *GNAQ*-mutated cancers, as a monotherapy or in combination with a c-Met inhibitor, such as crizotinib or binimetinib.

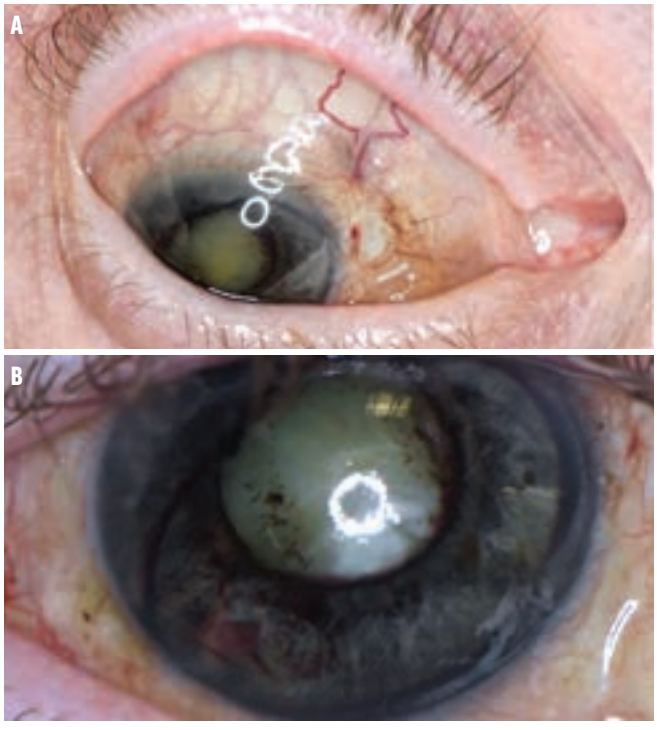

Figure 1. External photographs at presentation showed diffuse subconjunctival pigmentation (A). Note the scattered pigment in the anterior chamber and on the anterior lens capsule (B). Layered hemorrhage was visualized inferiorly, and a dense white cataract obstructed the posterior view.

Herein, we report a case of MUM that spread to the liver and was successfully treated with darovasertib and crizotinib, highlighting the dramatic response of the primary tumor and the potential role of this combination therapy for ocular treatment, particularly in the neoadjuvant setting.

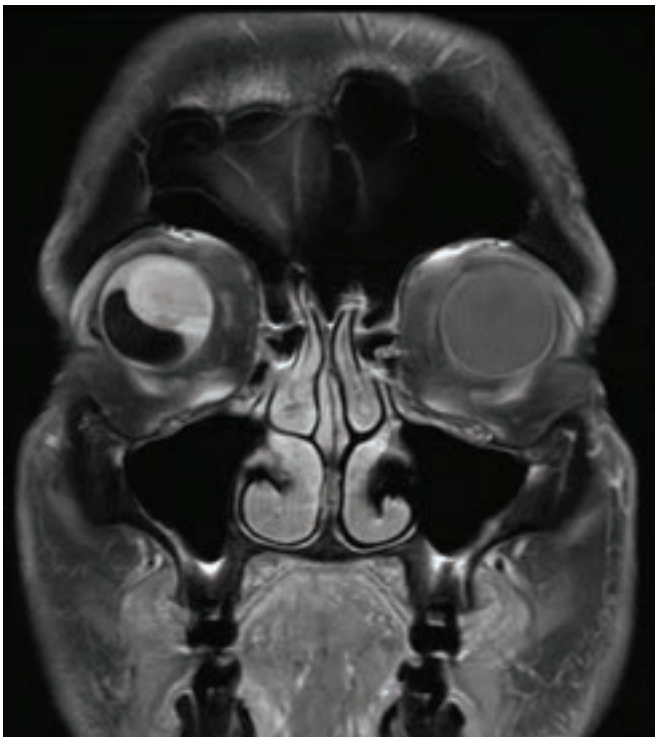

Figure 2. MRI of the orbits showed an enhancing intraocular mass occupying most of the globe in the T-1 post-contrast image.

