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RETINA WOMEN

An update from leaders in the field

With Guest Editor Judy E. Kim, MD

PEARLS FOR THE YAMANE TECHNIQUE

WOMEN IN LEADERSHIP: A CONVERSATION WITH JULIA A. HALLER, MD, AND JOAN W. MILLER, MD

JOURNAL CLUB WITH THE WILLS EYE HOSPITAL RETINA FELLOWS

THIS IS PRECISION

This is

FINESSE™ SHARKSKIN™ ILM Forceps

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

Optimized grasping platform and angled tip closure to help mitigate membrane shredding[2]

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.

Reference: 1. Data on File. Alcon Laboratories Inc; May 2018. **2.** Data on File. Alcon Laboratories Inc; September 2017.

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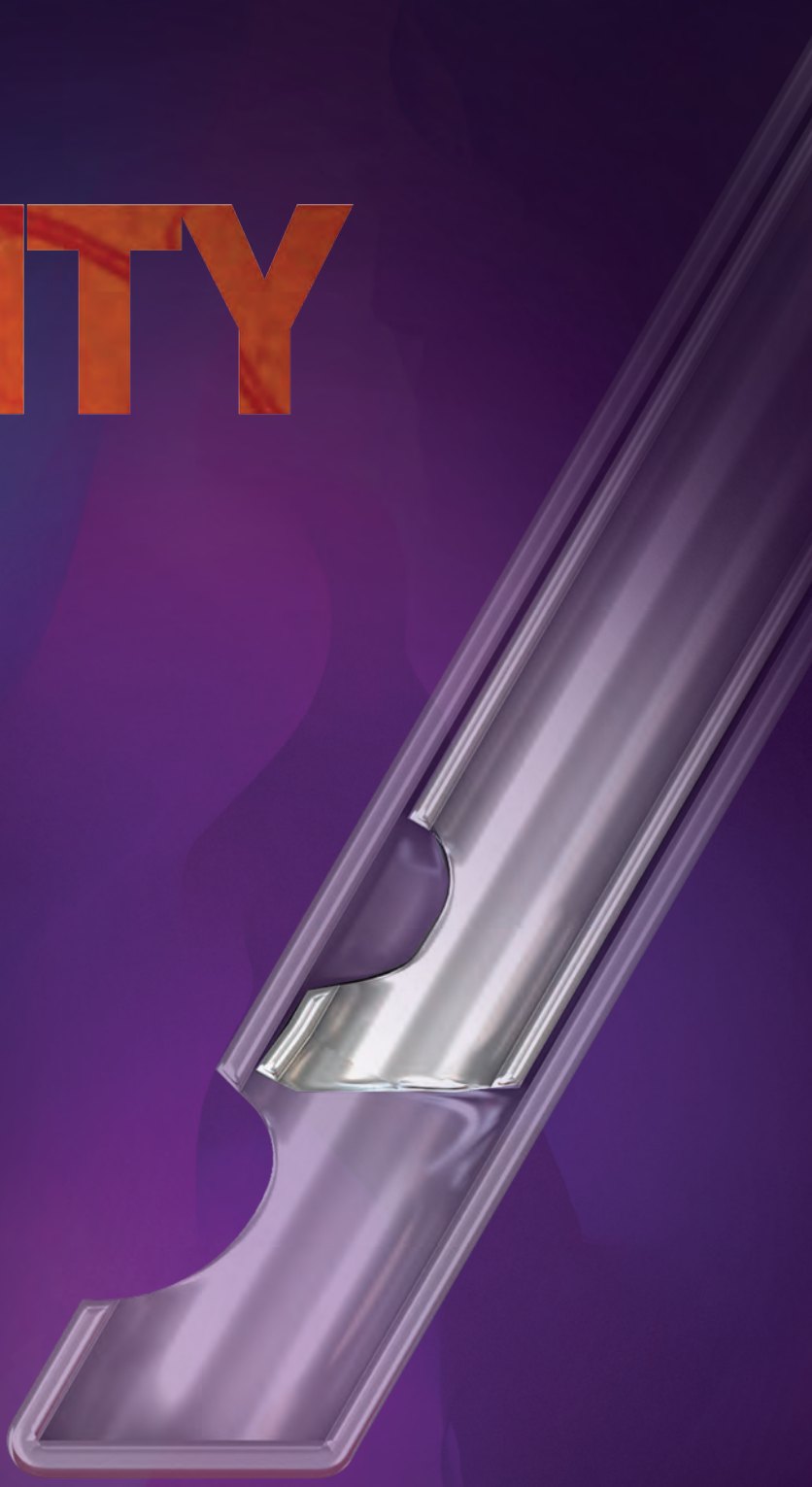
THIS IS STABILITY

This is HYPERVIT™

DUAL BLADE VITRECTOMY PROBE



Designed to:

- Enhance stability with a continuously open port and CONSTELLATION® Vision System's IOP compensation[1]
- Reduce pulsatile traction with **20 000 cuts per minute** using 25+® and 27+® gauge probes*, [2,3]
- Improve vitreous flow[4]
- Enable closer access to tissue plane with beveled tip[5]

*At similar single-blade flow rates

MIVS IMPORTANT PRODUCT INFORMATION

Caution: Federal law restricts this device to sale by, or on the order of, a physician. Indications for Use: The CONSTELLATION® Vision System is an ophthalmic microsurgical system that is indicated for both anterior segment (i.e., phacoemulsification and removal of cataracts) and posterior segment (i.e., vitreoretinal) ophthalmic surgery. The ULTRAVIT® Vitrectomy Probe is indicated for vitreous cutting and aspiration, membrane cutting and aspiration, dissection of tissue and lens removal. The valved entry system is indicated for scleral incision, canulae for posterior instrument access and venting of valved cannulae. The infusion cannula is indicated for posterior segment infusion of liquid or gas. **Warnings and Precautions:** • The infusion cannula is contraindicated for use of oil infusion. • Attach only Alcon supplied products to console and cassette luer fittings. Improper usage or assembly could result in a potentially hazardous condition for the patient. Mismatch of surgical components and use of settings not specifically adjusted for a particular combination of surgical components may affect system performance and create a patient hazard. Do not connect surgical components to the patient's intravenous connections. • Each surgical equipment/component combination may require specific surgical setting adjustments. Ensure that appropriate system settings are used with each product combination. Prior to initial use, contact your Alcon sales representative for in-service information. • Care should be taken when inserting sharp instruments through the valve of the Valved Trocar Cannula. Cutting instrument such as vitreous cutters should not be actuated during insertion or removal to avoid cutting the valve membrane. Use the Valved Cannula Vent to vent fluids or gases as needed during injection of viscous oils or heavy liquids. • Visually confirm that adequate air and liquid infusion flow occurs prior to attachment of infusion cannula to the eye. • Ensure proper placement of trocar cannulas to prevent sub-retinal infusion. • Leaking sclerotomies may lead to post operative hypotony. • Vitreous traction has been known to create retinal tears and retinal detachments. • Minimize light intensity and duration of exposure to the retina to reduce the risk of retinal photic injury. **ATTENTION:** Please refer to the CONSTELLATION® Vision System Operators Manual for a complete listing of indications, warnings and precautions.

References: 1. Irannejad A, Tambat S, Abulon DJK. Retropulsion and mass flow of 27-gauge vitrectomy probes: comparison of dual-blade/flat-tipped probes and single-blade/beveled probes. Poster presented at: 18th Congress of the European Society of Retina Specialists; September 20–23, 2018; Vienna, Austria. **2.** Alcon data on file. Alcon Laboratories, Inc; June 2018. **3.** Alcon data on file. Alcon Laboratories, Inc; June 2018. **4.** Alcon data on file. Alcon Laboratories, Inc; June 2018. **5.** Alcon data on file. Alcon Laboratories, Inc; May 2017.

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Discover continuous calm in uveitis

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg:

- **Proven to reduce uveitis recurrence at 6 and 12 months[1]***
  [At 6 months–18% for YUTIQ and 79% for sham for study 1 and 22% for YUTIQ and 54% for sham for study 2 (*P*<.01). At 12 months–28% for YUTIQ and 86% for sham for study 1 and 33% for YUTIQ and 60% for sham for study 2.]
- **Innovative Durasert® technology is designed for a sustained release of fluocinolone acetonide for up to 36 months with just 1 YUTIQ implant[2]**

For more information, visit **YUTIQ.com**

J code: J7314

*Study design: The efficacy of YUTIQ was assessed in 2 randomized, multicenter, sham-controlled, double-masked, phase 3 studies in adult patients (N=282) with noninfectious uveitis affecting the posterior segment of the eye. The primary endpoint in both studies was the proportion of patients who experienced recurrence of uveitis in the study eye within 6 months of follow-up; recurrence was also assessed at 12 months. Recurrence was defined as either deterioration in visual acuity, vitreous haze attributable to noninfectious uveitis, or the use of prohibited medications.[1,3]

INDICATIONS AND USAGE

YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic noninfectious uveitis affecting the posterior segment of the eye.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Ocular or Periocular Infections: YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases.

Hypersensitivity: YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

WARNINGS AND PRECAUTIONS

Intravitreal Injection-related Effects: Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection.

Steroid-related Effects: Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

Risk of Implant Migration: Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

ADVERSE REACTIONS

In controlled studies, the most common adverse reactions reported were cataract development and increases in intraocular pressure.

References: 1. YUTIQ® (fluocinolone acetonide intravitreal implant) 0.18 mg full U.S. Prescribing Information. EyePoint Pharmaceuticals, Inc. October 2018. **2.** EyePoint Pharmaceuticals Receives FDA Approval of YUTIQ™ (fluocinolone acetonide intravitreal implant) 0.18 mg. Global Newswire. https://www.globenewswire.com/news-release/2018/10/15/1621023/0/en/EyePoint-Pharmaceuticals-Receives-FDA-Approval-of-YUTIQ-fluocinolone-acetonide-intravitreal-implant-0-18-mg.html. Accessed February 7, 2020. **3.** Data on file.

Please see next page for Brief Summary of full Prescribing Information.

EyePoint PHARMACEUTICALS

480 Pleasant Street, Suite B300, Watertown, MA 02472

2/2020
US-YUT-2000020

YUTIQ™ (fluocinolone acetonide intravitreal implant) 0.18 mg, for intravitreal injection
Initial U.S. Approval: 1963

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

1. INDICATIONS AND USAGE. YUTIQ™ (fluocinolone acetonide intravitreal implant) 0.18 mg is indicated for the treatment of chronic non-infectious uveitis affecting the posterior segment of the eye.

4. CONTRAINDICATIONS. 4.1. Ocular or Periocular Infections. YUTIQ is contraindicated in patients with active or suspected ocular or periocular infections including most viral disease of the cornea and conjunctiva including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections and fungal diseases. **4.2. Hypersensitivity.** YUTIQ is contraindicated in patients with known hypersensitivity to any components of this product.

5. WARNINGS AND PRECAUTIONS. 5.1. Intravitreal Injection-related Effects. Intravitreal injections, including those with YUTIQ, have been associated with endophthalmitis, eye inflammation, increased or decreased intraocular pressure, and choroidal or retinal detachments. Hypotony has been observed within 24 hours of injection and has resolved within 2 weeks. Patients should be monitored following the intravitreal injection *[see Patient Counseling Information (17) in the full prescribing information]*. **5.2. Steroid-related Effects.** Use of corticosteroids including YUTIQ may produce posterior subcapsular cataracts, increased intraocular pressure and glaucoma. Use of corticosteroids may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses. Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection. **5.3. Risk of Implant Migration.** Patients in whom the posterior capsule of the lens is absent or has a tear are at risk of implant migration into the anterior chamber.

6. ADVERSE REACTIONS. 6.1. Clinical Studies 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. Adverse reactions associated with ophthalmic steroids including YUTIQ include cataract formation and subsequent cataract surgery, elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera. Studies 1 and 2 were multicenter, randomized, sham injection-controlled, masked trials in which patients with non-infectious uveitis affecting the posterior segment of the eye were treated once with either YUTIQ or sham injection, and then received standard care for the duration of the study. Study 3 was a multicenter, randomized, masked trial in which patients with non-infectious uveitis affecting the posterior segment of the eye were all treated once with YUTIQ, administered by one of two different applicators, and then received standard care for the duration of the study. Table 1 summarizes data available from studies 1, 2 and 3 through 12 months for study eyes treated with YUTIQ (n=226) or sham injection (n=94). The most common ocular (study eye) and non-ocular adverse reactions are shown in Table 1 and Table 2.

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Cataract[1]	63/113 (56%)	13/56 (23%)
Visual Acuity Reduced	33 (15%)	11 (12%)
Macular Edema	25 (11%)	33 (35%)
Uveitis	22 (10%)	33 (35%)
Conjunctival Hemorrhage	17 (8%)	5 (5%)
Eye Pain	17 (8%)	12 (13%)
Hypotony Of Eye	16 (7%)	1 (1%)
Anterior Chamber Inflammation	12 (5%)	6 (6%)
Dry Eye	10 (4%)	3 (3%)
Vitreous Opacities	9 (4%)	8 (9%)
Conjunctivitis	9 (4%)	5 (5%)
Posterior Capsule Opacification	8 (4%)	3 (3%)
Ocular Hyperemia	8 (4%)	7 (7%)
Vitreous Haze	7 (3%)	4 (4%)
Foreign Body Sensation In Eyes	7 (3%)	2 (2%)
Vitritis	6 (3%)	8 (9%)
Vitreous Floaters	6 (3%)	5 (5%)
Eye Pruritus	6 (3%)	5 (5%)
Conjunctival Hyperemia	5 (2%)	2 (2%)
Ocular Discomfort	5 (2%)	1 (1%)
Macular Fibrosis	5 (2%)	2 (2%)
Glaucoma	4 (2%)	1 (1%)
Photopsia	4 (2%)	2 (2%)

(continued)

Table 1: Ocular Adverse Reactions Reported in ≥ 1% of Subject Eyes and Non-Ocular Adverse Reactions Reported in ≥ 2% of Patients

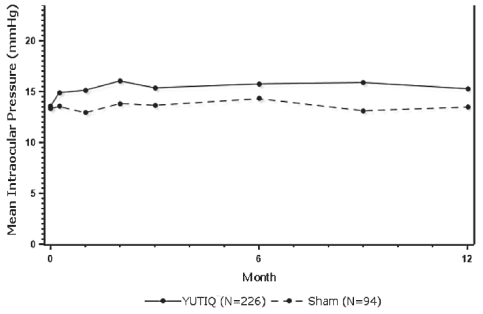
Ocular		
ADVERSE REACTIONS	**YUTIQ (N=226 Eyes) n (%)**	**Sham Injection (N=94 Eyes) n (%)**
Vitreous Hemorrhage	4 (2%)	0
Iridocyclitis	3 (1%)	7 (7%)
Eye Inflammation	3 (1%)	2 (2%)
Choroiditis	3 (1%)	1 (1%)
Eye Irritation	3 (1%)	1 (1%)
Visual Field Defect	3 (1%)	0
Lacrimation Increased	3 (1%)	0
Non-ocular		
ADVERSE REACTIONS	**YUTIQ (N=214 Patients) n (%)**	**Sham Injection (N=94 Patients) n (%)**
Nasopharyngitis	10 (5%)	5 (5%)
Hypertension	6 (3%)	1 (1%)
Arthralgia	5 (2%)	1 (1%)

1. Includes cataract, cataract subcapsular and lenticular opacities in study eyes that were phakic at baseline. 113 of the 226 YUTIQ study eyes were phakic at baseline; 56 of 94 sham-controlled study eyes were phakic at baseline.

Table 2: Summary of Elevated IOP Related Adverse Reactions

ADVERSE REACTIONS	YUTIQ (N=226 Eyes) n (%)	Sham (N=94 Eyes) n (%)
IOP elevation ≥ 10 mmHg from Baseline	50 (22%)	11 (12%)
IOP elevation > 30 mmHg	28 (12%)	3 (3%)
Any IOP-lowering medication	98 (43%)	39 (41%)
Any surgical intervention for elevated IOP	5 (2%)	2 (2%)

Figure 1: Mean IOP During the Studies



8. USE IN SPECIFIC POPULATIONS. 8.1 Pregnancy. Risk Summary. Adequate and well-controlled studies with YUTIQ have not been conducted in pregnant women to inform drug associated risk. Animal reproduction studies have not been conducted with YUTIQ. It is not known whether YUTIQ can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. Corticosteroids have been shown to be teratogenic in laboratory animals when administered systemically at relatively low dosage levels. YUTIQ should be given to a pregnant woman only if the potential benefit justifies the potential risk to the fetus. All pregnancies have a risk of birth defect, loss, or other adverse outcomes. In the United States general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2% to 4% and 15% to 20%, respectively. **8.2 Lactation.** Risk Summary. Systemically administered corticosteroids are present in human milk and can suppress growth, interfere with endogenous corticosteroid production. Clinical or nonclinical lactation studies have not been conducted with YUTIQ. It is not known whether intravitreal treatment with YUTIQ could result in sufficient systemic absorption to produce detectable quantities of fluocinolone acetonide in human milk, or affect breastfed infants or milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for YUTIQ and any potential adverse effects on the breastfed child from YUTIQ. **8.4 Pediatric Use.** Safety and effectiveness of YUTIQ in pediatric patients have not been established. **8.5 Geriatric Use.** No overall differences in safety or effectiveness have been observed between elderly and younger patients.

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THE PATHS TO SUCCESS

I believe in using our voices and the circle of influence to empower others, both men and women, to create positive changes. What better way to do this than to work with other exceptional physicians, learn and share their wisdom on issues facing retina specialists—especially women—and help guide others to success? In addition, 2020 is especially meaningful for women because it marks the 100th anniversary of women's suffrage in the United States. Therefore, I was honored to accept the invitation from *Retina Today*'s Chief Medical Editor Allen C. Ho, MD, and Associate Medical Editor Robert L. Avery, MD, to serve as Guest Editor for the "Women in Retina" issue.

Never short of ideas (I have constant a flood of ideas like a Times Square ticker tape!), my head was bursting with potential topics and authors, and choosing which topics to cover and with whom to collaborate was more difficult than I imagined; there were numerous facets of issues to consider and many qualified people to expertly address them. "Women in Retina" in the modern era is a complex topic that will continue to evolve, and I tried my best to balance complexity with accessibility and applicability. We know that the definition of success differs for everyone. Nevertheless, we present here paths that these physicians have chosen, experienced, and are advising, to offer some examples of success in the field of retina for readers to consider.

The authors of this issue aced the difficult task of explaining the reality for women in retina—describing the barriers and opportunities they encounter and foresee, and proposing solutions to the problems they've observed—in order for us to continue to pave the path to success. I thank them for sharing their insights and life experiences with thoughtfulness and honesty. I believe many of their comments are not uniquely applicable only to women in retina, but rather can be applied to other fields in which women are still a minority and to both men and women in their early careers.

Avni Finn, MD, MBA, and Caroline Baumal, MD, interviewed a number of women leaders for their piece "Closing the Gender Gap in Retina." María H. Berrocal, MD; Sharon Fekrat, MD; Nancy M. Holekamp, MD; Shlomit Schaal, MD, PhD; and Carol L. Shields, MD, offered their observations about the field's challenges. Dr. Fekrat's astute observation—"Medical schools are now more than 50% female, and, as a result, more women will choose ophthalmology and thus retina"—reminds us exactly why this issue of *Retina Today* is so timely.

Dr. Shields contributed to another cover article, this time with her husband, Jerry Shields, MD, to discuss their careers, their marriage, and the solutions they have found along the way. Not only is this profile of a retinal couple an integral component of this issue's focus on success inside and outside the clinic, but it also serves as a record of the lives of two people whose influence on our field cannot be measured.

It has long been observed that the proportion of women on the podium is not reflective of the population of retina specialists. Tala Al-Khaled, BA, and Ann-Marie Lobo-Chan, MD, address this topic in "Pathway to the Podium," a pearls piece that aspiring women and men in retina may find useful when navigating the meeting landscape. A discussion on mentorship with Audina M. Berrocal, MD; Zelia M. Correa, MD , PhD; and Adrienne W. Scott, MD, yields useful information for future retina leaders who are seeking a mentor or wishing to become one. Without mentors, as they point out, navigating the road to success would be far more difficult.

