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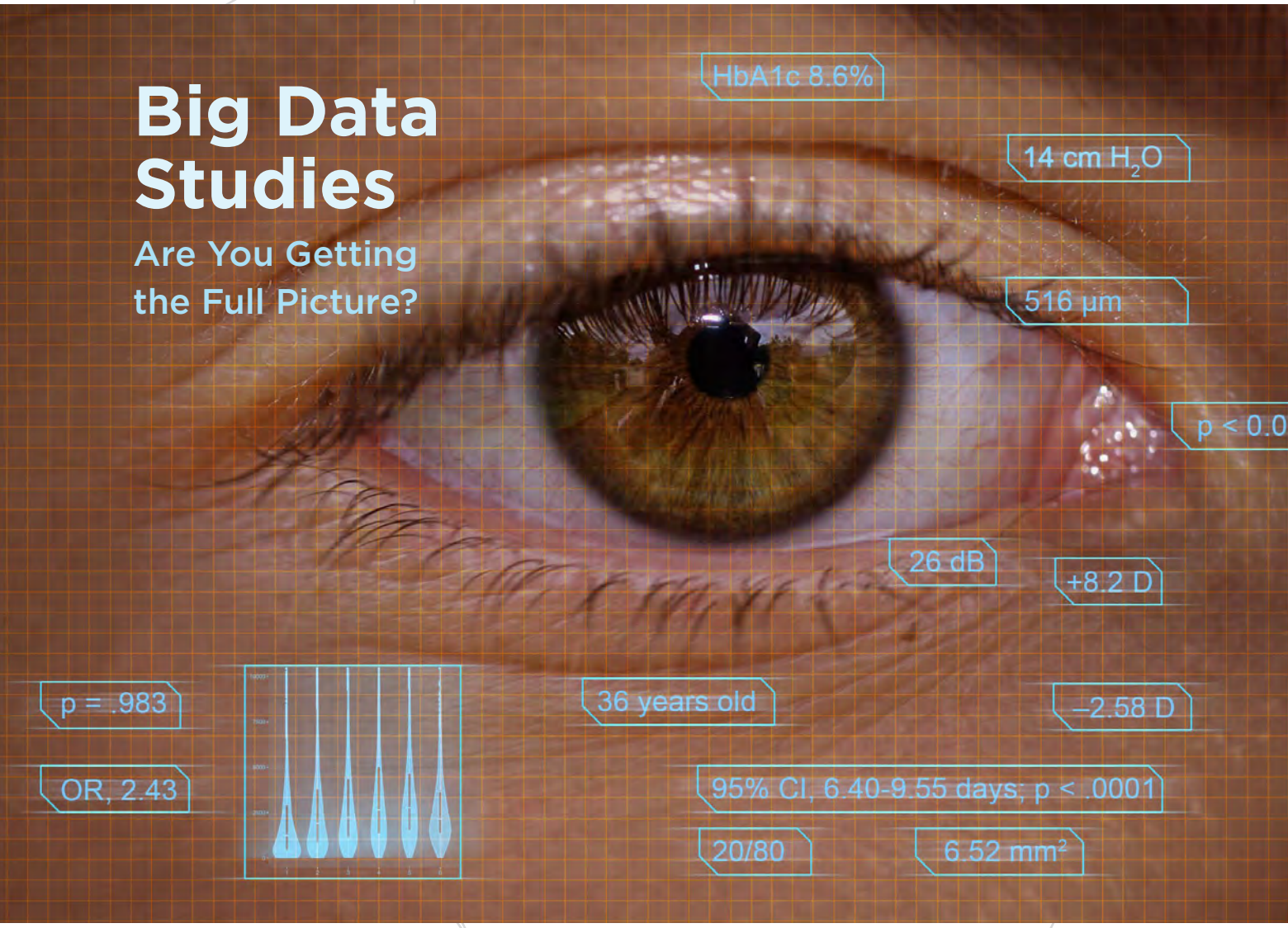
AUGUST 2021

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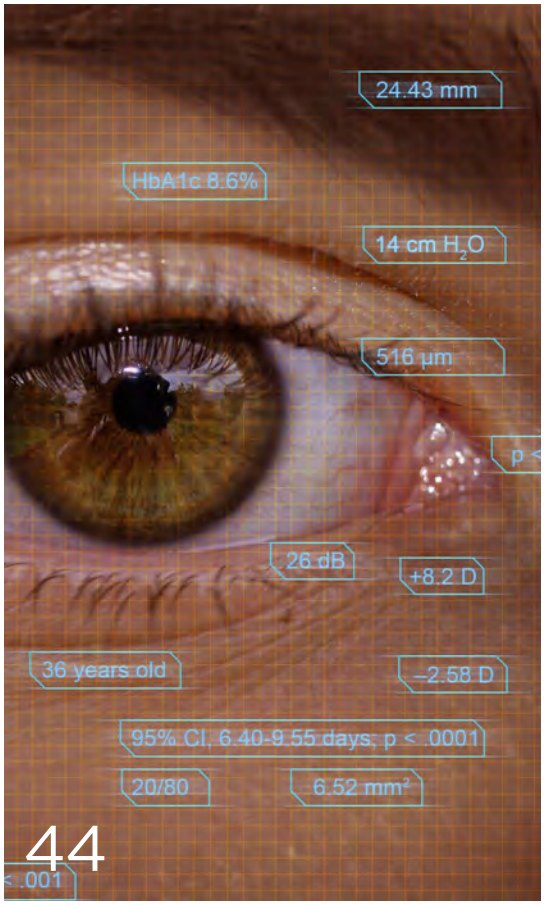


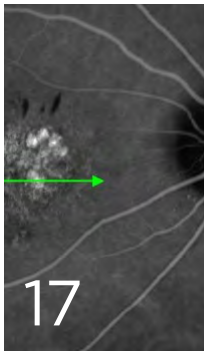


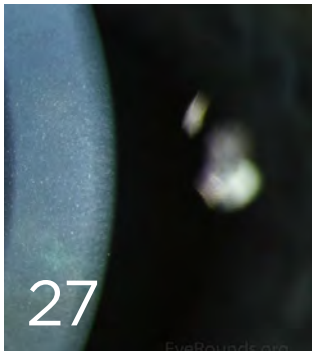



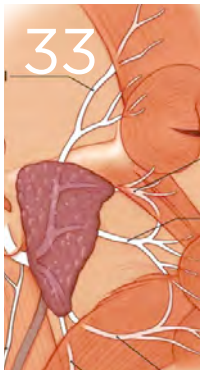


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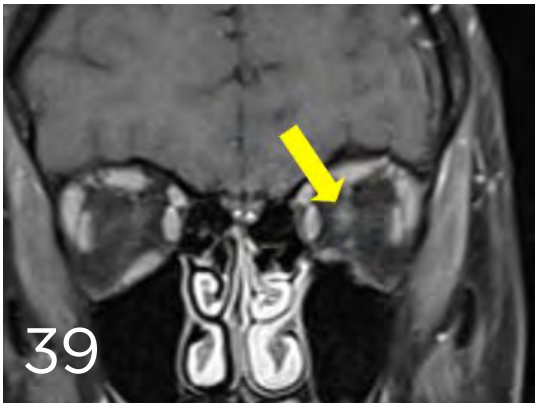
AUGUST 2021
VOLUME 25 • NUMBER 8

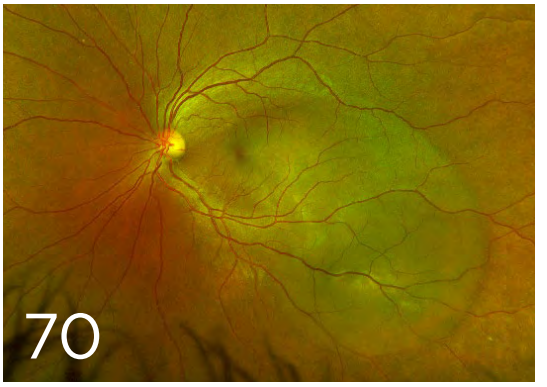


AMERICAN ACADEMY OF OPHTHALMOLOGY®

***EyeNet*® *Magazine*** (ISSN 1097-2986) is published monthly by the American Academy of Ophthalmology, 655 Beach St., San Francisco, CA 94109-1336, as a membership service. Subscription is included in U.S. members' annual dues. International Member, IMIT, $135 per year. Nonmember in U.S., $150 per year. Nonmember outside U.S., $210 per year. Periodicals Postage Paid at San Francisco, CA, and at additional mailing offices. POSTMASTER: Send address changes to *EyeNet*, P.O. Box 7424, San Francisco, CA 94120-7424. American Academy of Ophthalmic Executives®, EyeSmart®, EyeWiki®, IRIS®, ONE®, the Focus logo, and Protecting Sight. Empowering Lives ® among other marks are trademarks of the American Academy of Ophthalmology®. All other trademarks are the property of their respective owners.





# UPLIFTED

## Give Ptosis Patients an EYE-OPENING Lift With a Daily Drop of Upneeq® (oxymetazoline hydrochloride ophthalmic solution), 0.1%[1]

The only FDA-approved prescription eyedrop proven to lift upper eyelids in adults with acquired blepharoptosis (low-lying lids)[1]

**Learn more at Upneeq.com.**

## INDICATION

Upneeq® (oxymetazoline hydrochloride ophthalmic solution), 0.1% is indicated for the treatment of acquired blepharoptosis in adults.

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

- Alpha-adrenergic agonists as a class may impact blood pressure. Advise Upneeq patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension or hypotension to seek medical care if their condition worsens.
- Use Upneeq with caution in patients with cerebral or coronary insufficiency or Sjögren's syndrome. Advise patients to seek medical care if signs and symptoms of potentiation of vascular insufficiency develop.
- Upneeq may increase the risk of angle closure glaucoma in patients with untreated narrow-angle glaucoma. Advise patients to seek immediate medical care if signs and symptoms of acute narrow-angle glaucoma develop.
- Patients should not touch the tip of the single patient-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

### ADVERSE REACTIONS

Adverse reactions that occurred in 1-5% of subjects treated with Upneeq were punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation, and headache.

### DRUG INTERACTIONS

- Alpha-adrenergic agonists, as a class, may impact blood pressure. Caution in using drugs such as beta blockers, anti-hypertensives, and/or cardiac glycosides is advised. Caution should also be exercised in patients receiving alpha adrenergic receptor antagonists such as in the treatment of cardiovascular disease, or benign prostatic hypertrophy.
- Caution is advised in patients taking monoamine oxidase inhibitors which can affect the metabolism and uptake of circulating amines.

**To report SUSPECTED ADVERSE REACTIONS or product complaints, contact RVL Pharmaceuticals at 1-877-482-3788. You may also report SUSPECTED ADVERSE REACTIONS to the FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

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

**Reference: 1.** Upneeq® (oxymetazoline hydrochloride ophthalmic solution), 0.1%. [Prescribing Information].

RVL PHARMACEUTICALS, INC.

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PM-US-UPN-0197 01/21

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UPNEEQ®
(oxymetazoline hydrochloride ophthalmic solution), 0.1%*

*Each mL of Upneeq contains 1 mg of oxymetazoline hydrochloride, equivalent to 0.09 mg (0.09%) of oxymetazoline free base.

*Eye-Opening Possibilities*

**UPNEEQ® (oxymetazoline hydrochloride ophthalmic solution), 0.1%,* for topical ophthalmic use**

*Each mL of UPNEEQ contains 1 mg of oxymetazoline hydrochloride, equivalent to 0.09 mg (0.09%) of oxymetazoline free base.

**BRIEF SUMMARY: The following is a brief summary only; see full Prescribing Information at https://www.upneeq.com/Upneeq-PI.pdf for complete information.**

## 1 INDICATIONS AND USAGE

UPNEEQ is indicated for the treatment of acquired blepharoptosis in adults.

## 2 DOSAGE AND ADMINISTRATION

Contact lenses should be removed prior to instillation of UPNEEQ and may be reinserted 15 minutes following its administration.

If more than one topical ophthalmic drug is being used, the drugs should be administered at least 15 minutes between applications.

## 4 CONTRAINDICATIONS

None.

## 5 WARNINGS AND PRECAUTIONS

### 5.1 Potential Impacts on Cardiovascular Disease

Alpha-adrenergic agonists may impact blood pressure. UPNEEQ should be used with caution in patients with severe or unstable cardiovascular disease, orthostatic hypotension, and uncontrolled hypertension or hypotension. Advise patients with cardiovascular disease, orthostatic hypotension, and/or uncontrolled hypertension/hypotension to seek immediate medical care if their condition worsens.

### 5.2 Potentiation of Vascular Insufficiency

UPNEEQ should be used with caution in patients with cerebral or coronary insufficiency, or Sjögren's syndrome. Advise patients to seek immediate medical care if signs and symptoms of potentiation of vascular insufficiency develop.

### 5.3 Risk of Angle Closure Glaucoma

UPNEEQ may increase the risk of angle closure glaucoma in patients with untreated narrow-angle glaucoma. Advise patients to seek immediate medical care if signs and symptoms of acute angle closure glaucoma develop.

### 5.4 Risk of Contamination

Patients should not touch the tip of the single patient-use container to their eye or to any surface, in order to avoid eye injury or contamination of the solution.

## 6 ADVERSE REACTIONS

### 6.1 Clinical Trials Experience

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

A total of 360 subjects with acquired blepharoptosis were treated with UPNEEQ once daily in each eye for at least 6 weeks in three controlled Phase 3 clinical trials, including 203 subjects treated with UPNEEQ for 6 weeks and 157 subjects treated with UPNEEQ for 12 weeks. Adverse reactions that occurred in 1-5% of subjects treated with UPNEEQ were punctate keratitis, conjunctival hyperemia, dry eye, blurred vision, instillation site pain, eye irritation, and headache.

## 7 DRUG INTERACTIONS

### 7.1 Anti-hypertensives/Cardiac Glycosides

Alpha-adrenergic agonists, as a class, may impact blood pressure. Caution in using drugs such as beta-blockers, anti-hypertensives, and/or cardiac glycosides is advised.

Caution should also be exercised in patients receiving alpha adrenergic receptor antagonists such as in the treatment of cardiovascular disease, or benign prostatic hypertrophy.

### 7.2 Monoamine Oxidase Inhibitors

Caution is advised in patients taking MAO inhibitors which can affect the metabolism and uptake of circulating amines.

## 8 USE IN SPECIFIC POPULATIONS

### 8.1 Pregnancy

Risk Summary

There are no available data on UPNEEQ use in pregnant women to inform a drug-associated risk for major birth defects and miscarriage. In animal reproduction studies, there were no adverse developmental effects observed after oral administration of oxymetazoline hydrochloride in pregnant rats and rabbits at systemic exposures up to 7 and 278 times the maximum recommended human ophthalmic dose (MRHOD), respectively, based on dose comparison. [see Data]. The estimated background risks of major birth defects and miscarriage for the indicated population are unknown. All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data

*Animal Data*

Effects on embryo-fetal development were evaluated in rats and rabbits following oral administration of oxymetazoline hydrochloride during the period of organogenesis. Oxymetazoline hydrochloride did not cause adverse effects to the fetus at oral doses up to 0.2 mg/kg/day in pregnant rats during the period of organogenesis (28 times the MRHOD, on a dose comparison basis). Oxymetazoline hydrochloride did not cause adverse effects to the fetus at oral doses up to 1 mg/kg/day in pregnant rabbits during the period of organogenesis (278 times the MRHOD, on a dose comparison basis). Maternal toxicity, including decreased maternal body weight, was produced at the high dose of 1 mg/kg/day in pregnant rabbits and was associated with findings of delayed skeletal ossification.

In a rat prenatal and postnatal development study, oxymetazoline hydrochloride was orally administered to pregnant rats once daily from gestation day 6 through lactation day 20. Maternal toxicity was produced at the high dose of 0.2 mg/kg/day (28 times the MRHOD, on a dose comparison basis) in pregnant rats and was associated with an increase in pup mortality and reduced pup body weights. Delayed sexual maturation was noted at 0.1 mg/kg/day (14 times the MRHOD, on a dose comparison basis). Oxymetazoline hydrochloride did not have any adverse effects on fetal development at a dose of 0.05 mg/kg/day (7 times the MRHOD, on a dose comparison basis).

### 8.2 Lactation

Risk Summary

No clinical data are available to assess the effects of oxymetazoline on the quantity or rate of breast milk production, or to establish the level of oxymetazoline present in human breast milk post-dose. Oxymetazoline was detected in the milk of lactating rats. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for UPNEEQ and any potential adverse effects on the breastfed child from UPNEEQ.

### 8.4 Pediatric Use

Safety and effectiveness of UPNEEQ have not been established in pediatric patients under 13 years of age.

### 8.5 Geriatric Use

Three hundred and fifteen subjects aged 65 years and older received treatment with UPNEEQ (n = 216) or vehicle (n = 99) in clinical trials. No overall differences in safety or effectiveness were observed between subjects 65 years of age and older and younger subjects.

## 10 OVERDOSAGE

Accidental oral ingestion of topical intended solutions (including ophthalmic solutions and nasal sprays) containing imidazoline derivatives (e.g., oxymetazoline) in children has resulted in serious adverse events requiring hospitalization, including nausea, vomiting, lethargy, tachycardia, decreased respiration, bradycardia, hypotension, hypertension, sedation, somnolence, mydriasis, stupor, hypothermia, drooling, and coma. Keep UPNEEQ out of reach of children.

## PATIENT COUNSELING INFORMATION

Advise the patient to read the FDA-approved patient labeling (Instructions for Use).

RVL PHARMACEUTICALS, INC.

Manufactured for: RVL Pharmaceuticals, Inc.
Bridgewater, New Jersey 08807

PM-US-UPN-0203 01/21

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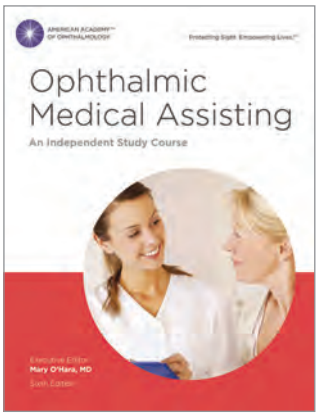


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# Letters


## Gratitude From a Trainee

Thank you very much to Ruth D. Williams, MD, for underscoring the effort put forth by ophthalmologists who practiced beyond their routine work during the COVID-19 pandemic (Opinion, May). It is worth adding that the extent to which ophthalmologists went above and beyond was certainly notable in the realm of medical academia.

The pandemic substantially disrupted traditional structures of educational curricula, including clinical clerkships, and dramatically altered the application season. As a student who just finished clinical clerkships in her third year of medical school, I appreciate all the ophthalmologists who spent additional time and made the extra effort to provide opportunities, mentorship, and guidance to trainees during the pandemic. To cite a few examples of this outreach: Virtual ophthalmology rotations were created.[1] Mentorship matchup opportunities were crafted through surveys and several online platforms. Webinars were held to teach trainees how to work effectively in a virtual environment, especially for conducting interviews. Residency program directors offered their insight and perspectives to applicants.[2] And the Academy provided extra resources for medical students on its website.[3]

The massive effort to help trainees has been a testament to the spirit and character within the community of ophthalmology. Importantly, the collaborative energy inspires the next generation of ophthalmologists to give back to future students.

*Gabriella Schmuter, BS*
*Incoming fourth-year medical student*
*City University of New York School of Medicine, New York*

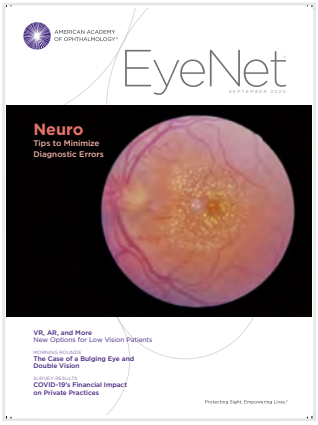
1 Wendt S et al. *Surv Ophthalmol.* 2021;66(2):354-361.
2 Duong AT et al. *Ophthalmology.* 2020;127(11):e95-e98.
3 aao.org/medical-students.

## Rural Practices Have Reached a Tipping Point

I read Dr. Parke's "An Open Letter to Congress: Medicare Payment Policies and a Tipping Point" (Current Perspective, September 2020) with great personal interest. My perspective is that, in rural America, we are not approaching that tipping point but rather have already reached it.

My practice is a long-standing, two-ophthalmologist partnership in rural northern California and southern Oregon. I am 70 years old; my partner is a few years younger. My partner, an excellent surgeon, elected to discontinue doing surgery on Jan. 1, 2020, because it simply was not worth the stress and risk. I've continued surgery only because it is a common need and there is no readily available alternative for our patients. We have both decided to fully retire at the end of 2021.

We are willing to almost give away our practice so that our employees can keep their jobs and our elderly patients can have continued access to care (the next nearest ophthalmologist is about 80 miles away over less-than-ideal roads). And while the pandemic created a tremendous demand for real estate in our relatively spared area, we have been unable to find a younger ophthalmologist who is willing to move to our rural area and take on the rigors and ever-increasing financial risks of private practice.




Reimbursement, particularly for bread-and-butter cataract surgery, is a big part of the issue for our patients. We have contacted other practices in the region to ask if any of the ophthalmologists would come here and do surgery occasionally. None are willing because it is not financially worthwhile for them to do so. A cluster of communities around 90 miles south of us with a combined population of over 60,000 are now served by only one ophthalmologist doing cataract surgery; the others have stopped due to declining reimbursements.

In short, the tipping point has come. The patients in our region will soon have great difficulty accessing ophthalmology care, the primary reason being the reimbursement cuts that have been made to cataract surgery.

*Larry A. Eninger, MD*
*Pacific Vision Medical Center*
*Crescent City, Calif.*

**WRITE TO US.** Send your letters of 150 words or fewer to us at *EyeNet Magazine,* American Academy of Ophthalmology, 655 Beach Street, San Francisco, CA 94109; e-mail eyenet@aao.org; or fax 415-561-8575. (*EyeNet Magazine* reserves the right to edit letters.)

DURYSTA™
(bimatoprost intracameral implant) 10 mcg

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IOP=intraocular pressure.
Not an actual patient.