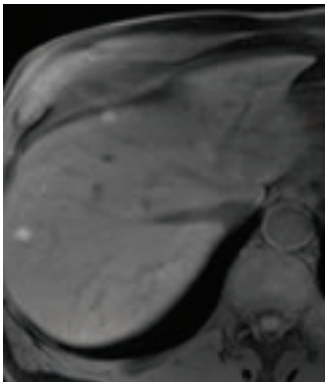

Figure 3. A pre-contrast axial T-1 image of the abdomen performed at the time of diagnosis demonstrated multiple intrinsically enhancing lesions consistent with MUM.

CASE REPORT

A 73-year-old man presented to our service for a tertiary opinion. Four months prior, he was diagnosed at an outside hospital with a retinal detachment and presumed subretinal and choroidal hemorrhage, for which he underwent pars plana vitrectomy. His postoperative course was complicated by multiple redetachments requiring two repeat surgeries; in the most recent surgery, the surgeon noted intraocular brown pigment.

The patient's past medical, family, and social history were noncontributory. At presentation, VA was light perception OD and 20/25 OS, and IOP was normal. On anterior examination, there was fine, diffusely scattered subconjunctival pigment; diffuse pigment on the corneal endothelium; iris neovascularization; and a dense cataract (Figure 1). Vitreous hemorrhage obscured the posterior view. He was taking oral acetazolamide (Diamox, Teva Pharmceuticals), as well as topical prednisolone acetate and 2%/0.5% dorzolamide HCl timodol maleate ophthalmic solution (Cosopt PF, Théa) in the right eye.

Ultrasonography of the right eye was limited due to the presence of silicone oil but suspicious for a large intraocular mass. Globe transillumination showed diffuse darkening without discrete borders. UM was suspected, and an MRI of the orbits was performed that revealed a 2.0 cm x 1.3 cm intraocular mass with intrinsic T-1 hyperintensity and relative diffuse restriction, consistent with a melanocytic tumor and UM (Figure 2). There was no gross orbital extension on MRI; however, the subconjunctival pigment was consistent with extraocular spread. Systemic workup with CT of the chest and MRI of the abdomen showed multiple small, T-1-enhancing liver lesions (Figure 3). CT-guided liver biopsy confirmed MUM with *GNAQ* mutation.

Treatment options were reviewed with the patient, including enucleation. Given the need for systemic management and that the patient was pain-free, surgery was deferred. Systemic treatment options included immune checkpoint blockade, liver-directed therapy, and clinical trials. The patient was HLA-A*02:01 negative and, thus, not a candidate for tebentafusp (Kimmtrak, Immunocore). He was enrolled in a clinical trial and started on treatment with oral darovasertib and crizotinib. He experienced moderate but tolerable side effects, including nausea, vomiting, edema, and facial rash; each was controlled medically.

At 2 months post-treatment, liver disease was reduced by 28%. At 3 months post-treatment, orbital MRI showed a greater-than 50% reduction of the ocular tumor (Figure 4). Six months post-diagnosis, the patient has decreased disease burden (Figure 5).

EMERGING NEOADJUVANT THERAPIES

Therapeutic options for MUM remain limited. Checkpoint inhibitors, which revolutionized the treatment of metastatic cutaneous melanoma, show disappointing results in UM.[9] Recent advances include the FDA approval of tebentafusp, a bispecific gp100-CD3 T-cell engager for HLA-A*02:01-positive patients that improves median overall survival to 21.6 months compared with 16 months in the control group. The overall survival benefit does not correlate with response rates, which are limited to 9% versus 5% in control populations.[10] While tebentafusp is currently first-line therapy for HLA-A*02:01-positive patients, eligibility for the drug is limited. HLA-A*02:01 seropositivity occurs in about 50% of the White population.[11]

There remains an urgent need for treatments that will target broader populations. Early trial data showed that darovasertib/crizotinib therapy for the treatment of MUM may have a 90% disease control rate and median