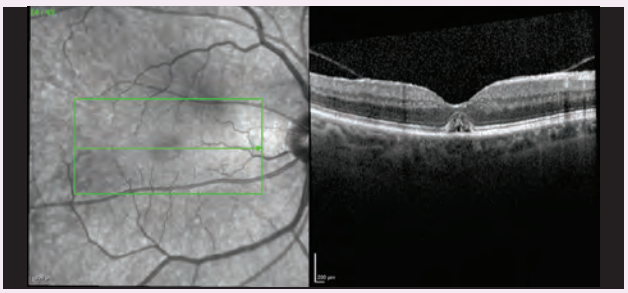
Julia A. Haller, MD, and Joan W. Miller, MD, sat down with me for a roundtable discussion about their pathways to leadership and their "views from the top" on women in retina as department leaders. Their perspectives on the price and benefits of departmental leadership serve as a useful glimpse inside the minds of two of retina's important leaders.

As I worked on this issue, I was reminded once again that the best ally we have as we pave the road to success in any endeavor is each other. The contributors to this issue worked hard to make it a success. I know you'll find these leading retina specialists' experience and knowledge useful. I thank them and the *Retina Today* editorial staff from the bottom of my heart. Enjoy the issue. Cheers! ■

— Judy E. Kim, MD, Guest Editor

UPDATE ON A CASE FROM A PAST ISSUE

After the January/February issue went to press, Brian C. Joondeph, MD, MPS, informed the editorial staff that the patient profiled in the cover series article "An Elusive Macular Hole Closed by Eye Drops Alone" returned to his office for follow-up. As of February 2020, the patient's VA was 20/30 and further fluid reduction had been demonstrated. To read this case, visit bit.ly/Joondeph0320.



RETINA WOMEN

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NOVARTIS RESPONDS TO ASRS NOTE ON SAFETY CONCERNS FOR BROLUCIZUMAB; DRUG RECEIVES EU APPROVAL

Novartis is launching an internal and external review of new information that raises serious safety concerns over its wet age-related macular degeneration (AMD) drug brolucizumab-dbll (Beovu), the company confirmed to Eyewire News in February. Separately, the company announced that the drug had received marketing approval from regulators in the European Union (EU).

On February 23, the American Society of Retina Specialists (ASRS) shared a note with its membership stating that, since Beovu was approved by the US FDA in October 2019, ASRS has received reports of 14 cases of vasculitis associated with the drug, of which 11 were designated by the reporting provider as occlusive retinal vasculitis, a vision-threatening inflammatory eye condition.

In a statement sent to Eyewire News, Novartis said it is aware of recently reported adverse events following treatment with brolucizumab and is evaluating the cases.

"Novartis stands behind the safety and efficacy of [brolucizumab]. In addition to our own internal assessment, we have engaged an external safety review committee to further evaluate these post-marketing cases. We will continue to share details as they become available," the Novartis statement said. "The FDA is aware of our ongoing review and we're in the process of informing other health authorities. Our clinical development and pharmacovigilance teams are working with healthcare professionals to quickly obtain and evaluate all available information in order to classify these events and identify potential risk factors."

An estimated 46,000 injections of brolucizumab have been administered in the United States as of February 21, 2020, according to Novartis.

The company noted that brolucizumab is contraindicated for patients with active intraocular inflammation, and that physicians should follow the guidance in the prescribing information that patients with active ocular inflammation should not be injected with brolucizumab. The product information for brolucizumab in the US lists a 4% rate of intraocular inflammation and a 1% rate of retinal artery occlusion as adverse events reported in the HAWK and HARRIER clinical trials of the drug.

WATCH IT NOW

bit.ly/Eyewire0320

In a separate development, Novartis in February received approval for brolucizumab from the European Medicines Agency, making it the first anti-VEGF agent approved in the EU to demonstrate superior resolution of retinal fluid (intraretinal fluid/subretinal fluid) compared with aflibercept (Eylea, Regeneron).

The EU approval was based on findings from the phase 3 HAWK and HARRIER clinical trials, in which brolucizumab met the primary endpoints, demonstrating gains in BCVA that were noninferior to aflibercept at year 1 (week 48). Vision gains at year 1 were maintained at year 2.

The approval is applicable in all 27 EU member states, as well as the United Kingdom, Iceland, Norway, and Liechtenstein.

RP UPDATE: PHASE 1/2A TRIAL FOR STEM CELL THERAPY WILL EXPAND; GENE THERAPY FOR XLRP SHOWED SAFETY IN PHASE 1 STUDY

A study evaluating the safety and efficacy of a human retinal progenitor cell (hRPC) stem cell therapy candidate for retinitis pigmentosa (RP) will be expanded based on interim efficacy data in an ongoing phase 1/2a study, according to the therapy's developer, the ReNeuron Group.

Three patients in the study successfully received treatment in one eye. Mean difference in VA improvement between treated eyes and untreated eyes was +7.3 letters at 12 months, the company stated in a February press release.

The company has submitted a protocol amendment to

the FDA to expand the phase 1/2a study to treat up to a further nine patients in the phase 2a segment of the study at a dosage of 2 million hRPC cells; a dose of 1 million cells has been used in the study thus far.

In an unrelated study also in patients with RP, no significant safety concerns were observed after application of the gene therapy AAV8-RPGR (NightStar Therapeutics; now Biogen) for the treatment of X-linked RP (XLRP).[1]

In a 6-month, phase 1/2 dose-escalation clinical trial evaluating the safety of gene therapy for XLRP in 18 patients, some visual field improvements were observed.

XLRP is caused by a mutation on the gene *RPGR*, which blocks production of a protein necessary for photoreceptor cell function. *RPGR* mutations account for approximately 70% of all cases of XLRP.

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NEWS BRIEFS

Read Eyewire's latest retina news at Eyewire.news/interests/retina.

>STUDY OF LIGHT THERAPY FOR DIABETIC RETINOPATHY WILL EXPAND

The Valeda System (LumiThera), a photobiomodulation platform being commercialized in Europe for the treatment of dry AMD, will also be investigated for use in treating diabetic retinopathy (DR), according to its maker.

LumiThera received the CE Mark to commercialize the Valeda System in the EU for the treatment of ocular diseases including dry AMD; the LIGHTSIDE II study is evaluating the safety and efficacy of the Valeda System for the treatment of dry AMD in the United States. Preclinical and clinical work has shown that the light therapy system also has potential benefits in treating diabetic edema, the company stated in a press release.

>>MARKET SCOPE: RETINAL SURGICAL DEVICE MARKET TO REACH NEARLY $2 BILLION BY 2025

The retinal surgical device market is expected to total more than $1.5 billion in 2020, with revenue rising to nearly $2 billion in 2025, according to the health care data firm Market Scope.

Market Scope estimated that 1.84 million vitrectomies will be performed globally in 2020.

The per-procedure revenue is typically 10 to 15 times greater than that for cataract surgery due to the numerous products required for a vitrectomy. Still, the number of vitrectomies is far lower than the 30 million cataract surgeries expected to be performed in 2020.

More than 55 companies compete in the global retinal surgical device market, but most specialize in only one or two product categories. Eight companies—Alcon, Bausch + Lomb, Dutch Ophthalmic Research Center (DORC), Geuder, Beaver-Visitec International (BVI), Nidek, Oertli, and Hoya—account for 82% of global revenue in this market.

REMEMBERING MINA CHUNG, MD

Mina Chung, MD, died in February. She was 51.

Dr. Chung was an associate professor of ophthalmology at the University of Rochester Medical Center Flaum Eye Institute and a faculty member at the University of Rochester's Center for Visual Science. She completed her fellowship in vitreoretinal surgery at the University of Iowa College of Medicine and residency at the USC University Hospital, where she was chief resident. She completed her undergraduate studies and medical degree at Yale. ■

HYPOTONY MACULOPATHY AFTER PHACOEMULSIFICATION


A late complication after cataract surgery was resolved with treatment.

BY WEE-MIN TEH, MD, MMED; AND WEI-CHI WU, MD, PHD

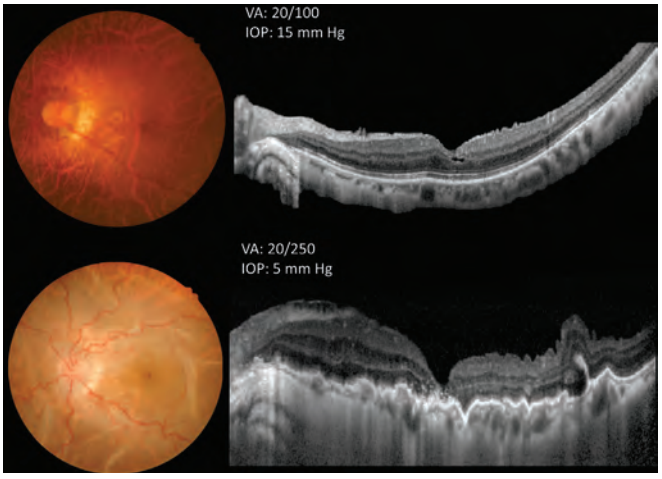
A 56-year-old man noted no visual improvement in his left eye (OS) 2 weeks after uneventful phacoemulsification surgery. He was a high myope (-10.00 D OS) with a history that included retinal detachment surgery in the same eye 1 year before the cataract operation was performed. BCVA before the cataract surgery was 20/100 OS (top left and top right images).

Examination revealed VA of 20/250 OS and IOP of 5 mm Hg. The cornea was clear, and the IOL was positioned well in the capsular bag without tilt or decentration. Dilated fundus examination showed a slightly blurred disc margin, dilated and tortuous retinal vessels, and multiple chorioretinal folds (bottom left image). Spectral-domain OCT (Spectralis, Heidelberg) demonstrated numerous characteristic undulations of the choriocapillaris and retina with retinal thickening. There was no serous detachment. Flattening of the posterior sclera was also seen (bottom right image).

On further inspection of the corneal wound, wound leak was suspected, and Seidel test was positive. A therapeutic bandage contact lens was applied. Over the next 6 months, the patient gradually improved, with IOP at 17 mm Hg and BCVA restored to 20/100 at 6 months.

The term *hypotony maculopathy* was coined by Gass in 1972.[1] It can be defined statistically (IOP < 6.5 mm Hg, or three standard deviations below mean IOP) or clinically (IOP low enough to cause visual loss).[2,3] Common causes of postoperative hypotony include wound leak, overfiltration, iridocyclitis, retinal detachment, cyclodialysis, and mitomycin C toxicity of the ciliary body.[4] Risk factors include younger age, myopia, and male sex.[5]

Successful treatment of hypotony maculopathy depends on timely and correct identification of its cause. Visual recovery is variable depending on the timing of intervention. The treatment goal in this patient was aimed at normalizing IOP to reverse the inward bowing of the sclera and resolve the chorioretinal folds. ■



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To share an image, contact Manish Nagpal, MS, DO, FRCS(Edin), at drmanishnagpal@yahoo.com.
Note: Images should be 400 dpi or higher and at least 10 inches wide.

A PRIMER ON PENTOSAN POLYSULFATE SODIUM MACULOPATHY

Evidence of a new maculopathy is emerging in the clinic.

BY MEERA S. RAMAKRISHNAN, MD; AMAR PATEL, MD; RONALD MELLES, MD; AND ROBIN A. VORA, MD

Mounting evidence links chronic exposure to pentosan polysulfate sodium (PPS; Elmiron, Janssen Pharmaceuticals) with the development of a novel pigmentary maculopathy. PPS is a semisynthetic heparin-like macromolecule used to treat interstitial cystitis (IC), a chronic, incurable bladder pain syndrome manifesting as relentless bladder or pelvic pain, incontinence, and dyspareunia. It is estimated that IC affects more than 1 million individuals in the United States, predominantly women.[1,2] PPS is the only oral option of the two US FDA–approved therapies for IC. Since compassionate use in 1986 and regulatory approval in 1996, PPS has been prescribed by urologists and gynecologists to hundreds of thousands of patients with IC.[3,4]

The association of PPS with maculopathy was first reported in 2018 by Pearce et al in a single-center case series of six patients (six white women, median age 60 years, age range 37-62 years) reporting difficulty reading, paracentral scotomas, and prolonged dark adaptation despite relatively preserved visual acuity.[5] Examination revealed paracentral retinal pigment epithelium (RPE) hyperpigmentation surrounded by subtle vitelliform-like deposits with highly irregular appearances on fundus autofluorescence (FAF) and near-infrared reflectance (NIR) imaging. These patients underwent genetic screening and evaluation for hereditary retinal dystrophies and mitochondrial cytopathies, all of which were negative. Diagnosis of IC and exposure to PPS was the common denominator in all patients.

MANY PATIENTS WITH PPS EXPOSURE MAY HAVE BEEN MISDIAGNOSED WITH AGE-RELATED MACULAR DEGENERATION OR RETINAL DYSTROPHIES, WHICH MAY HAVE LED TO PREVENTABLE, IRREVERSIBLE VISION LOSS ... .

Subsequent case series and cohort studies demonstrated a pattern of PPS exposure characteristics and clinical features.[6-8] In these studies, affected patients tended to be white women of median age 60 years (range 37-79 years). Symptoms most commonly reported were blurred

AT A GLANCE

- ▶ Patients exposed to pentosan polysulfate sodium (PPS) have increased risk of developing maculopathy.
- ▶ PPS is used to treat interstitial cystitis and has been used by patients since 1986.
- ▶ Annual exams with imaging are recommended for patients who have had chronic PPS exposure.

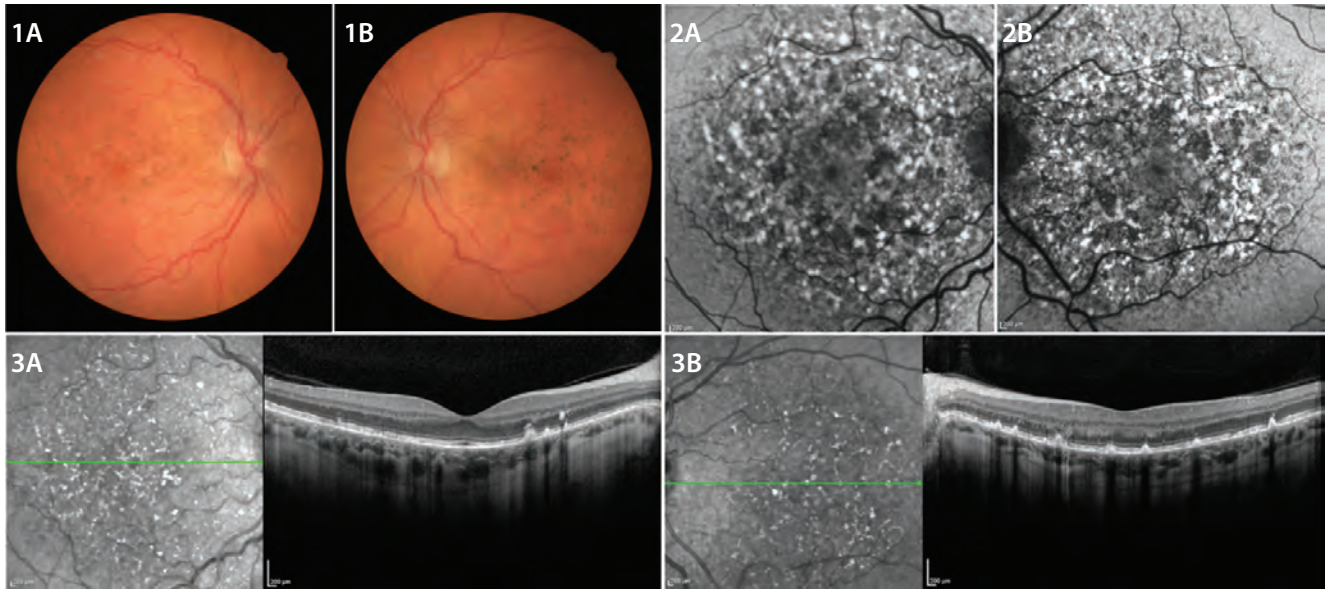

Figure. Clinical characteristics of PPS maculopathy are demonstrated here, with bilateral symmetric pathology centered on the fovea. Hyperpigmented spots, pale yellow-orange deposits, and/or patchy RPE atrophy are observed on color fundus photography (1 A, B). FAF imaging reveals a dense array of hyper- and hypoautofluorescent spots in the posterior pole that tend to be much more striking than relatively subtle fundus examination findings (2 A, B). OCT imaging demonstrates focal thickening or elevation of the RPE layer with associated hyperreflectance on NIR imaging (3 A, B).

vision, prolonged dark adaptation, and metamorphopsia. The most common presenting diagnoses for these cases were macular or pattern dystrophy and age-related macular degeneration (Figure).

Longitudinal follow-up suggests a progressive maculopathy that spreads centrifugally. Macular pigment clumps appear to be a sign of early disease and may ultimately progress to RPE atrophy in later stages. Visual acuity tends to be preserved, except in cases of center-involving RPE atrophy and cystoid macular edema.[6,8] To date, there is also a single case report of choroidal neovascularization associated with PPS maculopathy that resulted in vision loss.[9] Full-field electroretinography demonstrates variable mild attenuation of response amplitudes that is consistent with macular disease, and multifocal electroretinography reveals mild to severe attenuation.

RELATIONSHIP TO PPS EXPOSURE

In a cohort of 219 patients with IC and PPS exposure, the odds ratio for developing an unspecified pigmentary maculopathy was 11.25, and all 14 patients with definite clinical characteristics of PPS maculopathy had exposure to PPS.[7] No other IC therapy demonstrated a significant association with maculopathy. Patients with maculopathy reported duration of PPS intake ranging 3 to 22 years (median 16-17 years).[5-9] A retrospective cohort study by Jain et al involving a large US claims database found that, by 7 years, PPS users had significantly increased odds (odds ratio = 1.41) of developing maculopathy compared with matched controls.[10]

In a large cohort of patients, Vora et al reported definite signs of PPS maculopathy in 11% of patients taking 500 to 999 g PPS daily, and in 42% of those taking more than 1,500 g PPS daily.[8] Patients with maculopathy had ingested an average of 14,067 capsules compared with 10,561 capsules in those without maculopathy.[8]

IMPLICATIONS

It is unusual for a potential drug toxicity to manifest decades after initial FDA approval. PPS safety was not a major issue in clinical trials, and no ocular adverse events were identified.[11-13] Pathogenesis remains unclear. Based on the prolonged exposure time and cumulative dose, the mechanism is potentially related to toxic PPS metabolites accumulating in the RPE, thereby disrupting processing of photoreceptor outer segments or the interphotoreceptor matrix.[6]

These findings represent a major patient safety issue. Many patients with PPS exposure may have been misdiagnosed with age-related macular degeneration or retinal dystrophies, which may have led to preventable, irreversible vision loss or unwarranted genetic counseling. It remains unclear whether discontinuing PPS will halt or alter the course of maculopathy. For now, evidence suggests that the smallest effective dose should be used for the least amount of time.

It may be advisable to perform annual exams with imaging (ie, fundus photography, FAF, NIR, and OCT) of patients with chronic PPS exposure. Discussion with urology and gynecology colleagues is ongoing to raise awareness of PPS toxicity; at the time of publication, the FDA has not

To improve vision in DME,* macular edema following RVO,† or noninfectious posterior segment uveitis

- Achieves clinically significant 3-line gains in BCVA[2,‡]
- Significantly reduces vitreous haze vs sham in noninfectious posterior segment uveitis[2]
- Suppresses inflammation by inhibiting multiple inflammatory cytokines[2]

*Diabetic macular edema. †Retinal vein occlusion: branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO). ‡Best-corrected visual acuity.

Indications and Usage
Diabetic Macular Edema
OZURDEX® (dexamethasone intravitreal implant) is a corticosteroid indicated for the treatment of diabetic macular edema.