## INDICATIONS AND USAGE

DURYSTA™ (bimatoprost intracameral implant) is indicated for the reduction of intraocular pressure (IOP) in patients with open angle glaucoma (OAG) or ocular hypertension (OHT).

## IMPORTANT SAFETY INFORMATION

### Contraindications

DURYSTA™ is contraindicated in patients with: active or suspected ocular or periocular infections; corneal endothelial cell dystrophy (e.g., Fuchs' Dystrophy); prior corneal transplantation or endothelial cell transplants (e.g., Descemet's Stripping Automated Endothelial Keratoplasty [DSAEK]); absent or ruptured posterior lens capsule, due to the risk of implant migration into the posterior segment; hypersensitivity to bimatoprost or to any other components of the product.

### Warnings and Precautions

The presence of DURYSTA™ implants has been associated with corneal adverse reactions and increased risk of corneal endothelial cell loss. Administration of DURYSTA™ should be limited to a single implant per eye without retreatment. Caution should be used when prescribing DURYSTA™ in patients with limited corneal endothelial cell reserve.

DURYSTA™ should be used with caution in patients with narrow iridocorneal angles (Shaffer grade < 3) or anatomical obstruction (e.g., scarring) that may prohibit settling in the inferior angle.

Macular edema, including cystoid macular edema, has been reported during treatment with ophthalmic bimatoprost, including DURYSTA™ intracameral implant. DURYSTA™ should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Prostaglandin analogs, including DURYSTA™, have been reported to cause intraocular inflammation. DURYSTA™ should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Ophthalmic bimatoprost, including DURYSTA™ intracameral implant, has been reported to cause changes to pigmented tissues, such as increased pigmentation of the iris. Pigmentation of the iris is likely to be permanent. Patients who receive treatment should be informed of the possibility of increased pigmentation. While treatment with DURYSTA™ can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Intraocular surgical procedures and injections have been associated with endophthalmitis. Proper aseptic technique must always be used with administering DURYSTA™, and patients should be monitored following the administration.

### Adverse Reactions

In controlled studies, the most common ocular adverse reaction reported by 27% of patients was conjunctival hyperemia. Other common adverse reactions reported in 5%-10% of patients were foreign body sensation, eye pain, photophobia, conjunctival hemorrhage, dry eye, eye irritation, intraocular pressure increased, corneal endothelial cell loss, vision blurred, iritis, and headache.

**Please see Brief Summary of full Prescribing Information on the following page.**

**References: 1.** DURYSTA™ [Prescribing Information]. Irvine, CA: Allergan, Inc.; 2020. **2.** Data on file, Allergan, 2020. **3.** Standring S. Orbit and accessory visual apparatus. In: *Gray's Anatomy: The Anatomical Basis of Clinical Practice*. 41st ed. Philadelphia, PA: Elsevier Limited; 2016: 666-708.

Allergan
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# DURYSTA™
(bimatoprost intracameral implant) 10 mcg

**Brief Summary—Please see the DURYSTA™ package insert for full Prescribing Information**

## INDICATIONS AND USAGE
**DURYSTA™** is a prostaglandin analog indicated for the reduction of intraocular pressure (IOP) in patients with open angle glaucoma (OAG) or ocular hypertension (OHT).

## CONTRAINDICATIONS
DURYSTA™ is contraindicated in patients with active or suspected ocular or periocular infections; corneal endothelial cell dystrophy; prior corneal transplantation, or endothelial cell transplants; absent or ruptured posterior lens capsule, due to the risk of implant migration into the posterior segment; or hypersensitivity to bimatoprost or any other components of the product.

## WARNINGS AND PRECAUTIONS
**Corneal Adverse Reactions:** The presence of DURYSTA™ implants has been associated with corneal adverse reactions and increased risk of corneal endothelial cell loss. Administration of DURYSTA™ should be limited to a single implant per eye without retreatment. Caution should be used when prescribing DURYSTA™ in patients with limited corneal endothelial cell reserve.

**Iridocorneal Angle:** Following administration with DURYSTA™, the intracameral implant is intended to settle within the inferior angle. DURYSTA™ should be used with caution in patients with narrow iridocorneal angles (Shaffer grade < 3) or anatomical obstruction (e.g., scarring) that may prohibit settling in the inferior angle.

**Macular Edema:** Macular edema, including cystoid macular edema, has been reported during treatment with ophthalmic bimatoprost, including DURYSTA™ intracameral implant. DURYSTA™ should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

**Intraocular Inflammation:** Prostaglandin analogs, including DURYSTA™, have been reported to cause intraocular inflammation. DURYSTA™ should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

**Pigmentation:** Ophthalmic bimatoprost, including DURYSTA™ intracameral implant, has been reported to cause changes to pigmented tissues, such as increased pigmentation of the iris. Pigmentation of the iris is likely to be permanent. Patients who receive treatment should be informed of the possibility of increased pigmentation. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. While treatment with DURYSTA™ can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

**Endophthalmitis:** Intraocular surgical procedures and injections have been associated with endophthalmitis. Proper aseptic technique must always be used with administering DURYSTA™, and patients should be monitored following the administration.

## ADVERSE REACTIONS
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.

The most common ocular adverse reaction observed in two randomized, active-controlled clinical trials with DURYSTA™ in patients with OAG or OHT was conjunctival hyperemia, which was reported in 27% of patients. Other common ocular adverse reactions reported in 5-10% of patients were foreign body sensation, eye pain, photophobia, conjunctival hemorrhage, dry eye, eye irritation, intraocular pressure increased, corneal endothelial cell loss, vision blurred, and iritis. Ocular adverse reactions occurring in 1-5% of patients were anterior chamber cell, lacrimation increased, corneal edema, aqueous humor leakage, iris adhesions, ocular discomfort, corneal touch, iris hyperpigmentation, anterior chamber flare, anterior chamber inflammation, and macular edema.

The following additional adverse drug reactions occurred in less than 1% of patients: hyphema, iridocyclitis, uveitis, corneal opacity, product administered at inappropriate site, corneal decompensation, cystoid macular edema, and drug hypersensitivity.

The most common nonocular adverse reaction was headache, which was observed in 5% of patients.

## USE IN SPECIFIC POPULATIONS
**Pregnancy:** There are no adequate and well-controlled studies of DURYSTA™ administration in pregnant women to inform a drug associated risk. Oral administration of bimatoprost to pregnant rats and mice throughout organogenesis did not produce adverse maternal or fetal effects at clinically relevant exposures. Oral administration of bimatoprost to rats from the start of organogenesis to the end of lactation did not produce adverse maternal, fetal or neonatal effects at clinically relevant exposures.

In embryo/fetal developmental studies in pregnant mice and rats, abortion was observed at oral doses of bimatoprost which achieved at least 1770 times the maximum human bimatoprost exposure following a single administration of DURYSTA™ (based on plasma $C_{max}$ levels; blood-to-plasma partition ratio of 0.858).

In a pre/postnatal development study, oral administration of bimatoprost to pregnant rats from gestation day 7 through lactation resulted in reduced gestation length, increased late resorptions, fetal deaths, and postnatal pup mortality, and reduced pup body weight at 0.3 mg/kg/day (estimated 470-times the human systemic exposure to bimatoprost from DURYSTA™, based plasma $C_{max}$ and a blood-to plasma partition ratio of 0.858). No adverse effects were observed in rat offspring at 0.1 mg/kg/day (estimated 350-times the human systemic exposure to bimatoprost from DURYSTA™, based on plasma $C_{max}$).

**Lactation:** There is no information regarding the presence of bimatoprost in human milk, the effects on the breastfed infants, or the effects on milk production. In animal studies, topical bimatoprost has been shown to be excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when DURYSTA™ is administered to a nursing woman.

The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for DURYSTA™ and any potential adverse effects on the breastfed child from DURYSTA™.

**Pediatric Use:** Safety and effectiveness of DURYSTA™ in pediatric patients have not been established.

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

## NONCLINICAL TOXICOLOGY
**Carcinogenesis, Mutagenesis, Impairment of Fertility**
Bimatoprost was not carcinogenic in either mice or rats when administered by oral gavage at doses up to 2 mg/kg/day and 1 mg/kg/day respectively for 104 weeks (approximately 3100 and 1700 times, respectively, the maximum human exposure [based on plasma $C_{max}$ levels; blood-to-plasma partition ratio of 0.858]).

Bimatoprost was not mutagenic or clastogenic in the Ames test, in the mouse lymphoma test, or in the *in vivo* mouse micronucleus tests.

Bimatoprost did not impair fertility in male or female rats up to doses of 0.6 mg/kg/day (1770-times the maximum human exposure, based on plasma $C_{max}$ levels; blood-to-plasma partition ratio of 0.858).

## PATIENT COUNSELING INFORMATION
**Treatment-related Effects:** Advise patients about the potential risk for complications including, but not limited to, the development of corneal adverse events, intraocular inflammation or endophthalmitis.

**Potential for Pigmentation:** Advise patients about the potential for increased brown pigmentation of the iris, which may be permanent.

**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.

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# Opinion

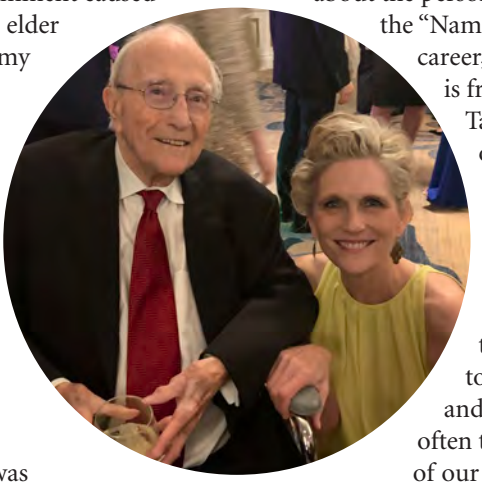
RUTH D. WILLIAMS, MD, CHIEF MEDICAL EDITOR, *EYENET*

## Ophthalmologist the Elder

Arnold Schwarzenegger recently referred to himself as an "elderly statesman," a statement that felt odd given his movie roles. But his comment caused me to reflect on the question: What is an elder statesman? A photo of a 95-year-old Jimmy Carter building houses with Habitat for Humanity comes to mind, a reminder that this former president has become a symbol for volunteerism, human rights, and economic development. An elder is someone who may or may not still have an active career but whose presence reminds us of our deeper values.

What are the qualities of an elder in the ophthalmology community?

I think of Stanley Truhlsen, now 100 years old. One of my favorite moments was kneeling beside his wheelchair at the 2019 Orbital Gala when I felt overwhelming respect and affection for him. Dr. Truhlsen certainly had a remarkable career in ophthalmology. He was Academy president in 1983, editor of the Academy's journal, and on the board of Nebraska Blue Cross Blue Shield, and he helped make the Truhlsen-Marmor Museum of the Eye possible. But it is his kindness, his humility, his integrity, and his life of service that makes him an elder. Stan Truhlsen, by his mere presence, is a reminder that our daily work and our achievements are in service of patients and the public good.



*Stanley Truhlsen, MD, and Ruth Williams, MD*

Closer to home, our practice has an annual award that recognizes a physician who embodies our idea of a great colleague. The awardee is selected by the previous year's honoree, who prepares a presentation about why the person was chosen. We struggled to name the award. After first calling it the Golden Globe Award and then the Collegiality Award (which reminded me of a Miss America contest), we finally decided to name it after a beloved and now retired partner. Doing so described the intent of the award better than any catchy phrase. He is our elder.

Named lectures are a tradition in academic medicine, and speakers are chosen each year for their expertise, innovative treatments, and fresh perspectives. One of the more interesting aspects of giving a named lecture is to prepare comments about the person for whom the lecture is named. Often the "Named" person had a remarkable academic career, but it's the person's character that is frequently highlighted in the speech. Talking about the giants in ophthalmology cultivates the values of an organization. What is said about previous leaders is a clue to the core values of a medical group or program.

Elders don't have to be elderly, though. Sometimes the people who teach us the most about what it means to be a physician are active clinicians and academicians. Fellowship training is often the most intense mentoring experience of our career, though it can be decades before the full impact of those relationships is realized. Sarwat Salim, who did her glaucoma fellowship with Bruce Shields, recently told me that he still stays in close contact with her. She credits Bruce with teaching her not only how to be a glaucoma specialist but also how to treat patients with dignity and colleagues with kindness.

Let's recognize our elders and our mentors. The Academy's Foundation is offering a unique opportunity to honor our mentors (aao.org/foundation/honor-a-mentor). Foundation Chair—and mentor to many—Greg Skuta said, "All of us have been profoundly impacted by special mentors during our careers, whether a particularly memorable teacher during our residency or fellowship or a treasured colleague who has helped guide us professionally and personally."

In a tribute to Dan Jones, Jane Edmond wrote, "I love and admire DBJ's brilliance, memorable bon mots, and instilling in me the drive to strive for excellence." With a tribute gift to the Foundation, you and your mentor will be acknowledged in next year's Foundation annual report.

I can't wait to read about the people who have shaped each of you and shaped our profession. And next month: Ophthalmologist the Younger.

# Current Perspective

DAVID W. PARKE II, MD

## The MOM Program

The goal of the Minority Ophthalmology Mentoring (MOM) program is to provide support to medical students from groups underrepresented in ophthalmology (relative to the patient population) so that they will strongly consider choosing ophthalmology as a career path. They come from a broad spectrum of backgrounds and medical schools. Most are rising second-year medical students.

The program was born not in response to the events of last year, but in 2016 after data emerged revealing that although certain minority groups make up over 30% of the U.S. population, they constituted only 6% of practicing ophthalmologists. Further, the percentage of ophthalmologists who are Black had not increased in decades.

Why is this so important? Studies have shown that, in general, patients prefer to go to physicians of the same color or ethnicity. They see physicians more often and have better outcomes of care. And physicians of color practice in communities of color more often than other physicians. This is important to the health of our communities.

This is not just an issue in ophthalmology, but throughout medicine. The racial and ethnic groups underrepresented in medicine (URIM) constitute only about 8% of the physician population. There are a host of factors contributing to this disparity, and at the top of the list is a paucity of compelling role models and mentors. Think about why you chose ophthalmology. The odds are that either in your personal life or in your medical school career you had an ophthalmologist role model. You said, "I want to be like that person."

What happens if you can't envision that? One Black physician colleague said, "You have to be able to see your own dreams." And it's not just a single version of the dream—each person has their own narrative. There is not one standard image of a Black male ophthalmologist any more than there is of any subgroup of physicians—women/men; Black/Brown/White; rural/urban; privileged/poor upbringing.

There is also what has been called "the soft bigotry of low expectations." It is a special challenge to excel when those around you—be it friends, teachers, colleagues, and even patients—don't anticipate excellence.

The MOM program exists to provide mentorship and preparatory resources to enable ophthalmology resident applicants to succeed. The Academy serves as a steward both for our profession and for eye care in our communities. Helping to develop and support an ophthalmology workforce that meets the needs of our diverse American community is part of our collective mission.

***David W. Parke II, MD***
*Academy CEO*

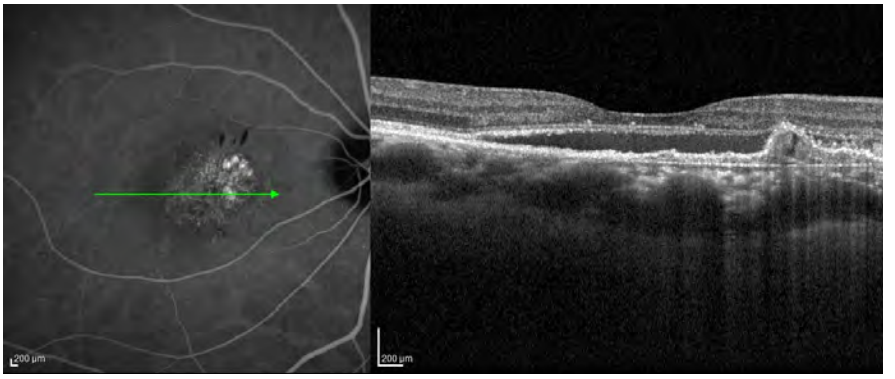
The yearlong MOM program has increased from 25 students in its first year to about 100 this year. It includes sessions in preparing for standardized exams; career choice; networking with faculty, residents, and community ophthalmologists; skills transfer; a visit to the Annual Meeting; and ongoing mentorship.

Does it work? One student wrote, "It was empowering to see such diverse physicians make it to their dream field. I am inspired . . ." MOM graduates have already been accepted at over 15 residency programs. More than 240 Academy member ophthalmologists have been mentors or program participants!

This is not solely an Academy program. The Association of University Professors of Ophthalmology is a multiyear (and critically important) partner. The Alcon Foundation, Genentech, Mallinckrodt Pharmaceuticals, and Dompé are major corporate supporters. The Academy Leadership Development Program XXI Class of 2019 came together with a major gift. The American Board of Ophthalmology, Women in Ophthalmology, and most ophthalmology subspecialty societies stepped up as well.

Finally, this would not be possible without the leadership over these years of some of our volunteer colleagues who have a shared passion. It is a very long list, but I must in particular mention Drs. Keith Carter, Michelle Latting, Cesar Briceno, Mildred Olivier, and Susan Forster.

For more information about the program, its sponsors, and its incredible volunteers, please go to aao.org/minority-mentoring.




***CRITICAL CLUE.*** *PCV is characterized by subretinal neovascularization between the RPE and Bruch membrane, dilated polypoidal lesions, and a branching vascular network. In these images, an inverted U-shape elevation of the RPE on the OCT B-scan (right) corresponds to the polypoidal lesion on the ICG angiogram (left). The green arrow on the angiogram identifies the location of the image on the OCT B-scan.*

RETINA

## OCT B-Scans Pin Down Dx of PCV

**TO DATE, CLINICIANS HAVE HAD** trouble distinguishing polypoidal choroidal vasculopathy (PCV) from age-related macular degeneration (AMD). But researchers at the University of Hawaii have found that OCT B-scans can detect a characteristic structural feature of PCV.[1]

**Tell-tale sign.** Gregg T. Kokame MD, MMM, at the University of Hawaii in Honolulu, and his coauthors conducted a retrospective study of case records on 112 eyes with AMD (106 patients). Sixty-nine of the eyes had been diagnosed with PCV using indocyanine green angiography (ICGA). Comparison to the patients' pre- and post-treatment OCT B-scans showed that there was a characteristic sign of PCV: an inverted U-shaped elevation of the retinal pigment epithelium (RPE) that was usually located between the RPE and Bruch membrane. The location of this feature on OCT B-scans correlated to the sites of polypoidal lesions on ICGA.

**Critical timing.** However, the U-shaped elevations were visible primarily before beginning treatment, Dr. Kokame said. "We showed that if you only looked at the after-treatment OCT B-scan, only a quarter of the eyes with PCV were diagnosed. But if you looked at the before-treatment B-scan, the correct diagnosis was reached in 56% of the known PCV cases," he said.

**A cause of anti-VEGF resistance?** PCV is a subtype of exudative AMD that predominates among Asian populations, although it occurs, to a lesser degree, in other ethnic groups. Awareness of the clinical importance of this subtype has risen in the last decade as researchers sought to explain why some AMD eyes were resistant to anti-VEGF therapy. It now is thought that unrecognized PCV might be a factor, Dr. Kokame said.

**Need to tailor treatment.** According to a recent report from the EVEREST II clinical trial, PCV responds better to combined photodynamic therapy plus ranibizumab than it does to ranibizumab alone.[2]

Consequently, it is important for ophthalmologists who treat AMD to be able to identify possible PCV cases early, even though the traditional technology for doing so often is not available in many clinical settings, Dr. Kokame said. "Usually to get the best diagnosis of PCV requires specialized equipment, such as ICGA with the scanning laser ophthalmoscope, plus the ability to read an ICG angiogram, which most practitioners don't have access to," he said. "But almost every practice in ophthalmology has access to OCT, and the B-scan is one thing that just about every ophthalmologist knows how to look at."

As ICGA is often not available, not ordered, or not comfortably read, OCT could help practices identify many patients who otherwise might not be considered for combination therapy, Dr. Kokame said. He added, "We want all ophthalmologists treating exudative macular degeneration to understand that polypoidal choroidal vasculopathy is the most important subtype of AMD."

Specifically, PCV "acts differently from typical exudative macular degeneration, with higher resistance to current medications; it might be susceptible to alternative therapy; and it is predictive of response to different medications," Dr. Kokame said. "We want them to learn to diagnose PCV in the majority of cases with the equipment that they do have available, the OCT B-scan."

*—Linda Roach*

1 Kokame GT et al. *Ophthalmol Retina.* Published online May 19, 2021.
2 Lim TH et al. *JAMA Ophthalmol.* 2020;138(9):935-942.

**Relevant financial disclosures**—Dr. Kokame: None.

Gregg T. Kokame, MD, MMM

DRUG DELIVERY

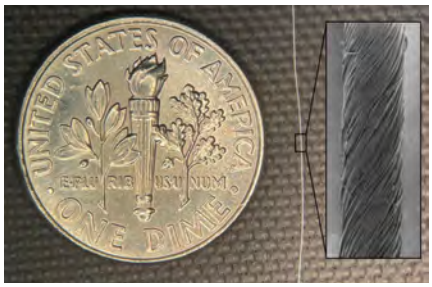
# Drug-Loaded Sutures Developed

**BY TWISTING NANOMETER-SCALE** polymer strands into thin ropes, researchers at the Wilmer Eye Institute in Baltimore have found their way to what arguably represents a Holy Grail of ophthalmic surgery: a resilient ultrathin suture material capable of delivering an antibiotic to ocular wound sites for days or weeks.[1]

**Tackling a challenge.** Currently, the only globally marketed drug-eluting sutures are coated with the antibacterial and antifungal agent triclosan. Given their size (U.S.P. sizes 6-0 through 0), these triclosan-loaded sutures are used only in general surgery.[1]

In ophthalmology, the advent of ultrathin drug-loaded sutures could virtually vanquish a number of infection-control challenges, including poor patient compliance with topical eyedrops and suture-related infections. Moreover, the researchers wrote, they could "reduce the need for oral antibiotic use, decrease the risk of infection associated with implantable ocular devices, and serve as an alternative to the more than 12 million nylon sutures used [globally] in ocular procedures each year."[1]

**Starting with levofloxacin.** The researchers reported on incorporating the broad-spectrum antibiotic levofloxacin into nanofibers made from polycaprolactone (PCL), which is a biocompatible polymer. But other tests, not yet published, have shown that the methodology also works with other antibiotics and with steroids, said co–corresponding author Laura M. Ensign, PhD, at Wilmer's Nanomedicine Division.