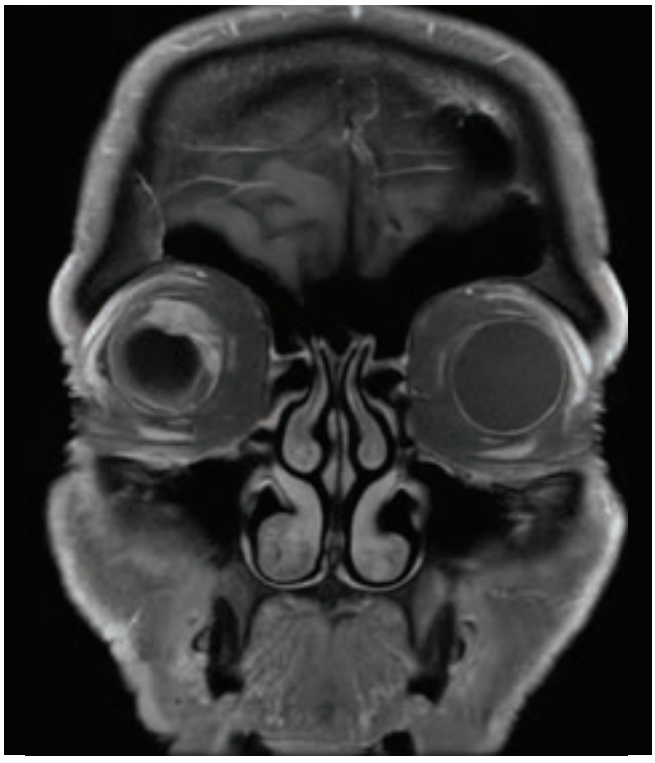

Figure 4. MRI of the orbits 3 months post-treatment initiation showed that the mass had decreased by more than half.

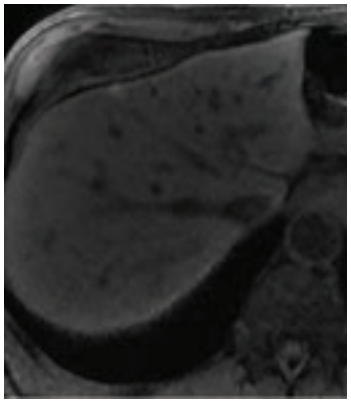

Figure 5. A pre-contrast, axial T-1 image of the abdomen performed 6 months post-treatment showed that the lesions had significantly reduced in size and number.

progression-free survival of 7 months, offering a potential first-line treatment for HLA-A*02:01-negative patients.[12]

Research focuses on the potential of neoadjuvant treatments for primary UM. Neoadjuvant treatment is used to shrink the ocular tumor prior to definitive therapy. Current treatment with tebentafusp and immune checkpoint inhibitors offers poor response rates of 0% to 9%, making them unsuitable for neoadjuvant use.[10,13,14] Our patient experienced 50% shrinkage of his ocular tumor with darovasertib/crizotinib therapy; this marked response is supported by clinical data. Darovasertib/crizotinib combination has an overall response rate of 45% and decreased tumor size in 100% of patients with UM to date.[12] Hoing et al recently published the first prospective case of successful neoadjuvant treatment using combined darovasertib/crizotinib in a patient with a large UM in his only seeing eye. At 4 months, there was an 80% reduction in tumor size, sparing the patient enucleation and allowing for plaque brachytherapy.[15] These data have prompted a phase 2 clinical trial evaluating darovasertib as a neoadjuvant therapy in ocular melanoma.

POTENTIAL TO SPARE ENUCLEATION

Decreasing tumor size prior to definitive therapy has the potential to allow for malignancies to be treated with globe-salvaging approaches and improved visual outcomes post-brachytherapy through lowering radiation dosage, a known risk factor for visual impairment.[16] ■

Acknowledgement: The authors would like to thank Volkan Beylergil, MD, radiologist at Memorial Sloan Kettering Cancer Center, New York City, for his contributions to the article.