Retinal Vein Occlusion
OZURDEX® is a corticosteroid indicated for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

Posterior Segment Uveitis
OZURDEX® is indicated for the treatment of noninfectious uveitis affecting the posterior segment of the eye.

Dosage and Administration
FOR OPHTHALMIC INTRAVITREAL INJECTION. The intravitreal injection procedure should be carried out under controlled aseptic conditions. Following the intravitreal injection, patients should be monitored for elevation in intraocular pressure and for endophthalmitis. Patients should be instructed to report any symptoms suggestive of endophthalmitis without delay.

IMPORTANT SAFETY INFORMATION
Contraindications
Ocular or Periocular Infections: OZURDEX® (dexamethasone intravitreal implant) is contraindicated in patients with active or suspected ocular or periocular infections including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.

Glaucoma: OZURDEX® is contraindicated in patients with glaucoma, who have cup to disc ratios of greater than 0.8.

Torn or Ruptured Posterior Lens Capsule: OZURDEX® is contraindicated in patients whose posterior lens capsule is torn or ruptured because of the risk of migration into the anterior chamber. Laser posterior capsulotomy in pseudophakic patients is not a contraindication for OZURDEX® use.

Hypersensitivity: OZURDEX® is contraindicated in patients with known hypersensitivity to any components of this product.

Warnings and Precautions
Intravitreal Injection-related Effects: Intravitreal injections, including those with OZURDEX®, have been associated with endophthalmitis, eye inflammation, increased intraocular pressure, and retinal detachments. Patients should be monitored regularly following the injection.

Steroid-related Effects: Use of corticosteroids including OZURDEX® may produce posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses.

Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

CALL OZURDEX®

Adverse Reactions
Diabetic Macular Edema
Ocular adverse reactions reported by greater than or equal to 1% of patients in the two combined 3-year clinical trials following injection of OZURDEX® (dexamethasone intravitreal implant) for diabetic macular edema include: cataract (68%), conjunctival hemorrhage (23%), visual acuity reduced (9%), conjunctivitis (6%), vitreous floaters (5%), conjunctival edema (5%), dry eye (5%), vitreous detachment (4%), vitreous opacities (3%), retinal aneurysm (3%), foreign body sensation (2%), corneal erosion (2%), keratitis (2%), anterior chamber inflammation (2%), retinal tear (2%), eyelid ptosis (2%). Non-ocular adverse reactions reported by greater than or equal to 5% of patients include: hypertension (13%) and bronchitis (5%).

Increased Intraocular Pressure: IOP elevation greater than or equal to 10 mm Hg from baseline at any visit was seen in 28% of OZURDEX® patients versus 4% of sham patients. 42% of the patients who received OZURDEX® were subsequently treated with IOP-lowering medications during the study versus 10% of sham patients.

The increase in mean IOP was seen with each treatment cycle, and the mean IOP generally returned to baseline between treatment cycles (at the end of the 6-month period).

Cataracts and Cataract Surgery: The incidence of cataract development in patients who had a phakic study eye was higher in the OZURDEX® group (68%) compared with Sham (21%). The median time of cataract being reported as an adverse event was approximately 15 months in the OZURDEX® group and 12 months in the Sham group. Among these patients, 61% of OZURDEX® subjects versus 8% of sham-controlled subjects underwent cataract surgery, generally between Month 18 and Month 39 (Median Month 21 for OZURDEX® (dexamethasone intravitreal implant) group and 20 for Sham) of the studies.

Retinal Vein Occlusion and Posterior Segment Uveitis
Adverse reactions reported by greater than 2% of patients in the first 6 months following injection of OZURDEX® for retinal vein occlusion and posterior segment uveitis include: intraocular pressure increased (25%), conjunctival hemorrhage (22%), eye pain (8%), conjunctival hyperemia (7%), ocular hypertension (5%), cataract (5%), vitreous detachment (2%), and headache (4%).

Increased IOP with OZURDEX® peaked at approximately week 8. During the initial treatment period, 1% (3/421) of the patients who received OZURDEX® required surgical procedures for management of elevated IOP.

Please see Brief Summary of full Prescribing Information on adjacent page.

References: 1. Data on file, Allergan. **2.** OZURDEX® Prescribing Information.

Treat early with

Ozurdex®
(dexamethasone intravitreal
implant) 0.7 mg

Allergan

OZURDEX®

(dexamethasone intravitreal implant) 0.7 mg

Brief Summary—Please see the OZURDEX® package insert for full Prescribing Information.

INDICATIONS AND USAGE

Retinal Vein Occlusion: OZURDEX® (dexamethasone intravitreal implant) is a corticosteroid indicated for the treatment of macular edema following branch retinal vein occlusion (BRVO) or central retinal vein occlusion (CRVO).

Posterior Segment Uveitis: OZURDEX® is indicated for the treatment of non-infectious uveitis affecting the posterior segment of the eye.

Diabetic Macular Edema

OZURDEX® is indicated for the treatment of diabetic macular edema.

CONTRAINDICATIONS

Ocular or Periocular Infections: OZURDEX® (dexamethasone intravitreal implant) is contraindicated in patients with active or suspected ocular or periocular infections including most viral diseases of the cornea and conjunctiva, including active epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, varicella, mycobacterial infections, and fungal diseases.

Glaucoma: OZURDEX® is contraindicated in patients with glaucoma, who have cup to disc ratios of greater than 0.8.

Torn or Ruptured Posterior Lens Capsule: OZURDEX® is contraindicated in patients whose posterior lens capsule is torn or ruptured because of the risk of migration into the anterior chamber. Laser posterior capsulotomy in pseudophakic patients is not a contraindication for OZURDEX® use.

Hypersensitivity: OZURDEX® is contraindicated in patients with known hypersensitivity to any components of this product *[see Adverse Reactions]*.

WARNINGS AND PRECAUTIONS

Intravitreal Injection-related Effects: Intravitreal injections, including those with OZURDEX®, have been associated with endophthalmitis, eye inflammation, increased intraocular pressure, and retinal detachments.

Patients should be monitored regularly following the injection *[see Patient Counseling Information]*.

Steroid-related Effects: Use of corticosteroids including OZURDEX® may produce posterior subcapsular cataracts, increased intraocular pressure, glaucoma, and may enhance the establishment of secondary ocular infections due to bacteria, fungi, or viruses *[see Adverse Reactions]*.

Corticosteroids are not recommended to be used in patients with a history of ocular herpes simplex because of the potential for reactivation of the viral infection.

ADVERSE REACTIONS

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

Adverse reactions associated with ophthalmic steroids including OZURDEX® include elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

Retinal Vein Occlusion and Posterior Segment Uveitis

The following information is based on the combined clinical trial results from 3 initial, randomized, 6-month, sham-controlled studies (2 for retinal vein occlusion and 1 for posterior segment uveitis):

Adverse Reactions Reported by Greater than 2% of Patients

MedDRA Term	OZURDEX® N=497 (%)	Sham N=498 (%)
Intraocular pressure increased	125 (25%)	10 (2%)
Conjunctival hemorrhage	108 (22%)	79 (16%)
Eye pain	40 (8%)	26 (5%)
Conjunctival hyperemia	33 (7%)	27 (5%)
Ocular hypertension	23 (5%)	3 (1%)
Cataract	24 (5%)	10 (2%)
Vitreous detachment	12 (2%)	8 (2%)
Headache	19 (4%)	12 (2%)

Increased IOP with OZURDEX® peaked at approximately week 8. During the initial treatment period, 1% (3/421) of the patients who received OZURDEX® required surgical procedures for management of elevated IOP.

Following a second injection of OZURDEX® (dexamethasone intravitreal implant) in cases where a second injection was indicated, the overall incidence of cataracts was higher after 1 year.

In a 2-year observational study, among patients who received >2 injections, the most frequent adverse reaction was cataract 54% (n=96 out of 178 phakic eyes at baseline). Other frequent adverse reactions from the 283 treated eyes, regardless of lens status at baseline, were increased IOP 24% (n=68) and vitreous hemorrhage 6.0% (n=17).

Diabetic Macular Edema

The following information is based on the combined clinical trial results from 2 randomized, 3-year, sham-controlled studies in patients with diabetic macular edema. Discontinuation rates due to the adverse reactions listed in the table below were 3% in the OZURDEX® group and 1% in the Sham group. The most common ocular (study eye) and non-ocular adverse reactions are as follows:

Ocular Adverse Reactions Reported by ≥ 1% of Patients and Non-ocular Adverse Reactions Reported by ≥ 5% of Patients

MedDRA Term	OZURDEX® N=324 (%)	Sham N=328 (%)
Ocular		
Cataract[1]	166/243[2] (68%)	49/230 (21%)
Conjunctival hemorrhage	73 (23%)	44 (13%)
Visual acuity reduced	28 (9%)	13 (4%)
Conjunctivitis	19 (6%)	8 (2%)
Vitreous floaters	16 (5%)	6 (2%)
Conjunctival edema	15 (5%)	4 (1%)
Dry eye	15 (5%)	7 (2%)
Vitreous detachment	14 (4%)	8 (2%)
Vitreous opacities	11 (3%)	3 (1%)
Retinal aneurysm	10 (3%)	5 (2%)
Foreign body sensation	7 (2%)	4 (1%)
Corneal erosion	7 (2%)	3 (1%)
Keratitis	6 (2%)	3 (1%)
Anterior Chamber Inflammation	6 (2%)	0 (0%)
Retinal tear	5 (2%)	2 (1%)
Eyelid ptosis	5 (2%)	2 (1%)
Non-ocular		
Hypertension	41 (13%)	21 (6%)
Bronchitis	15 (5%)	8 (2%)

[1] Includes cataract, cataract nuclear, cataract subcapsular, lenticular opacities in patients who were phakic at baseline. Among these patients, 61% of OZURDEX® subjects vs. 8% of sham-controlled subjects underwent cataract surgery.

[2] 243 of the 324 OZURDEX® subjects were phakic at baseline; 230 of 328 sham-controlled subjects were phakic at baseline.

Increased Intraocular Pressure

Summary of Elevated IOP Related Adverse Reactions

	Treatment: N (%)	
IOP	**OZURDEX®** N=324	**Sham** N=328
IOP elevation ≥10 mm Hg from Baseline at any visit	91 (28%)	13 (4%)
≥30 mm Hg IOP at any visit	50 (15%)	5 (2%)
Any IOP lowering medication	136 (42%)	32 (10%)
Any surgical intervention for elevated IOP*	4 (1.2%)	1 (0.3%)

* OZURDEX®: 1 surgical trabeculectomy for steroid-induced IOP increase, 1 surgical trabeculectomy for iris neovascularization,1 laser iridotomy, 1 surgical iridectomy
Sham: 1 laser iridotomy

The increase in mean IOP was seen with each treatment cycle, and the mean IOP generally returned to baseline between treatment cycles (at the end of the 6 month period).

Cataracts and Cataract Surgery

At baseline, 243 of the 324 OZURDEX® subjects were phakic; 230 of 328 sham-controlled subjects were phakic. The incidence of cataract development in patients who had a phakic study eye was higher in the OZURDEX® group (68%) compared with Sham (21%). The median time of cataract being reported as an adverse event was approximately 15 months in the OZURDEX® group and 12 months in the Sham group. Among these patients, 61% of OZURDEX® subjects vs.

8% of sham-controlled subjects underwent cataract surgery, generally between Month 18 and Month 39 (Median Month 21 for OZURDEX® group and 20 for Sham) of the studies.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

There are no adequate and well-controlled studies with OZURDEX® in pregnant women. Topical ocular administration of dexamethasone in mice and rabbits during the period of organogenesis produced cleft palate and embryofetal death in mice, and malformations of the abdominal wall/intestines and kidneys in rabbits at doses 5 and 4 times higher than the recommended human ophthalmic dose (RHOD) of OZURDEX® (0.7 milligrams dexamethasone), respectively.

In the US general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2 to 4% and 15 to 20%, respectively.

Data

Animal Data

Topical ocular administration of 0.15% dexamethasone (0.75 mg/kg/day) on gestational days 10 to 13 produced embryofetal lethality and a high incidence of cleft palate in mice. A dose of 0.75 mg/kg/day in the mouse is approximately 5 times an OZURDEX® injection in humans (0.7 mg dexamethasone) on a mg/m^2 basis. In rabbits, topical ocular administration of 0.1% dexamethasone throughout organogenesis (0.20 mg/kg/day, on gestational day 6 followed by 0.13 mg/kg/day on gestational days 7-18) produced intestinal anomalies, intestinal aplasia, gastroschisis and hypoplastic kidneys. A dose of 0.13 mg/kg/day in the rabbit is approximately 4 times an OZURDEX® injection in humans (0.7 mg dexamethasone) on a mg/m^2 basis. A no-observed-adverse-effect-level (NOAEL) was not identified in the mouse or rabbit studies.

Lactation

Risk Summary

Systemically administered corticosteroids are present in human milk and can suppress growth and interfere with endogenous corticosteroid production or cause other unwanted effects. There is no information regarding the presence of dexamethasone in human milk, the effects on the breastfed infants, or the effects on milk production to inform risk of OZURDEX® to an infant during lactation. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for OZURDEX® and any potential adverse effects on the breastfed child from OZURDEX®.

Pediatric Use: Safety and effectiveness of OZURDEX® in pediatric patients have not been established.

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility

Animal studies have not been conducted to determine whether OZURDEX® (dexamethasone intravitreal implant) has the potential for carcinogenesis or mutagenesis. Fertility studies have not been conducted in animals.

PATIENT COUNSELING INFORMATION

Steroid-related Effects

Advise patients that a cataract may occur after repeated treatment with OZURDEX® If this occurs, advise patients that their vision will decrease, and they will need an operation to remove the cataract and restore their vision.

Advise patients that they may develop increased intraocular pressure with OZURDEX® treatment, and the increased IOP will need to be managed with eye drops, and, rarely, with surgery.

Intravitreal Injection-related Effects

Advise patients that in the days following intravitreal injection of OZURDEX®, patients are at risk for potential complications including in particular, but not limited to, the development of endophthalmitis or elevated intraocular pressure.

When to Seek Physician Advice

Advise patients that if the eye becomes red, sensitive to light, painful, or develops a change in vision, they should seek immediate care from an ophthalmologist.

Driving and Using Machines

Inform patients that they may experience temporary visual blurring after receiving an intravitreal injection. Advise patients not to drive or use machines until this has been resolved.

Rx only

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Madison, NJ 07949

issued any warnings.[14-17] Further investigation is warranted to explore pathogenesis and to inform screening guidelines for this sight-threatening condition. ■

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UP AGAINST GLOBAL POVERTY

A closer look at the challenges of achieving health equity around the world.

BY ZAIBA MALIK, MD

In 2015, the World Bank reset the international poverty line to $1.90 per day. This figure represents a picture of the costs of basic food, clothing, and shelter. Individuals who live on less than this amount are considered to be living in extreme poverty. According to the most recent estimates, this includes more than 702 million people worldwide, or 10% of the global population.[1]

The percentage of individuals living below the international poverty line has decreased significantly since 1990 (36%); however, a disparity in the distribution of the world's poor remains. For example, the number of people living in extreme poverty has decreased in most countries within East and Southeast Asia, but it continues to increase in Sub-Saharan Africa. This region is home to more than half of the world's extremely poor population, and 42% of its inhabitants currently live below the international poverty line.[2]

The international poverty line is determined by an individual's purchasing power to fulfill his or her daily needs. Although most of the daily $1.90 is allocated to food, the food that it affords might be low in quality and nutritional value. Shelter, education, and health care must be covered by this amount as well. When an individual is forced to choose between health care and other necessities such as food or housing, health care often takes a back seat.

CAUSES OF GLOBAL POVERTY

A multitude of diverse factors contribute to global poverty, and the lines between cause and effect are often blurred. Historically, the poorest nations in the world are former colonies, where resources were systematically removed and conditions were created to prevent people from accessing capital, land, and education. War and political upheaval continue to strain the stability, safety, and security of these regions, thereby preventing inhabitants from harnessing basic resources such as clean water and nutritious food. In addition to a lack of stable infrastructure, conflict zones such as these provide little to no access to formal education or employment.

Additionally, in some low-income areas, recurrent catastrophic natural disasters pose significant obstacles to eradicating poverty. Flooding in Bangladesh, drought in Africa, and earthquakes and hurricanes in Haiti are just some examples of the destructive natural disasters that affect impoverished regions.

POVERTY AND HEALTH

Poverty and poor health are interwoven.[3] Poverty is a major cause of poor health as well as a barrier to health care access. Conversely, poor health is a major cause of poverty. The costs associated with consultations, medications, and tests—as well as transportation and missed work—can make accessing health care burdensome for those living in poverty. These inequalities further lead to disparities in education, literacy, health, nutrition, sanitation, and mortality.[4] Such disparities result in a lack of health equity.

Health equity occurs when every individual has a fair and just opportunity to be healthy. Its achievement requires the removal of several obstacles, including discrimination and socioeconomic barriers to education, employment, housing, and food. Health disparity is, in actuality, health inequality, and it results in differences in health between various groups.

PICTURES OF GLOBAL POVERTY

The concept of global poverty may, for some, conjure up images of malnourished children living on a roadside or multigenerational families living in one room and sharing a bowl of porridge. However, poverty presents in many ways. Even in the United States, one of the wealthiest nations in the world, examples of health disparities can be seen. In my under- and uninsured patient population in Dayton, Ohio, I frequently see patients who must choose between undergoing vision-saving treatments and paying their monthly rent.

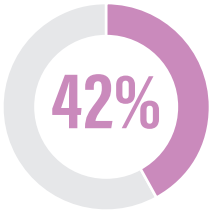
Health inequality can look like Mr. Hendrix, an elderly underinsured patient who decided it was so important for him to get his glaucoma drops that he resorted to eating canned cat food in order to afford them. When the technician asked him why he didn't call our practice once he found out his copay charge, she heartbreakingly realized he hadn't considered that we could change his class of medication or find him a drug assistance program; he assumed his doctor knew best and that he had no other option.

Health inequality can look like Mrs. Noor, a refugee who sleeps with the lights on, flinches at loud noises, has lost

Individuals in extreme poverty are defined as those living below the international poverty line of **$1.90 PER DAY**

More than **700 MILLION** people worldwide, or 10% of the global population, live below the international poverty line

More than half of the world's extremely poor live in Sub-Saharan Africa, and **42% of the region's inhabitants** live below the international poverty line



family members in war-torn Syria, and refuses to attend a health and wellness workshop because she believes doing so implies she has a mental disease. Or health inequality can look like the people of Vanua Levu, the second largest island in Fiji, where, despite a population of more than 135,000, not a single ophthalmologist exists. Here, all I can offer as a visiting ophthalmologist is 40 cataract cases per week, leaving the remaining patients untreated until the next group of volunteers comes through.

ENDING GLOBAL POVERTY

The World Bank and the United Nations have set a lofty goal of ending extreme poverty by 2030.[1] With only a decade left, it is unclear whether this can be achieved.

There is no single solution to ending global poverty. Reaching this goal requires cross-collaboration between governments and communities. By working with nonprofits and governmental aid organizations to increase food security, promote child survival, strengthen health systems, and improve education, we can reach this goal.[5] Innovations in economic development, health care access, job growth, and pay equity all contribute to inclusive economic growth and health equity.

For physicians, acquiring knowledge of the problem is the first step. The second step is to become involved in advocacy efforts. Our involvement in health care delivery and advocacy can have a significant impact on communities. Of course, making donations to reputable organizations is a step that all people can take. But, as physicians, we have the skill set to work directly with those in need and provide on-the-ground services, training, and mobilization both locally and abroad. Our local inner-city and rural communities often face socioeconomic barriers to health care that mirror what is seen in developing countries.

Globally, building self-sustaining health care systems is crucial to allow communities to develop and thrive instead of relying on one-time efforts of volunteers. One way to create a longer-term impact is to invest in the community's economy by procuring medicine and equipment locally. Most US medical groups partner with country-specific nongovernmental organizations to provide humanitarian trips and intra-country specialty training. Skills transfer, therapeutic indications, procedure training, and community development projects are all means through which physicians can help make a difference. In addition, physician mentorship (via webinar, for example) is important for providing ongoing education of local staff.