***COMPARISON.*** *In this composite image, a 10-0 size antibiotic-eluting multifilament nanofiber suture is shown next to a U.S. dime. The high-resolution scanning electron microscopy image (right) shows nanoscale structural detail.*

**Novel application of an old lab technique.** The group chose PCL for the sutures because it degrades slowly over 12 to 24 months, making it usable for suturing corneal grafts, and because PCL is already a component of several

NEURO-OPHTHALMOLOGY

# Subretinal Fluid in NAION

**USING SPECTRAL-DOMAIN OCT, RESEARCHERS OB-**served subretinal fluid in the macula in a substantial number of patients with nonarteritic anterior ischemic optic neuropathy (NAION).[1] The findings, consistent with earlier studies, confirm that NAION is not just an isolated optic nerve process but is associated with retinal abnormalities that may contribute to vision loss.

"Documenting the presence of subfoveal fluid is important since it can be associated with reduced visual acuity, which is classically preserved in nonarteritic AION, as well as in papilledema," said Thomas R. Hedges III, MD, at Tufts University School of Medicine and the New England Eye Center (NEEC) in Boston.

In previous OCT studies, NEEC researchers observed the presence of subretinal fluid in patients with papilledema, and they subsequently saw fluid in patients with NAION.[2] This latest study, using higher-resolution OCT, affirms those findings.

**Findings.** For this study, 20 patients (25 eyes) diagnosed with NAION between 2013 and 2017 were evaluated using SD-OCT. All patients presented within four weeks of symptom onset; five had a history of NAION in the fellow eye. NAION was diagnosed on the basis of typical clinical presentation, including, among other findings, painless sudden vision loss and altitudinal visual field defects accompanied by swelling of the optic disc with hemorrhages.

Peripapillary subretinal fluid was present in 16 eyes (64%). Of those, subretinal fluid extended into the macula to produce subfoveal edema in four eyes (16%). About one month after initial presentation, the subfoveal fluid resolved in three of these eyes, and visual acuity (VA) improved in two. VA declined in one eye and remained unchanged in another.

Other retinal findings included intraretinal cysts and hyperreflective dots. However, their significance is unclear, the researchers said.

**Looking for vitreoretinal changes.** OCT revealed a variety of vitreopapillary interface abnormalities, but their presence does not suggest that the vitreous plays any role in the pathogenesis of AION, Dr. Hedges said. Specifically, there was no evidence of a primary role for vitreopapillary traction (VPT) in the presence of optic disc edema. What's more, neither of the two asymptomatic patients with optic disc swelling had VPT.

**Treatment implications.** Dr. Hedges stressed the importance of these findings in treatment trials of NAION, where determining which patients have subfoveal fluid in different treatment groups is critical to interpreting the results. "The reduction in central vision spontaneously resolves in most patients, which can be helpful for prognosis," he said. "It will be important to understand what is being treated, the optic neuropathy or the secondary effects on the retina." *—Miriam Karmel*

1 Molaie AM et al. *J Neuro-Ophthalmol.* Published online April 26, 2021.

2 Hedges TR et al. *Arch Ophthalmol.* 2008;126:812-815.

**Relevant financial disclosures**—Dr. Hedges: None.

Aditya Josyula, Johns Hopkins University

medical products, including thicker general surgery sutures, Dr. Ensign said.

Early tests showed that levofloxacin could be loaded into single, extruded monofilaments, but this reduced their tensile strength to 10% of what is required for ophthalmic sutures, she said. Instead, the researchers created a new electrospinning process to produce and twist nanofibers together.

"Electrospinning is a very old lab technique. The idea is that you're using a syringe system and voltage to shoot out polymer threads," Dr. Ensign said. "The uniqueness of the way we set it up is that, instead of the fibers randomly shooting onto a flat plate, we collect them in a perpendicular fashion, and a rotating motor twists the fibers together to give you a strong, composite nanofiber suture in the end."

**Finished product.** The finished product consists of hundreds of levofloxacin-loaded nanofibers, twisted together 1,576 times to make 10-0 sutures that are 28 µm in diameter. According to the researchers, the new nanofiber sutures demonstrated biocompatibility comparable to conventional nylon sutures. In addition, they retained 96% of breaking strength over 31 days and delivered levofloxacin at detectable levels in rat eyes for at least 30 days.[1]

The team also evaluated their manufacturing platform's ability to produce sutures equivalent in size to 9-0 and 8-0 ophthalmic sutures.

**What's next?** Several Wilmer surgeons are now testing the sutures' ease of use in a wet lab, and, with the right investment, clinical testing could begin within two years, Dr. Ensign said. "We really want to make something that works as well as nylon and that the surgeon can actually enjoy using," she said. "We don't want a product that doesn't do what the surgeon needs."

*—Linda Roach*

1 Parikh KS et al. *Bioeng Transl Med.* 2021;6(2): e10204.

**Relevant financial disclosures**—Dr. Ensign: Co-inventor on patent applications describing the suture technology; Research to Prevent Blindness: S; Robert H. Smith Family Foundation: S.

GLAUCOMA

# Avoiding Glaucoma Malpractice Cases

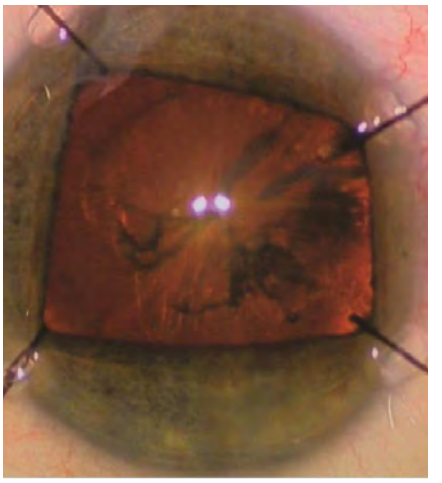
**AN ANALYSIS OF CAUSES AND OUT-**comes of malpractice litigation among patients with glaucoma suggests that risk to both patients and providers can be reduced by conducting careful examinations and documenting detailed conversations with patients.[1] The analysis revealed that nearly 40% of cases involved allegations of mismanagement or failure to diagnose and treat. Adverse drug effects and surgical complications also resulted in litigation.

"Our study confirms much of what has been reported, and it reinforces the need for risk management to be a part of clinical care," said Ashvini K. Reddy, MD, in private practice in San Antonio, Texas.

**Disproportionately high awards.** The researchers identified 69 glaucoma malpractice cases in the WestLaw database occurring between 1962 (the first year in which cases were reported) and 2014. Well over half (62.3%) resolved in favor of defendants. Eight jury verdicts awarded a mean of $994,260 to plaintiffs, while 10 cases settled with a mean indemnity of $1.2 million. (Amounts were adjusted for inflation in 2015 dollars.)

Although the rate of glaucoma plaintiff verdicts mirrored ophthalmology overall, median awards were 1.7 times higher than the whole—$977,474 in glaucoma versus $604,352 for all of ophthalmology.

**Common scenarios.** Of the 69 cases, 35 (50.7%) involved allegations of insufficient intervention, such as failure to diagnose or treat, and failure to monitor properly through intraocular pressure (IOP) checks, dilated examinations, and visual field (VF) testing. Thirteen cases (18.8%) involved failure to diagnose or treat and/or mismanagement of angle-closure glaucoma, and 12 cases (17.4%) involved failure to diagnose open-angle glaucoma. Of 10 varied surgical and procedural claims, six involved trabeculectomy.



***COMMON MISTAKES.*** *Nearly 25% of the claims involved either angle-closure glaucoma (shown here) or open-angle disease.*

**An unexpected finding.** While adverse effects of glaucoma medications were not common (10; 14.5%), the median award value of nearly $1 million was a surprise, Dr. Reddy said. All but two of 10 cases involving topical glaucoma medication resulted in payments, including a $1.3 million settlement for an elderly woman with a known history of asthma who sustained permanent brain damage after being administered timolol.

**Examine, talk, document.** Challenges inherent to glaucoma—such as its chronicity and the ongoing need to revise disease management—may explain the disproportionately high awards, the researchers noted. They advised routine IOP measurements, visual field testing, and dilated exams for all glaucoma suspects.

Dr. Reddy stressed the importance of communication, especially with patients who have aggressive disease, guarded prognoses, or poor outcomes. "These patients are particularly high risk and need to be very involved in decisions. Documentation of their involvement is also important."

*—Miriam Karmel*

1 Engelhard SB et al. *Ophthalmol Glaucoma.* 2021; 4(4): in press.

**Relevant financial disclosures**—Dr. Reddy: Alimera: C; Clearside: C; Eyepoint: C; Heidelberg: C.

**See the financial disclosure key,** page 10. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.

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*Low-dose OTC brimonidine. †Low-dose brimonidine is an α2-AR agonist that primarily constricts the venule. [1]McLaurin E, et. al. *Optom Vis Sci*. 2018;95(3):264-271. ‡In clinical trials, one case of rebound redness was reported. §In Home Use Test, March 2018. n=301.



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# Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

## *Ophthalmology*

Selected by Stephen D. McLeod, MD

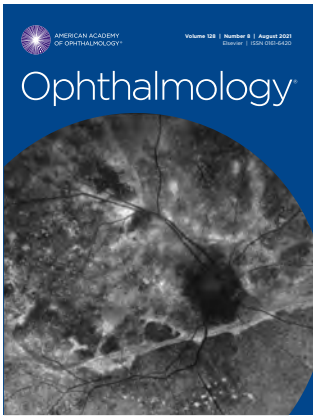
### Ophthalmology Faculty: Diversity Needed

August 2021

**Fairless et al.** assessed the ethnic demographics of the faculty members in U.S. medical school departments. They found that ophthalmology departments have among the fewest minority faculty members (6.8%). In contrast, the obstetrics and gynecology sector has the most (15.7%).

For this study, the researchers analyzed data from the 2019 faculty roster of the Association of American Medical Colleges. The proportions of underrepresented minority (URM) faculty, including chairs, were calculated for ophthalmology and 17 other clinical departments. In addition, the percentage of URM ophthalmology faculty was compared with the proportion of URM persons among graduates of medical schools and with the U.S. population at large. For this study, URM denoted persons who are Black, Hispanic/Latinx, Native American, Native Hawaiian, or Pacific Islander.

The dataset included nearly 158,000 faculty members. Of these, 3,060 were from ophthalmology departments. URM prevalence was significantly higher among all faculty combined (9.8%) than in the ophthalmology sector (6.8%). Moreover, ethnic diversity was lower for ophthalmology faculty than for graduating medical students or the overall U.S. population.




Of the 18 medical departments studied, ophthalmology had the third-lowest percentage of URM faculty; only radiology and orthopedics fell further behind. The difference between ophthalmology and other departments was statistically significant for 12 of the 18 comparisons.

To achieve parity with other clinical education programs and the diverse populations that physicians serve, work is needed to increase URM ophthalmology faculty, said the authors.

### Which LPI Location Is Best?

August 2021

Laser peripheral iridotomy (LPI) is a common treatment for angle closure. However, consensus is lacking on the optimal location for iridotomy. **Xu et al.** looked at anatomic changes after LPI and developed statistical models to determine predictors of angle widening and angle opening. They found that angle widening was significantly greater when the LPI location was superior as opposed to temporal or nasal.

The study population included Chinese patients between 50 and 70 years (84% female), identified from the Zhongshan Angle Closure Prevention study. At baseline, all patients were suspected of having primary angle closure, defined as inability to visualize pigmented trabecular meshwork in two or more quadrants on static gonioscopy. Each patient had LPI performed on one eye in the superior location (between 11 and 1 o'clock; n = 219) or the temporal or nasal location (at or below 10:30 or 1:30 o'clock, respectively; n = 235). OCT imaging of the anterior segment and gonioscopy were performed at baseline and two weeks after LPI. One or two images per eye, oriented along the horizontal and/or vertical meridians, were analyzed with software that automatically segmented anterior segment structures and produced biometric measurements that corresponded to scleral spur markings. Thirteen biometric parameters that describe the anterior segment were explored.

The analyses showed significant differences in all biometric parameters from baseline to two weeks post-treatment ($p < .006$), except for iris thickness at 2,000 μm from the scleral spur. Residual signs of angle closure after LPI were evident in 120 eyes (26.4%). According to multivariate regression analyses, predictors of greater angle widening were superior LPI location, smaller angle-opening distance measured 750 μm from the scleral scar, and greater iris curvature. Predictors of insufficient widening were temporal and nasal LPI locations and smaller mean gonioscopy grades.

Based on these findings, the authors recommend that eye care providers consider the superior LPI location to optimize anatomic changes after LPI. Even so, they cautioned that long-term clinical outcomes and potential risks are unclear at this time.

### Young Children Need Higher Atropine Doses

August 2021

Although low-dose atropine has shown promise for myopia control in children, the responses to treatment vary widely. In the Low-Concentration Atropine for Myopia Progression (LAMP) study, the spherical equivalent (SE) reductions over one year ranged from 27% to 67% for atropine concentrations of up to 0.05%. In a secondary analysis of LAMP data, **Li et al.** aimed to elucidate factors related to poor treatment response. They found that younger age predicts lower response, whereas baseline SE and parental myopia status did not affect the responses.

Of the original 438 children recruited for the LAMP study, 350 completed two years and were included in the follow-up study. Patients were categorized by age (4-6 years, 7-9 years, and 10-12 years) and were assigned randomly to receive atropine 0.05%, 0.025%, 0.01%, or placebo. In the second year, those initially given placebo received 0.05% atropine. Generalized estimating equations were used to evaluate potential predictors of change in SE and axial length (AL); these included age, gender, baseline refraction, parental myopia status, and other factors.

During both years of treatment, younger age was the only predictor of faster SE progression and AL elongation; the youngest group had the weakest treatment response. During the two-year period, myopia progression of 10-year-olds in the 0.01% group was similar to that of 8-year-olds in the 0.025% group and of 6-year-olds in the 0.05% group. For each younger-age year, the mean SE change was 0.14 D larger in the 0.05% group, 0.15 D larger in the 0.025% group, and 0.20 D larger in the 0.01% group. Although age and atropine concentration were significant risk factors for SE progression and AL elongation, there was no interaction between the two, indicating that they influence myopia progression independently.

All concentrations of atropine were well tolerated, regardless of age. The mean accommodation amplitude decreased with age, but the mean changes in photopic pupil size were similar among treatment and age groups, as were the rates of photophobia and use of photochromic glasses. These results suggest that among the factors studied, age was the only predictor of response to atropine treatment. For children under 7 years of age, the highest concentration (0.05%) is required to attain efficacy similar to that of smaller doses in older children. *(Also see Clinical Update, page 30.)*

*—Summaries by Lynda Seminara*

## Ophthalmology Glaucoma

Selected by Henry D. Jampel, MD, MPH

### Marijuana, Glaucoma, and Social Media

July/August 2021

**Jia et al.** conducted an analysis of social media content on glaucoma and medical cannabis. They found robust support of cannabis for glaucoma patients, despite recommendations against its use by such organizations as the American Glaucoma Society and the Academy.

For this internet-based study, the researchers identified online information on Google, Facebook, and YouTube. The top 20 searches for Google and YouTube and the posts from the top nine patient-based glaucoma groups on Facebook were aggregated and analyzed. Each post, website, or video was evaluated for quality using Sandvik and risk scoring methodology. Additional analysis included whether the source was professional; these were further separated into ophthalmology/optometry and non–eye care sources.

The search resulted in an aggregate of 51 websites on Google, 126 posts from Facebook groups, and 37 videos on YouTube. Of note, the number of members in the Facebook support groups ranged from 600 to more than 16,000. A significant portion of online material promoted cannabis use by glaucoma patients (24% of Google, 59% of YouTube, and 21% of Facebook results). Content from professional sources had a higher content quality score and a lower risk score and was less likely to support cannabis use. However, 11% and 27% of professional opinions on Google and YouTube, respectively, were pro-cannabis use. Upon further clarification, these professional opinions either were outdated, from non–eye care sources, or linked to cannabis organizations.

"It is important for physicians to be aware of the different platforms and opinions that are readily shared among patients," the authors said, and they recommended directing patients to better-quality professional information on the topic. *—Summary by Jean Shaw*

## Ophthalmology Retina

Selected by Andrew P. Schachat, MD

### Changes in Treatment Paradigms and AMD Outcomes

August 2021

**Schwartz et al.** set out to describe treatment strategies for neovascular age-related macular degeneration (AMD) over a decade and determine their impact on visual outcomes. They found that, despite the evolution in treatment, patients continue to lose vision after the first year of anti-VEGF injections.

For this retrospective study, the researchers analyzed electronic health records from 27 National Health Service secondary care providers in the United Kingdom. Treatment-naive patients who received at least three intravitreal anti-VEGF injections in their first six months of follow-up were included. Those with a previous diagnosis of retinal vein occlusion, diabetic macular edema, or proliferative diabetic retinopathy were excluded. Eyes with at least three years of follow-up were grouped by years of treatment initiation, and three-year outcomes were compared between the groups.

A total of 13,705 patients (15,810 eyes) were included. All patients were

treated between September 2008 and December 2018, and 194,904 injections were provided. Visual acuity (VA) improved from baseline during the first year but dropped in the second and third years of treatment, a trend that did not change over time. Although an increasing proportion of patients retained functional VA and were able to continue driving as the decade progressed, this was linked to a trend of better baseline VA at start of treatment.

The data suggest that these results may be related to suboptimal treatment patterns, the researchers said. They noted that rethinking treatment strategies may be warranted, "possibly on a national level or through the introduction of longer-acting therapies."

*—Summary by Jean Shaw*

## Ophthalmology Science

Selected by Emily Y. Chew, MD

### Choroidal Thickness and Systemic Health of Preterm Infants

June 2021

**Michalak et al.** used handheld OCT to analyze the impact of systemic health factors on choroidal thickness in preterm infants. They found that a thinner choroid in these infants may be related to a slower growth rate in the first weeks of life and the need for prolonged use of supplemental oxygen.

The researchers enrolled 118 preterm infants as part of the prospective, longitudinal BabySTEPS study. Both eyes of the infants were imaged with a handheld investigational swept-source OCT system at multiple time points during their stay in the intensive care nursery. Custom segmentation software was used to delineate the central 1 mm subfoveal choroidal thickness on OCT images. Errors in segmentation were manually corrected. Univariable and multivariable linear regression analyses were performed to evaluate factors associated with choroidal thickness. Maternal and infant clinical health data were collected. The main outcome was the association between infant health factors and choroidal thickness.

For this analysis, data were used from 85 infants (170 eyes) at 36 ± 1 weeks postmenstrual age (PMA). Subfoveal choroidal thickness could be measured in 82 of the 85 infants (159 eyes). Mean choroidal thickness was 233 ± 75 µm. The infants' mean birth weight was 968 ± 271 g, and their mean gestational age was 28 ± 2 weeks.

The results showed that a thinner choroid is independently associated with slower postnatal growth velocity and the use of supplemental oxygen. In addition, a thinner choroid was associated with several other systemic health conditions, including baseline health metrics and cardiac and pulmonary abnormalities. Of these, the most common systemic factors were pulmonary and were related to the need for supplemental oxygen, which was the one statistically significant factor in the multivariable analyses.

As BabySTEPs is a longitudinal study, these children will be studied up to school age, with follow-up data on visual outcomes to be published at that time.

*—Summary by Jean Shaw*

## American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

### Characteristics of Uveitis in Spondyloarthritis

August 2021

Spondyloarthritis denotes a spectrum of diseases with overlapping skeletal and extra-articular features. Although its most common extra-auricular sign is acute anterior uveitis (AAU), spondyloarthritis goes undiagnosed in nearly 40% of patients with uveitis. **Bilge et al.** looked at the frequency and features of AAU in a nationwide cohort of Turkish patients with spondyloarthritis of various subtypes. They found that radiographically observed damage and long duration of disease were linked to elevated uveitis risk.

The data source for this study was the TReasure registry, which includes detailed information on patients with inflammatory arthritis in regions throughout Turkey. The authors recorded data for patients with concurrent spondyloarthritis and uveitis, including the timing of uveitis diagnosis, the number of attacks, and whether the involvement was unilateral or bilateral. History of uveitis was defined as AAU diagnosed by an ophthalmologist.

The study cohort included 4,297 patients; of these, 475 (11%) had experienced at least one episode of uveitis. Uveitis was more common in patients older than age 60 years ($p < .001$) and in those with a smoking history ($p = .004$), arthritis ($p < .001$), diagnostic delay ($p = .001$), disease lasting at least five years ($p < .001$), HLA-B27 positivity ($p < .001$), family history of spondyloarthritis ($p < .001$), or radiographic evidence of damage ($p < .001$). Uveitis was most prevalent in patients with ankylosing spondylitis and was less common in those with psoriasis or psoriatic arthritis.

Given these results, the authors recommend that eye care providers ask patients with uveitis about back pain and arthritis and refer them to a rheumatologist for a full spondyloarthritis workup. Collaboration between rheumatology and ophthalmology is crucial for optimal care of patients with uveitis, said the authors. To their knowledge, this study represents the largest cohort of patients with coexisting spondyloarthritis and uveitis.

### Cluster of TASS Cases After Cataract Surgery

August 2021

Toxic anterior segment syndrome (TASS) is characterized by acute noninfectious inflammation of the anterior segment. **Imamachi et al.** reviewed seven cases (four patients) of TASS that occurred shortly after placement of the same type of IOL during cataract surgery. The procedures were performed by three surgeons at two facilities. The author stressed the importance of prompt diagnosis and treatment to preserve vision.

Among 162 eyes that received the Lentis Comfort/LS-313 MF15 IOL from July through November 2020, seven eyes (4.3%) displayed acute inflammation of the anterior chamber including fibrin formation within 15 days of uneventful surgery, which con-

sisted of cataract surgery alone (four eyes) or combined with minimally invasive glaucoma surgery (three eyes). During the same period, TASS did not occur with any other IOL model. The authors believe that this is the first study of TASS associated with the Lentis Comfort/LS-313 MF15 IOL. The seven incidents were reported to the lens manufacturer, who investigated the corresponding lens lots and found no deviations from the standard manufacturing protocol.