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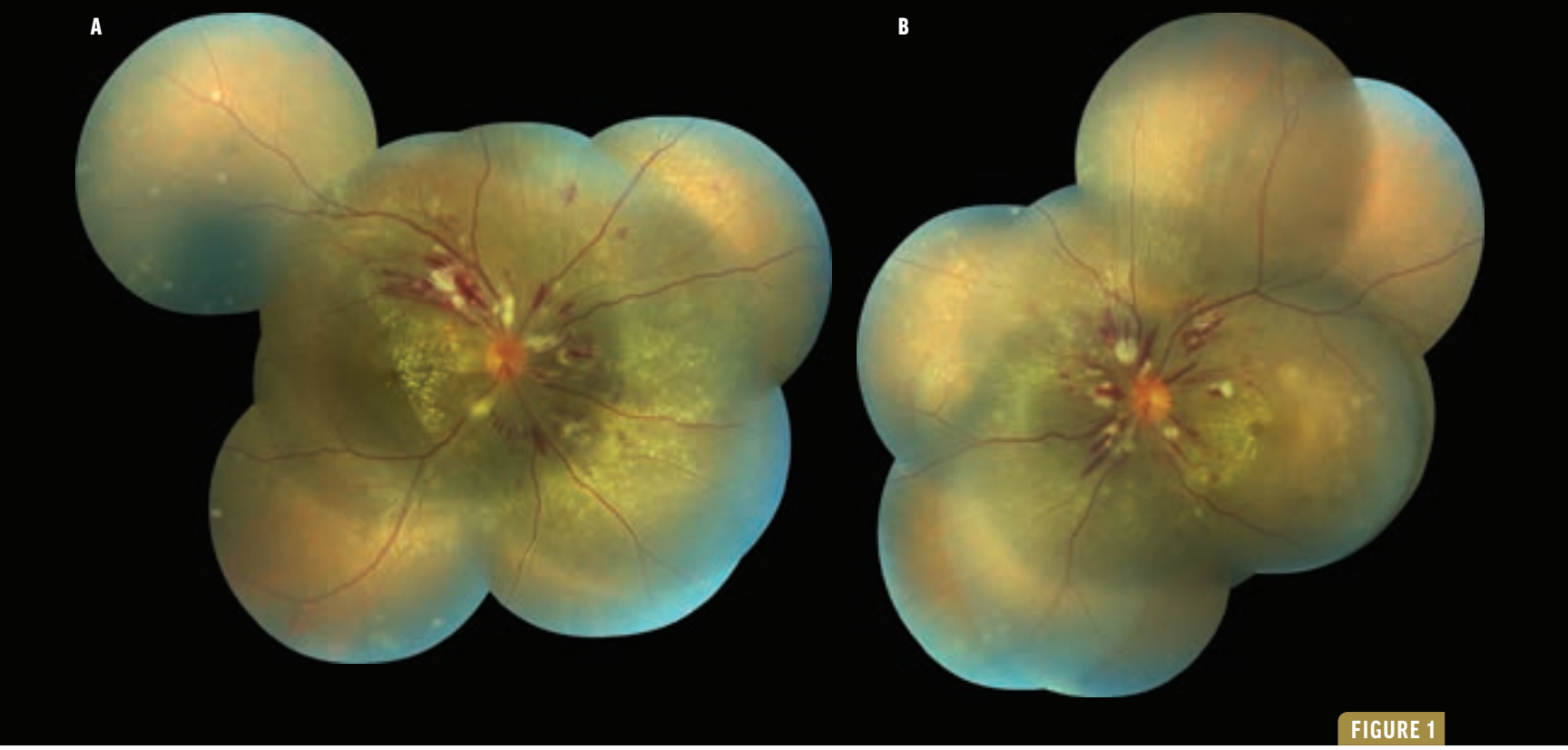

FIGURE 1

A COMPLICATED CASE OF OCULAR TUBERCULOSIS


This patient's pulmonary tuberculosis led to decreased vision 7 years later.

BY JHON EDUARDO ZANS, MD, AND DIEGO FLORES, MD

A 31-year-old woman presented with ocular tuberculosis with many clinical symptoms, including progressive central vision loss, blurry vision, headache, and weight loss that began 5 months earlier. Her condition was aggravated by meningoencephalitis and brain hemorrhage, which required surgery. After recovery, she experienced visual improvement but developed neurological sequelae, including homonymous hemianopsia in three quadrants, that continued for almost 1 year.