CONCLUSION

Global poverty is a complex and multifactorial challenge, and a great deal of work must still be done to combat it. Although progress has been made, in some nations it has been slow, and in others poverty has only worsened. As 2030 nears, we must strive to identify solutions to alleviate global poverty and all of its consequences, including health inequality. When communities and governments around the world begin to treat health care as a human right and commit to improving access to health care for everyone, we will be much closer to breaking the cycle of global poverty. ■

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Summaries of two recent journal pieces.

BY THOMAS L. JENKINS, MD; AND RAVI R. PANDIT, MD, MPH

Delayed Retinal Breaks and Detachments After Acute Posterior Vitreous Detachments

Uhr JH, Obeid A, Wibbelsman TD, et al.[1]

Patients frequently present to retinal specialists for evaluation after an acute posterior vitreous detachment (PVD). The incidence of retinal tear after an acute symptomatic PVD ranges widely, from 8% to 43%,[2] but less is known about the development of new retinal tears or detachments following an initial examination despite the common practice of scheduling follow-up examinations within 6 weeks.[3]

Uhr and colleagues conducted a study to determine the timing and incidence of delayed PVD-related complications after an initial examination.[1]

STUDY DESIGN

Researchers at Wills Eye Hospital Retina Service and Mid Atlantic Retina performed this retrospective case-control study of eyes diagnosed with a PVD and undergoing an extended ophthalmoscopic examination on presentation from October 2015 to August 2018. They subsequently

TABLE. HAZARD RATIOS FOR RISK FACTORS FOR DEVELOPMENT OF A DELAYED BREAK OR DETACHMENT

	Eyes With Delayed Retinal Breaks		Eyes with Delayed Retinal Detachments	
	Hazard Ratios (95% Confidence Interval)	*P* Value	Hazard Ratios (95% Confidence Interval)	*P* Value
Vitreous Hemorrhage	2.53 (1.84-3.49)	< .001	2.88 (1.51-5.17)	.001
Intraretinal Hemorrhage	0.88 (0.60-1.30)	.52	0.69 (0.36-1.33)	.27
Lattice Degeneration	1.21 (0.89-1.65)	.22	1.27 (0.67-2.39)	.47
Pseudophakia*	1.09 (0.75-1.58)	.64	2.10 (1.27-3.50)	.004
Male Gender	1.36 (1.04-1.80)	.03	1.87 (1.12-3.11)	.02
Age	0.99 (0.97-1.01)	.39	0.96 (0.93-0.99)	.01

*This includes one aphakic eye in the retinal detachment cohort.
Table adapted from Uhr JH, Obeid A, Wibbelsman TD, et al. Delayed retinal breaks and detachments after acute posterior vitreous detachments [published online ahead of print October 23, 2019]. *Ophthalmology*.

compared the dates of initial examination to those of subsequent treatment with laser retinopexy, cryotherapy, or retinal detachment repair to determine the duration to development of new peripheral pathology.

The study's primary outcome measure was the development of a retinal break or detachment after initial evaluation. Secondary outcomes included incidence of retinal tear on initial visit and risk factors for the development of delayed retinal tear or detachment.

RESULTS

Of the 7,999 eyes diagnosed with an acute PVD, 1,280 (16%) and 499 (6.2%), respectively, were found to have a retinal tear or retinal detachment at presentation. Delayed retinal tears were found in 209 (2.6%) eyes and delayed retinal detachments in 80 (1%) eyes. Of the eyes with a delayed retinal tear, 116 (55.5%) occurred within 6 weeks of initial examination and 93 (44.5%) occurred more than 6 weeks after initial examination. Delayed retinal detachments tended to occur later, with 54 (67.5%) occurring more than 6 weeks after presentation. New or worsening symptoms were present in 84 (40.2%) eyes at the time of delayed retinal tear and 54 (67.5%) eyes when a delayed retinal detachment was diagnosed.

Vitreous hemorrhage and male gender were both associated with the development of a delayed retinal break. The only risk factor associated with greater incidence of a delayed break within 6 weeks was vitreous hemorrhage. Risk factors for the development of delayed retinal detachments included vitreous hemorrhage, pseudophakia at presentation, younger age, and male gender (Table).

SIGNIFICANCE

This study demonstrated that delayed retinal tears and detachments occur after initial examination for acute PVD. A substantial percentage of patients with delayed pathology were asymptomatic and were diagnosed at more than 6 weeks after presentation. The study showed the importance of follow-up examinations after acute PVD to detect potentially treatable pathology.

Effect of Initial Management With Aflibercept vs Laser Photocoagulation vs Observation on Vision Loss Among Patients With Diabetic Macular Edema Involving the Center of Macula and Good Visual Acuity: A Randomized Clinical Trial (DRCR Protocol V)

Baker CW, Glassman AR, Beaulieu WT, et al; DRCR Retina Network[4]

Center-involving diabetic macular edema (CI-DME) is a frequent cause of vision loss worldwide. Intravitreal anti-VEGF injections have been shown in numerous trials to reduce CI-DME and improve visual acuity; however, these trials have historically excluded patients with 20/25 vision or better (good vision). Many patients will nevertheless present with CI-DME and good vision; the optimal management for these patients is unclear. This study sought to determine whether initial anti-VEGF treatment in eyes with CI-DME and good vision resulted in better long-term visual acuity outcomes as compared with observation or focal/grid laser photocoagulation.

STUDY DESIGN

The Protocol V study was conducted at 91 sites across North America.[4] A total of 702 treatment-naïve (or with no treatment within 12 months) adult diabetic patients were randomly assigned to receive 2 mg aflibercept (Eylea, Regeneron), photocoagulation, or observation. In the aflibercept group, injections were administered every 4 weeks if visual acuity or central subfield thickness (CST) on OCT improved or worsened; injections were deferred if measurements were stable for two consecutive visits. Patients in the photocoagulation group received treatment at baseline and every 13 weeks as needed. Patients in the photocoagulation and observation groups could receive aflibercept if their visual acuity declined by at least 10 letters at one visit or by 5 to 9 letters at two consecutive visits. Individuals who required aflibercept rescue were still grouped according to their initial randomization in an intention-to-treat approach.

RESULTS

At 2 years, 25% of patients in the photocoagulation group and 34% of patients in the observation group required aflibercept rescue. Sixteen percent of patients in the aflibercept group, 17% of patients in the photocoagulation group, and 19% of patients in the observation group lost at least 5 letters from baseline; this finding was not statistically significant.

No difference was detected in change in mean visual acuity at 2 years among all groups. Seventy-seven percent of patients in the aflibercept group, 71% of patients in the photocoagulation group, and 66% of patients in the observation group retained 20/20 VA or better at 2 years; the difference between the aflibercept group and observation group was statistically significant ($P = 0.03$).

When considering cumulative improvement in vision over time (area under the curve), aflibercept therapy was superior to photocoagulation (+1.9 letters) and observation (+2.1 letters; $P < .001$ for both).

No difference was detected among the groups in mean change of CST on OCT or 2-step improvement in diabetic retinopathy severity level,

(Continued on page 48)

DISTINGUISHING VKH FROM CSCR

A patient's undisclosed medication makes for a difficult differential diagnosis in this case report.

BY SNEHA PADIDAM, MD; BRIAN K. DO, MD; JORDANA G. FEIN, MD; AND HEERAL SHAH, MD

A 58-year-old white man presented with a 1-week history of blurred vision in both eyes. He reported no photophobia or eye pain and no history of ocular trauma. The patient's ocular history was relevant for primary open-angle glaucoma in both eyes. He had undergone trabeculectomy in his right eye in 2015 and was taking brinzolamide, bimatoprost, and a fixed combination of brimonidine and timolol in the left eye at the time of presentation to our center. He had no significant past medical history and was not taking any oral medications. In the review of systems, he reported no headaches, hearing loss, or joint pains. At the time of initial evaluation, the patient denied the use of any topical, inhaled, or oral corticosteroid-based medications.

On examination, his Snellen BCVA was counting fingers at 1 foot in his right eye and 20/200 in his left eye. IOP was 2 mm Hg in his right eye and 22 mm Hg in his left eye. Anterior segment evaluation revealed corneal endothelial pigment deposition in both eyes. Posterior segment examination revealed serous retinal detachments in both eyes and choroidal effusions in the right eye (Figure 1).

Imaging with spectral-domain OCT (SD-OCT) showed subretinal fluid with sub–external limiting membrane fluid in the right eye and subretinal fluid in the left eye (Figure 2). Fluorescein angiography revealed multifocal pinpoint leakage in the posterior pole in both eyes (Figure 3) without evidence of disc leakage.

Our initial differential diagnosis included causes of an inflammatory exudative choroidopathy, such as Vogt-Koyanagi-Harada (VKH) disease or sympathetic ophthalmia. Other causes of panuveitis, such as tuberculosis, sarcoidosis, and syphilis, had to be excluded. The patient was started on oral prednisone 80 mg daily and was referred to a uveitis specialist for further workup. Further evaluation included testing for *Toxoplasma gondii* (negative), QuantiFERON-TB Gold (Qiagen; negative), angiotensin-converting enzyme and lysozyme levels (normal), rapid plasma reagin and fluorescent treponemal antibody absorption testing (nonreactive; negative), and chest x-ray (normal).

Over the next month, the patient's serous retinal detachments improved slightly while the dose of prednisone was tapered. When the taper reached 40 mg/day, the exudation once again worsened. At this time, the decision was made to inject a dexamethasone intravitreal implant 0.7 mg (Ozurdex, Allergan) into the patient's left eye.

At the next visit, no significant improvement of the subretinal fluid in the left eye was seen. At this visit, upon further questioning, the patient revealed that he had been taking oral oxymetholone, a strong androgenic and anabolic steroid, for physique-enhancement purposes—something which he had not reported at previous visits.

Given these findings and the patient's variable response to steroids, it is most likely that the patient had a variant of central serous chorioretinopathy (CSCR). The oral steroids were stopped, and the patient was instructed to cease using the oxymetholone pills. At the most recent follow up visit, 2 months after stopping the oral prednisone, BCVA was 20/70 in the patient's right eye with resolving subretinal fluid and 20/30 in the left eye

AT A GLANCE

- ▶ The acute stages of Vogt-Koyanagi-Harada (VKH) disease and central serous chorioretinopathy (CSCR) share characteristics and can sometimes be confused with one another.
- ▶ In this case report, the patient was initially thought to have VKH and was treated for that condition.
- ▶ When additional information emerged, the diagnostic picture changed.

with no subretinal fluid (Figure 4). Observation of the patient continues, awaiting further improvement.

DISCUSSION

CSCR is a common condition characterized by accumulation of subretinal fluid in the macula along with pigment epithelial detachments (PEDs). The pathogenesis of CSCR is not fully elucidated, but studies have shown that it may be related to abnormally hyperpermeable choroidal capillaries.[1] CSCR has a strong association with exogenous and endogenous corticosteroids.[2] An association has been suggested between CSCR and certain personality factors, including type A personality and psychological stress.[3]

Our patient was taking oxymetholone, a powerful synthetic androgenic and anabolic steroid, for body-building purposes. Nudleman et al reported on a series of nine patients using exogenous testosterone therapy who developed CSCR.[4] Those authors hypothesized that exogenous testosterone may lead to increased choroidal blood flow and hence increased choroidal permeability.

VKH is an autoimmune disorder affecting pigmented tissues. Acute VKH is characterized by bilateral exudative retinal detachments and increased choroidal thickness on SD-OCT. VKH commonly affects darkly pigmented individuals and usually has a prodromal stage with influenza-like symptoms. Patients can also have various neurologic and auditory symptoms, such as headaches, dizziness, orbital pain, and sensorineural hearing loss.[5] Initial treatment of VKH consists of high-dose oral corticosteroids, and some patients later require immunomodulatory therapy.

Our patient was initially thought to have VKH, given his bilateral exudative retinal detachments with subretinal septa in his right eye on OCT, as well as fluorescein angiogra-

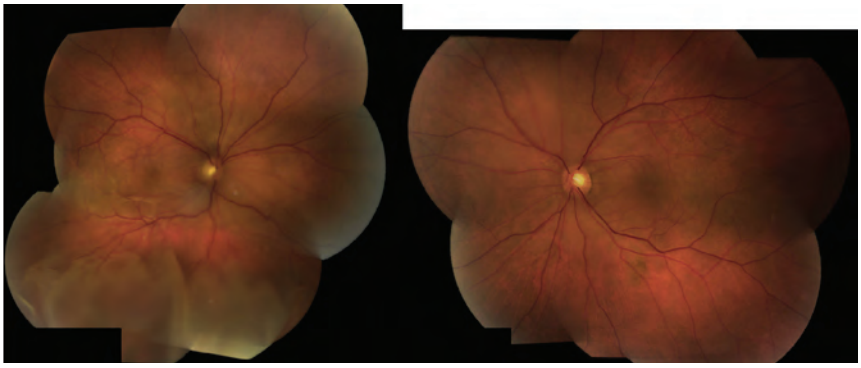

Figure 1. Fundus photographs of the right and left eyes show serous retinal detachment in each eye.

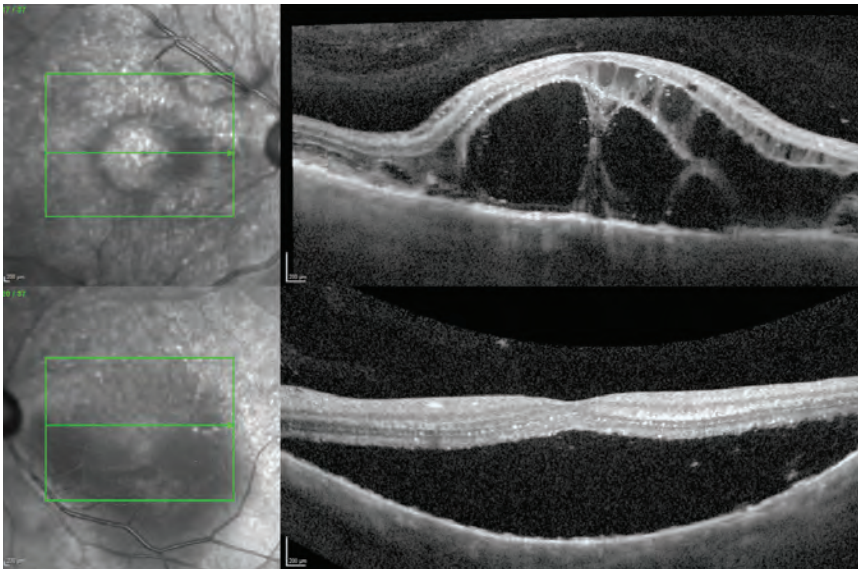

Figure 2. OCT of the right eye (top) demonstrates extensive intraretinal cystic fluid. OCT of the left eye (bottom) demonstrates subretinal/subexternal limiting membrane fluid.

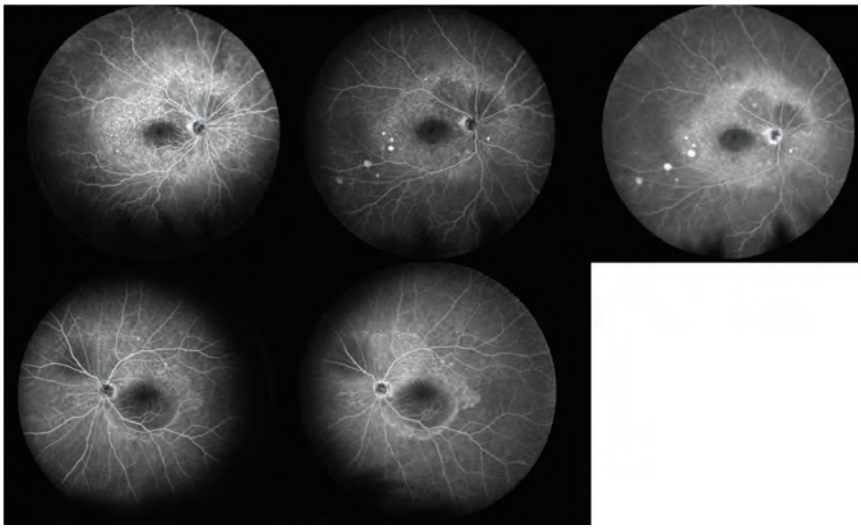

Figure 3. Fluorescein angiography of the right (top) and left (bottom) eyes shows multifocal areas of pinpoint leakage in each eye.

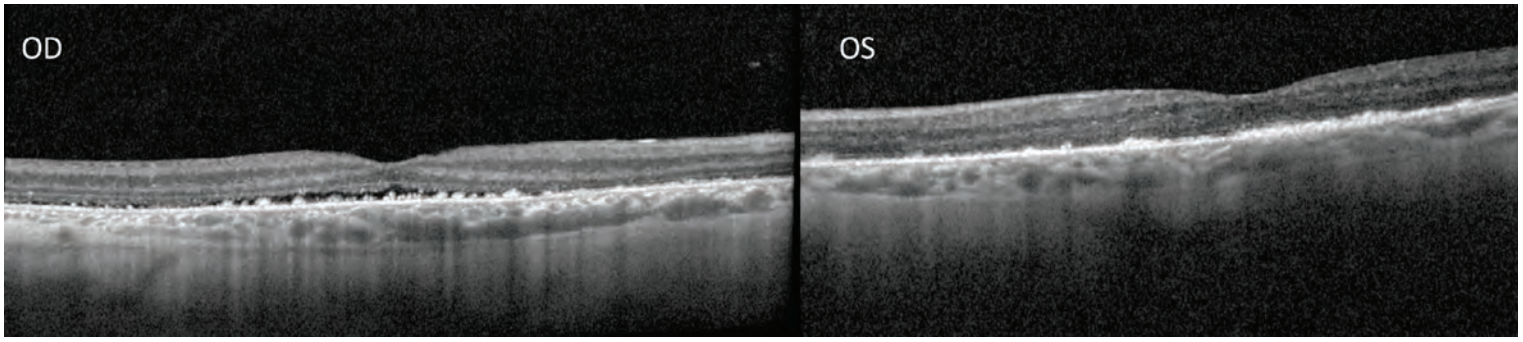

Figure 4. OCT was taken 2 months after the discontinuation of the patient's steroids. OCT of the right eye (left photo) shows interval improvement in the subretinal fluid. OCT of the left eye (right photo) shows resolution of the subretinal fluid.

phy showing multifocal macular leakage in both eyes. The patient also had a dome-shaped mass of intraretinal fluid, termed a bacillary detachment, which is commonly seen in patients with VKH. Of note, our patient did not have optic nerve leakage on fluorescein angiography, which is often seen in VKH.

The patient demonstrated a variable response to high-dose corticosteroids. Given his (initially concealed) consumption of oxymetholone and his clinical improvement after stopping the oral prednisone, the clinical picture is more consistent with atypical CSCR.

The acute stages of VKH and CSCR can sometimes be confused with one another. In one report, 90 of 410 patients with VKH disease had initially been misdiagnosed as CSCR.[6] In a study including 35 patients with VKH and 25 with CSCR, Shin et al found that PED in CSCR and optic disc hyperemia in VKH had the highest positive predictive values (100%), respectively.[7] Of note in that study, during late-phase fluorescein angiography, multifocal leakage was observed in 90% of eyes in the CSCR group. Lin et al found that subretinal septa and folds of retinal pigment epithelium were seen only in eyes with acute VKH, whereas patients with CSCR had significant PEDs and bulging of retinal pigment epithelium.[8]

CONCLUSION

The case presented here demonstrates the importance of making the correct differential diagnosis of VKH versus CSCR. Initial therapy for VKH usually consists of high-dose corticosteroids, which can worsen CSCR. Making a correct diagnosis helps prevent negative visual outcomes.