One patient was 60 years old; the others were in their 70s. Treatment of the inflammation and/or secondary angle closure (due to pupillary obstruction) varied by severity. For mild TASS cases, the authors recommend initial treatment of frequent instillation of a topical steroid (four to eight times daily), especially 0.1% dexamethasone. If this fails, a steroid can be injected.

In this series, one eye was treated conservatively with success, one eye required vitreous surgery, and another required Nd:YAG laser fibrin membranotomy. The fibrin membrane was removed in two eyes, and two others had anterior chamber washout. In all cases, the inflammation and angle closure responded to treatment, and there was no recurrence of fibrin or inflammation. However, the authors cautioned that TASS can cause irreversible corneal endothelial damage and other long-term sequelae.

*—Summaries by Lynda Seminara*

## *JAMA Ophthalmology*

Selected and reviewed by Neil M. Bressler, MD, and Deputy Editors

### Revised Estimate of VA Loss or Blindness in the United States

July 2021

**Flaxman et al.** set out to estimate the prevalence of visual acuity (VA) loss and blindness within the United States. They found that more than 7 million people are living with VA loss—and that, of this group, more than 1 million are living with blindness. They also found that a significant number of people with VA loss or blindness are younger than 40 years of age.

For this study, the researchers summarized data from the CDC's Vision and Eye Health Surveillance System, which includes information on visual difficulty or blindness from four national surveys. Using Bayesian meta-regression methods, they then stratified the data by location (U.S. state), age, sex, and ethnicity for the year 2017.

For all VA loss, the researchers estimated that 7.08 million people (95% uncertainty interval [UI], 6.32-7.89 million) live with VA loss (defined as best-corrected VA of 20/40 or worse). This corresponds to a crude prevalence rate of 2.17% (95% UI, 1.94% to 2.42%). By location, crude prevalence rates range from 1.35% in Maine to 3.59% in West Virginia.

In a second calculation, the researchers found that an estimated 1.08 million people (95% UI, 0.82-1.3) live with blindness (BCVA of 20/200 or worse). This corresponds to a crude prevalence rate of 0.33% (95% UI, .02% to .4%), with state-based findings ranging from a crude prevalence of 0.19% in Utah to 0.65% in West Virginia.

Unsurprisingly, rates of VA loss or blindness increase by age—but an estimated 1.62 million persons with VA loss are younger than 40 years, and 141,000 with blindness are younger than 40.

Overall, the estimated number of cases of VA loss or blindness in this study is 68.7% higher than the previous estimate from the Vision Problems in the United States (VPUS) study, although the estimate of blindness alone is lower. *(Also see related commentary by Emily Y. Chew, MD, in the same issue.)*

### Link Between Visual Impairment and Depression

July 2021

**Parravano et al.** evaluated the prevalence of depression in patients with visual impairment who seek eye care. They found that 1 in 4 of these patients experience depression, making it a health problem in patients with such common eye diseases as age-related macular degeneration (AMD).

For this meta-analysis, the researcher evaluated 27 studies with a median sample size of 125 patients (range, 42-990 patients). All told, data on 6,992 patients (18 years or older) were included. The patients' mean age was 76 years, and the majority (60%) were female.

Although the studies adopted various definitions of visual impairment and used different tools to assess depression, the pooled analysis indicated that the prevalence of depression was high both in clinic-based studies and in those conducted in rehabilitation settings. Moreover, the prevalence did not vary by the extent of disease severity.

Thus, the researchers said, "the results of our review suggest the need for depression screening in patients attending eye clinics who are 65 years or older and have mild to severe visual loss, regardless of comorbidities."

In addition to this increased need for screening, the researchers noted that all eye care professionals need experience not only in recognizing the signs and symptoms of depression but also in determining which patients need to be referred for mental health treatment.

### Protocol W: Two-Year Results in Diabetic Retinopathy

July 2021

In Protocol W of the DRCR Retinal Network, **Maturi et al.** investigated whether treatment with intravitreal aflibercept could prevent vision-threatening complications in eyes with moderate to severe nonproliferative diabetic retinopathy (NPDR). They found that aflibercept was more effective than sham in reducing the likelihood that a patient would develop PDR or center-involved diabetic macular edema (CI-DME). However, the mean change in visual acuity (VA) from baseline to the two-year mark was similar between the two groups.

For this study, the researchers enrolled 328 adults (399 eyes) with moderate to severe NPDR and no CI-DME. Participants' mean age was 57 years, and 57.6% were male. Baseline characteristics were balanced between treatment groups. Participants' eyes were randomly assigned to either sham injections (n = 199) or 2 mg

aflibercept (n = 200). Injections were given at baseline and at months 1, 2, and 4. After that, they were given every four months through year 2. Aflibercept injections were administered as needed if CI-DME developed or when eyes progressed to PDR.

At the two-year mark, preventive treatment with aflibercept resulted in a more than threefold reduction in CI-DME with decreased VA and a more than twofold reduction in new-onset PDR. Even so, 16.3% of aflibercept-treated eyes developed PDR or CI-DME with VA loss by two years. Moreover, VA was roughly equivalent between the two groups: The adjusted mean difference in VA between aflibercept and sham was 0.5 letters.

Protocol W is ongoing and is scheduled to be completed in 2022. *(Also see related commentary by Rajendra S. Apte, MD, PhD, and Christopher K. Hwang, MD, PhD, in the same issue.)*

*—Summaries by Jean Shaw*

## OTHER JOURNALS

Selected by Prem S. Subramanian, MD, PhD

### Targeted OCRL Modulation Reduces Steroid-Elevated IOP

*Translational Vision Science & Technology*
2021;10(6):10

Open-angle glaucoma can be induced by prolonged use of topical glucocorticoids and involves elevated intraocular pressure (IOP) with outflow resistance and abnormal trabecular meshwork (TM) function. **Kowal et al.** have used an optogenetic approach in TM to regulate 5-phosphatase (5ptase) OCRL, which contributes to regulating phosphatidylinositol 4,5-bisphosphate (PIP2). In a subsequent study, they applied this system with the intent of reversing compromised outflow in a steroid-induced murine model of ocular hypertension. They found that blue-light stimulation caused CRY2-OCRL-5ptase to translocate to plasma membrane and cilia in TM cells, which normalized IOP and outflow activity. Moreover, in cultured human TM cells, they noted that optogenetic stimulation reduced the aberrant actin structures caused by dexamethasone.

For this study, the authors induced elevated IOP by subconjunctival injection of dexamethasone into wild-type mice. Following this, they injected adeno-associated viruses containing optogenetic modules of CRY2-OCRL-5ptase and CIBN-GFP into the anterior chamber. Four weeks after incubation, they measured IOP by tonometry and assessed outflow facility by perfusion analysis. In a separate evaluation of actin structures, they explored the effects of light stimulation on human TM cells exposed to dexamethasone.

As expected, the dexamethasone raised IOP and lowered outflow facility in the mice. Optogenetic constructs were expressed in the TM of mouse eyes, and light stimulation caused CRY2-OCRL-5ptase to translocate to the plasma membrane (CIBN-CAAX-GFP) and cilia (CIBN-SSTR3-GFP) of TM cells, which rescued the IOP and outflow facility. In human cells, the aberrant actin structures were minimized by optogenetic stimulation.

Subcellular targeting of inositol phosphatases to remove PIP2 is "a promising strategy to reverse defective TM function in steroid-induced ocular hypertension," said the authors. Their findings support the hypothesis that cytoskeletal alterations and formation of cross-linked actin networks (CLANs) are responsible for the abnormal outflow facility and IOP observed in mice. They concluded that their study offers a new framework for a therapeutic approach based on signaling and emphasized the need to identify precise pathways that lead to formation of OCRL-dependent CLANs.

### Intracameral Versus Topical Mydriasis

*Journal of Cataract & Refractive Surgery*
2021;47(5):570-578

Topical mydriatics for cataract surgery require advance preparation, and multiple instillations are needed during the procedure. In a phase 4 trial, **Souki et al.** compared eyedrops alone to a protocol including a mydriatic-anesthetic solution given intracamerally. They found that intracameral (IC) mydriasis resulted in better ocular surface integrity and higher satisfaction for patients and surgeons.

For this study, researchers enrolled 50 patients between the ages of 40 and 88 years who were slated for bilateral cataract surgery. The patients were assigned randomly to receive either topical drops or an IC mydriatic-anesthetic solution (Mydrane plus Fydrane) plus topical anesthetic drops in one eye for the first surgery. The other treatment was given to the fellow eye for the second surgery. Assessments were performed before surgery, immediately after surgery, at post-op day 1, and at post-op day 7. The primary endpoint was change from baseline in corneal and conjunctival surfaces. Secondary outcomes were epithelial alterations, point-spread function, ocular surface disease index (OSDI), tear film stability assessed by vision breakup time, adverse events (AEs), corrected distance visual acuity (CDVA), intraocular pressure (IOP), patient/investigator satisfaction, and surgery duration.

All eyes received pre-op topical anesthesia (one to two drops of oxybuprocaine chlorhydrate 0.4% + tetracaine chlorhydrate 0.1%). Control eyes also received one drop of tropicamide 1% and phenylephrine 10% at three 10-minute intervals beginning 30 minutes preoperatively, to achieve pupillary dilation. Those randomized to Mydrane/Fydrane received 0.2 mL of the solution, administered slowly into the anterior chamber, just after the first corneal incision.

Changes in corneal and conjunctival surfaces from baseline to day 1 did not differ significantly between treatments, but the Mydrane/Fydrane group had fewer epithelial alterations ($p < .005$), fewer folliculopapillary reactions ($p < .05$), shorter procedures ($p < .001$), less post-op discomfort ($p < .05$), and greater patient and provider satisfaction ($p < .05$). AEs were minimal in both groups. Outcomes for point-spread function, CDVA, IOP, and OSDI did not differ significantly but were better with Mydrane/Fydrane.

*—Summaries by Lynda Seminara*

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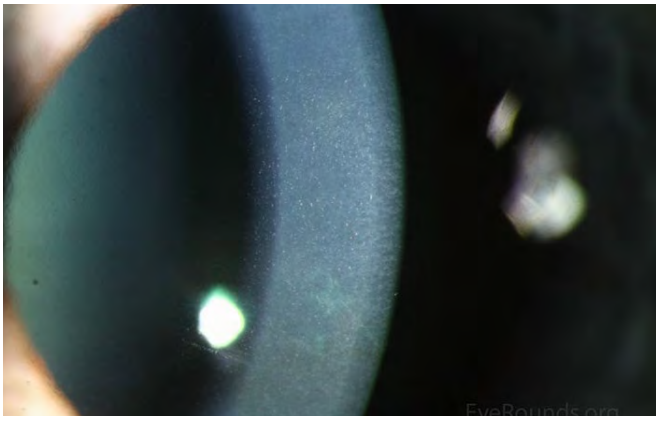
# MD Roundtable: Cataract Surgery in Eyes With Compromised Corneas, Part 1

A question that cornea specialists often hear from their anterior segment colleagues is "How do I modify my approach to cataract surgery in an eye with an abnormal cornea?" In this first installment of a three-part series, Kavitha R. Sivaraman, MD, at the Cincinnati Eye Institute, hosts a discussion with Nicole R. Fram, MD, at Advanced Vision Care in Los Angeles, and Joshua C. Teichman, MD, MPH, at Prism Eye Institute and the University of Toronto. The trio share their pearls for cataract surgery in the context of autoimmune-related dry eye and endothelial dysfunction. Parts 2 and 3 will address cataract surgery in patients with other corneal diseases and will appear in the September and October issues of *EyeNet*.




***GUTTAE**. Cataract surgery in eyes with Fuchs endothelial corneal dystrophy may require special considerations during surgical evaluation.*

## Pre-Op Prep in Severe Dry Eye

***Dr. Sivaraman:*** *For a patient with severe autoimmune-type dry eye—such as Sjögren's syndrome, graft-vs.-host disease (GVHD), or mucus membrane pemphigoid—what do you look for preoperatively, and what are your criteria for offering cataract surgery?*

**Dr. Fram:** Cataract surgery in these patients can be challenging. For a good outcome, you need to make sure that the ocular surface is healthy enough for measurements so that you can get reliable topography and biometry results. It's also important to minimize inflammation preoperatively, whether that's with an anti-inflammatory, like cyclosporine or lifitegrast, preservative-free dexamethasone, or even serum tears. You should have a conversation about how to use these medications properly. Serum tears, for example, contain no preservatives, so you should discuss with the patient the importance of using a refrigerated fresh bottle every three to seven days and making sure to store the remainder in the freezer.

The patient's disease stage dictates my preoperative plan. If the patient has early stage Sjögren's syndrome or very early mucous membrane pemphigoid, I focus on the eyelids, making sure that there is no keratinization of the lid margins. If there is keratinization of the eyelids, there is typically overgrowth of bacteria, which increases endophthalmitis risk. Before cataract surgery, I pretreat every patient with a hypochlorous acid antiseptic, which is particularly important in autoimmune dry eye.

If the dry eye is relatively mild, the patient may be a candidate for a toric IOL, an extended depth of focus lens (e.g., Vivity [Alcon]), or an enhanced monofocal IOL (e.g., Eyhance [Johnson & Johnson]). However, if the dry eye is severe and the cornea is irregular despite aggressive preoperative treatment, it is best to place a traditional monofocal lens for the most reliable outcome.

## Managing Autoimmune Dry Eye During Cataract Surgery

***Dr. Sivaraman:*** *What are some perioperative pearls for cataract surgery in the setting of autoimmune dry eye?*

**Dr. Fram:** Intraoperatively, I coat the eye with methylcellulose or OcuCoat (Bausch + Lomb) to keep the surface moist because an epithelial defect can be particularly problematic when corneal dysfunction is present. After the procedure, I place a disposable soft contact lens or a bandage contact lens; I've found that this helps avoid many complications that are common in the early post-op period.

ROUNDTABLE HOSTED BY **KAVITHA R. SIVARAMAN, MD,** WITH **NICOLE R. FRAM, MD,** AND **JOSHUA C. TEICHMAN, MD, MPH.**

It's crucial that you maintain the eye with the same intensity postoperatively as you did preoperatively. For my patients with GVHD or mucous membrane pemphigoid, I may give a subconjunctival injection of triamcinolone or dexamethasone to help them through the perioperative period.

**Dr. Teichman:** When treating mucus membrane pemphigoid in particular, you need to be extremely cautious to avoid injuring the conjunctiva. As much as possible, I try to avoid touching the conjunctiva, and I anchor the eye with a dry Weck-Cel sponge (Beaver-Visitec).

**Dr. Sivaraman:** I tend to avoid topical NSAIDs preoperatively because epithelial toxicity can occur in autoimmune-type dry eye, even from a once-daily NSAID formulation. The rare cases that I have seen of NSAID-related melts have been in patients with autoimmune disease, such as in rheumatoid arthritis and Sjögren's syndrome.

I sometimes prescribe a preservative-free formulation of methylprednisolone, dexamethasone, or Lotemax ointment (Bausch + Lomb) because autoimmune dry eye patients patients tend to be very sensitive to benzalkonium chloride and other preservatives.

And I learned a trick from one of my partners: At the end of the case, any unused dispersive viscoelastic is placed on the cornea and the eye is patched shut for a couple of hours. It seems that the effect is like that of a bandage contact lens—letting the eye recover from the betadine and preserved drops that you use perioperatively.

## Challenging Corneal Topographies

***Dr. Sivaraman:*** *Despite our best efforts to optimize the ocular surface, sometimes the corneal topography is still problematic. Maybe the eye is still very dry, even though it's not actively inflamed. Maybe the patient is dependent on a scleral lens or bandage contact lens but visual acuity is 20/400 from a posterior subcapsular cataract, and it's time to choose an IOL. What is your approach?*

**Dr. Teichman:** I do my best to get the contact lenses out for as long as possible. In theory, a properly placed scleral lens should vault completely over the cornea and shouldn't need to be out for very long, but you're making an assumption in trusting that the fit is good. When it comes to soft contact lenses, ophthalmologists vary in how long they want patients to have them out preoperatively—from as little as three days to as long as two weeks. Once the patient is ready for testing, the first thing I look at are the mires on topography, to get an idea of corneal curvature and the quality of the scan, and I look for consistency among multiple test results over time. You want to have reliable results in terms of all your measurements: biometry, refraction, keratometry, topography, and tomography. Tomography is less influenced by tear film than topography, so tomography can be more informative than topography for dry eye/ocular surface patients.

## Surgical Evaluation in Endothelial Disease

***Dr. Sivaraman:*** *What is your approach to the initial evaluation and IOL selection for cataract surgery in eyes with endothelial disease?*

**Dr. Sivaraman:** For example, maybe the case involves Fuchs dystrophy, posterior polymorphous corneal dystrophy, or prior glaucoma surgery, and the endothelium is known to be compromised. I'm always thinking about whether the patient is likely to need endothelial keratoplasty (EK) in their lifetime. Some cases have obvious edema, so you know that a graft or maybe a Descemet-stripping only procedure will be needed. The trickier cases are those patients with a compact stroma who have advanced endothelial disease because you need to predict if manifest edema is likely to occur after cataract surgery. I like to think that I'm getting better the longer I do this, but you can't always predict which eyes will decompensate.

Characteristics that I consider are patient age and cataract density, especially in the context of a shallow anterior chamber. I tend to perform specular microscopy on these patients to check the endothelial mosaic preoperatively, but it's not just about the cell count; the cell morphology and functional status also matter. An endothelial cell count over, say, 1,000 can bring a false sense of security, and some surgeons use criteria of cell count <1,000 per $mm^2$ and pachymetry findings >640 µm as an indication for a triple procedure (i.e., phacoemulsification, IOL implantation, and endothelial transplantation). I don't find pachymetry results at a single point in time to be particularly useful. Without longitudinal data, you can't know if corneal thickness of, say, 610 µm is normal for that person; if, for example, the native cornea is 480 µm, that would indicate gross edema.

**Dr. Teichman:** I agree. Surgical planning based on cell count and pachymetry results is dated for many reasons. First, phaco technology has significantly improved (with corneas that may have previously decompensated now doing very well). Second, the study we are all referring to[1] was when cataract surgery was to be combined with penetrating keratoplasty, which has a poorer risk/benefit profile than EK. So both cataract and cornea surgery have really improved.

Pre-op planning involves determining whether the visual problem stems from the endothelial disease, the cataract, or both. The first question I always ask patients is "Do you have blurry vision in the morning?" I think that morning edema, on its own, is an indication for EK nowadays.

I avoid hydrophilic acrylic IOLs in endothelial disease. If the patient needs EK in the future, the procedure's air bubble can calcify these lenses. Additionally, if I think the eye is at risk of decompensating, I typically aim to keep the patient a little myopic during the cataract surgery. If I'm doing a Descemet's membrane endothelial keratoplasty (DMEK), I usually aim for somewhere between –0.5 D and –1.0 D. If you're performing the cataract surgery but would be referring the patient to a cornea specialist should decompensation occur, you want to account for the hyperopic shift that your local cornea specialist would have after EK.

Another consideration is astigmatism and toric lenses. If there's corneal

edema, the astigmatism can increase, decrease, and/or change axes in response to DMEK. As an unofficial rule, if the eye has more than 2 D of cylinder, it is probably indicative of inherent cylinder in the cornea. If the patient likely will require DMEK, I'm happy to place a toric lens in these cases, as I know it should help to debulk the astigmatism, even if it does not eliminate it completely. I generally avoid toric lenses for eyes with 1.5 D or less of cylinder in the context of edema, as the results are more variable.

**Dr. Sivaraman:** I agree, especially for against-the-rule astigmatism. I may consider a toric lens if the pattern is regular and the eye has more than 2 D of cylinder, but I stipulate that the patient should still expect to wear glasses, albeit hopefully a lower-strength prescription.

**Dr. Fram:** I will also consider a toric IOL if I have reliable data on the patient over time, the pachymetry results show that the cornea has stable thickness (e.g., <600 µm), and there's roughly a minimum of 2.5 D of cylinder. However, if the cornea has significant edema and >2.5 D of astigmatism that is not reproducible on multiple measurements, I typically offer a phakic DMEK. This technique is relatively simple to perform, provides information on the corneal shape, and expands the range of future therapeutic options. One caveat: It is critical to use air in phakic DMEK—not gas—and before surgery, you should perform a laser peripheral iridotomy (LPI) in the office if possible. If the cornea is so edematous that the iris features are not visible, the surgeon can perform a surgical peripheral iridotomy using a 23-gauge vitrector with an I/A cut setting, >700 mm Hg vacuum, and cut rate of 50-100 cuts/minute.

**Dr. Sivaraman:** It's not just the astigmatism that's labile in these operations; the spherical equivalent can shift as well because of post-DMEK corneal deturgescence. If a patient undergoes implantation with a costly premium IOL and still needs a +3 D spherical prescription postsurgically, you may be thrilled that the astigmatism is corrected, but the benefit to the patient is less apparent. The possible need for corrective lenses is worth including in the informed consent discussion preoperatively.

**Dr. Fram:** You bring up an important point! The thicker the cornea is preoperatively, the more likely that you will get a hyperopic result. I tend to aim even more myopic in these cases. For example, I typically aim –0.50 D for DMEK triple and –1.25 D for DSEK triple for a distance result. In the case of an edematous cornea (>700 µm) and DMEK triple, I will aim –1.00 D to achieve a plano result.

In general, less-complicated cases (e.g., Fuchs, early pseudophakic bullous keratopathy) are managed with DMEK. More complex eyes receive nanothin DSEK (<50 µm), which is easier to perform in postvitrectomized eyes or eyes with multiple filtering tubes. I will even aim as high as –1.50 D to achieve a plano result in these complex eyes.