At presentation, her VA was 20/150 OD and 20/100 OS. Her medical history was significant for pulmonary tuberculosis 7 years prior with isoniazid resistance during lab analytics, a positive result for purified protein derivative (16 mm), and negative results for human immunodeficiency virus and venereal disease research laboratory. Her chest X-ray indicated pulmonary tuberculosis.

Fundus imaging showed a clear media and optic nerve with poorly defined edges with peripapillary flame hemorrhages accompanied by cotton-like exudates in the right (Figure 1A) and left (Figure 1B) eye. Exudates observed at the macular level suggested neuroretinitis. In the posterior pole of the left eye, there was a choroidal granulomatous lesion of elevated appearance (Figure 1B), and in the periphery of each eye, grayish ovoid punctate lesions suggestive of multifocal choroiditis were observed.

Macular OCT showed an absence of vitreomacular interface lesions in the right (Figure 2A) and left (Figure 2B) eye. Hyperreflective and hyporeflective lesions in the intraretinal

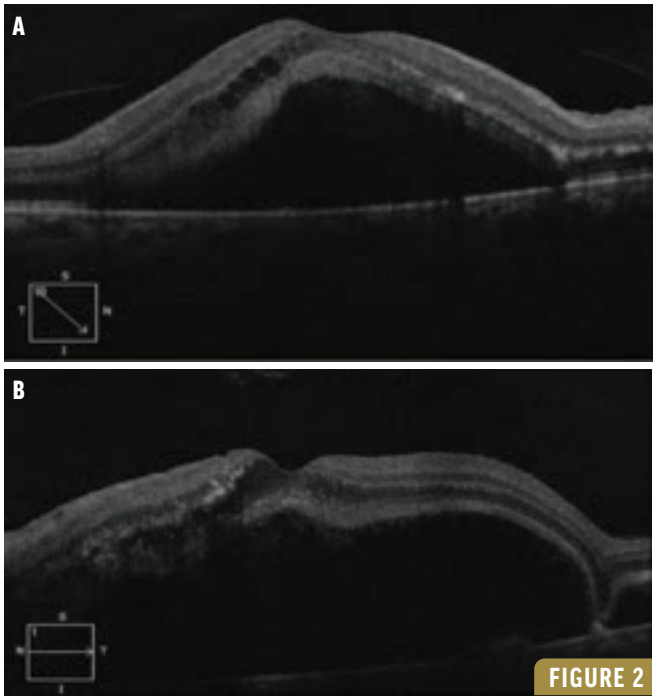

FIGURE 2

tissue suggested exudates and cystoid macular edema, respectively, and extensive hyporeflectivity at the subretinal level was a sign of serous retinal detachment.

TREATMENT APPROACH

We initiated a multidisciplinary management approach with infectiology and neurology and recommended treating the patient with oral antibiotics in the hospital. We based our decision on the Collaborative Ocular Tuberculosis Study consensus.[1]

At the hospital, she received treatment with oral levofloxacin, rifampicin, ethambutol, and pyrazinamide, which continued for 1 year. She underwent surgery for decompressive craniotomy due to subdural and subarachnoid hemorrhage. Her VA improved to 20/60 OD and 20/25 OS post-treatment. ■

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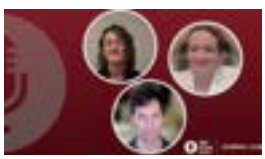