Noting the presence or absence of optic disc hyperemia, subretinal septae, PEDs, systemic symptoms, and use of any medications can be of benefit in distinguishing these two entities. Our patient had initially withheld information regarding his use of a high-dose anabolic and androgenic steroid. Despite initially starting treatment with oral prednisone, the patient has improved with observation after cessation of the androgenic steroid. ■

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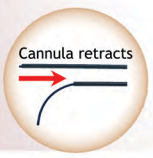

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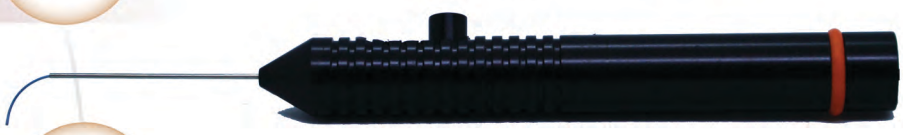

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PEARLS FOR THE YAMANE TECHNIQUE

A RUNDOWN OF THE STEPS INVOLVED IN PERFORMING THIS SUTURELESS TECHNIQUE FOR IOL FIXATION IN THE ABSENCE OF CAPSULAR SUPPORT, AND PEARLS FOR MASTERING IT.

BY BRANDON D. AYRES, MD; ZAINA AL-MOHTASEB, MD; STEVEN G. SAFRAN, MD; AND MANJOOL SHAH, MD

There has been plenty of buzz in the retina community about the Yamane technique. When the team at Retina Today *was strategizing how best to cover the topic, we decided that deferring to our colleagues in the anterior segment was a good starting place. This article, which is a modified version of a cover story from* Retina Today*'s sister publication* Cataract & Refractive Surgery Today, *can be viewed in its entirely online at bit.ly/RetinaTodayYamane.*

—Chief Medical Editor Allen C. Ho, MD; and Associate Medical Editor Robert L. Avery, MD

BY BRANDON D. AYRES, MD

The Yamane technique: Step by step.

Pseudoexfoliation syndrome is one of the most common reasons for lens dislocation during cataract surgery. For such cases, and for eyes in which capsular support is absent, multiple IOL fixation techniques have been used over the years. In my practice, we have transitioned from suture techniques to an elegant sutureless haptic fixation technique, the Yamane technique.

This has been our primary technique for scleral fixation of an IOL for the past 2 years. The procedure has its complexities and involves performing multiple components in a specific order. Now, the technique can be simplified using the Scleral IOL Fixation Solutions Pack (SFP; MicroSurgical Technology), which provides all the tools required to use the Yamane approach for scleral fixation of IOLs.

THE CONCEPT

The idea behind the Yamane technique is to externalize the haptics of a three-piece IOL using thin-walled 30- or 27-gauge needles through two transconjunctival sclerotomies. The haptics of the IOL are carefully laced into the lumen of the needles using intraocular forceps. Then the needles are used to externalize the haptics on the conjunctival surface. Next, low-temperature cautery is used to make a flange at the end of the haptics. This flange or bulb prevents the haptics from prolapsing back into the posterior chamber, and the three-piece IOL is thereby fixated efficiently in the posterior segment in the absence of capsular support.

STEP BY STEP

The Yamane technique involves the following steps:

▶ Step No. 1

Carefully measure for the exact placement of the haptics at the beginning of the case (Figure 1). This is critical to minimize the risk of decentration or tilt of the IOL.

- *Hint: Before inserting the IOL into the anterior chamber it is important to ensure that no vitreous is present.*

▶ Step No. 2

Once the measuring is completed,

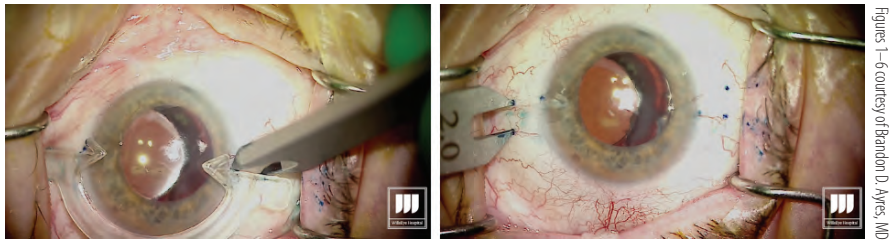

Figure 1. Measuring and marking of the needle insertion sites.

Figures 1–6 courtesy of Brandon D. Ayres, MD

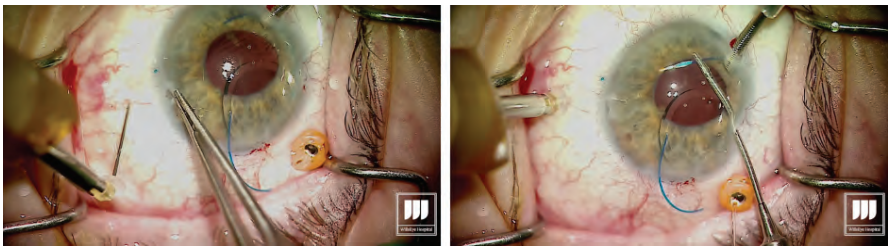

Figure 2. After the first sclerotomy is created, the leading haptic is placed into the lumen of the needle.

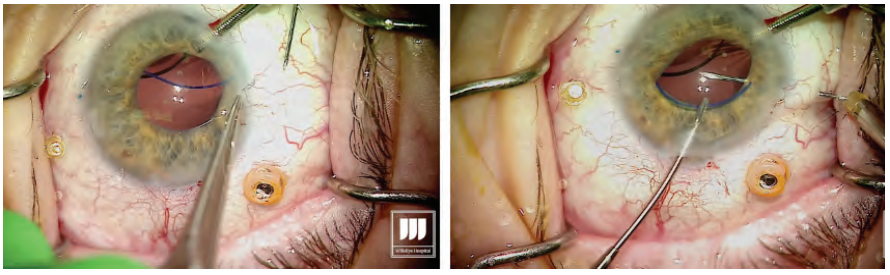

Figure 4. Externalization of the trailing haptic.

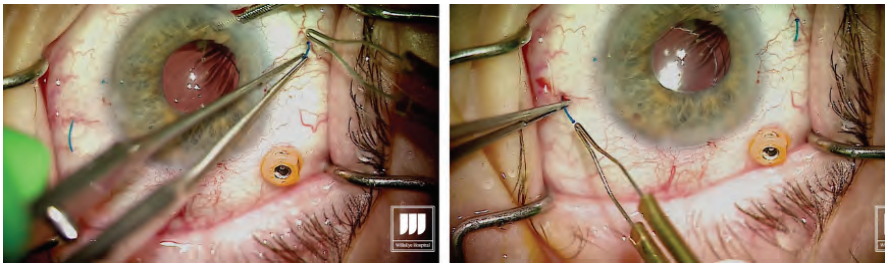

Figure 5. Cauterization of the externalized haptics.

place the three-piece IOL in the anterior chamber. My preferred IOL for haptic fixation is the CT Lucia 602 (Carl Zeiss Meditec) due to the durability of its PVDF haptics. Typically at this point, I place the leading haptic in the nasal anterior chamber and leave the trailing haptic hanging out through the main incision.

▶ Step No. 3

Maintain the anterior chamber. I like to use an anterior chamber maintainer in the eye in order to prevent hypotony.

▶ Step No. 4

Make the transconjunctival sclerotomy with the thin-walled 30-gauge needle.

▶ Step No. 5

Make the first sclerotomy 2.5 mm posterior to the limbus. The intrascleral length of the tunnel is about 2 to 2.5 mm as well.

▶ Step No. 6

Grasp the leading haptic using intraocular 25-gauge microforceps and carefully lace it into the lumen of the needle (Figure 2).

▶ Step No. 7

Once the first haptic is securely laced into the lumen of the needle, the hub is released from the holding forceps, allowing the IOL to move into the eye.

- *Hint: Externalizing the trailing haptic is the point when surgeons can experience problems. To avoid challenges with the trailing haptic, do not externalize the leading haptic first. When the haptic is fixated in the needle, let the needle go. Externalizing the needle with the leading haptic at this point would lead to rotation of the IOL in the eye, moving the trailing haptic into a challenging position for lacing the haptic into the second needle. Placing the main incision slightly to the left will help ease placement of the trailing haptic (Figure 3).*

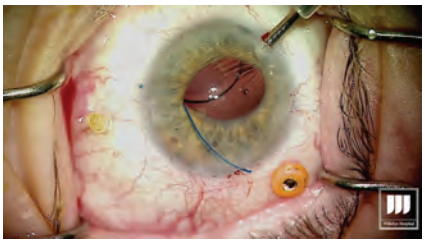

Figure 3. The leading haptic is left fixed inside the needle to avoid potential difficulties with externalization of the trailing haptic.

▶ Step No. 8

Introduce the trailing haptic into the anterior chamber, then grasp the second needle to perform the transconjunctival sclerotomy about 2.5 mm posterior to the limbus with core length of about 2 mm. This second sclerotomy is made exactly 180° across from the first one.

- *Hint: Ensure that the eye is pressurized with the anterior chamber maintainer whenever you make a sclerotomy.*

▶ Step No. 9

Once the second sclerotomy is made, visualize the lumen of the needle through the cornea and pupillary space. I always aim to achieve a similar angle of the haptic and the needle for even alignment of the IOL. Using the microforceps, grasp the second haptic and place it in the lumen of the needle.

▶ Step No. 10

With the second haptic now introduced into the lumen of the needle, externalize the haptic by removing the needle through the transconjunctival sclerotomy, then carefully grasp the haptic (Figure 4).

▶ Step No. 11

With low-temperature cautery, melt about 1 to 2 mm of the terminal end of the haptic to create a flange or bulb that will prevent the haptic from

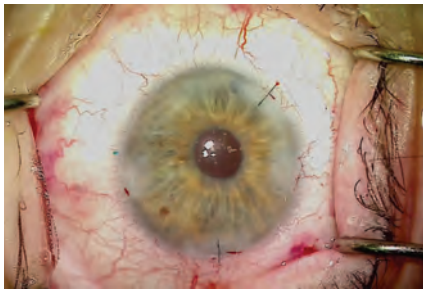

Figure 6. A well-centered three-piece IOL placed using the Yamane technique.

prolapsing through the scleral incision (Figure 5).

▶ Step No. 12

Go to the other side of the eye, 180° across, where the needle is still penetrating the sclera holding the leading haptic of the IOL. Externalize the needle and grasp the haptic on the conjunctival surface. Again, melt the end using low-temperature cautery.

▶ Step No. 13

Prolapse the haptic through the conjunctiva and force it into the scleral channel.

▶ Step No. 14

The result should be a well-centered three-piece IOL suspended in the posterior segment with no sutures (Figure 6).

CONCLUSION

The learning curve for this technique to place an IOL without capsular support is steep, but once it is mastered it should take only 15 to 20 minutes to complete. In my experience, the greatest challenges with this technique are measuring for placement of the needle insertion sites and lacing the trailing haptic into the lumen of the needle. The most difficult intraocular maneuver is probably lacing the trailing haptic. This is very challenging, but with the right approach and instrumentation, unnecessary complications can be avoided.

BY ZAINA AL-MOHTASEB, MD

A few pearls for the Yamane technique.

The small-incision, sutureless, transconjunctival scleral fixation technique first described by Yamane et al[1] for use in eyes with absence of capsular support involves the creation of small-gauge sclerotomies and a small clear corneal incision, resulting in a fast visual recovery and a low risk of postoperative hypotony. A few pearls can help surgeons overcome the challenges of performing this technique.

PEARL NO. 1

Technically any three-piece IOL can be used in the Yamane technique; however, we have found that IOLs with PVDF haptics are durable and resistant to kinking and breaking. For this reason, the CT Lucia 602 is our preferred IOL for performing this procedure.

PEARL NO. 2

Loosely attach each 30-gauge needle and do not use a luer-lock syringe. This will avoid the possibility of experiencing difficulty detaching the syringe.

PEARL NO. 3

Fill syringes with a small amount of balanced saline solution and make sure to irrigate the needle before the scleral pass. This can help to avoid air bubbles that can interfere with the view for needle insertion during haptic fixation.

PEARL NO. 4

Use an anterior chamber maintainer to ensure a firm eye during the creation of the sclerotomies.

PEARL NO. 5

If the IOL is poorly centered or tilted, the three most common causes are:

- The needle insertions are not 180° apart;
- The needle insertions are not the same distance from the limbus; or
- The scleral pathways vary in length and/or direction.

If the needle insertion points are different distances from the limbus or are not 180° apart, one of the haptics must be reinserted into the eye and refixated with a new needle pass. If the scleral tunnels are of different lengths, one or both haptics can be trimmed and recauterized to improve centration.

1. Yamane S, Sato S, Maruyama-Inoue M, Kadonosono K. Flanged intrascleral intraocular lens fixation with double-needle technique. *Ophthalmology*. 2017;124(8):1136-1142.

BY STEVEN G. SAFRAN, MD

Adequate vitrectomy and an infusion cannula are must-haves.

For me, the most important aspects of the Yamane technique are ensuring an adequate vitrectomy and placing an infusion cannula. I always use a trocar and perform a pars plana vitrectomy when performing the Yamane technique. The vitrectomy is essential because I am going to be maneuvering behind the iris, and I don't want to be disturbing the vitreous. Additionally, the vitreous must be adequately and completely removed. Even if the eye has had a vitrectomy previously, I make sure that it was adequate and that all vitreous was removed.

An infusion cannula should be in place to control IOP because I don't want to be sticking needles into a soft eye. Doing so will increase the risk of bleeding and choroidal hemorrhage. It is helpful to use an infusion line that is under footpedal control, so that it can be turned on and off as needed during the procedure.

IOL SELECTION

I use the CT Lucia 602 IOL because this lens has PVDF haptics, which are robust and do not kink or break easily. Additionally, even when the haptics of this IOL have been bent acutely, they return to their original configuration.

MARKING AND NEEDLE TUNNEL CREATION

Controlling the entry point into the eye and the length of the tunnels is vital for this technique. It's important to mark the patient carefully and to make sure that the marks are exactly 180° apart and exactly the same distance from the limbus, and that the tunnel length and angle of entry are symmetric. If anything is off, the IOL will be decentered. I put both of my marks exactly 2 mm behind the limbus.

Each tunnel should be about 1 to 1.5 mm in length. An infusion line is useful when making the tunnels. If the eye is at a constant and firm IOP, I can control the tunnel length and there will be less bleeding. I enter a little acutely with the needle, then create the tunnel, then enter acutely again. The tunnels should be more or less parallel to the limbus; they can be angled ever so slightly posterior, about 5° away from the limbus, but no more than that. For a myopic patient, I may angle the tunnels a bit more than 5°, and a bit less if the patient is hyperopic. This is because the bigger the eye is, the less haptic there will be to work with.

INSERTING THE HAPTICS

The next step is to feed both haptics into the needles. I feed one haptic into one needle, let go of it, then move to the second needle, feed that haptic in, and then rotate them simultaneously. I pull both needles out of the eye at the same time, and as I do that both haptics come out of the eye at the same time. When I do it this way, the lens has to rotate. If the lens doesn't rotate, then one haptic will pull out, but the other haptic won't come out because it hasn't rotated. But if both haptics are rotated by extracting both at the same time, the lens will rotate and both haptics will come out at the same time. With a 30-gauge needle, the haptics will not slip back into the eye. I can just pull the haptics out, let go, and the haptics won't go anywhere.

Next I grab both haptics with the forceps and push them so that each side is only a little bit out, to see if the lens is centering the way I want it to. If I've done everything symmetrically, the lens should center. If it looks like it's going to center well, I do a small haptic melt on each side and push it into its tunnel, and I'm done.

The haptic melt should not be too big. If it is too big, it will sit on the surface of the eye and not go into the tunnel. I just make a little mushroom tip, and that can be pushed into the tip of the tunnel.

ADDITIONAL POINTERS

Inject OVD before performing the vitrectomy. A vitrectomized eye will not hold an OVD; it will just drop into the back of the eye. I inject dispersive OVD into the eye using the iris and vitreous as a kind of backboard that allows me to press the OVD up against the cornea and create protection for the cornea. In the vitrectomized eye, the IOL will serve as the backboard.

Use self-sealing incisions. Self-sealing incisions are important for the Yamane technique—and any other technique, for that matter. If the eye is leaking, the surgeon will not have control. I make sure that my incisions—even larger incisions—are fashioned so that when I put the infusion line in, they seal themselves or close off.

A redock is my last resort. After I pull both haptics out, I test the centration and tilt of the optic by manipulating the haptics so that there is an equal amount of externalized haptic—about 1 to 2 mm on each side. If everything has been done symmetrically, the lens should center well at this point, and if it does, I will go ahead and melt the haptic tips and be done. If, on the other hand, there appears to be some tilt or decentration, I pull one haptic out a bit more than the other to see if I can compensate and center the IOL. If that does not fix the problem, I melt the side I consider the most optimal and redock the other side. What I mean by *redock* is that I will create a flange on one side to secure it and I make another needle path with the 30-gauge needle, designed to correct for whatever centration or tilt issue is present by compensating for the asymmetry causing the positioning

problem. For example, I may make the second pass more anterior, posterior, nasal, or temporal to the first pass as indicated by the centration or tilt issue to compensate for it and thereby fix the problem. After creating a new needle pass, I pull that externalized haptic back into the eye and dock it again in the lumen of the needle once to externalize it again and create a new haptic position. I refer to this process as *redocking*. I do this on one side in about 30% to 40% of my cases because I want excellent centration, and with this maneuver I am usually able to improve the lens position to achieve that.

Perform peripheral iridotomy using the vitrector or after the IOL is successfully fixated. This is an important step in order to prevent reverse pupillary block. I generally put the peripheral iridotomy temporally.

BY MANJOOL SHAH, MD

Measure posteriorly from the scleral spur, not the limbus.

As a glaucoma and complex anterior segment specialist, I am aware that some IOL fixation techniques can cause real problems. Specifically capsule-independent IOL fixation runs the risk of resulting in uveitis-glaucoma-hyphema (UGH) syndrome, which is purely iatrogenic. When the eye is marked for needle passes, one often measures from the limbus, and it is easy to mischaracterize where vital intraocular structures such as the ciliary body are located. Instead, I advocate measuring posteriorly from the scleral spur, which can often be visualized even without making a conjunctival peritomy as the end of the blue zone. The spur, or the surgical limbus, always correlates to intraocular anatomy.[1] I routinely place my needle tracks at least 2 mm posterior to the spur, and in this way I avoid running into the ciliary body. Additionally, I try to ensure that the needle is perpendicular to the surface of the sclera, which keeps the internal entry at the same distance from the spur as the external entry. If the needle is angled in the iris plane, there is risk of the internal needle entry emerging relatively anterior, again putting the ciliary body and posterior iris at risk for IOL-induced chafe.

Another key pearl for any scleral-fixated IOL procedure is to place a peripheral iridotomy. In eyes lacking capsular and zonular stability, the iris can exhibit a great degree of iridodonesis, increasing the risks of intermittent contact between the IOL and the iris, reverse pupillary block, and even pupil capture of the optic.[2,3] A simple iridotomy placed at the time of IOL fixation can mitigate that risk greatly. I typically use a vitreous cutter at a 1 cut per minute rate so I can get a single, small, clean opening. ■

1. Van Buskirk, EM. The anatomy of the limbus. *Eye*. 1989;3:101-108.
2. Singh H, Modabber M, Safran SG, Ahmed II. Laser iridotomy to treat uveitis-glaucoma-hyphema syndrome secondary to reverse pupillary block in sulcus-placed intraocular lenses: Case series. *J Cataract Refract Surg*. 2015;41(10):2215-2223.
3. Singh H, Safran SG, Ahmed II. Laser iridotomy for pseudophakic reverse pupillary block in patients with pupillary optic capture after sulcus-placed intraocular lenses. *J Cataract Refract Surg*. 2017;43(2):299.

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Profiles in Retina: Drs. Carol and Jerry Shields

A landmark interview with one of the power couples of retina.

AN INTERVIEW WITH CAROL SHIELDS, MD, AND JERRY SHIELDS, MD

When I asked *Retina Today* if profiling Carol L. Shields, MD, and Jerry A. Shields, MD, was a good fit for the Women in Retina issue, they agreed that an intimate portrait answering the questions we all have—How do they do it? What's the secret?—was long overdue.