**Dr. Sivaraman:** I do, too.

## Endothelial Disease and Cataract Surgery: Post-Op Care

***Dr. Sivaraman:*** *For post-op care in patients with endothelial disease, I often taper the steroid more slowly. What is your approach for a tenuous endothelium?*

**Dr. Fram:** I augment the steroid intensity in the early post-op period. I give these patients Durezol (Novartis) or prednisolone acetate, and I focus on the counseling. I tell patients that it's normal to have blurry vision in the first two weeks. If I see deep folds and edema centrally and clearing of the periphery, I can be confident in telling the patient that vision will be clear. If the edema and folds are wall to wall, I have a conversation with the patient about options and what to expect. In such cases, I prescribe Muro drops (Bausch + Lomb) and ointments to give the endothelium a break.

Even if the eye hasn't improved by, say, the three-month mark, I don't give ripasudil or netarsudil as a last-ditch wound-healing effort as I have found these eyes to be more susceptible to honeycomb keratopathy.

**Dr. Teichman:** Sometimes as cornea specialists, we forget that not every surgeon is as comfortable with corneal edema as we are. It's worth revisiting the basics. When trying to determine the cause of edema postoperatively, keep in mind that there are risk factors besides endothelial damage. For instance, patients with Fuchs dystrophy are more likely to have a Descemet's detachment, but you may not be able to see the detachment through a cloudy cornea. It might be apparent only with anterior segment OCT.

I've had very good surgeons refer cases of corneal edema to me. On gonioscopy, I find a retained lens fragment, or viral keratitis, or a haptic out of the capsular bag causing an IOP spike. With a thorough examination, you might find other causes of edema that are treatable without EK.

**Dr. Sivaraman:** Yes, retained lens fragments can be an issue. When the lens is dense, I'm liberal with the dispersive viscoelastic; I'll apply it periodically during nucleus disassembly if the cumulative dissipated energy (CDE) is climbing. However, this increases the risk of a trapped lens fragment. Keep careful track of what you're phacoing. When you're trying to salvage the endothelium and spare the patient a graft, the last thing you want is a retained lens fragment in the angle.

1 Seitzman GD et al. *Ophthalmology*. 2005;112(3):441-446.

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**MORE AT THE MEETING.** Don't miss the 20th Spotlight on Cataract session at AAO 2021. It takes place Monday, Nov. 15, in New Orleans.

**NOTE:** This article has been updated since print publication. In the original article, the Further Reading box (next page) incorrectly attributed the Pineles study to the Academy's Task Force on Myopia. It is actually attributable to the Academy Ophthalmic Technology Assessment Committee Pediatric Ophthalmology/Strabismus Panel. This version of the article corrects the mistake.



# Low-Dose Atropine to Slow Myopia: Evidence and Adoption Are Growing

The first studies about low-dose atropine to slow myopic progression in children were published about 20 years ago, eliciting a trickle of interest among pediatric ophthalmologists. As the worldwide prevalence of myopia grew to epidemic proportions, the influential Atropine for the Treatment of Myopia (ATOM1 and ATOM2) and LAMP (Low-Concentration Atropine for Myopia Progression) studies came out, and early adopting ophthalmologists started to integrate the drug into their practices. Then COVID hit, possibly pushing the myopia epidemic to new levels.[1]

This confluence of factors has raised awareness of low-dose atropine for myopia not only among ophthalmologists but also among pediatricians, primary care physicians, and parents. Nonetheless, questions remain, even as scientific evidence and clinical experience among ophthalmologists accrue.

## Analyzing the Research

The ATOM and LAMP studies in particular have been instrumental in capturing the attention of ophthalmologists. The ATOM1 study found atropine to be superior to placebo, and ATOM2 found that low dosages also slowed the progression of myopia. The LAMP study used a range of low dosages of atropine to see which was most effective.

In the wake of these major studies, research continues.

**Age matters.** Recently, a secondary analysis of LAMP data by Li et al. found that younger children require higher concentrations of the drug to achieve a benefit similar to older children on lower dosages. Specifically, the researchers stated that 6-year-old children who used 0.05% atropine had mean spherical equivalent progression similar to 8-year-olds on 0.025% atropine and 10-year-olds on 0.01% atropine.[2]

***ATROPINE.*** *Public awareness is growing about low-dose atropine for slowing myopia progression in children.*

**Diverse population.** K. David Epley, MD, a pediatric ophthalmologist in Kirkland, Washington, and an early adopter of low-dose atropine drops, joined with colleagues in a multicenter retrospective case review to assess the effectiveness of 0.01% atropine drops in a diverse group of pediatric patients in the United States.[3]

This review published in 2019 included myopic children of a variety of ethnicities aged 6-15 years. Controls were matched to study participants by age and spherical equivalent refraction. Patients were primarily Asian and White, with much smaller percentages of mixed-race children, Hawaii/Pacific Islanders, Blacks, and Native Americans. Study subjects received nightly atropine in addition to their typical eye care (e.g., single-vision eyeglasses or no glasses for low myopes). Controls received only typical eye care.

After one year, atropine-treated patients had progressed by –0.2 ± 0.8 D, versus controls who progressed by –0.6 ± 0.4 D ($p < 0.001$). At two years, progression was –0.3 ± 1.1 D and –1.2 ± 0.7 D, respectively ($p < 0.001$). The authors concluded that atropine 0.01% could be safe and effective in reducing myopia progression in an ethnically diverse population.

**Studies in progress.** Currently, numerous studies are in progress, including ATOM3,[4] a study at the Singapore National Eye Centre, which involves the use of low-dose atropine in children who are 5-9 years old either to prevent myopia in those whose parents are myopes or to slow progression in those with low myopia.

The Pediatric Eye Disease Investigator Group in collaboration with the NEI is studying the efficacy of 0.01% atropine in children aged 5-12 years in a sample that is no more than 25% East

BY KATHRYN MCKENZIE, CONTRIBUTING WRITER, INTERVIEWING **K. DAVID EPLEY, MD, JENNIFER A. GALVIN, MD, FAAP,** AND **STACY L. PINELES, MD, MS.**

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Asian.[5] It is studying the children over a treatment course of two years, and for six months after end of treatment.

And several prospective phase 3 trials are underway, such as Sydnexis's STAAR trial of its patented SYD-101,[6] the Childhood Atropine for Myopia Progression (CHAMP) looking at Nevakar's NVK-002,[7] and the CHALLENGE study of EyeNovia's Micropine novel dosing device.[8] FDA approval of one or all of these products could make low-dose atropine more widely available, because at present, the drops can be obtained only from compounding pharmacies and are not typically covered by insurance, said Dr. Epley.

## Putting Studies Into Practice

Ophthalmologists are finding that the 0.01% concentration is optimal as a starting dose, said Jennifer A. Galvin, MD, FAAP, at Yale School of Medicine in New Haven, Connecticut.

**Starting dose.** Dr. Galvin has been using 0.01% atropine eyedrops with her patients since 2014, based upon findings from ATOM2. She has treated some 60 patients between the ages of 6 and 13 years during this time. Citing observations from her practice, she said, "In the majority of my patients, especially the patients with strong family history of high myopia, there has been a stabilization and slowing of the myopic refractive error as well as the axial length measurement."

Stacy L. Pineles, MD, MS, also starts patients on this lowest dose. "I typically start with 0.01%, and if patients progress, I increase to 0.05%," she said, adding, "a lot of other physicians are starting with 0.05% based on LAMP." Dr. Pineles is at the University of California Stein Eye Institute in Los Angeles.

In fact, Dr. Galvin said that in summer 2020, based on results from LAMP, she increased the dosage for most of her patients from 0.01% to 0.05%. After she found that many patients had side effects of light sensitivity, she switched nearly all of them back to 0.01%.

For his part, Dr. Epley starts patients at 0.01% to avoid any unwanted side effects. "If the child's not stable or steady at 0.01%, I don't hesitate to move them up the scale a little bit. Combining atropine in our practice with the new MiSight lenses from CooperVision and orthokeratology, I think we have a pretty effective protocol for slowing down myopia." (For more about MiSight, see "Beyond Atropine and Ortho-K: Contact Lenses for Mitigating Myopia Progression," *EyeNet*, February 2021 at aao.org/eyenet.)

**Link to growth cycle.** Dr. Epley said he now typically keeps younger children on the drops for five to seven years, usually to age 14. "If they're an older child and they started treatment at 11 or 12 years of age, then I'll usually stop them after five years," he said. He has observed among his own patients that those who start progressing at earlier ages are on the medication longer, since they have a lengthier growth cycle than youngsters whose myopia started to progress in the pre-teen or teen years.

**Rebound effect.** Dr. Epley noted the potential of a rebound effect when treatment is stopped. In his experience, the myopia is more likely to worsen if a patient has been on higher-concentration drops. "Over time, I have kept children on the drops longer to avoid this rebound effect, not stopping until the child is 14 to 15 years of age and less likely to continue to progress," he said.

**Dilation observations.** Dr. Epley has also noticed that lower doses are well tolerated with few side effects, which may increase as the percentage is bumped up. Even in White patients with light irides, who tend to have a little more pupil dilation than those with darker eyes, he noted that there are few problems. "At 0.05%, there's definitely a bit of blurring up close, which is tolerated by most kids. It's not so blurred that they can't do what they need to do," he said.

**Unanswered questions.** However, as treatment with low-dose atropine is relatively new and not FDA approved, questions remain.

**Duration of treatment.** Dr. Epley, who has treated about 190 patients with low-dose atropine since 2012, said he would like to see studies address how long to keep patients on the drops, and at what age to stop.

"It's clear that there are some kids who are done with their growth process in terms of increasing myopia by the age of 12 or 13, and there are definitely a lot who are not," he said. "Initially, I was stopping kids at 13, which is what they did with the ATOM studies. And I found so many kids—a large percentage—who were not stable at that point, and their myopia would increase again."

**Ethnicity.** Dr. Pineles noted that some physicians are still hesitant to prescribe atropine because many of the larger studies thus far have involved only patients of Asian ethnicity. She said that she hopes more studies like that conducted by Dr. Epley and colleagues will address questions around ethnicity. And she looks forward to results from the PEDIG study.

**Other questions.** Dr. Pineles raised several additional questions: "First, what is the optimal age to start? Then, should we be waiting until the myopia rapidly progresses or trying to intervene even before that in high-risk families? And, when—and how—should we stop treatment?" She also noted that combination therapy is an important area for inquiry, for example combining low-dose atropine with multifocal lenses prescribed off-label, the latter of which was reported the BLINK study.[9]

## Rising Awareness

Word is spreading that low-dose atropine is proving to be a worthwhile solution to childhood myopia—pediatricians, optometrists, and primary care physicians are referring patients specifically for this type of treatment, said Dr. Epley. Parents are also becoming more savvy; nearsighted parents

### FURTHER READING


Pineles S et al. for the Academy's Task Force on Myopia. **Atropine for the Prevention of Myopia Progression in Children.** *Ophthalmology*. 2017;124:1857-1866.

Modjtahedi BS et al. for the Academy's Task Force on Myopia. **Reducing the Global Burden of Myopia by Delaying the Onset of Myopia and Reducing Myopic Progression in Children.** *Ophthalmology*. 2021;128(6):816-826.

are particularly concerned that their myopic children may follow in their footsteps, he said.

Dr. Pineles has also observed increased interest in low-dose atropine during the last year or two. "Given the low side-effect profile and the demonstrated efficacy in a disease that doesn't have many other treatment options, families are asking for the drops, and physicians are recommending them."

Finally, Drs. Epley, Galvin, and Pineles noted, getting the word out about low-dose atropine can be an enormous step forward in curbing the global myopia epidemic. "If we can reduce the number of kids who are –6 D or higher, over time, that will have a huge impact on eye health as they become adults," said Dr. Epley. "So it's worth doing. I'm eagerly awaiting the day that CHAMP and some of these other trials are finished so that we can get an FDA-approved product."

1 Wang J et al. *JAMA Ophthalmol.* 2021;139(3):293-300.
2 Li FF et al. *Ophthalmology.* 2021;128(8):1180-1187.
3 Larkin GL et al. *Ophthalmol Ther.* 2019;8(4):589-598.
4 ATOM3. www.clinicaltrials.gov/ct2/show/NCT03140358.
5 PEDIG. www.clinicaltrials.gov/ct2/show/NCT03334253.
6 STAAR. www.clinicaltrials.gov/ct2/show/NCT03918915.
7 CHAMP. www.clinicaltrials.gov/ct2/show/NCT03350620.
8 EyeNovia. www.clinicaltrials.gov/ct2/show/NCT03942419.
9 Walline JJ et al. *JAMA.* 2020;324(6):571-580.

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**Dr. Galvin** is a principal investigator for the Pediatric Eye Disease Investigator Group at Eye Physicians & Surgeons PC and assistant clinical professor of ophthalmology and visual science at Yale School of Medicine in New Haven, Conn. *Financial disclosures: None.*
**Dr. Pineles** is associate professor of ophthalmology and residency program director at the Stein Eye Institute, University of California, Los Angeles. *Financial disclosures: None.*
**See disclosure key,** page 10.

# Diagnosis and Management of Bell Palsy

Bell palsy (BP) is an idiopathic, unilateral facial nerve palsy of acute onset that leads to facial muscle weakness. BP accounts for approximately half of all facial nerve palsies. The etiology is not fully understood, although some studies have investigated herpes simplex virus as a possible disease trigger.[1] As many patients recover at least partial muscle function, treatment is aimed at protecting the ocular surface. For persistent disease, newer therapies such as surgical facial reanimation show promise.

## Epidemiology and Risk Factors

BP is a relatively rare disease with an annual incidence of 32 cases per 100,000. It is most common between the ages of 15 and 45 years,[2] and younger patients have a better prognosis. Risk factors include diabetes, hypertension, respiratory disease, obesity, pregnancy, and preeclampsia. There are no significant disparities in risk or outcomes between men and women. Recurrent disease is seen in 7% of patients, usually within 1.5 years of initial onset.[2]

## Pathophysiology

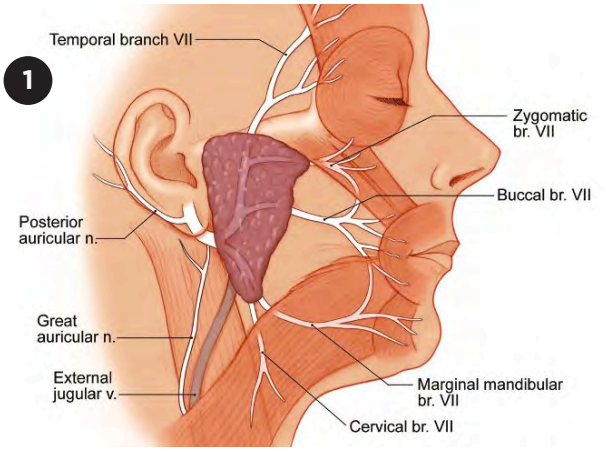
BP is thought to result from inflammation of the peripheral facial nerve (cranial nerve [CN] VII) as it exits the skull via the stylomastoid foramen. Inflammation at the level of the geniculate ganglion can lead to obstruction, ischemia, demyelination, and subsequent nerve dysfunction.[3] Herpesviruses and other viruses are under investigation as causative agents, although definitive proof has not been established.[1]

The facial nerve induces facial movement and expression via five motor branches, any of which can be affected by BP (Fig. 1):

- The **temporal branch** innervates the frontalis, orbicularis oculi, and corrugator supercilii muscles.
- The **zygomatic branch** innervates the orbicularis oculi muscle.
- The **buccal branch** innervates the orbicularis oris, buccinator, and zygomaticus muscles.
- The **marginal mandibular branch** innervates the mentalis muscle.
- The **cervical branch** innervates the platysma muscle.

CN VII performs several other functions. It stimulates the stapedius muscle of the ear, which protects against auditory damage by dampening vibrations in loud environments; supplies parasympathetic innervation of the lacrimal, salivary, and mucous glands; innervates the external auditory meatus, tympanic membrane, and pinna; and carries the sensation of taste from the anterior region of the tongue.

Facial nerve deficits may stem from central or peripheral causes. BP and other peripheral palsies present with ipsilateral findings affecting the upper and lower half of the face. Central lesions affect the lower contralateral side of the face, with relative sparing of the upper face due to bilateral innervation to the upper half of the face.



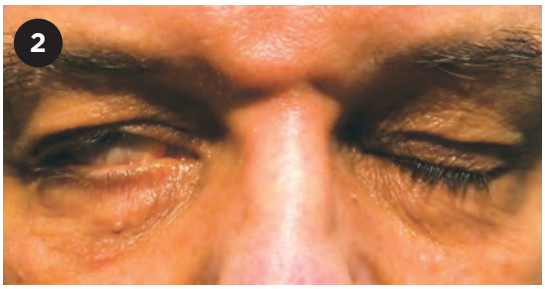

***ANATOMY.*** *Illustration depicts the facial nerve branches and distribution.*

## Clinical Presentation

BP is characterized by unilateral weakness and partial or total paralysis of facial muscles that occurs over a period of hours to days. Clinical manifestations include facial droop, asymmetric smile, drooling, and poor eyelid closure (Fig. 2). Other symptoms include jaw pain, loss of taste, headache, and sensitivity to sound on the affected side. The overall severity of facial nerve dysfunction can be measured using the House-Brackmann grading scale[4] (HBGS; see "House-Brackmann Grading Scale for Bell Palsy," page 35).

Ocular-specific signs indicative

BY **ANNA KOZLOVA, MD, CHISOM T. MADU, BS, VICTORIA S. NORTH, MD,** AND **ELEANORE T. KIM, MD.** EDITED BY BENNIE H. JENG, MD.



***EYELID EFFECT.*** *Patient has right-sided lagophthalmos secondary to Bell palsy.*

of BP include widened eyelid fissure, lower eyelid ectropion, lagophthalmos, and decreased lacrimation.[5] Each of these findings can contribute to ocular surface dryness and, ultimately, lead to exposure keratopathy. This is especially true in patients with an impaired Bell phenomenon (palpebral oculogyric reflex), as the inability to supraduct the eye with attempted closure further increases the risk of ocular surface disease, exposure keratopathy, and corneal ulceration.[5] Neurotrophic keratopathy can manifest in cases with concomitant trigeminal (CN V) neuropathy.

Following facial nerve injury, aberrant regeneration (synkinesis) may occur. Synkinesis creates linkage between voluntary and involuntary muscle contractions, such as blinking with oral movement, hyperlacrimation, and abnormal facial/neck tightness.[5] These aberrant movements may interfere with essential tasks such as chewing or swallowing.

## Diagnosis

BP is a diagnosis of exclusion that is typically established with clinical findings alone. A thorough clinical history can help exclude alternate diagnoses (see "Differential Diagnosis for Bell Palsy," page 36). The clinician should inquire about new medications; recent illnesses; travel to Lyme-endemic areas; pregnancy; and a history of herpes infections, inflammatory conditions, or malignancy, including prior cutaneous malignancy (perineural invasion). An accurate timeline is important for the diagnosis: Maximal weakness is typically reached within one week in BP, whereas a more gradual onset is suspicious for mass lesions.

Complete ophthalmologic examination of a patient with suspected BP includes assessment of bilateral orbicularis strength, eyelid position, lagophthalmos, and Bell phenomenon. Careful slit-lamp examination of the ocular surface is crucial. It is important to be aware that several features of the ocular exam, including motility, pupil examination, and trigeminal nerve sensation (including corneal sensation), may reveal deficits of multiple cranial nerves. Such findings should prompt critical consideration of other diagnoses such as stroke or tumors.

The clinician should also assess for facial rashes, mass lesions, and gross auditory abnormalities that could point to alternative causes. The auditory canal should be examined for herpes zoster lesions, which support a diagnosis of Ramsay Hunt syndrome.

Basic laboratory studies can be obtained to establish a baseline evaluation and to rule out other inflammatory or infectious causes of facial nerve palsy (e.g., complete blood count, erythrocyte sedimentation rate, C-reactive protein, Lyme antibody, syphilis screen). If the physical exam or reported history is suspicious for other etiologies, additional blood work or imaging may be useful.

**Imaging and electrodiagnostic testing.** When examination suggests a central source or when the timeline or additional clinical features argue against acute idiopathic facial nerve palsy, neuroimaging is indicated. Magnetic resonance imaging (MRI) of the brain and orbits, with and without contrast, effectively highlights the soft tissues of the cranial nerves and associated parenchyma. A dedicated facial nerve MRI can be helpful when perineural invasion or an inflammatory process is suspected. Computed tomography scans can identify bony fragments impinging on CN VII in cases of trauma.

Electrodiagnostic testing modalities such as electromyography (EMG) and electroneurography (ENoG) can be useful in patients with severe BP.[6] These tests measure electrical activity of a muscle or nerve to quantify the extent of nerve damage. Ideally, they are performed seven days after symptom onset, when Wallerian degeneration of the nerve is optimally measured. A 90% or greater loss in ENoG or EMG signal amplitude indicates a low likelihood of spontaneous recovery and may help identify patients who would benefit from facial nerve decompression surgery.[3]

## Prognosis

The majority of BP patients experience near-complete or complete spontaneous recovery within three weeks of onset, and nearly all patients will recover within five weeks.[3] In a large study of the natural history of BP, 100% of patients achieved some degree of muscular recovery, and 71% achieved complete recovery.[2] The extent of eventual recovery was associated with severity of palsy at presentation and with patient age. Among patients who had incomplete palsy, 94% recovered fully, compared with 61% of patients who had complete palsy.

The recovery time was also associated with disease severity: within two months for incomplete palsy versus three to five months for complete palsy. No patients who had residual deficits after six months achieved complete recovery. An early recovery was also associated with better final prognosis, whereas later recovery was associated with sequelae such as aberrant regeneration.[2]

Patients aged 5 to 14 years were found to have the most favorable prognosis, with 90% achieving full recovery. Likelihood of full recovery decreased with age, with only about one-third of patients above the age of 60 years regaining normal function.[2]

## Medical Management

Although most patients with BP recover spontaneously, treatment can speed recovery and potentially prevent permanent sequelae. In general, patients with more severe clinical findings may benefit from more aggressive management in order to prevent permanent complications such as exposure keratopathy.

**Corticosteroids.** Treatment with oral

steroids is associated with increased rates of complete recovery[7] and should be initiated within 72 hours of symptom onset. Clinical guidelines recommend a 10-day course of oral steroids with five days at a high dose (prednisolone 50 mg/day for 10 days or prednisone 60 mg/day for five days) followed by a five-day taper.[6] Caution should be taken in patients with diabetes, and close monitoring of glucose levels is essential.