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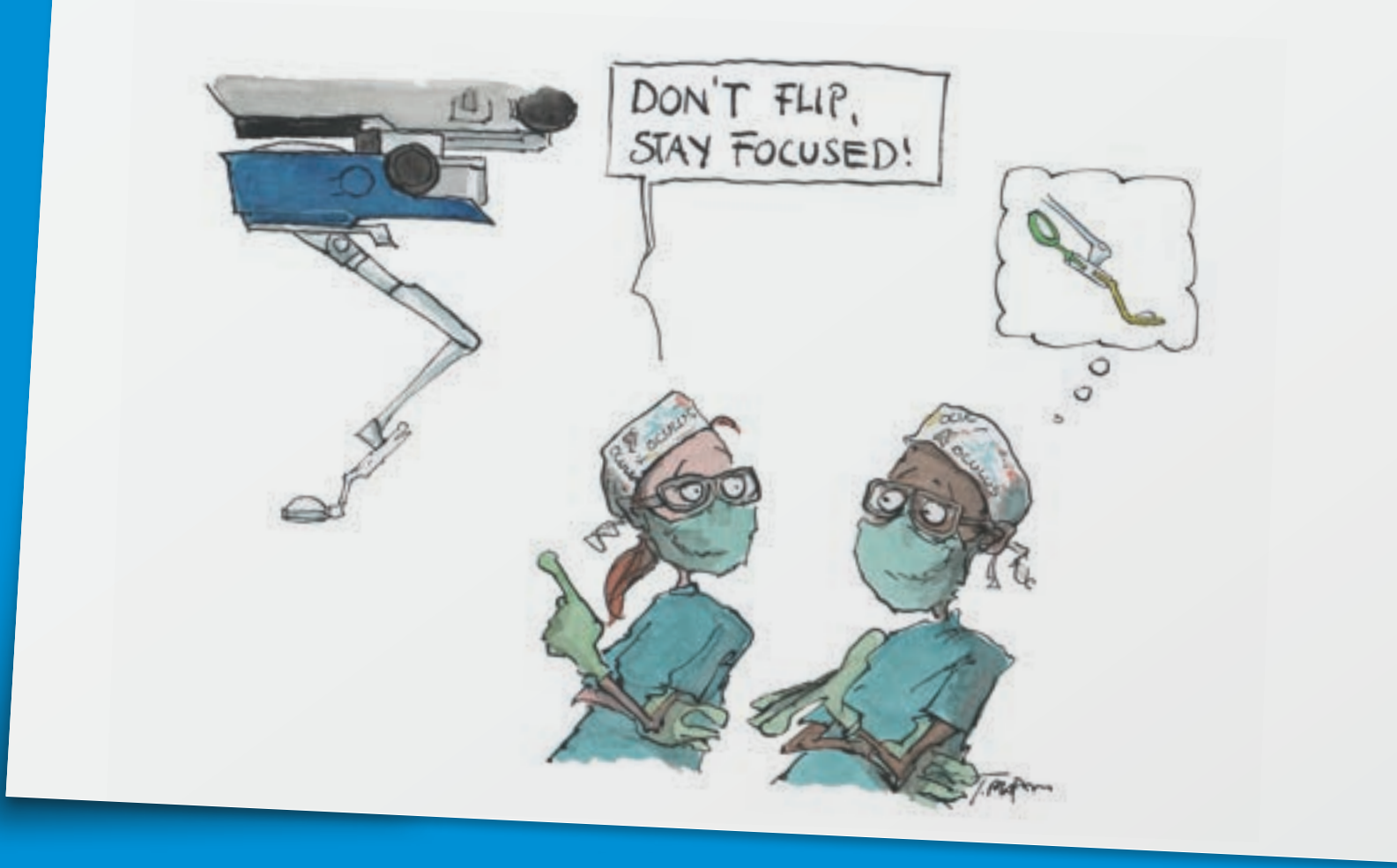

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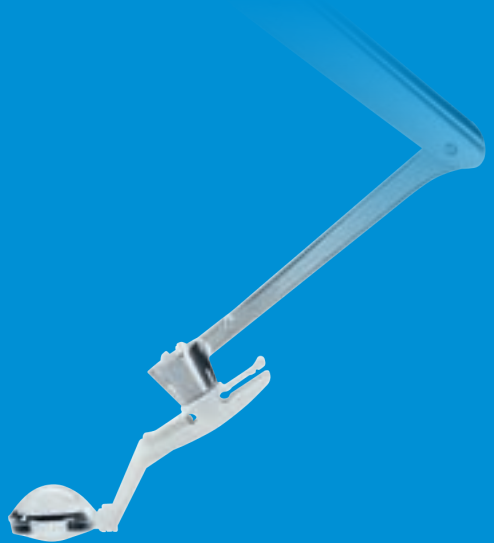

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