Here, two leaders in ocular oncology sit down for an all-too-brief discussion about their partnership. The interview has been edited for length and clarity.

—Judy Kim, MD
Guest Editor, *Retina Today*

Retina Today: Tell us about how you first met.

Jerry A. Shields, MD: We first met when Carol came to Philadelphia for her ophthalmology residency. I was already on staff there and was fortunate enough to meet her when she joined Wills Eye Hospital.

Carol L. Shields, MD: It was 1984 and I was fresh out of my internship, and I was sort of dating a nice young man from Pittsburgh. I had no intention of meeting anybody at Wills and was happy-go-lucky on my own. When I arrived, I had never even heard the words *Jerry Shields*.

Wills had a mixed doubles tennis event, and they needed someone to fill in, so I volunteered. Tennis wasn't my favorite (my sport is basketball), but I said sure, I'll play. My partner was Jerry Shields. We played tennis—he was pretty good—and when the evening was over, I thought that was it. We just went our separate ways.

Jerry: And then I asked her to join me at a Philadelphia 76ers game because I knew that she played college basketball at the University of Notre Dame.

Carol: It was a lot of fun. And about a month later, I hosted a Christmas party for my class at Wills. And who shows up? Jerry Shields. I had only invited my class to the party, so I knew he was up to something.

Jerry: After that, I invited her to join me on New Year's Eve for dinner with Bill Benson, MD, and his wife.

Carol: I looked at him cross-eyed and said, "Are you kidding me? I'm not sure we're a couple yet." So we laid low for a while, and then later we went public.

Jerry: People were pretty surprised, but that's how life goes, right?

Carol: Jerry was a bachelor—and a desperately handsome young doctor—who was married to his work.

Jerry: Carol had a brother in Pittsburgh, and she wanted to return there and practice with him. If she did that, it would have been the end of me.

Carol: That was 36 years ago. I still haven't made up my mind if I'll join my brother or not.

Carol L. Shields, MD, and Jerry A. Shields, MD, offered *Retina Today* a pictorial view into their personal lives. Here is a selection of photographs spanning the three decades.

Drs. Carol and Jerry Shields are flanked by their children. Left to right, they are Jerry F., John, Charlotte Nelle, Jerry A. Shields Sr., Carol L. Shields, Mary Rose, Margaret, William, and Patrick.

Drs. Carol and Jerry Shields paused for a picture in the Wills Eye Hospital OR.

Photo credit: Roger Barone

CHALLENGES IN RETINA

RT: What were some of the challenges you faced from being a couple in the same field and workplace?

Carol: I can name three things that I felt were challenges. The first challenge: I was his wife, and Jerry would introduce me as his wife, not as Dr. Carol Shields. So that was a little difficult.

The second challenge: I took his last name. I've often wondered if I should've just kept my maiden name because that would have made us two different people.

The third challenge: Wills Eye Hospital was 99% male doctors back then, and it was a challenge to get referrals. But I have to say, there were a couple of doctors at Wills who started referring to me—it's just nice to get your own referrals. It makes you feel like you're actually making an impact.

Jerry: I knew Carol was a great person and we didn't compete in any way.

Carol: It's true, we never competed. If you're a married couple, you should never compare yourselves. I mean, he was already very well established and knew everyone; I was just starting out.

We actually had a very good working relationship because I crossed all the T's and dotted all the I's and made the patient care seamless, which was a completely different job than what Jerry was doing. He was out lecturing and bringing in patients and was an international figure.

Jerry: It's fair to say that we worked in the same office but had two very different jobs.

Carol: Being in same business and attending the same meetings can be a lot of work, and a lot of fun.

Jerry: But that's part of the benefit. Every time we went to a Macula Society meeting or a Retina Society meeting, it was like a vacation.

Carol: It was so nice because it was just us. We would always carve out one evening for the two of us go out and have a dinner together. Jerry always wanted to go out and socialize with everyone, but we made sure to keep one evening to just spend time together and reminisce on how things are going with the kids and our lives.

THE INTERSECTION OF FAMILY AND CAREERS

RT: When you decided to start a family, did you think about how it was going to affect your careers?

Carol: I knew it would affect my career. When our kids were young, I couldn't go to the AAO Annual Meeting or any of the big retina meetings because it was too much work to leave the kids with babysitters. But after the kids were in grade school and things started going smoothly, I started attending more meetings and becoming more career-oriented.

We both come from large families; each family had eight children. I really wanted to have as normal a life as possible. I definitely wanted children.

Drs. Carol and Jerry Shields with a copy of *Intraocular Tumors: An Atlas and Textbook, Second Edition*, which they coauthored. The book's third edition was released in 2016.

A picture of the happy couple on the day of their wedding.

Drs. Carol and Jerry Shields (left photo) set out on a bike riding adventure with their seven children (right photo) approximately 15 years ago.

Jerry: I didn't worry about it because I knew that I'd finally met a fantastic woman who believes everything like I do. We were good buddies.

Carol: Yeah, we're soul mates.

Jerry: We have a total of seven children, and during all of that time she was taking fellowships.

Carol went to England for fellowship training a few months right after we had our first baby, and this was a giant step in our marriage. Following fellowship, we went ahead and had a few additional children. Every time she would have another baby, I would hang in there as best I could. She was hanging in there better than I was.

Carol: We realized that we probably needed really skilled home-help for our growing family. We soon found a husband and wife couple to help us with the kids. We moved out of the city of Philadelphia to a little farm that had a cottage on it. We hired a couple who worked full-time at our house; the husband did some cleaning and fixed broken doorknobs and drove the kids to school, while the wife got the kids up in the morning, got breakfast ready, and later prepared dinner. There was enough to keep them both busy.

Jerry: The first couple we hired were Polish immigrants. We're still in touch with them. They are wonderful people; they actually raised their daughter with our seven children. It was like a family of eight kids.

Carol: When we were looking to hire a second couple after the first couple moved on, we turned to a woman who worked at Wills Eye as a typist. She wanted to have a career as a housekeeper. She took over the job, and her husband joined her in the cottage. We employed them until the kids were grown and gone.

Jerry: Carol and I were very close to our respective families, and both of us came from large families. Our other siblings had children, and our kids grew up with their children and those in the neighborhood.

Carol: Every child was a blessing. I've never looked back for one minute and ever regretted having a family, skipping this meeting to go to a lacrosse game, or cutting out of clinic a little early to go watch one of our kids play in a tennis match. We've had a lot of fun watching the kids grow up.

Jerry: Absolutely. I wouldn't trade that for anything.

RESERVING TIME FOR EACH OTHER AND FAMILY

***RT*: You had a family with seven children and the rigorous calendars of retina specialists. Your schedules must have been packed. How did you reserve that time for yourselves?**

Carol: Every day is busy, but if I could line up all the things in our joint career, the best thing was having a family. Don't you think?

Jerry: Absolutely. We worked hard

(Continued on page 44)

Hear It From the Attendings: Mentorship in Retina

An honest, casual conversation about mentorship from those who lead.

INTERVIEWS WITH AUDINA M. BERROCAL, MD; ZELIA M. CORREA, MD, PHD; AND ADRIENNE W. SCOTT, MD

What qualities do you look for in a potential mentee?

Audina M. Berrocal, MD: The perfect mentee is the individual who is either early in their training or at a crossroads in their career. The mentee needs to be open to guidance even when that guidance requires introspection or comes at a perceived personal cost. A great mentee needs to be ready to grow, which, at times, requires honesty and focus. For mentoring to impact your life, you must be willing to be mentored.

Zelia M. Correa, MD, PhD: I look for those with drive, goals, and talent, in that order. But none of those features are worth investing in if the mentee is not respectable, trustworthy, humble, and open to advice and counseling. An individual with energy and drive aims to be prepared and competent and is, therefore, better equipped to overcome obstacles, stay on task, and work on their goals.

What makes a good mentor?

Adrienne W. Scott, MD: A good mentor is someone with whom you can build a relationship. Keep in mind that a mentor is not necessarily a friend. It is usually someone who is senior to you, who has walked the path to success that you're trying to achieve. A mentor must be available and supportive, and it must be someone that the mentee feels comfortable going to when they are challenged. "I'm having trouble and struggling with this next step," is a sentence that a mentor must be willing to respond to by explaining how they navigated it.

Dr. Correa: A good mentor opens doors and opportunities for their mentee. A good mentor establishes a positive relationship, carefully listens before offering advice, and allows the mentee to make their own decisions.

Dr. Berrocal: A good mentor understands who you are, where you come from, and where you want to go. A great mentor helps you to find your personal path. Mentorship requires self-knowledge, assessment of strengths and weaknesses, and comfort with one's career and life. Self-knowledge allows a mentor to learn a mentee's strengths and weaknesses and helps the mentee take the steps that allow them to grow.

How does one find a mentor?

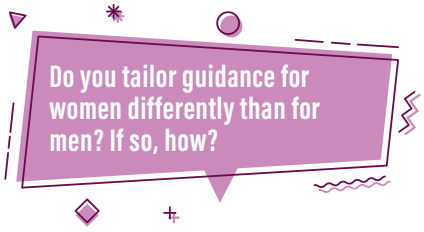
Dr. Berrocal: I believe that we are surrounded by mentoring opportunities. The best mentoring occurs naturally and it is not forced. But if you are not open to mentoring, then you will not recognize those opportunities. Fixed mentoring, in which you are assigned a mentor, has a place in many organizations, but often doesn't have the depth of an organic mentoring relationship.

Dr. Correa: Finding a mentor can happen by chance, but it is more productive as an intentional action. The first step is to identify people you would like to mirror, then study their attitude, circle of influence, and professionalism. If there is still interest,

request a meeting to establish a rapport and discuss a mentoring relationship. Be sure that your potential mentor has the time to advise you. Finally, it is important to realize that anyone can have multiple mentors who may advise on different aspects of life, including professional, academic, and family mentors.

Dr. Berrocal: I think there are differences, but these are more based on personality, career goals, personal life, and ethnicity rather than gender. Nonetheless, I sometimes address some of the classic stereotypes to be the best mentor for each of my mentees.

Dr. Scott: I've not noticed differences between the genders of the mentees that I have or have had. I think it's very individual depending on how driven somebody is and how focused someone is. So I can't generalize a man mentee versus a woman mentee. I think it all comes from your own internal drive.



Dr. Berrocal: I do not tailor guidance based on gender, but rather based on the individual. That said, as a woman I can help women mentees in the many aspects of becoming a better woman physician-surgeon. There are experiences, challenges, and hurdles for women that men will never experience. At the same time, I like to guide my mentees and teach them how to recognize and understand the silent and hidden biases that exist for both men and women.

Dr. Scott: I wouldn't advise a man or a woman differently as mentees. I do think, however, that women in this space might have to work harder to prove themselves, as this is a field that has been traditionally male-dominated. I do think that as a woman, particularly as a woman from an underrepresented minority background, I have experienced a unique path.

In general, I do give the same advice to anyone I'm mentoring, regardless of gender, ethnicity, or professional achievement: The most important part of achieving any goal is to be a very hard worker and to stay focused on what it is you're trying to achieve.

Dr. Correa: I don't mentor based on gender, but I do alert women to the challenges we face, especially regarding moving up the professional ladder. I make sure junior women around me get equal access to opportunities, and I always tell them that they don't need to fit any particular mold and that diversity is the secret ingredient to the most successful teams.

Dr. Berrocal: It is so important to understand that, if you don't find that *one* lifelong mentor, look for mentors that come into your life at important moments. I call these *situational mentors* or *temporary mentors*. They are very valuable. For many, it is ideal to have an ideal single mentor; for most that is impossible to find. Learn to be mentored by many different people for different moments and different parts of your life.

Dr. Correa: Every situation and experience should be an opportunity to learn, not only professionally but personally. Even when the experience is negative, it is an opportunity to figure out what not to do. An important part of our profession is to be in continual learning mode.

Dr. Scott: Work hard, particularly in training when you have a dedicated support system and an opportunity to learn everything about the field. Being a fellow, particularly in a field like retina, it's a unique opportunity to learn literally at the side of an expert. Work as hard as possible, learn as much as possible, ask as many questions as possible because when you're out of training you will not have the same opportunities to learn. Take advantage of every resource, including your attendings.

Of course, when you're in the real world, you can always go back to a mentor and ask him or her questions. But there's nothing like a full-time apprenticeship, which is what vitreoretinal fellows have. ■

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Closing the Gender Gap in Retina


The landscape is changing, but more is yet to come.

BY AVNI FINN MD, MBA; AND CAROLINE BAUMAL, MD;
WITH CONTRIBUTIONS FROM MARÍA H. BERROCAL, MD; SHARON FEKRAT, MD;
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"More gender diversity… can translate to increased productivity, greater innovation, better decision-making… ."
—2017 Report on Gender Diversity, Morgan Stanley[1]

Research in the business world has shown that greater gender balance in a company translates into better returns and less volatility for investors. The case for greater gender balance in medicine is similarly compelling.

Most retina physicians, men and women alike, are proponents of gender diversity within our field, but increasing diversity remains challenging. The reasons behind continued gender inequality are complex. They are not limited to medical education and physician practice, but rather stem from all aspects of society. Among the ophthalmology subspecialties, retina attracts the smallest percentage of women. As of 2018, 19% of US retina specialists were women, compared to 26% in oculoplastics, 29% in cornea, 34% in glaucoma, and 47% in pediatric ophthalmology.[2]

A major step toward improving gender balance in our field is understanding why the imbalance exists. Lack of leadership, support, and mentorship during surgical training, sponsorship of research, and equality in pay are all potential barriers to gender balance in retina.[3-7] For this article, we interviewed several female leaders who are at the forefront of mentorship, research, and clinical care in retina and asked them to share their thoughts on gender imbalance in the field.

NOT JUST RETINA

Shlomit Schaal, MD, PhD, Professor and Chair of the Department of Ophthalmology and Visual Sciences at the University of Massachusetts Medical School, commented, "I see evidence of gender inequality not only in our field of retina, but also in academic medicine as a whole. The 2019 report from the Association of American Medical Colleges clearly shows that at the highest levels of academic medicine (department chairs and deans) women are underrepresented. I'm optimistic that this is going to change in the future as more women take on these challenges and serve as role models for the younger generation, both for women and for men."

This anticipated change is likely to have a trickle-down effect: Having women in leadership roles not only sets an example for younger trainees but also broadly changes the perceptions of what a woman in ophthalmology can achieve.

As Carol L. Shields, MD, Director of the Ocular Oncology Service at Wills Eye Hospital and a Professor of Ophthalmology at Thomas Jefferson University, noted, "It is difficult to break into a field without support from a seasoned player, whether that be a male or female physician. Those of us in retina and ocular oncology have a special opportunity to influence younger women and men, and this likely impacts their choice of specialty.

"Once in the field, there is another factor to consider, and that is the sense of belonging," Dr. Shields added. "This depends on all of us welcoming new members and including them in all the aspects of our field, regardless of age, race, or gender. This allows these new members to grow into their careers and contribute to their fullest."

BEYOND LEADERSHIP

The gender imbalance extends beyond the leadership gap. The very nature of the specialty—the challenges that interest and captivate us—may be the same ones that turn some trainees away.

Nancy M. Holekamp, MD, a Professor of Clinical Ophthalmology and Visual Sciences at Washington University School of Medicine and the Director of Retina Services for Pepose

Vision Institute, had some thoughts on this. She said, "I think a gender imbalance exists in retina for the same reason it exists in general surgery and neurosurgery: Extra years of training, more emergency calls, less predictable schedules. We are the ones getting called in the middle of the night to surgically fix emergency problems—infections, posteriorly ruptured globes, retinal detachments. Retina is distinct enough from other ophthalmology specialties to create a gender disparity not observed in those specialties."

Sharon Fekrat, MD, a Professor of Ophthalmology, Associate Professor in the Department of Surgery, and Surgical Retina Fellowship Director at Duke University School of Medicine, agreed. "Although many women definitely think that vitreoretinal surgery is fun and exciting, they likely make a work-life balance decision not to enter the field," she said. "However, what they may not realize is that, irrespective of which ophthalmic specialty they choose, they still have to deal with complex ophthalmic conditions."

María H. Berrocal, MD, Director of Berrocal & Associates, noted that changes and innovation in the field may increasingly attract more women and calls attention to the need to close disparities in salaries between male and female retina specialists.

"Fortunately, with retina cases being shorter and with the trend toward in-office, pharmaceutical treatment of diseases, I think more women will be choosing retina as a subspecialty," she said.

"Transparency in salaries is necessary, particularly in academia, to reduce the gender disparity in wages," she added. "Sadly, women retina specialists' base salaries in many academic settings are less than their male counterparts' salaries. This practice persists because of the lack of transparency."

Emily Y. Chew, MD; María H. Berrocal, MD; Shlomit Schaal, MD, PhD; and Caroline Baumal, MD, are among the women leaders in retina. Here, they were gathered at the Retina Society annual meeting in Paris in 2015.

Female vitreoretinal surgeons at the Duke Eye Center.

ATTITUDES ARE CHANGING

Despite what may seem like a gloomy landscape as described above, thoughts and attitudes toward gender in the workplace are changing due to the work of leaders and pioneers in the field. The leaders we interviewed pointed to important ways to close the gender gap and shared their optimism for the future.

Dr. Fekrat noted that the field is already evolving.

"Medical schools are now more than 50% female, and, as a result, more women will choose ophthalmology and thus retina," she said. "In fact, an increasing percentage of retina fellows are female, so we are almost there. Seeing strong and accomplished female role models within our field who have both a successful career and personal life will ultimately attract more women to our field."

Dr. Shields remarked, based on her own experience, that barriers may be a matter of perception.

"I did not see the gender gap as a problem, but rather as an opportunity," she said. "Women can be exquisitely talented, both intellectually and surgically, and achieve high standards similar to men. Women tend to be precise, with excellent delicate fine motor skills—traits that are of utmost importance to our field."

Dr. Shields said she has observed the

increasing number of women in the field during the tenure of her career.

"Over the past 33 years of my career, there has been a slow rise in the number of women in both retina and ocular oncology. Now, when I attend an ocular oncology symposium, I estimate that 50% or more of the attendees and speakers are women. This has been a gradual evolution. Part of this is due to female (and male) mentorship, changing workplace philosophies, and women believing in their skills. I feel that the presence of women in both retina and ocular oncology has and will continue to push these fields forward and to higher levels, with top performers providing new insights and more creative thinking."

MENTORS CRUCIAL

Our interviewees agreed that mentorship is crucial to bring about change. As Dr. Holekamp remarked, "Young, talented, and smart women in ophthalmology training programs simply need encouraging role models (both female and male) to tell them they can do it."

Dr. Schaal similarly underscored the importance of female leadership and guidance within the field.

"It may seem quite daunting for a young rising female retina specialist to adequately balance her life between her developing demanding career and her beloved growing family," she said. "As a mother of four daughters, I can certainly relate to these feelings of anxiety, restlessness, and uncertainty. It is not easy to navigate an ambitious career with a happy home. We must recognize that support, reassurance, and guidance are needed, both from mentors and from peers."

Just as our patient populations are diverse, a diverse group of vitreoretinal surgeons is necessary to best serve the individual patient's needs. Dr. Berrocal noted how women can increase value in the field of retina: "Women can bring a lot to the field and to their practices—connection with patients, improved patient satisfaction, greater empathy, and, as a recent article showed, better outcomes and reduced mortality.[8] At present, we have a system that values and remunerates seeing as many patients as possible, as quickly as feasible. With the current trend toward valuing results-oriented outcomes, I am sure women will start to be valued more. Also, as more women enter the field, we will become not a rarity but a familiarity."

RAISING AWARENESS

Raising awareness of potential barriers can help lead to transformation. There have already been incredible changes in our field in the past few decades. Female membership in the American Society of Retina Specialists has increased from 11% to 19% over the past decade.[9] The proportion of female fellows-in-training members is even higher, at 30%.