**Antivirals.** Antiviral treatment for BP is controversial; some research shows no benefit when these drugs are added to corticosteroids.[7] However, there is evidence for benefit in severe or complete BP, particularly with the use of higher-bioavailability antivirals such as valacyclovir and famciclovir.[8] In one study, a dosing regimen of oral famciclovir (750 mg/day) for seven days led to increased rates of recovery.[8]

## Ocular Surface Protection

BP can be a vision-threatening disease if persistent lagophthalmos leads to significant exposure keratopathy, corneal ulceration, or eventual neurotrophic keratopathy. It is essential to initiate measures such as the following to protect the ocular surface while facial paralysis is present[5]:

- Lubrication: artificial tears, ointments, moisture chambers, punctal occlusion, humidifiers.
- Temporary induced ptosis: chemodenervation with botulinum toxin, application of external gold weight.
- Temporary eyelid closure: eyelid taping or suture tarsorrhaphy.
- Corneal surface coverage: bandage contact lens.

Longer-term solutions can be considered to address persistent corneal exposure, lacrimal apparatus malfunction, aberrant regeneration, and poor cosmesis:

- Ocular surface coverage: scleral contact lens.
- Eyelid implants: upper eyelid gold or platinum weights, palpebral springs.
- Upper lid retraction repair: müllerectomy or levator recession.
- Lower lid ectropion repair: medial and/or lateral canthoplasty, wedge resection, medial canthal Royce-Johnston suture, or autologous fascial sling.
- Facilitation of drainage/tear reduction: botulinum toxin to lacrimal gland. Epiphora is multifactorial in nature in facial nerve palsy patients, due to loss of tear pump, lower eyelid malposition, reflex epiphora from exposure, and hyperlacrimation. Certain cases may ultimately benefit from dacryocystorhinostomy or use of a Jones tube.

## Surgical Management

**Facial nerve decompression.** CN VII passes through rigid bony structures that restrict expansion during inflammation, resulting in nerve ischemia and damage when inflamed. Surgical decompression relieves this structural constraint but is controversial.

A recent meta-analysis found higher rates of complete recovery in patients with complete palsy (HBGS V and VI) or severe nerve degeneration (>90% degeneration on electrodiagnostic testing) who underwent surgical decompression versus conservative management. Optimal results were seen with decompression within 14 days of symptom onset, with some possible improvement after that window.[9]

**Facial reconstruction and reanimation.** Finally, surgical static and dynamic techniques can be considered in patients with lasting damage and limited potential for recovery in order to improve functional and aesthetic outcomes.[5,10] Static techniques (slings) improve resting symmetry of face without restoring movement. Dynamic techniques include the following:

- nerve interposition grafting: bridges the gap of a nerve defect;
- hypoglossal-facial nerve end-to-end anastomosis of CN XII and CN VII;
- contralateral facial nerve graft: uses donor nerve to bridge a damaged facial nerve to the contralateral (unaffected) facial nerve;
- muscle bundle transfer (e.g., tempo-

### House-Brackmann Grading Scale for Bell Palsy

| GRADE | CHARACTERISTICS |
|---|---|
| I | Normal facial function in all areas. |
| II | Gross: Slight weakness noticeable on close inspection; may have very slight synkinesis.<br>At rest: Normal symmetry and tone.<br>Motion: Forehead, moderate to good function; eye, complete closure with minimum effort; mouth, slight asymmetry. |
| III | Gross: Obvious but not disfiguring difference between two sides; noticeable but not severe synkinesis, contracture, and/or hemifacial spasm.<br>At rest: Normal symmetry and tone.<br>Motion: Forehead, slight to moderate movement; eye, complete closure with effort; mouth, slightly weak with maximum effort. |
| IV | Gross: Obvious weakness and/or disfiguring asymmetry.<br>At rest: Normal symmetry and tone.<br>Motion: Forehead, none; eye, incomplete closure; mouth, asymmetric with maximum effort. |
| V | Gross: Only barely perceptible motion.<br>At rest: Asymmetry.<br>Motion: Forehead, none; eye, incomplete closure; mouth, slight movement. |
| VI | Total paralysis: No movement. |

**SOURCE:** Adapted from House JW, Brackmann DE. *Otolaryngol Head Neck Surg.* 1985;93(2):146-147.

ralis muscle): employed when affected muscle is no longer viable; and
- microneurovascular free flap transfers: transplants from remote donor sites.

Aberrant regeneration can be managed with facial physical therapy for muscular weakness and synkinesis. Neurectomy and chemical denervation with botulinum toxin can be useful, especially in cases of hyperlacrimation (i.e., crocodile tears).

## Recent Developments

Facial reanimation is a growing field, with research into the use of flaps or grafts from small muscles and muscle units such as the platysma to reconstruct a dynamic blink.[11] There have also been advancements in the use of nerve conduits and acellular autografts. Improved harvesting and microsurgical techniques have allowed for greater success in these surgeries.

Advances have also been made in the management of neurotrophic keratopathy, which may develop with long-standing exposure. These include biopolymer drops that mimic the corneal component heparan sulfate, and coenzyme Q10 drops to suppress connexin 43 and speed epithelial healing.[12] Topical cenegermin (Oxervate) has recently been found effective in the management of neurotrophic keratopathy. The active ingredient is a recombinant nerve growth factor (NGF) structurally identical to human NGF, mechanistically supporting corneal epithelial cell health and stimulating corneal reinnervation. When long-term recovery is not anticipated, corneal neurotization with nerve grafting may improve corneal structure, sensation, and function.

## Conclusion

BP is an acute, idiopathic facial nerve palsy that resolves fully in the majority of patients within two months. Patients with incomplete palsy at onset have a better prognosis and a speedier recovery. Corticosteroids and, possibly, antivirals can hasten recovery and prevent long-term sequelae. Protection of the ocular surface with conservative measures or surgical eyelid repair is key to ameliorating exposure and preventing exposure keratopathy and vision loss. Other surgical strategies include decompression of the facial nerve canal and facial reanimation techniques; however, because the majority of patients recover spontaneously, these methods should be reserved to address permanent complications.

**Differential Diagnosis for Bell Palsy**

| | |
|---|---|
| **Infectious** | Lyme disease, viral (e.g., herpes simplex, varicella zoster, adenovirus), bacterial otitis media |
| **Inflammatory/ Autoimmune** | Sarcoidosis, Guillain-Barré syndrome, Hashimoto encephalopathy, multiple sclerosis |
| **Compressive Lesions** | Cerebellopontine angle tumors, metastatic neoplasms, benign cysts, cholesteatoma |
| **Trauma** | Fracture of bony fallopian canal, facial nerve lacerations, blunt force trauma, penetrating trauma |
| **Ischemic** | Stroke affecting vasculature supplying CN VII, atherosclerosis |
| **Miscellaneous** | Influenza vaccination (reported from intranasal version, since recalled) |

**SOURCE:** Adapted from Tiemstra JD, Khatkhate N. *Am Fam Physician.* 2007;76(7):997-1002.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**Dr. Kozlova** is a resident, **Dr. North** is an oculoplastics fellow, and **Dr. Kim** is assistant professor of ophthalmology at New York University Grossman School of Medicine in New York; **Mr. Madu** is a medical student at Sophie Davis School of Biomedical Education, City University of New York School of Medicine, in New York. *Financial disclosures: None.*

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- NCELL helps improve the delivery of cyclosporine to where it is needed[2,3]
- Significant improvement in tear production at 3 months[1]
- Significant improvement in corneal staining as early as 1 month[2,4]
- In a comfort assessment at 3 minutes post instillation, 90% (Day 0) and 85% (Day 84) of patients had no or mild ocular discomfort[4]

Cequa™
(cyclosporine ophthalmic solution) 0.09%
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## INDICATIONS AND USAGE

CEQUA™ (cyclosporine ophthalmic solution) 0.09% is a calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye).

## IMPORTANT SAFETY INFORMATION

### WARNINGS AND PRECAUTIONS

**Potential for Eye Injury and Contamination:** To avoid the potential for eye injury and contamination, advise patients not to touch the vial tip to the eye or other surfaces.

**Use with Contact Lenses:** CEQUA should not be administered while wearing contact lenses. If contact lenses are worn, they should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following administration of CEQUA ophthalmic solution.

### ADVERSE REACTIONS

The most common adverse reactions reported in greater than 5% of patients were pain on instillation of drops (22%) and conjunctival hyperemia (6%). Other adverse reactions reported in 1% to 5% of patients were blepharitis, eye irritation, headache, and urinary tract infection.

**Please see brief summary of Full Prescribing Information on the adjacent page.**

**References: 1.** CEQUA [package insert]. Cranbury, NJ: Sun Pharmaceutical Industries, Inc.; 2018. **2.** Data on file. Cranbury, NJ: Sun Pharmaceutical Industries, Inc. **3.** US Patent 9,937,225 B2. **4.** Tauber J, Schechter BA, Bacharach J, et al. A Phase II/III, randomized, double-masked, vehicle-controlled, dose-ranging study of the safety and efficacy of OTX-101 in the treatment of dry eye disease. *Clin Ophthalmol*. 2018;12:1921-1929.


PM-US-CQA-0327 10/2019

SUN OPHTHALMICS

**Brief Summary of Prescribing Information for CEQUA™ (cyclosporine ophthalmic solution) 0.09%, for topical ophthalmic use**

**CEQUA™ (cyclosporine ophthalmic solution) 0.09%**
**See package insert for Full Prescribing Information.**

## INDICATIONS AND USAGE

CEQUA ophthalmic solution is a calcineurin inhibitor immunosuppressant indicated to increase tear production in patients with keratoconjunctivitis sicca (dry eye).

## CONTRAINDICATIONS

None.

## WARNINGS AND PRECAUTIONS

### Potential for Eye Injury and Contamination

To avoid the potential for eye injury and contamination, advise patients not to touch the vial tip to the eye or other surfaces.

### Use with Contact Lenses

CEQUA should not be administered while wearing contact lenses. If contact lenses are worn, they should be removed prior to administration of the solution. Lenses may be reinserted 15 minutes following administration of CEQUA ophthalmic solution.

## ADVERSE REACTIONS

### Clinical Trials Experience

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

In clinical trials, 769 patients received at least 1 dose of cyclosporine ophthalmic solution. The majority of the treated patients were female (83%).

The most common adverse reactions reported in greater than 5% of patients were pain on instillation of drops (22%) and conjunctival hyperemia (6%). Other adverse reactions reported in 1% to 5% of patients were blepharitis, eye irritation, headache, and urinary tract infection.

## USE IN SPECIFIC POPULATIONS

### Pregnancy

Risk Summary

There are no adequate and well-controlled studies of CEQUA administration in pregnant women to inform a drug-associated risk. Oral administration of cyclosporine to pregnant rats or rabbits did not produce teratogenicity at clinically relevant doses.

Data

*Animal Data*

Oral administration of cyclosporine oral solution (USP) to pregnant rats or rabbits was teratogenic at maternally toxic doses of 30 mg/kg/day in rats and 100 mg/kg/day in rabbits, as indicated by increased pre- and postnatal mortality, reduced fetal weight, and skeletal retardations. These doses (normalized to body weight) were approximately 3200 and 21,000 times higher than the maximum recommended human ophthalmic dose (MRHOD) of 1.5 mcg/kg/day, respectively. No adverse embryofetal effects were observed in rats or rabbits receiving cyclosporine during organogenesis at oral doses up to 17 mg/kg/day or 30 mg/kg/day, respectively (approximately 1800 and 6400 times higher than the MRHOD, respectively).

An oral dose of 45 mg/kg/day cyclosporine (approximately 4800 times higher than MRHOD) administered to rats from Day 15 of pregnancy until Day 21 postpartum produced maternal toxicity and an increase in postnatal mortality in offspring. No adverse effects in dams or offspring were observed at oral doses up to 15 mg/kg/day (approximately 1600 times greater than the MRHOD).

### Lactation

Risk Summary

Cyclosporine blood concentrations are low following topical ocular administration of CEQUA. There is no information regarding the presence of cyclosporine in human milk following topical administration or on the effects of CEQUA on breastfed infants and milk production. Administration of oral cyclosporine to rats during lactation did not produce adverse effects in offspring at clinically relevant doses. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for CEQUA and any potential adverse effects on the breastfed child from cyclosporine.

### Pediatric Use

The safety and efficacy of CEQUA ophthalmic solution have not been established in pediatric patients below the age of 18.

### Geriatric Use

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

## PATIENT COUNSELING INFORMATION

### Handling the Vial

Advise patients to not allow the tip of the vial to touch the eye or any surface, as this may contaminate the solution. Advise patients also not to touch the vial tip to their eye to avoid the potential for injury to the eye.

### Use with Contact Lenses

CEQUA should not be administered while wearing contact lenses. Patients with decreased tear production typically should not wear contact lenses. Advise patients that if contact lenses are worn, they should be removed prior to the administration of the solution. Lenses may be reinserted 15 minutes following administration of CEQUA ophthalmic solution.

### Administration

Advise patients that the solution from one individual single-use vial is to be used immediately after opening for administration to one or both eyes, and the remaining contents should be discarded immediately after administration.

**Rx Only**

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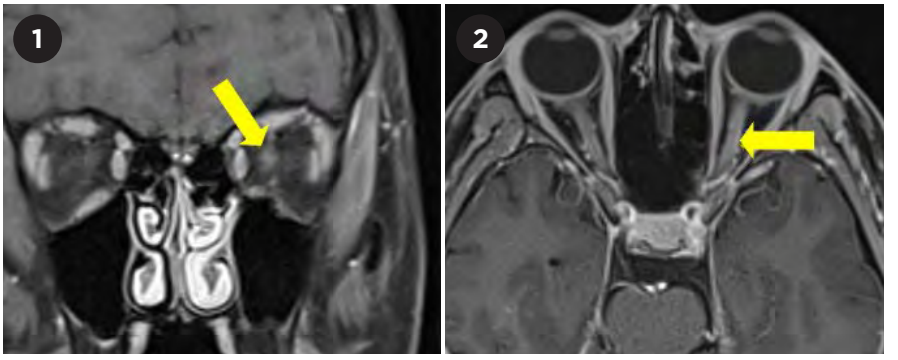
PLR-00020 2018

SUN OPHTHALMICS

# The Case of Visual Loss in a Teenager

Mona Morley,* a 17-year-old girl, experienced vision loss in her left eye. She initially kept this to herself, but after two months, with the problem getting worse, she confided in her parents. They took her to the community ophthalmologist, who noted that Mona's vision was hand motion with a relative afferent pupillary defect (RAPD). The ophthalmologist ordered magnetic resonance imaging (MRI) of the brain and orbits, which were interpreted as normal. Mona was then referred to our clinic for further evaluation.




***A SECOND MRI.*** *T1-weighted, fat-suppressed, contrast-enhanced axial MRI of the orbits in (1) coronal and (2) axial views. Left optic nerve enhancement noted (yellow arrows).*

## We Take Her History

When we first saw Mona, her medical history included anxiety and depression. She also had been treated for Lyme disease four years previously. Her ocular history included dry eye syndrome, meibomian gland dysfunction, and punctate keratitis in both eyes. Her medications included lamotrigine and venlafaxine for anxiety and depression, and levonorgestrel/ethinyl estradiol for contraception. There was no family history of significant eye disease, autoimmune disease, or episodes of sudden vision loss. Mona stated that she was sexually active with males and always used barrier protection.

She said that the vision loss started two months earlier as a "black splotch" in the middle of her vision in her left eye. The splotch began centrally and spread peripherally. She told us that her left eye had always been the weaker eye. She said that she hadn't been experiencing headaches, pain with eye movements, or photosensitivity during this two-month period. From the onset of her symptoms, she said that it took a few weeks for her vision to decline to hand motion. During those last few weeks before we saw her, it remained consistently poor.

## The Exam

On general examination, Mona was alert and oriented; her mood and affect were appropriate under the circumstances.

In her right eye, visual acuity was 20/20, and color vision, motility testing, confrontation field testing, and pupillary exam were within normal limits.

In her left eye, central vision was reduced to hand motion; she saw 0/11 Ishihara plates; and she had constricted confrontation visual fields with an RAPD. Motility was normal.

Intraocular pressures and the slit-lamp exam were normal in both eyes.

In the right eye, the dilated fundus exam revealed a cup-to-disc ratio of 0.3 with a sharp disc margin, absence of pallor and edema, a flat macula, and normal vasculature. In the left eye, cup-to-disc ratio was 0.5 with a sharp disc margin, no edema, and global pallor. The macula was flat, and the retinal vasculature and periphery were normal.

Humphrey 24-2 visual field testing revealed full fields in the right eye and unreliable results in the left. Follow-up Goldmann visual field testing in the left eye showed just a few scattered responses.

## A Second Look

The clinical findings of RAPD and painless visual loss suggested optic neuropathy. However, MRI of the brain and orbit performed one week earlier was interpreted by a radiologist as normal,

BY **ABID HASEEB, MD, KIMBERLEE CURNYN, MD,** AND **PETER W. MACINTOSH, MD.** EDITED BY AHMAD A. AREF, MD, MBA.

with no evidence of acute ischemia, intracranial hemorrhage, space-occupying lesions, edema, or lesions of the optic nerves. However, on our review of the MRI, we noticed some subtle enhancement of the left optic nerve. We ordered a repeat MRI of the brain and orbits (Fig. 1). MRI of the brain was within normal limits. But on MRI of the orbits, the left optic nerve had increased in size with enhancement, consistent with a diagnosis of left optic neuritis. The rest of the MRI orbit findings were within normal limits.

## Differential and Workup

**Differential diagnosis.** Given clinical findings of unilateral painless vision loss and imaging findings consistent with optic neuritis, we developed a broad differential. Possible autoimmune etiologies included multiple sclerosis (MS), neuromyelitis optica (NMO), Sjögren syndrome, and sarcoidosis. Possible infectious etiologies included HIV, syphilis, cat-scratch disease, John Cunningham virus, adenovirus, Epstein-Barr virus, and varicella zoster virus.

**What we ordered.** We recommended an inpatient admission for thorough workup of autoimmune and infectious etiologies. A lumbar puncture was performed, and cerebrospinal fluid (CSF) studies were obtained. Because of Mona's poor spontaneous visual recovery, an MRI of the spine was ordered to investigate for a demyelinating process indicating multiple sclerosis. Inflammation control and immunosuppression can promote vision recovery in the acute phase of optic neuritis. Even though she was no longer in the acute phase, she received 1 g of IV methylprednisolone treatment daily for three days, but this didn't improve her vision.

**Workup's findings.** Mona's workup revealed the presence of antiaquaporin-4 (AQP4) antibody, also known as NMO antibody. There was also a positive Lyme antibody, consistent with the fact that she had previously undergone treatment for Lyme disease, although she had no symptoms consistent with the disease. MRI of the spine was unrevealing for evidence of demyelination. The rest of the workup, including CSF studies, was within normal limits.

Based on the clinical picture, imaging studies, and serological results, we diagnosed Mona with NMO.

## Treatment and Follow-Up

Mona was discharged from the hospital on an oral steroid taper and started on treatment with rituximab. She was also started on prophylactic trimethoprim-sulfamethoxazole. At a three-month follow-up phone conversation, she said that her vision had been stable, and she reported no new symptoms.

## Discussion

NMO is an autoimmune inflammatory disease that leads to demyelinating lesions and, when untreated, consequential vision loss and paralysis. A major development in NMO research was the finding of a detectable serum immunoglobulin G (IgG) against AQP4, a channel that regulates fluid homeostasis across the blood-brain barrier.[1]

**Epidemiology.** NMO predominantly presents in women in the fourth or fifth decade of life, though one large study found that 5% of AQP4-IgG–positive patients are younger than 18.[2] That same study found AQP4-IgG to be seven times more prevalent in females than in males. In terms of demographics, one study reported that 37% of pediatric NMO patients were White, 37% were Black and 13% were Hispanic/Latinx; the frequency of non-White race in that study (63%) was greater than in MS (39%), which predominantly affects White patients.[3]

**Symptoms.** Clinically, NMO presents with optic neuritis and transverse myelitis with poor recovery. Presenting symptoms in pediatric NMO include vision loss, motor deficiencies, and constitutional symptoms such as fevers, hiccups, and seizures. A large case series of NMO spectrum disorders in pediatric patients found that 65% presented with optic neuritis, 55% with spinal cord involvement, and 13% involved both.[3]

**NMO in pediatric patients.** Most of the clinical, imaging, and laboratory findings in pediatric-onset NMO are similar to those in adult-onset disease. However, in pediatric patients, the female preponderance is lower; there is longer time to increased disease severity; there is a longer time to first treatment; a monophasic disease course is more common; and MRI lesions associated with acute myelitis may be less specific for NMO spectrum diseases.[1,4]

**Making the diagnosis.** When NMO is suspected, an appropriately detailed history and physical exam should be obtained. This should be followed by a workup that includes hematologic and metabolic studies, cerebrospinal fluid studies, serologic studies for antibodies associated with autoimmune etiologies, and evidence of infectious etiologies underlying vision loss. For patients with AQP4-IgG seropositivity, a diagnosis of NMO can be confirmed—according to consensus diagnostic criteria from the International Panel for NMO Diagnosis—if at least one core clinical characteristic (such as optic neuritis or myelitis) is present and alternative diagnoses can be excluded.[1] Our patient satisfied these criteria. In patients without confirmed AQP4-IgG, there are additional diagnostic requirements: The patient should have at least two core clinical characteristics and, to enhance diagnostic specificity, MRI scans should show supportive characteristics. For example, if one of the core clinical characteristics is acute myelitis, a longitudinal MRI scan that shows a lesion extending over three or more contiguous segments would be needed.[1]

**Treatment.** Treatment of NMO focuses on minimizing disease progression by mitigating acute attacks and preventing future exacerbations. Treatment of acute attacks involves the use of IV methylprednisolone. Since 2019, three new targeted therapeutic agents for NMO—eculizumab (complement C5), inebilizumab (CD19+ B cells), and satralizumab (interleukin-6)—have become available and are FDA-approved for first-line therapy of patients with this disorder. Newly diagnosed patients should be considered for one of these agents. Additionally, some mainstays of MS treatment, namely interferon-beta and natalizumab, may increase relapse rate in NMO, underscoring the importance of distinguishing between these two disease processes.[5]

**Prognosis.** One study of 106 patients with AQP4-IgG–positive NMO found

that, after a median disease duration of 75 months, 18% of patients developed permanent bilateral visual disability, 34% had permanent motor disability, and 23% had become wheelchair-dependent.[6] In the small number of patients who were treated before their first relapse, none developed permanent visual disability. However, early treatment did not protect against motor disability. Patients with monophasic disease courses were treated earlier than patients with relapsing disease (three months vs. 54 months). While the understanding around prognosis in NMO-spectrum diseases is developing, these findings suggest that delays in treatment portend worse disease courses. Timely diagnosis and treatment are critical.

## Conclusion

This case emphasizes the importance of putting NMO on the differential diagnosis for vision loss, even in pediatric patients, who may experience significant vision loss before reporting it to parents. Furthermore, it highlights the need for ophthalmologists to thoroughly re-interrogate the findings and assumptions in referred cases because the finding of optic neuritis may initially be missed, as it was in this instance. Imaging alone may not be sufficient for diagnosis, and clinicians should be aware of the laboratory testing available for a thorough workup.

* Patient name is fictitious.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**Dr. Haseeb** is in his internship year at the University of Illinois Hospital in Chicago. **Dr. Curnyn** and **Dr. MacIntosh** are at the Illinois Eye and Ear Infirmary in Chicago; Dr. Curnyn is clinical assistant professor of ophthalmology in the Pediatric Ophthalmology and Adult Strabismus Service, and Dr. MacIntosh is assistant professor of ophthalmology and director of the Residency Program. *Financial disclosures: Mr. Haseeb and Dr. Curnyn: None. Dr. MacIntosh: NEI: S; Research to Prevent Blindness: S.*


**See disclosure key,** page 10.


## MORE AT AAO 2021

**What Are "NMOSDs" and "MOGs" and How Are They Different From MS? What the Comprehensive Ophthalmologist Needs to Know About Optic Neuritis (event code 285).** *Senior instructor: Howard D. Pomeranz, MD, PhD.* This course will discuss several etiologies for demyelinating optic neuritis, along with characteristic radiological and laboratory treatments. **When:** Saturday, Nov. 13, 3:45-5:00 p.m. **Where:** Room 338.

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# AAO 2021

## The Many Paths to Leadership

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## Program Highlights

**Jackson Memorial Lecture**
Russell N. Van Gelder, MD, PhD

**Spotlight on Cataract Complications**
David F. Chang, MD and
Nicole R. Fram, MD

**Charles D. Kelman Lecture**
Michael E. Snyder, MD

**C. Stephen and Frances Foster Lecture on Uveitis and Immunology**
Narsing A. Rao, MD

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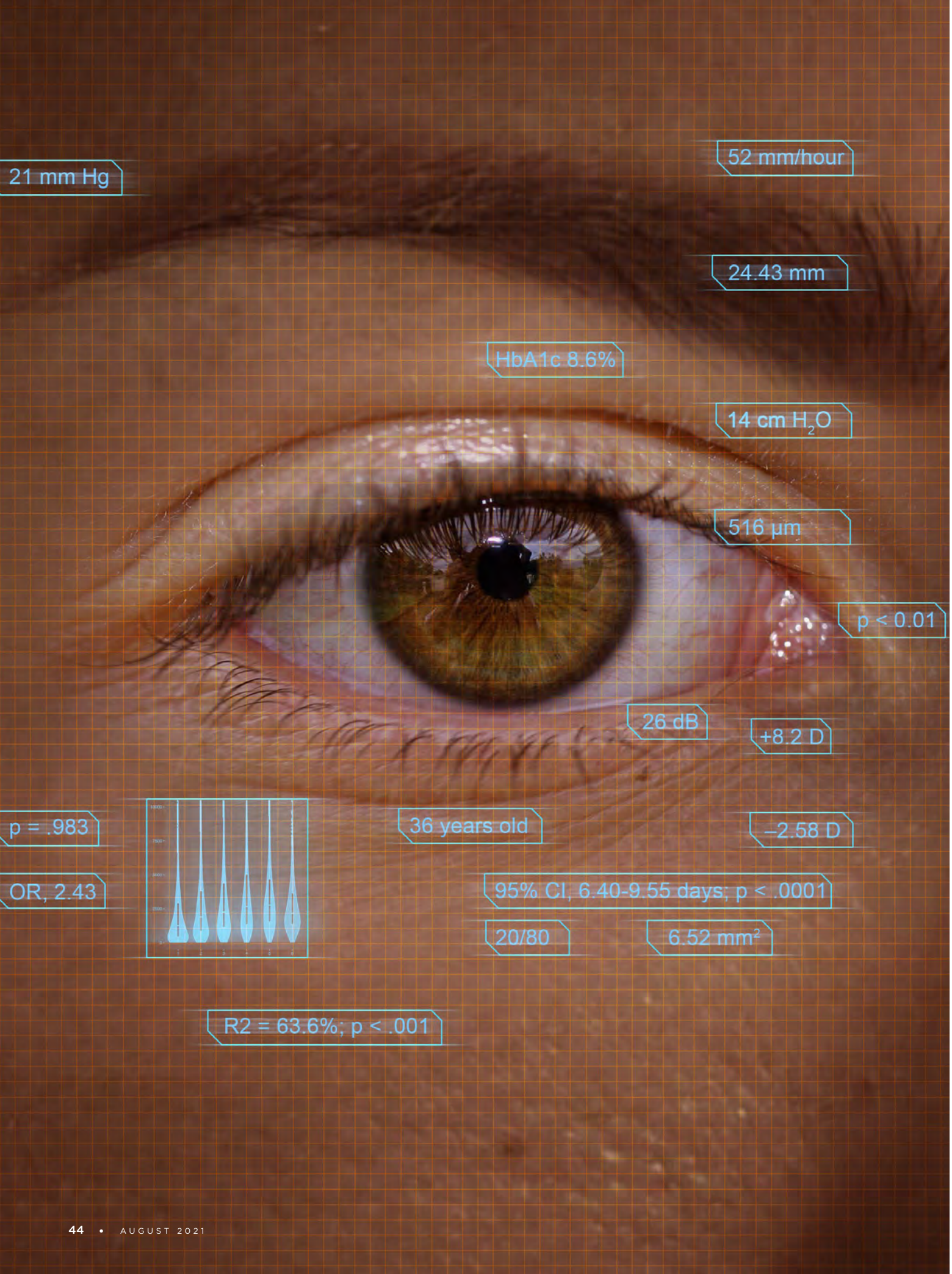

21 mm Hg
52 mm/hour
24.43 mm
HbA1c 8.6%
14 cm $H_2O$
516 µm
p < 0.01
26 dB
+8.2 D
p = .983
36 years old
–2.58 D
OR, 2.43
95% CI, 6.40-9.55 days; p < .0001
20/80
6.52 mm²
R2 = 63.6%; p < .001

# Big Data Studies

How to tell when the analysis might be falling short.

By Mike Mott, Contributing Writer

BIG DATA, A ONCE-NICHE BUZZWORD, has become mainstream. And its wealth of clinical and patient information—from electronic health records (EHRs), health insurance and Medicare claims databases, clinical data registries, national biobanks, and mobile and wearable devices—has spawned a boom in population-based research. The ophthalmic literature is now flooded with studies that incorporate patient cohorts in the millions—datasets that are too large for traditional statistical methodologies.

Consequently, many physicians find themselves reading literature that involves unfamiliar data analysis techniques, said Marion R. Munk, MD, PhD, at the University of Bern in Switzerland, and this increasing complexity is now becoming an issue for the practicing ophthalmologist.

A 2014 review of the peer-reviewed ophthalmic literature, for example, found that a reader with basic statistical knowledge was only able to critically evaluate 20% of studies.[1] To successfully assess the results of more than 90% required a working knowledge of at least 29 different statistical methods. "Seven years have passed since that publication," said Dr. Munk, "and it's safe to say that big data might be pushing many of us into murky waters."

So the next time you come across a paper investigating the efficacy of treatments X, Y, and Z distilled from hundreds of thousands of patients, how can you decipher when the analysis is sound and when the data are being misused? Here's what to watch for when navigating big data.

## Use Care When Interpreting Significance

Commonly, readers of big data studies misunderstand the word "significance," said Aaron Y. Lee, MD, MSc, at the University of Washington in Seattle. "Too often, readers conflate statistical significance with clinical significance, and that confusion largely stems from not truly understanding what a 'p' value measures," he said.

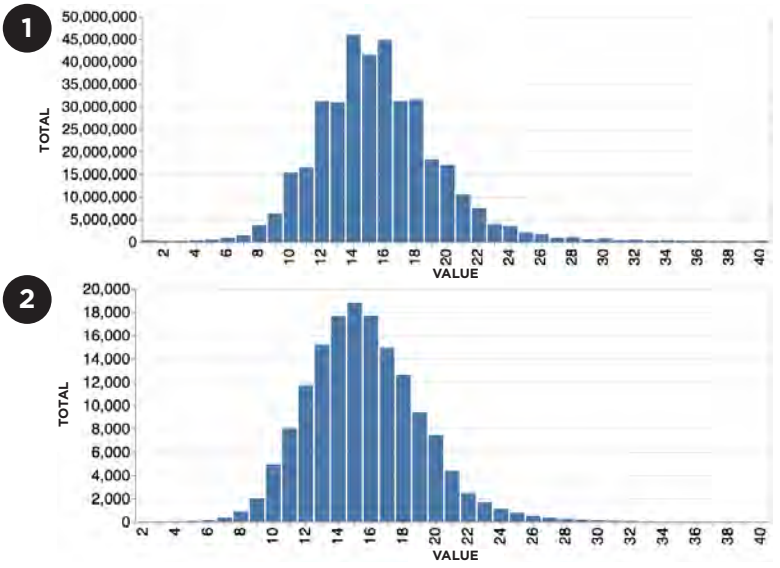
**P basics.** P value is a commonly used measurement of statistical significance, said Dr. Lee. Readers need to be aware that it measures the probability that a study's result is due to chance and does not necessarily demonstrate a treatment effect of clinical significance. For example, the traditional cutoff for a statistically significant p value is 0.05. $P < 0.05$ means there's less than a 5% possibility that the result is a random event.

**P meets big data.** What's more, because statistical significance is positively correlated with sample size, these conventional metrics break down when used in large population-based research, said Dr. Lee. "P values were never designed to be used with millions and millions of patients. Now we have the ability to obtain so much data that achieving statistical difference between groups has become almost trivial—seemingly everything becomes statistically significant."

So when you come across a big data study and see multiple p values that are all extraordinarily small, you might be led to believe there are very strong associations there, he said, when in fact it's just an artifact of the number of patients included.

**When is it clinically significant?** While p values

Peter Bollinger




***DATA FROM THE ENTIRE IRIS REGISTRY DATABASE.*** *(1) Goldmann applanation tonometry compared with (2) other forms of tonometry shows that pressures of 12, 14, 16, 18, and 20 are much more common than 13, 15, 17, and 19. Why? Because applanation tonometers are marked for the even numbers, and ophthalmologists tend to round up or down to the nearest even number.*

are important, readers need to take a deeper look at the size of the real treatment effect that would connote clinical significance, said Maureen G. Maguire, PhD, FARVO, at the University of Pennsylvania in Philadelphia.

**Sample scenario.** For example, a glaucoma study might look at the effect of two drugs on lowering the intraocular pressure (IOP) of 100,000 patients. Drug A decreased IOP by 5 mm Hg and drug B by 5.1 mm Hg—a mean difference of 0.1 mm Hg. With a p value well below the conventional 0.05 threshold, the researchers found the difference to be highly statistically significant.

"But as the reader, you have to dig in a bit more," said Dr. Maguire. "That p value only tells you whether the difference between the two drugs is zero or not. It doesn't tell you anything about how big the difference is." For that you need to look for effect estimates with corresponding confidence intervals to interpret whether the difference is meaningful, she said. "In this example, let's say the confidence interval is 0.05 to 0.15 mm Hg," said Dr. Maguire. "That's the range of values in which we are fairly sure our mean IOP difference lies. Is that clinically meaningful? No. That's not going to drive a change in treatment."

## Were the Researchers Fishing for P Values?

With the sheer amount of information available from resources like health insurance databases, researchers are better able to investigate multiple hypotheses, said Dr. Munk. But the more statistical tests they employ on a single dataset, the better the chance they will draw an erroneous conclusion.

**Errors of commission and omission.** In understanding p values, it is critical to frame the hypothesis—the question under investigation. Many questions in medical research involve determining differences between subpopulations. Did patients receiving treatment X have a different outcome than patients receiving treatment Y? Is group X at higher risk of disease than group Y? The null hypothesis states that there is no difference between groups and is akin to "innocence before proof of guilt" in a criminal trial. Two types of errors can occur in reaching a conclusion about the null hypothesis. It can be rejected due to spurious data—a Type I error, akin to convicting an innocent defendant due to chance circumstantial evidence. Alternatively, the null hypothesis can be accepted when it is actually false, a Type II error comparable to acquitting a guilty defendant.

**False positives.** At the conventional p threshold of 0.05, a single statistical hypothesis has a 1 in 20 probability of significance due to chance—in other words, a 5% chance that it will produce a false positive. This probability dramatically increases as the number of tests increase. For example, testing 14 individual hypotheses on the same dataset using the p threshold of 0.05 will result in a greater than 50% chance of one false positive, and thus a Type I error.[2]

**P-hacking.** This is what statisticians call the multiple testing problem, said Dr. Munk, and it can lead to the purposeful misuse of the data, otherwise known as data dredging or p-hacking, in which researchers conduct arbitrary post hoc analyses searching for any type of reportable outcome if their original hypothesis didn't pan out.

"Massive datasets allow researchers to conduct so many different types of association tests, but they might also be falsely discovering importance," said Dr. Munk. "Ophthalmologists, for example, can search for relationships by gender, age group, race, presenting visual acuity, IOP, and on and on, but exhaustively testing multiple hypotheses to see

what sticks on the wall can be very misleading."

As a reader, Dr. Munk wants to see clearly formulated, prespecified research questions as well as detailed methods that the researchers have used to conclusively prove or reject each hypothesis. "But if you open a journal and you're staring down at tables with 50, 60, 70 p values and the writers are correlating everything with everything, you should be cautious," she said. "That's definitely a sign of fishing for significance."

**A fix.** If the probability of false positives increases as the number of statistical comparisons increase, how can researchers correct for this phenomenon? The simplest method is using a Bonferroni correction, said Dr. Lee, in which the probability threshold (here using the conventional cutoff of 5%) for each individual test is adjusted to 0.05/N (where N is the total number of tests performed), thus ensuring that the study-wide error rate remains at 0.05.

However, this method may also increase the researcher's risk of an inadvertent Type II error, failing to reject a false null hypothesis. Because reducing the risk of false positives can also increase the risk of missing true positives, many critics believe the Bonferroni correction to be too conservative, said Dr. Lee. "Regardless of what method a researcher uses, by correcting for multiple comparisons, readers can worry less about the false discoveries and spurious associations that the researcher might have produced from slicing and dicing the data," he said.

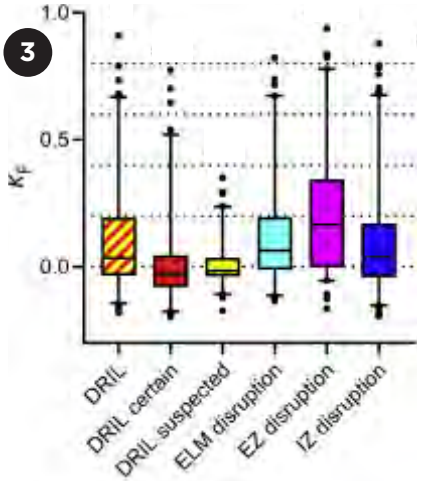
Unfortunately, the use of correction factors by ophthalmologists may not be as prevalent as might be expected, added Dr. Lee. For example, in a 2012 review of more than 6,000 abstracts from a

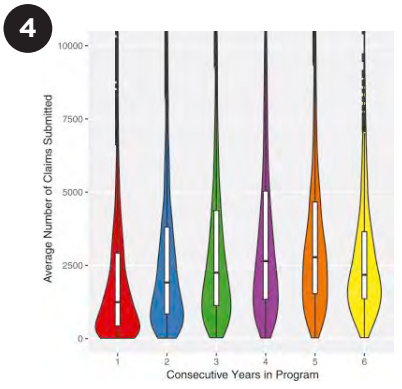
## Visualizing Big Data

Given the size of big data, researchers may represent their datasets in a number of ways for easier consumption. But these pictures can say a thousand words, or none at all, said Dr. Lee.

"For example, you probably won't come across many bar graphs in this type of research because of their simplicity," he said. "Data transparency is paramount, and a basic distribution plot showing mean values with standard deviations is going to hide a lot of the messiness that needs to be visible to the reader."

To provide the fullest picture of variability, current best practice is to present as much of the data as possible, oftentimes with the help of box-and-whisker or violin plots, said Dr. Lee.




**Distribution plots.** To visualize multiple statistical components of the data, the box-and-whisker plot (Fig. 3) provides a five-part graphical snapshot, including:

- a "box," which shows the median and the first and third quartiles of the dataset, and
- two "whiskers," which extend outward from each quartile and represent the minimum and maximum data points.

These plots are helpful because they can provide insight into the outliers (represented by dots), any symmetry and grouping, and how the data skews, said Dr. Lee. They're limited in value, though, because they don't show how all of the data points are distributed around these five markers.

**The best picture.** Likewise, violin plots (Fig. 4) include a snapshot of the median and the interquartile range, said Dr. Lee. But they are extremely useful because they show the full distribution of the data via overlaid density curves—what gives the plot its "violin" shape.

It's an easy-to-read representation, said Dr. Lee, because the width of the violin corresponds to the frequency of the values along each region of the internal box plot. "This method allows for transparency of the raw distributions for all of the variables in your study. It provides the entire data story."

## The IRIS Registry

The Academy's IRIS Registry has aggregated EHR information on 68 million patients from close to 16,000 participating clinicians. It includes a range of data points across 387 million patient visits, from demographics and medical history, to clinical examination findings, diagnoses, procedures, and medications.

Grants are available to clinicians and others who are interested in conducting IRIS Registry research.

**Learn more** at aao.org/iris-registry/data-analysis/requirements then scroll to "Current research opportunities."

major ophthalmic research conference, 8% of the submissions reported at least five p values, 95% of which did not correct for multiple comparisons. In a statistical simulation, the authors estimated that failure to do so could have resulted in 185 false-positive outcomes.[2]

### Be Aware of Treatment and Patient Bias

Readers should also have a healthy skepticism about any bias that researchers unwillingly—or purposefully—introduce in these big data studies, said Dr. Maguire, especially in terms of treatment and patient selection.

**Scenario #1: Treatment selection.** Imagine a retina study looking at the use of anti-VEGF drugs A and B for the treatment of neovascular age-related macular degeneration (AMD), said Dr. Maguire. The researchers want to know whether the number of injections needed for each drug is the same. A good source of data for this hypothesis would be an insurance claims database, which captures each injection based on specific billing and diagnostic codes.

But what could those data be hiding from the reader? More than you might think, said Dr. Maguire. First, there's likely no information regarding the size of the neovascular lesion, whether it was classic or occult, or the amount of retina fluid on OCT, she said. "Also, certain ophthalmologists might favor a specific treatment for a specific patient. For example, they might select anti-VEGF drug A, which they think is the best at drying the retina, for patients who have the highest likelihood of requiring multiple injections."

In doing so, they would overload drug group A with patients who have the worst prognosis so that the average number of injections would be greater than for drug group B, said Dr. Maguire. But a data analyst alone would never know this by just looking at the claims data, she said. And that's the problem: the bias toward using drug A in worst cases. On the other hand, a randomized masked trial between the drugs, in which the severity of cases was identical, might reach the conclusion that the two drugs are equally effective. "The reader who is accustomed to reading randomized controlled trials might assume that all of the patients in the claims database were of the same need for injections. So to create an even playing field, a study like this would require collaboration with a retina specialist to identify potential selection factors and provide insight into the likely magnitude of treatment bias."

**Scenario #2: Patient selection.** When selecting groups of patients who will undergo analysis, some exclusions that sound very reasonable can also cause trouble when interpreting results, said Dr. Maguire.

Imagine a second retina study using the same insurance claims database to compare bevacizumab and aflibercept for improving visual acuity (VA) one year after treatment for neovascular AMD. The researchers utilize two cohorts: those patients who receive only bevacizumab for the full year and those who receive only aflibercept for the full year.

That might sound sensible on the surface, said Dr. Maguire, but that would be concerning for retina specialists because, in today's practice, patients often start on low-cost bevacizumab first and, if their vision doesn't improve sufficiently, they are switched to aflibercept. Thus, in this example, "a set of patients doing poorly on bevacizumab would be excluded from the study because of the switch," she said, "while every aflibercept patient doing poorly would be retained." Bevacizumab would therefore appear to provide better VA. "The data are again hiding important information that the reader is not aware of," Dr. Maguire added. "It sounds clean to use only patients who stayed on the same drug, but the data are still biased."

### Keep Data Quality in Mind

"A large dataset like the IRIS Registry includes information in EHRs for patients across the United States," said Leslie G. Hyman, PhD, at Wills Eye Hospital in Philadelphia. "But this information was captured for clinical, administrative, and reimbursement purposes, not specifically for research.

While these data can provide ophthalmologists with important information pertaining to diagnostics, exam findings, demographics, and treatment provided, they are not captured in a systematic, consistent manner across the board, she said. There can be missing data fields, data entry

errors, and differing EHR formats, which cause high variability in the information available.

**Cases for concern.** "From a researcher's perspective, it's important to be aware of the data source and recognize the strengths and weaknesses of the dataset itself," said Dr. Hyman. "That understanding drives how researchers will interpret the study findings, how the data apply to patients, and ultimately whether or not these large data sources allow researchers to answer the questions they want to pose."