Mentorship of women by both men and women, including sponsorship and promotion, in addition to societal changes in perceptions of gender roles, will bring about change. Women must take their seats at the table by seeking and accepting committee memberships, speaking engagements, and leadership roles. We in the field must collectively and continually analyze shortcomings in gender diversity. The retina community must strive to be at the forefront of change to improve gender balance in our field and propel our subspecialty to its fullest potential. ■

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Departmental Leadership

Retina Today Guest Editor Judy Kim, MD, sat down with two women who lead academic departments to discuss the view from the top.

INTERVIEW BY JUDY E. KIM, MD; WITH JULIA A. HALLER, MD; AND JOAN W. MILLER, MD

When I sketched out the topics for this issue of *Retina Today,* I wanted to include women in leadership roles commenting on how they achieved professional success, the price of their ambition, and their proposed solutions for both real and perceived barriers. Julia A. Haller, MD, is Ophthalmologist-in-Chief and William Tasman, MD, Endowed Chair at Wills Eye Hospital and Professor and Chair of Ophthalmology at Sidney Kimmel Medical College at Thomas Jefferson University in Philadelphia. Joan W. Miller, MD, is the David Glendenning Cogan Professor of Ophthalmology and Chair of the Department of Ophthalmology at Harvard Medical School and is Chief of Ophthalmology at Mass Eye and Ear and Mass General, and Ophthalmologist-in-Chief at Brigham and Women's Hospital in Boston.

I was fortunate to have these amazing women share their insights on these topics of interest. We had so much to talk about! Therefore, the interview has been edited for brevity and clarity. I hope you enjoy learning from their perspectives as much as I did!

—Judy E. Kim, MD

PATHWAY TO LEADERSHIP

Judy E. Kim, MD: No two leaders arrive in their positions via identical paths. How did you wind up a chairperson?

Julia A. Haller, MD: Well, I can't claim that I ever set out to be the Ophthalmologist-in-Chief at Wills Eye Hospital, although in retrospect, had I known I would love my job this much, I certainly would have made it a goal! The opportunity to fill this role arose, as many opportunities do, by my just putting one foot in front of the other—sometimes with missteps—and working hard, trying to make contributions where I could, and then having chance favor the prepared woman!

There are many routes to leadership positions in academic medicine, and everyone's path is different, but there are some basic common denominators. Mine included clinical research productivity and the lucky opportunity to work with teams advancing the field in many groundbreaking

projects—which were exciting in and of themselves! That also gave me experience with academic teamwork in an environment in which teaching and mentoring were prioritized at every level, and fed excellence and breakthroughs in patient care.

Alternatively, some people follow paths through basic research or educational and administrative leadership roles, on to departmental vice chair and ultimately chair positions. I was drawn to the technical surgical excitement and trajectory of the field of retina, and the hugely valuable experience of serving as Chief Resident at the Wilmer Eye Institute after my fellowship with Ron Michels, MD. That was great preparation for being a department chair! I then had many opportunities to be involved in numerous trials and projects in which I could move into leadership roles, and moved up the professorial ladder, and eventually had the huge honor of Morton Goldberg, MD, a wonderful mentor, naming me the inaugural Katharine Graham Chair in Ophthalmology at Wilmer—what a thrill!

Meanwhile I found opportunities in important organizations in our field, such as the Retina Society and the American Society of Retina Specialists. I served on the first planning committee for AAO Retina Subspecialty Day and helped launch organizations such as the Diabetic Retinopathy Clinical Research Network. So much transformational work has been done in our field during my career, and it has been a privilege to be associated with that evolution. When the chance came to interview for the Wills Eye Hospital position, it was the opportunity of a lifetime. I threw my hat in the ring, and I was lucky enough that they picked it up.

Joan W. Miller, MD: I'm Canadian, and most Canadians stay in Canada for university. But I considered the United States because a good friend was applying for golf scholarships there. I wouldn't describe my decision-making at that time as a well-thought-out process.

I knew of only three schools—Princeton, Yale, and MIT—and put those three down on my SAT application. I heard back from MIT and thought that it looked like a great place. I was admitted and moved in without ever having seen it. I ended up at Harvard Medical School and was drawn to retina because the surgery was fascinating—you had to think on your feet in the OR—and because the research opportunities were plenty. I was involved in developing photodynamic therapy and the foundational work on anti-VEGF technology.

I enjoyed my life as a clinician-scientist and retina surgeon, and I wasn't looking for leadership opportunities. But in the late 1990s and early 2000s, there were some leadership opportunities at Harvard Medical School. One of my mentors, Ephraim Friedman, MD, told me it was my turn to give back to the institution, and to build an environment for young people that fostered success. That appealed to me, and I was chosen to lead the organization. I have really enjoyed my role, but a department chair position was certainly not the plan.

Dr. Kim: When you move from a clinician-scientist-surgeon to department chair, there are personal and professional sacrifices. What adjustments did you make when becoming a department leader?

Dr. Miller: Before adopting a role like department chairperson, you need to understand that it's a service role. You're leading a department, and it's all about the success of faculty and trainees.

When accepting a department chair position, you need to be at a stage where you've met your personal satisfaction and professional goals. Your decision must be a thoughtful one.

All department chair positions differ, and mine includes serving on the Board of Directors of Mass Eye and Ear, involved in institutional strategy as well as the financial wellbeing of Mass Eye and Ear. It's no small task. When I took on the role, I stopped taking retina call, limited my practice hours, and transferred a number of my patients to other doctors. About 7 years ago, I stopped operating as well, choosing to focus on medical retina for clinical work.

Those were big changes, and they aren't something to think about when you're coming out of training and passionate about performing surgery. Still, the challenges you encounter when moving into a new role keep your career exciting.

Dr. Haller: Everything has a price. Henry David Thoreau said something like, "The value of anything is the amount of life you exchange for it." Bullseye there. And as Teddy Roosevelt said, "Far and away the best prize that life has to offer is the chance to work hard at work worth doing." The cause of preserving and restoring vision (and with it, our patients' quality of life) is a noble one, and well worth the price we pay for it in years of training and hard work and sacrifices that we and our families make. I truly believe that.

Moving into my new chair role meant leaving behind an institution and a city that I knew and loved, as well as cutting back on a large surgical practice that was in many ways my identity, and changing gears into strategic planning and recruitment and fundraising. But part of the rewarding challenge of life is reinvention, and one of the really special aspects of academic medicine is that there are so many different roles and contributions to make. It keeps us engaged and energized.

Dr. Miller: Having difficult conversations with people is a challenge. And when you mentor physicians and train them for leadership, sometimes you

feel like you take two steps forward and one step back. Attending long institutional logistics meetings is not always a good use of one's time, and in the meetings I convene and run, I really try never to waste people's time. Managing difficult human resources– related issues is not invigorating, and you need to balance it with fun tasks such as mentoring emerging leaders.

Dr. Haller: Timing is part of the problem that women face as they advance through the academic ranks. The period of our life when we'd most like to start a family often coincides with the period of our professional careers that requires the most hours and where there is the least flexibility. Woman are joining as junior faculty or still in training in their mid 20s through early 30s, which is when many women consider having children. Thus their timeline is compressed and the challenges for balance can become more concentrated as these competing interests intensify. This is probably the time point at which the personal and professional sacrifices to which you allude are most obvious and need the most intentional thought.

Dr. Kim: How does one balance professional ambitions with family needs?

Dr. Haller: I don't think any of us ever feel like we've achieved perfect balance. I am lucky to have a husband who is also in academic ophthalmology, who understands the stresses of my lifestyle, and who is a great friend and partner. We were also fortunate in having great kids, and finding wonderful childcare helped bolster our support system; my parents, who were both local physicians, were wonderful grandparent resources. But there were plenty of times when the kids got packed up and dragged into the hospital for a few hours on weekends—I hope it was character-building!

EGALITARIAN ASPIRATIONS IN RETINA LEADERSHIP

Dr. Kim: What institutional barriers to success have you identified that may affect women in retina who seek to become leaders?

Dr. Haller: Mentorship is a major factor in the success of anyone. I see a lot of well-trained women get to the assistant professor level and then step off the track. They don't get the encouragement and mentoring and support that they need. They know that they can still be a good doctor, but they feel that they must choose between spending time with their family and dedicating time to ambitions.

Some academic institutions have dedicated themselves to figuring out how to solve some institutional barriers. Johns Hopkins Medicine was an early proponent of strategically restructuring the work week. Historically, Hopkins grand rounds in medicine and surgery were held on Saturday morning, which meant that that time could not be spent with family. After moving grand rounds to a weekday morning, more woman began participating and getting recognized as clinical leaders.

Hopkins also made an effort to delineate the steps of academic progress. The team there clearly defined deadlines, steps, and milestones of academic promotion. If there were an old boys' club membership that previously had been key to department leadership, it was rendered moot—at least a good bit—by this transparency.

Dr. Kim: Do the barriers become less obstructive as your career advances and you take on leadership roles?

Dr. Miller: It wasn't until I was actually in a leadership role that I paid much attention to being a woman professional. I realized that there is a representation problem at the leadership level. I found even within my own organization that sometimes it was hard to be heard. At other times, ideas that I articulated were attributed to others; I had heard about this happening, but it was something else to actually experience it. I also learned that, as a woman academic leader, I had a new role in advocating for women as speakers, as award recipients, and for leadership roles.

The lack of women in leadership positions is not, in my estimation, an issue with the talent pipeline. There is a bias in how we select leaders, and hopefully it will change. Having women leaders is the first fix, and having women leaders and male colleagues advocating for the development of women in leadership positions is an important next step.

Dr. Kim: During your training, did you experience the biases you have observed in your role as chairperson?

Dr. Miller: When I was in my training, I never framed the field in terms of a male-to-female ratio. There were many more men than women, but I never felt like I was treated differently. I took the attitude that you should work hard, be yourself, do a good job, and things will work out on a merit basis. That held true for me through those stages. But again, my perspective shifted somewhat after I moved into leadership.

Dr. Haller: Absolutely true—having women in leadership positions is very important, and it is our responsibility to pay it forward. When a young person sees a woman in a position of responsibility, then it becomes clear that she can do it, too.

I recently heard a talk by Jeffrey Goldberg, MD, PhD, at Stanford that made some great points about leveling the playing field for recruiting and interviewing. Let's say a department head (or someone in a similar position

of power) is meeting a potential new colleague for dinner. If it's someone you know or someone from a similar background, then you might talk about mutual friends or experiences. If it's someone you don't know or someone who has less societal overlap with you, then you might restrict conversation to research and professional accomplishments. Obviously the more engaging social conversation is more appealing than the more stilted professional one, and the interviewer may end up feeling that they have a closer connection with the person whose background and life mirrors theirs, and that they would be a better choice for the job. We tend to choose and promote and recommend people like ourselves; seeking diversity and inclusiveness requires intentional thought and preparation and practice in order to really compare apples to apples professionally.

FINDING THE NEXT GENERATION OF LEADERS

Dr. Kim: What qualities do you look for in potential leaders while you're mentoring them?

Dr. Miller: First and foremost, you want physicians who care about patients. Then, identifying future leaders is about finding people who are willing to engage outside of their comfort zone. This could start with leading a program or a group, and their leadership potential can be assessed on how they handle these assignments. If the emerging leaders enjoy the assignment, and use it as an opportunity to grow, then you might have a future leader on your hands.

Communication skills are also important. This includes the ability to communicate one's ideas and thoughts, but also the ability to listen, digest, and respond to others. If they can generate a plan and execute it based on input, then their communication skills are high.

Over time, I've challenged my own preconceived notions of what I'm looking for—just as I want to see potential mentees outside of their comfort zone, I have to be outside of mine from time to time.

Dr. Haller: A future leader must have a stick-to-it-iveness to be successful. When I see superb physicians who also have grit, drive, tenacity, and ambition, I try to find opportunities for them to grow and lead. These are the people who do twice as much work as you ask, who finish projects, for whom it is an absolute pleasure to write letters of recommendation and to nominate for awards and committees and jobs—those for whom you will pick up the phone and call a fellowship director or a chair.

Everyone has different talents. Some strengths are obvious from the beginning of our interactions, even with medical students, and I'm sure everyone has experienced this. You might see right away after one wet lab who in a group of residents or fellows will be a crackerjack surgeon, or who has the temperament to laugh off setbacks, dust themselves off, and get back into the fray. The pressures of a busy residency like the one we have at Wills bring out the diplomats and the negotiators, the clinicians who get to the bottom line immediately, the insightful questioners with a flair for the key research question. One of the joys of this job is getting to know these brilliant young people, and helping launch them into the most rewarding field in the world.

Dr. Miller: I have a final note about leadership. Leadership is engaging, and it gives you a different perspective on the field of retina. Being a chairperson has encouraged me to improve my communication skills and to seek out advice on areas where I need improvement. If you're considering leadership, know that it's an exciting opportunity that will keep you interested in retina in a new way.

Dr. Kim: Thank you, Joan and Julia! I am certain that many will appreciate your wonderful wisdom and candor on leadership. I hope you continue to be successful and enjoy the view from the top! ■

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THE PATHWAY TO THE PODIUM


Get involved in as many activities as you can.

BY TALA AL-KHALED, BA; AND ANN-MARIE LOBO-CHAN, MD

A career path is a journey involving various phases of development. Traveling along that path requires you to demonstrate initiative and dedication to the field. Consider taking some of the following steps during ophthalmology training and your early years of practice to direct your path toward establishing yourself in your profession.

GETTING INVOLVED

During residency and fellowship training, immerse yourself in each subspecialty rotation, and identify the unique surgical or clinical aspects of that subspecialty that may interest you. When you work alongside faculty, keep an eye out for their regularly scheduled lab meetings or journal clubs. By joining these activities, you can expand your knowledge and identify mentors and potential projects. Early in practice, join your local ophthalmologic and subspecialty societies as a way of staying informed and involved; this will also give you opportunities to meet colleagues in your field.

SHOWING UP

At every stage in your career, it is important to attend annual ophthalmology meetings, including both large-scale international conferences and more intimate subspecialty symposia. International meetings allow you to connect with colleagues from around the world and learn about diagnostic and surgical advances occurring in other countries. Exposure to current developments allows you to ask questions and may inspire new ideas. Smaller meetings can provide more interpersonal communication with presenters and facilitate opportunities for collaboration and mentorship.

When you attend an annual meeting, step outside the conference rooms to network at the social events, as this is where colleagues become friends and seeds of ideas for future projects and collaborations may develop.

If your ability to attend meetings is limited, participate in webinars and online discussions. These are becoming more readily available and are now provided by many meetings and societies.

FINDING YOUR NICHE

Identify a subject about which you are passionate, such as a specific disease, and choose the realm in which you wish to work (benchwork, clinical trials, educational programs, global ophthalmology, etc.). Before initiating your project, it is of great value to conduct a search of the published literature on your topic of interest. This allows you to familiarize yourself with progress that has already been made in that field and can help you to identify aspects that have yet to be explored. After you have selected your unique focus, the key is to strive toward becoming an expert on that topic.

Building your reputation stems from sharing your work with the community. It is important to set goals for each stage of your projects so that you can prepare updates to present at annual meetings. Delivering oral presentations at smaller meetings, academic institutions, or through webinars is a way to highlight your findings and create forums for discussion.

When you submit an abstract, allow time for you and your team to compose and later revise your submission. Ultimately, contributing to the scientific community through publications

AT A GLANCE

- Join committees and societies to get involved, informed, and noticed.
- Seek out what's interesting to you and become the expert; know your topic and share your knowledge.
- Find a mentor who can guide you toward opportunities in your field for presenting and developing research; as you advance, you can then in turn be a mentor to others.

is the cornerstone to establishing your expertise in your chosen field.

When you communicate your interests and end goals to your mentors, they can help guide you on the submission and presentation processes.

VOLUNTEERING

In addition to attending and presenting at meetings, consider joining a committee and taking on a designated role. Actively participating on a committee year after year will not only demonstrate your dedication to the field but may also introduce you to senior members who may invite you to partake in other committees or activities. As you establish your presence among your colleagues, opportunities to take on leadership roles may arise, such as organizing meetings, inviting speakers, and constructing panel discussions.

MENTORING

Throughout your career, your mentors play an important part in paving your way to speaking roles. As a mentee, you look to your career mentors for advice on meetings to attend and opportunities to become involved. Express your interests to them, including presenting your work at meetings, as your mentors may be able to help you through their roles in meeting organizations or on planning committees. As you rise through the professional ranks, and when your path to the podium has already been paved, you can then take on a mentorship role yourself. Trainees or recently specialized ophthalmologists may wish to learn about your work and to take on positions in your ongoing projects. By promoting these junior colleagues, you can not only improve your own contributions to the field but also help them to foster their own independent projects. If you are unable to attend a meeting, you can send a junior colleague or mentee in your place to gain experience in presenting and a wider recognition from those in your field.

CONCLUSION

As you progress along the pathway of your career, it is important to remain proactive. Partake in ongoing activities in your subspecialty, investigate subject areas that intrigue you, and become the expert. By building your career with these steps, you'll be able to succeed in your career path and make your way to the podium. ■

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in our practice, but always slipped time aside to take vacations with the family and then later to build the practice.

Carol: We didn't initially have time to go on a date night when we first started a family, but we organized our office around our lives to give us more time. Our office opened early in the morning, so we could check in patients, complete imaging tests, provide examination, and have everything wrapped up so that we could finish in time to get home for dinner with our children. Jerry and I made it a point to be home by 5:00 or 6:00 so that we ate dinner as a family every single night.

We always had a lit candle on the table. We still do. It symbolizes the family unit and that we are all here for each other.

Jerry: It takes a lot of organization to have a big family. No matter what field you're in, whether or not it's medicine, when there are two working people in the family, it's a big job having a lot of kids.

ADVICE FOR YOUNG DOCTORS IN SIMILAR CIRCUMSTANCES

RT: Imagine two young retina specialists who have hit it off are going on their first date. Given your experience, what piece of advice would you give?

Carol: I would tell them three things. Number 1, be yourself, and don't try to be anybody else. Number 2, as this relationship matures, make sure you always communicate. And number 3, always be careful to consider all the needs of yourselves as a couple or as a family, and not just you as single person.

Jerry: I would tell them to develop a close relationship and try to keep it that way. We've been very successful in that regard, always supporting our own children and our family.

Carol: When you find a person who understands you and your specialty, that's a treasure. They will understand why every Thursday night you want to prepare for grand rounds the next day.

Jerry: Yes, you need to mesh very well.

Carol: We're a strong couple and we have similar interests, but Jerry and I, we're not exactly alike. Jerry is, I think, a more happy-go-lucky guy, and I'm more of an organizer. And our differences have complemented each other well. ■

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The Role of the New Generation of Lasers in Retina

BY VICTOR CHONG, MD, FRCS, FRCOPHTH

Through the years, laser has evolved dramatically. Although intravitreal injections have become the first line of treatment of macular pathologies such as diabetic macular edema (DME), laser application within clinical settings continues to prove efficacious in macular conditions.

When introduced more than 50 years ago, macular laser was initially used as a photocoagulator to destroy lesions. Today, the newest lasers can be customized to deliver energy in different ways by varying power settings, shortening duration, and employing a train of pulses to achieve a targeted endpoint. To fully comprehend how new lasers are different from each other, and to ensure its proper clinical use, it is important to examine how and why lasers work, how laser is delivered, and how the target tissue in the retina reacts.

The evolution of the laser treatment of DME illustrates this topic well:

At the very beginning, we simply learned to "shoot the red dots," in order to perform a direct coagulation of the leaking microaneurysms. However, it was not uncommon to miss these microaneurysms and to discover that the treatment remained effective.

We gradually learned that most of the laser energy is absorbed primarily by melanin in the retinal pigment epithelium (RPE) and the choroid. Furthermore, it is believed that the energy induces a change in the RPE cells, changing the micro-environment, which improves the edema instead of directly destroying the microaneurysms. This led to a debate of "light" versus "classic" laser treatment for clinically significant DME. The idea was to reduce power to obtain a barely visible burn but still have microaneurysm absorption.

SUBTHRESHOLD LASERS AVAILABLE ON THE MARKET

	SubLiminal	Endpoint management/ Non-damaging	Nanosecond/Rejuvenation
Duration of laser in each pulse	0.1 ms	10 to 20 ms	0.000003 ms
OCT change after treatment	None visible	Clearly visible	Seen in some cases
AF imaging after treatment	None visible	Clearly visible	No published data but RPE changes visible on color fundus photos
Randomized controlled trials published	Several in DME and CSC	None	Reduced AMD progression (in post-hoc analysis)

Figure 1. Comparison of available subthreshold lasers available on the market.

This was considered to be the threshold point separating the power needed to cause a color change in the neurosensory retina during the procedure visible to the surgeon. As some retinal specialists alternatively defined threshold as needing a clearly visible reaction, this inherently led to the question, "If we don't see a reaction, is the treatment effective?"

CONVENTIONAL VERSUS SUBTHRESHOLD LASER PHOTOCOAGULATION

Conventional continuous-wave laser photocoagulation has been used to treat different macular retinal diseases for many years. As an example, the treatment settings for DME were defined by the ETDRS study in 1987.[1] These treatment settings were thermal laser therapy and based on the idea of obtaining a clearly visible reaction while lasering. Reported complications in patients with DME who undergo ETDRS laser include scotoma, visual field defects, and chorioretinal atrophy.[2]

To address these risks, and to implement a process of delivering more energy with minimal damage, less-invasive laser treatments were introduced. This paved the way for subthreshold laser photocoagulation. Subthreshold, using micropulsing, has shown efficacy without any visible changes on the retina.[3] Indeed, if the energy is reduced, the reaction can barely be seen, and we are able to achieve a positive clinical effect with no visible scarring.

Nowadays, three main types of subthreshold retina lasers are available on the market:

Endpoint Management (Topcon) is based on continuous delivery with decreased power levels and duration in an attempt to achieve no visible scarring with positive clinical effect. Though this approach makes sense in theory, it is unclear how this translates in clinical practice. To date, there is only one case series[4] showing clinical success without retinal damage on central serous chorioretinopathy (CSC). There are no controlled trials published in the treatment of DME, however, independent investigators have reported scarring and changes to RPE visible by using fundus autofluorescence imaging and OCT.

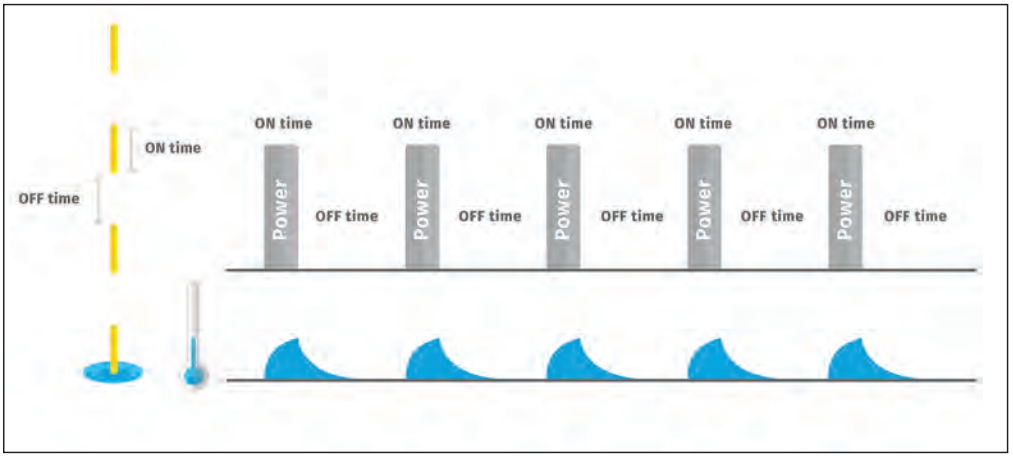

Figure 2. SubLiminal laser therapy treatment: Train pulse.

The 2RT nanosecond laser (Ellex) is using similar specifications to selective laser trabeculoplasty (SLT laser). 2RT treatment energy is based on power testing to a threshold color change and uses short pulse duration (0.000003 ms) and multiple beams delivered at 400-µm spot size (Figure 1). 2RT is thought to cause RPE death without damage to the retina. Nevertheless, it is causing some "RPE changes," which could be considered as scarring.

Its use to stimulate a natural, biological healing response to slow the degenerative process that causes retinal diseases, such as intermediate age-related macular degeneration (iAMD), has recently started to garner some attention. However, a controlled clinical trial (LEAD study[5]) demonstrating the slowing of AMD progression failed to meet its targeted endpoint. Only a post-hoc analysis excluding the reticular pseudodrusen demonstrated a slowing of the pathology, so it remains to be seen how effective 2RT will be.

SubLiminal laser therapy (Quantel Medical) offers laser energy delivery through a series of extremely short (microsecond) laser pulses (Figure 2). SubLiminal laser therapy is based on a stimulation concept, which allows for a cooling period between pulses resulting in no visible scarring (even with fundus autofluorescence imaging and OCT), and no detectable photoreceptor loss. This further results in the improvement of retinal sensitivity in edematous retina and reading speed, while also preventing retinal damage.

The latest SubLiminal laser uses a 577-nm true yellow wavelength that provides peak absorption of oxyhemoglobin, excellent lesion visibility, low intraocular light scattering and pain, and negligible xanthophyll absorption. With these absorption characteristics, the subliminal laser 577-nm yellow wavelength has the versatility of the 532-nm green wavelength yet causes less scatter, uses lower energy levels,[6] and also allows titration as compared with 810-nm infrared laser.

CLINICAL STUDIES SHOWING THE BENEFITS OF SUBLIMINAL LASER

Quantel Medical's technology allows a combination of multispot and SubLiminal delivery modes and features a customizable macular grid allowing the surgeon to customize the treatment area of the edema on the macula. In CSC, studies[7] have demonstrated that SubLiminal laser therapy is a promising alternative treatment strategy. The study concluded that SubLiminal laser is an effective treatment even in patients without sufficient improvement after photodynamic therapy. As I am confident in SubLiminal laser therapy for treating DME and CSC, I wonder what other retinal diseases could be treated? Evidence supports SubLiminal laser therapy can be used to supplement treatment in idiopathic polypoidal choroidal vasculopathy cases with suboptimal response to anti-VEGF treatment. Currently, there are several clinical trials using SubLiminal laser therapy for AMD. The goal is to show that SubLiminal laser therapy could also remove drusen and potentially slow the evolution of AMD without the limits of 2RT.

CONCLUSION

What we know today about SubLiminal laser therapy encourages us to move away from using conventional laser for macular treatment. In addition to the study of SubLiminal laser therapy on AMD, there are other exciting studies taking place right now to examine SubLiminal laser contributions to other retinal diseases, including retinitis pigmentosa, Stargardt disease, and geographic atrophy. I encourage you to monitor future updates, follow industry leaders conducting ongoing studies, and implement the technologies available to you today. ■

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PREDICTORS OF NEOVASCULAR GLAUCOMA IN CENTRAL RETINAL VEIN OCCLUSION


Investigators explored ways to identify patients at increased risk of developing glaucoma or experiencing disease progression.

BY CISSY YANG, MD; AND NOGA HARIZMAN, MD

Rong AJ, Swaminathan SS, Vanner EA, Parrish RK 2nd[1]
Industry support: No

ABSTRACT SUMMARY

For this retrospective cohort study, investigators identified clinical risk factors for the development of neovascular glaucoma (NVG) after central retinal vein occlusion (CRVO). They reviewed the charts of 646 patients with CRVO who presented to the Bascom Palmer Eye Institute between 2013 and 2017. Ninety-eight of these patients met the study's inclusion criteria: CRVO onset within 90 days of presentation, no anterior segment neovascularization on presentation, and no history of receiving an intravitreal anti-VEGF injection. Thirteen of the 98 patients (13%) developed NVG during an average follow-up duration of 17 months (range, 0.4–66.6 months). The mean time to NVG onset was 421 days after initial presentation and 212 days after the last intravitreal anti-VEGF injection.

Patients who had a history of systemic hypertension ($P = .026$), a worse visual acuity on initial presentation ($P = .034$), or a relative afferent pupillary defect (RAPD, $P = .002$) were found to be at high risk of developing NVG. Age at presentation, sex, body mass index, systolic or diastolic blood pressure at the initial visit, a history of diabetes, degree of diabetic retinopathy, and IOP at presentation did not differ significantly between patients who developed NVG and those who did not. An anti-VEGF injection at the first visit did not reduce the risk of developing NVG, but it did delay the onset of NVG. Neither the presence of macular edema nor central retinal thickness at presentation was associated with an increased risk of NVG, which suggests that macular edema and NVG are independent sequelae of CRVO.

STUDY IN BRIEF

- A retrospective cohort study found that a history of systemic hypertension, worse visual acuity, and the presence of a relative afferent pupillary defect at presentation were risk factors for developing neovascular glaucoma (NVG) after central retinal vein occlusion (CRVO) and that intravitreal anti-VEGF injections delayed but did not prevent the onset of NVG.

WHY IT MATTERS

- NVG is a rare but potentially visually devastating complication of CRVO. To date, physicians' ability to predict which patients will develop NVG after CRVO is limited. These investigators examined demographic data, systemic health data, and ophthalmologic examination findings to identify potential risks factors that may signal which patients are at increased risk of developing NVG. These patients may then be monitored more closely and for longer durations to allow prompt identification and treatment of neovascularization and thus prevent vision loss from glaucoma.

DISCUSSION

What was the relationship between intravitreal anti-VEGF injection and a patient's risk of developing NVG?

Commonly referred to as *100-day glaucoma*, the conversion to

NVG after CRVO has been thought to occur within the first 3 months after CRVO onset. This impression is based on CRVO natural history studies conducted before the era of anti-VEGF therapy. Rong and colleagues found the time to NVG onset to be significantly longer than the commonly accepted 100 days, and they found no significant difference in the rate of NVG between patients who received anti-VEGF therapy and those who did not. The researchers concluded that anti-VEGF therapy may reset the clock, so to speak, and delay NVG onset but that therapy does not decrease a patient's risk of developing NVG. Their findings suggest that eye care providers should observe CRVO patients receiving anti-VEGF injections closely for neovascularization beyond the traditional 90 days.

What is the relationship between macular edema and the risk of developing NVG?

Rong and colleagues did not find an association between macular edema or central retinal thickness and the risk of developing NVG. Furthermore, although anti-VEGF therapy has been shown to be effective for treating CRVO–related macular edema, this form of therapy did not decrease patients' risk of developing NVG in this study. Macular edema and NVG therefore may be independent sequelae of CRVO, as noted earlier. The researchers cautioned against mistakenly associating improved macular edema with decreased NVG risk because the assumption could give physicians a false sense of security about extending the duration between follow-up visits after CRVO.

How can the findings from this study affect the clinical management of patients with CRVO?

Clinical features associated with an increased risk of NVG included a history of hypertension and worse visual acuity or RAPD on presentation. There was an increased risk of NVG for every 0.5-logMAR decrease in visual acuity at presentation. Furthermore, of the 25 eyes with an initial visual acuity of 20/50 or better, only one (4%) developed NVG. The investigators recommended monitoring patients who present with these clinical signs at closer intervals and informing them of their increased risk of neovascularization so as to facilitate timely treatment and referral for subspecialty care. Patients with CRVO who later develop an RAPD or who experience a sudden decrease in vision should alert their providers; these changes may signal conversion from nonischemic to ischemic CRVO and a higher risk of NVG. ■

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WANT TO DIVE DEEPER ON PROTOCOL V?

In the September issue of *Retina Today*, Chirag Jhaveri, MD, an executive committee member for the DRCR Retina Network, examined Protocol V. Read "DME and Good Vision: Do We Need to Treat Early?" at bit.ly/Jhavari0320.

(Continued from page 21)

although there was a borderline statistically significant decrease in 2-step worsening of diabetic retinopathy severity level in the aflibercept group compared with the observation group (4% vs 11%, $P = 0.05$).

SIGNIFICANCE

Overall, this study lends confidence that patients with CI-DME and good vision can be observed initially. With this strategy, most patients will retain good vision, and those with functional or anatomic worsening may be treated with anti-VEGF without sacrificing final visual acuity at 2 years. This has significant implications for individual treatment burden as well as the public health expenditures associated with anti-VEGF treatment. ■

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KIRK PACKO, MD, FACS

YOU'VE STATED THAT WHEN YOU DISCOVERED OPHTHALMOLOGY, IT FELT LIKE HOME. WHY IS THAT?

One of the biggest influences in my life was my father. He was a professional photographer, so I grew up with optics and lingo like diopters, iris, and focus. Ophthalmology spoke the same language to me because photography is, of course, all about the visual. When my dad learned I wanted to go into ophthalmology he was thrilled. He was a perfectionist in his work, but also an extraordinary artist. I've tried to emulate those qualities, which are not only terrific for a photographer but are also vital for a surgeon. Our surgical efforts must be perfect, but there certainly is an art to what we do. My dad would have made a great eye doctor.

DESCRIBE YOUR INTEREST IN SURGICAL INSTRUMENT DEVELOPMENT.

As a kid, I loved to take toys apart to see how things worked and to think of ways to make them better. My first patent in the early 1990s was for vibrating intraocular scissors. The idea came during my fellowship and was based on a toy I had as a child called Snippy. Snippy was a plastic fish with vibrating jaws, but tremendous shear. The science behind the toy lent itself perfectly to the retinal surface. I also teach my residents and fellows how critical it is to thoroughly know your instruments and the science behind them. This principle not only fueled my interest in making instruments better, but also made me a better surgeon. To this day, I still try to scientifically understand every tool I use.

WHICH PROFESSIONAL ACCOMPLISHMENT ARE YOU MOST PROUD OF?

Although my role as a teacher to my residents and fellows is probably the most personally rewarding, the accomplishment I'm proudest of is my involvement for 20 years on the board of the American Society of Retina Specialists (ASRS). Founded as the Vitreous Society, it was the only truly open society for retina. I viewed this as a great opportunity to help make it representative for all—an organization that does all things retina. I brokered the name change to ASRS and started the PAT Survey, Film Festival, and *Retina Times*. In recognition of this, at the 2019 annual meeting the board established the Packo Award, which recognizes exceptional contributions to the ASRS and our field. This is an overwhelming honor for me and my family. To think that, 100 years from now, someone will be honored with the Packo Award is mind-boggling. Whatever that person has accomplished to deserve the award, I hope he or she is as proud of the honor as the guy behind the name.

Dr. Packo with his show-stopping 1956 Thunderbird. His love of toys shows.

AS A PROLIFIC AND IN-DEMAND PUBLIC SPEAKER, WHAT ADVICE DO YOU GIVE TO NOVICE SPEAKERS?

Remember, you're on stage. Make it memorable, make it visually exciting, not just a boring sea of numbers and text. Also, don't try to give too much information at once—keep it moving and keep it entertaining. Put a smile on audience members' faces while you teach them something, and have fun.

HOW WOULD YOUR COLLEAGUES DESCRIBE YOU?

Most people describe me as creative, a bit of a workaholic, and someone who gives great presentations. The creativity came from my father and the fact that I was a drama major in college. I actually studied acting in New York and planned to do that for a living. My acting and directing days served as a great backbone to my life as a teacher and public speaker. Seeing patients is similar to improv, in that listening and reacting, not just speaking, are all important. Doctors need to do the same. Listening to your patients and working with their comments is key. ■

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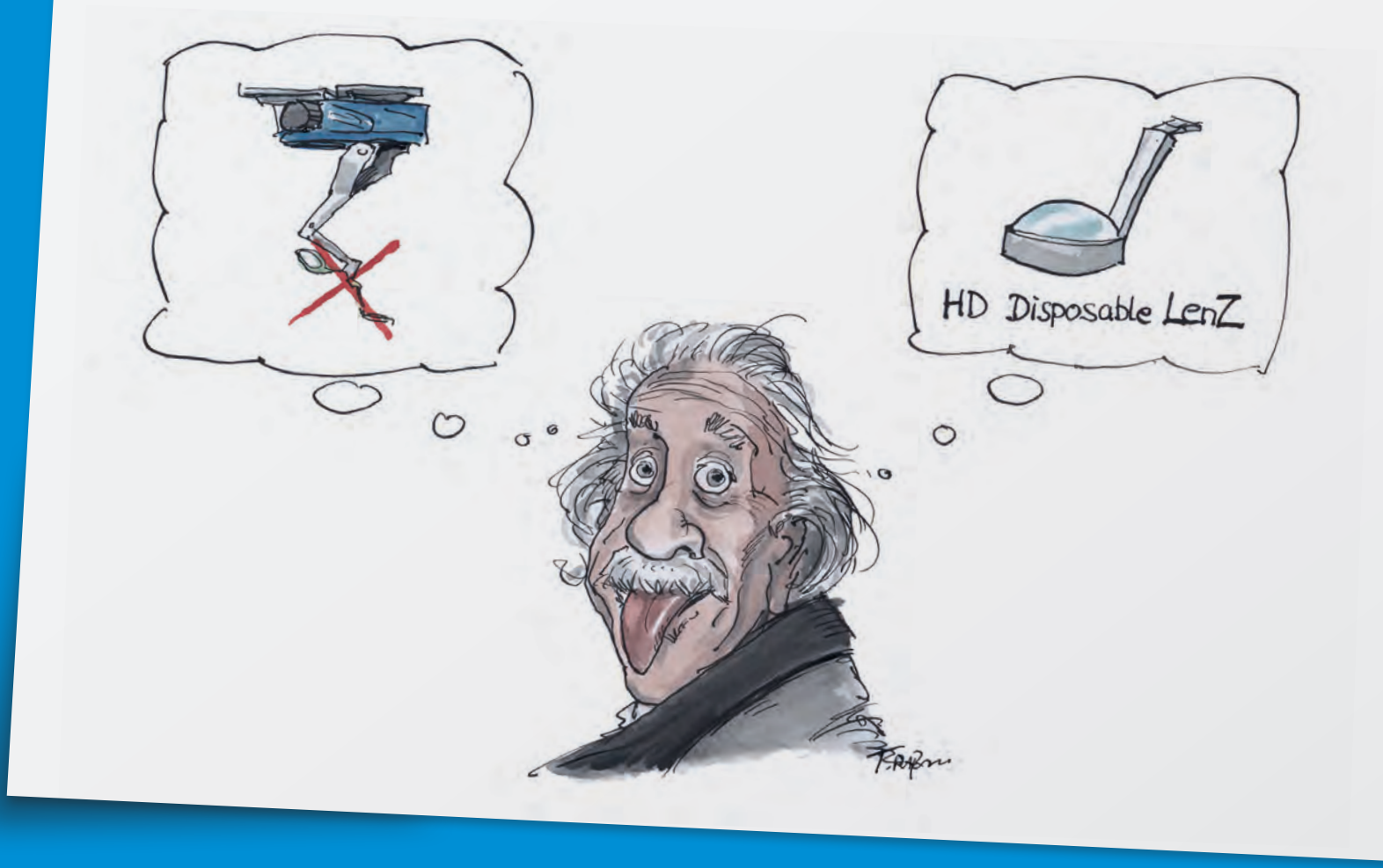

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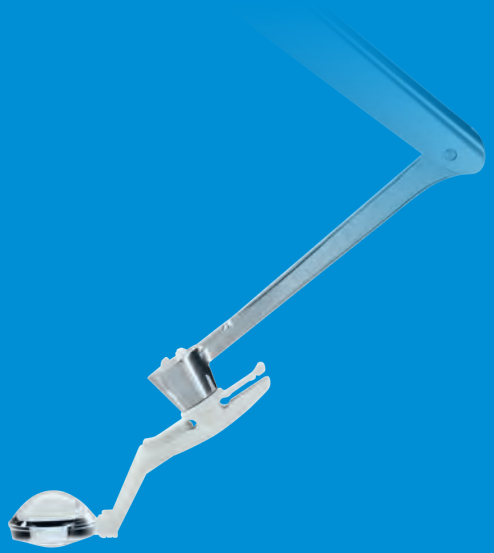

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