**Scenario #1: Variable data.** A good example of uneven data quality is the variability of VA measurements, said Dr. Hyman. VA is one of the most important pieces of information for evaluating the severity and impact of eye disease and treatment outcomes. In a traditional clinical study, researchers will measure VA using specific, standardized, detailed protocols, she said. But that's often not the case in big datasets.

"Visual acuity measures captured by an EHR lack consistency," said Dr. Hyman. For example, an eye care professional might measure acuity multiple times in a visit, with different methods, or when a patient is close to a target or far away. "Because of this variability, researchers have to think carefully about which of these measures best represent the visual acuity of a patient at a given time for a given visit," in order for the study to be based on the most appropriate data, she said.

**Scenario #2: Missing data.** What if a researcher is interested in health disparities regarding the treatment of diabetic retinopathy, said Dr. Hyman, but 20% of the records in the dataset fail to include key information such as ethnicity of an individual, which is needed to answer the question?

"If researchers don't have that vital information, they have to think about why it might be missing and how that might influence interpretation of the results," said Dr. Hyman. Are there certain biases with respect to why people don't report ethnicity? Would those reasons be related to having more severe disease or worse outcomes? Or is it just an omission? "Again, the investigator must consider the available data when posing a research question and make sure they are appropriate to the question that's being asked," she said.

## With Big Data, Big Challenges

Big data applications such as the IRIS Registry are indeed providing unprecedented ways to investigate the natural history of disease, the prevalence of rare diseases, practice pattern changes, the diffusion of technology, and more, all in a cost-effective, real-world setting.

"Yet despite this tremendous promise, big data simply doesn't have the answer for everything," said Dr. Maguire. "These data studies are just difficult to do well given the different levels of expertise required—you need physicians, you need data scientists, you need experts in billing and coding." Nevertheless, big data are becoming ubiquitous, she said, and as consumers, ophthalmologists need to be more mindful of when the answers are valuable and when they're not, what they can tell us and what they can't.

1 Lisboa R et al. *Ophthalmology*. 2014;121(7):1317-1321.
2 Stacey AW et al. *Invest Ophthalmol Vis Sci*. 2012;53(4):1830-1834.

## Meet the Experts

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**See disclosure key,** page 10. **For full disclosures,** view this article at aao.org/eyenet.

# WHAT COULD SHE SEE THIS YEAR?

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

## 36 FAMILY RECIPES

*Inspired by a real patient with MEfRVO.*

## IMPORTANT SAFETY INFORMATION

## CONTRAINDICATIONS

- EYLEA is contraindicated in patients with ocular or periocular infections, active intraocular inflammation, or known hypersensitivity to aflibercept or to any of the excipients in EYLEA.

## WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately. Intraocular inflammation has been reported with the use of EYLEA.
- Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with VEGF inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.
- There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

# CLINICALLY SIGNIFICANT VISION GAINS IN MEfRVO ACROSS 3 ROBUST CLINICAL TRIALS

Proportion of patients who gained ≥15 ETDRS letters (primary endpoint) and mean change in BCVA (ETDRS letters) (secondary endpoint) at Month 6 from baseline vs control[1-4,*]

| VIBRANT (MEfBRVO) | | COPERNICUS (MEfCRVO) | | GALILEO (MEfCRVO) | |
|---|---|---|---|---|---|
| Gained ≥15 ETDRS letters | Mean change in ETDRS letters | Gained ≥15 ETDRS letters | Mean change in ETDRS letters | Gained ≥15 ETDRS letters | Mean change in ETDRS letters |
| **EYLEA (n=91)** | **EYLEA (n=91)** | **EYLEA (n=114)** | **EYLEA (n=114)** | **EYLEA (n=103)** | **EYLEA (n=103)** |
| **53%** vs 27% in the control group (n=90) | **+17.0** vs +6.9 in the control group (n=90) | **56%** vs 12% in the sham control group (n=73) | **+17.3** vs -4.0 in the sham control group (n=73) | **60%** vs 22% in the sham control group (n=68) | **+18.0** vs +3.3 in the sham control group (n=68) |

*P*<0.01 vs control and sham control.

**VIBRANT study design:** Randomized, multicenter, double-masked, controlled study in which patients with MEfBRVO (N=181; age range: 42-94 years, with a mean of 65 years) were randomized to receive: 1) EYLEA 2 mg Q4 or 2) laser photocoagulation administered at baseline and subsequently as needed (control group). The primary efficacy endpoint was the proportion of patients who gained ≥15 letters in BCVA at Week 24 compared with baseline.[1]

**COPERNICUS and GALILEO study designs:** Randomized, multicenter, double-masked, sham-controlled studies in patients with MEfCRVO (N=358; age range: 22-89 years, with a mean of 64 years). Patients were assigned in a 3:2 ratio to either: 1) EYLEA 2 mg Q4 for the first 6 months or 2) sham injections (control) Q4 for a total of 6 injections. In both studies, the primary efficacy endpoint was the proportion of patients who gained ≥15 letters in BCVA at Week 24 compared with baseline.[1]

*Last observation carried forward; full analysis set.

**SEE WHAT EYLEA COULD DO FOR YOUR PATIENTS WITH MEfRVO AT HCP.EYLEA.US**

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; Q4, every 4 weeks.

## ADVERSE REACTIONS

- Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment.
- The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.
- Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

## INDICATIONS

EYLEA® (aflibercept) Injection 2 mg (0.05 mL) is indicated for the treatment of patients with Neovascular (Wet) Age-related Macular Degeneration (AMD), Macular Edema following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), and Diabetic Retinopathy (DR).

**References: 1.** EYLEA® (aflibercept) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc. August 2019. **2.** Campochiaro PA, Clark WL, Boyer DS, et al. Intravitreal aflibercept for macular edema following branch retinal vein occlusion: the 24-week results of the VIBRANT study. *Ophthalmology*. 2015;122(3):538-544. doi:10.1016/j.ophtha.2014.08.031 **3.** Boyer D, Heier J, Brown DM, et al. Vascular endothelial growth factor Trap-Eye for macular edema secondary to central retinal vein occlusion: six-month results of the phase 3 COPERNICUS study. *Ophthalmology*. 2012;119(5):1024-1032. doi:10.1016/j.ophtha.2012.01.042 **4.** Holz FG, Roider J, Ogura Y, et al. VEGF Trap-Eye for macular oedema secondary to central retinal vein occlusion: 6-month results of the phase III GALILEO study. *Br J Ophthalmol*. 2013;97(3):278-284. doi:10.1136/bjophthalmol-2012-301504

**Please see Brief Summary of Prescribing Information on the following page.**

03/2021
EYL.21.02.0050

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

**BRIEF SUMMARY—Please see the EYLEA full Prescribing Information available on HCP.EYLEA.US for additional product information.**

**1 INDICATIONS AND USAGE**
EYLEA is a vascular endothelial growth factor (VEGF) inhibitor indicated for the treatment of patients with:

**Neovascular (Wet) Age-Related Macular Degeneration (AMD), Macular Edema Following Retinal Vein Occlusion (RVO), Diabetic Macular Edema (DME), Diabetic Retinopathy (DR).**

**4 CONTRAINDICATIONS**

**4.1 Ocular or Periocular Infections**
EYLEA is contraindicated in patients with ocular or periocular infections.

**4.2 Active Intraocular Inflammation**
EYLEA is contraindicated in patients with active intraocular inflammation.

**4.3 Hypersensitivity**
EYLEA is contraindicated in patients with known hypersensitivity to aflibercept or any of the excipients in EYLEA. Hypersensitivity reactions may manifest as rash, pruritus, urticaria, severe anaphylactic/anaphylactoid reactions, or severe intraocular inflammation.

**5 WARNINGS AND PRECAUTIONS**

**5.1 Endophthalmitis and Retinal Detachments**
Intravitreal injections, including those with EYLEA, have been associated with endophthalmitis and retinal detachments [*see Adverse Reactions (6.1)*]. Proper aseptic injection technique must always be used when administering EYLEA. Patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment without delay and should be managed appropriately [*see Patient Counseling Information (17)*].

**5.2 Increase in Intraocular Pressure**
Acute increases in intraocular pressure have been seen within 60 minutes of intravitreal injection, including with EYLEA [*see Adverse Reactions (6.1)*]. Sustained increases in intraocular pressure have also been reported after repeated intravitreal dosing with vascular endothelial growth factor (VEGF) inhibitors. Intraocular pressure and the perfusion of the optic nerve head should be monitored and managed appropriately.

**5.3 Thromboembolic Events**
There is a potential risk of arterial thromboembolic events (ATEs) following intravitreal use of VEGF inhibitors, including EYLEA. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause). The incidence of reported thromboembolic events in wet AMD studies during the first year was 1.8% (32 out of 1824) in the combined group of patients treated with EYLEA compared with 1.5% (9 out of 595) in patients treated with ranibizumab; through 96 weeks, the incidence was 3.3% (60 out of 1824) in the EYLEA group compared with 3.2% (19 out of 595) in the ranibizumab group. The incidence in the DME studies from baseline to week 52 was 3.3% (19 out of 578) in the combined group of patients treated with EYLEA compared with 2.8% (8 out of 287) in the control group; from baseline to week 100, the incidence was 6.4% (37 out of 578) in the combined group of patients treated with EYLEA compared with 4.2% (12 out of 287) in the control group. There were no reported thromboembolic events in the patients treated with EYLEA in the first six months of the RVO studies.

**6 ADVERSE REACTIONS**
The following potentially serious adverse reactions are described elsewhere in the labeling:
- Hypersensitivity [*see Contraindications (4.3)*]
- Endophthalmitis and retinal detachments [*see Warnings and Precautions (5.1)*]
- Increase in intraocular pressure [*see Warnings and Precautions (5.2)*]
- Thromboembolic events [*see Warnings and Precautions (5.3)*]

**6.1 Clinical Trials Experience**
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in the clinical trials of a drug cannot be directly compared to rates in other clinical trials of the same or another drug and may not reflect the rates observed in practice.
A total of 2980 patients treated with EYLEA constituted the safety population in eight phase 3 studies. Among those, 2379 patients were treated with the recommended dose of 2 mg. Serious adverse reactions related to the injection procedure have occurred in <0.1% of intravitreal injections with EYLEA including endophthalmitis and retinal detachment. The most common adverse reactions (≥5%) reported in patients receiving EYLEA were conjunctival hemorrhage, eye pain, cataract, vitreous detachment, vitreous floaters, and intraocular pressure increased.

**Neovascular (Wet) Age-Related Macular Degeneration (AMD).** The data described below reflect exposure to EYLEA in 1824 patients with wet AMD, including 1223 patients treated with the 2-mg dose, in 2 double-masked, controlled clinical studies (VIEW1 and VIEW2) for 24 months (with active control in year 1).
Safety data observed in the EYLEA group in a 52-week, double-masked, Phase 2 study were consistent with these results.

**Table 1: Most Common Adverse Reactions (≥1%) in Wet AMD Studies**

| | Baseline to Week 52 | | Baseline to Week 96 | |
|---|---|---|---|---|
| **Adverse Reactions** | **EYLEA (N=1824)** | **Active Control (ranibizumab) (N=595)** | **EYLEA (N=1824)** | **Control (ranibizumab) (N=595)** |
| Conjunctival hemorrhage | 25% | 28% | 27% | 30% |
| Eye pain | 9% | 9% | 10% | 10% |
| Cataract | 7% | 7% | 13% | 10% |
| Vitreous detachment | 6% | 6% | 8% | 8% |
| Vitreous floaters | 6% | 7% | 8% | 10% |
| Intraocular pressure increased | 5% | 7% | 7% | 11% |
| Ocular hyperemia | 4% | 8% | 5% | 10% |
| Corneal epithelium defect | 4% | 5% | 5% | 6% |
| Detachment of the retinal pigment epithelium | 3% | 3% | 5% | 5% |
| Injection site pain | 3% | 3% | 3% | 4% |
| Foreign body sensation in eyes | 3% | 4% | 4% | 4% |
| Lacrimation increased | 3% | 1% | 4% | 2% |
| Vision blurred | 2% | 2% | 4% | 3% |
| Intraocular inflammation | 2% | 3% | 3% | 4% |
| Retinal pigment epithelium tear | 2% | 1% | 2% | 2% |
| Injection site hemorrhage | 1% | 2% | 2% | 2% |
| Eyelid edema | 1% | 2% | 2% | 3% |
| Corneal edema | 1% | 1% | 1% | 1% |
| Retinal detachment | <1% | <1% | 1% | 1% |

Less common serious adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal tear, and endophthalmitis.

**Macular Edema Following Retinal Vein Occlusion (RVO).** The data described below reflect 6 months exposure to EYLEA with a monthly 2 mg dose in 218 patients following central retinal vein occlusion (CRVO) in 2 clinical studies (COPERNICUS and GALILEO) and 91 patients following branch retinal vein occlusion (BRVO) in one clinical study (VIBRANT).

**Table 2: Most Common Adverse Reactions (≥1%) in RVO Studies**

| | CRVO | | BRVO | |
|---|---|---|---|---|
| **Adverse Reactions** | **EYLEA (N=218)** | **Control (N=142)** | **EYLEA (N=91)** | **Control (N=92)** |
| Eye pain | 13% | 5% | 4% | 5% |
| Conjunctival hemorrhage | 12% | 11% | 20% | 4% |
| Intraocular pressure increased | 8% | 6% | 2% | 0% |
| Corneal epithelium defect | 5% | 4% | 2% | 0% |
| Vitreous floaters | 5% | 1% | 1% | 0% |
| Ocular hyperemia | 5% | 3% | 2% | 2% |
| Foreign body sensation in eyes | 3% | 5% | 3% | 0% |
| Vitreous detachment | 3% | 4% | 2% | 0% |
| Lacrimation increased | 3% | 4% | 3% | 0% |
| Injection site pain | 3% | 1% | 1% | 0% |
| Vision blurred | 1% | <1% | 1% | 1% |
| Intraocular inflammation | 1% | 1% | 0% | 0% |
| Cataract | <1% | 1% | 5% | 0% |
| Eyelid edema | <1% | 1% | 1% | 0% |

Less common adverse reactions reported in <1% of the patients treated with EYLEA in the CRVO studies were corneal edema, retinal tear, hypersensitivity, and endophthalmitis.

**Diabetic Macular Edema (DME) and Diabetic Retinopathy (DR).** The data described below reflect exposure to EYLEA in 578 patients with DME treated with the 2-mg dose in 2 double-masked, controlled clinical studies (VIVID and VISTA) from baseline to week 52 and from baseline to week 100.

**Table 3: Most Common Adverse Reactions (≥1%) in DME Studies**

| | Baseline to Week 52 | | Baseline to Week 100 | |
|---|---|---|---|---|
| **Adverse Reactions** | **EYLEA (N=578)** | **Control (N=287)** | **EYLEA (N=578)** | **Control (N=287)** |
| Conjunctival hemorrhage | 28% | 17% | 31% | 21% |
| Eye pain | 9% | 6% | 11% | 9% |
| Cataract | 8% | 9% | 19% | 17% |
| Vitreous floaters | 6% | 3% | 8% | 6% |
| Corneal epithelium defect | 5% | 3% | 7% | 5% |
| Intraocular pressure increased | 5% | 3% | 9% | 5% |
| Ocular hyperemia | 5% | 6% | 5% | 6% |
| Vitreous detachment | 3% | 3% | 8% | 6% |
| Foreign body sensation in eyes | 3% | 3% | 3% | 3% |
| Lacrimation increased | 3% | 2% | 4% | 2% |
| Vision blurred | 2% | 2% | 3% | 4% |
| Intraocular inflammation | 2% | <1% | 3% | 1% |
| Injection site pain | 2% | <1% | 2% | <1% |
| Eyelid edema | <1% | 1% | 2% | 1% |

Less common adverse reactions reported in <1% of the patients treated with EYLEA were hypersensitivity, retinal detachment, retinal tear, corneal edema, and injection site hemorrhage.
Safety data observed in 269 patients with nonproliferative diabetic retinopathy (NPDR) through week 52 in the PANORAMA trial were consistent with those seen in the phase 3 VIVID and VISTA trials (see Table 3 above).

**6.2 Immunogenicity**
As with all therapeutic proteins, there is a potential for an immune response in patients treated with EYLEA. The immunogenicity of EYLEA was evaluated in serum samples. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to EYLEA in immunoassays. The detection of an immune response is highly dependent on the sensitivity and specificity of the assays used, sample handling, timing of sample collection, concomitant medications, and underlying disease. For these reasons, comparison of the incidence of antibodies to EYLEA with the incidence of antibodies to other products may be misleading.
In the wet AMD, RVO, and DME studies, the pre-treatment incidence of immunoreactivity to EYLEA was approximately 1% to 3% across treatment groups. After dosing with EYLEA for 24-100 weeks, antibodies to EYLEA were detected in a similar percentage range of patients. There were no differences in efficacy or safety between patients with or without immunoreactivity.

**8 USE IN SPECIFIC POPULATIONS**

**8.1 Pregnancy**
Risk Summary
Adequate and well-controlled studies with EYLEA have not been conducted in pregnant women. Aflibercept produced adverse embryofetal effects in rabbits, including external, visceral, and skeletal malformations. A fetal No Observed Adverse Effect Level (NOAEL) was not identified. At the lowest dose shown to produce adverse embryofetal effects, systemic exposures (based on AUC for free aflibercept) were approximately 6 times higher than AUC values observed in humans after a single intravitreal treatment at the recommended clinical dose [*see Animal Data*].
Animal reproduction studies are not always predictive of human response, and it is not known whether EYLEA can cause fetal harm when administered to a pregnant woman. Based on the anti-VEGF mechanism of action for aflibercept, treatment with EYLEA may pose a risk to human embryofetal development. EYLEA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.
All pregnancies have a background risk of birth defect, loss, or other adverse outcomes. The background risk of major birth defects and miscarriage for the indicated population is unknown. In the U.S. general population, the estimated background risk of major birth defects and miscarriage in clinically recognized pregnancies is 2-4% and 15-20%, respectively.

Data
*Animal Data*
In two embryofetal development studies, aflibercept produced adverse embryofetal effects when administered every three days during organogenesis to pregnant rabbits at intravenous doses ≥3 mg per kg, or every six days during organogenesis at subcutaneous doses ≥0.1 mg per kg.
Adverse embryofetal effects included increased incidences of postimplantation loss and fetal malformations, including anasarca, umbilical hernia, diaphragmatic hernia, gastroschisis, cleft palate, ectrodactyly, intestinal atresia, spina bifida, encephalomeningocele, heart and major vessel defects, and skeletal malformations (fused vertebrae, sternebrae, and ribs; supernumerary vertebral arches and ribs; and incomplete ossification). The maternal No Observed Adverse Effect Level (NOAEL) in these studies was 3 mg per kg. Aflibercept produced fetal malformations at all doses assessed in rabbits and the fetal NOAEL was not identified. At the lowest dose shown to produce adverse embryofetal effects in rabbits (0.1 mg per kg), systemic exposure (AUC) of free aflibercept was approximately 6 times higher than systemic exposure (AUC) observed in humans after a single intravitreal dose of 2 mg.

**8.2 Lactation**
Risk Summary
There is no information regarding the presence of aflibercept in human milk, the effects of the drug on the breastfed infant, or the effects of the drug on milk production/excretion. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, EYLEA is not recommended during breastfeeding.
The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for EYLEA and any potential adverse effects on the breastfed child from EYLEA.

**8.3 Females and Males of Reproductive Potential**
Contraception
Females of reproductive potential are advised to use effective contraception prior to the initial dose, during treatment, and for at least 3 months after the last intravitreal injection of EYLEA.

Infertility
There are no data regarding the effects of EYLEA on human fertility. Aflibercept adversely affected female and male reproductive systems in cynomolgus monkeys when administered by intravenous injection at a dose approximately 1500 times higher than the systemic level observed humans with an intravitreal dose of 2 mg. A No Observed Adverse Effect Level (NOAEL) was not identified. These findings were reversible within 20 weeks after cessation of treatment.

**8.4 Pediatric Use**
The safety and effectiveness of EYLEA in pediatric patients have not been established.

**8.5 Geriatric Use**
In the clinical studies, approximately 76% (2049/2701) of patients randomized to treatment with EYLEA were ≥65 years of age and approximately 46% (1250/2701) were ≥75 years of age. No significant differences in efficacy or safety were seen with increasing age in these studies.

**17 PATIENT COUNSELING INFORMATION**
In the days following EYLEA administration, patients are at risk of developing endophthalmitis or retinal detachment. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise patients to seek immediate care from an ophthalmologist [*see Warnings and Precautions (5.1)*].
Patients may experience temporary visual disturbances after an intravitreal injection with EYLEA and the associated eye examinations [*see Adverse Reactions (6)*]. Advise patients not to drive or use machinery until visual function has recovered sufficiently.

REGENERON

Manufactured by:
**Regeneron Pharmaceuticals, Inc.**
777 Old Saw Mill River Road
Tarrytown, NY 10591



Issue Date: 08/2019
Initial U.S. Approval: 2011

Based on the August 2019
EYLEA® (aflibercept) Injection full
Prescribing Information.

EYL.20.09.0052

# E/M Nuances: Determining the Level of Medical Decision-Making

Which level of evaluation and management (E/M) code should you use? There are two ways to determine this: One is physician-time based and the other is based on the level of medical decision-making (MDM) that is required. The MDM level is dependent on the 1) problems, 2) data, and 3) risk that the physician must contend with (see "E/M Rules for Office Visits: What Level of Medical-Decision Making?" Savvy Coder, June).

**Some clarifications.** Although new E/M rules have been in force for eight months, practices are still getting to grips with the nuances of the new system. Here is a refresher on two of MDM's components, including responses from the American Medical Association (AMA), which maintains the Current Procedural Terminology (CPT) codes, including the E/M codes.

## MDM's Data Component

The "amount and/or complexity of data to be reviewed and analyzed" helps to determine the MDM level.

**Q. What does analyzed mean?**

**AMA's response.** "It is the process of using and anticipating using the test in the MDM process. If a test is ordered outside of an encounter, the ordering has not yet been part of the MDM level determination, so the results will be included in the subsequent E/M visit, if analyzed in the MDM of that encounter. For a test that is recurring, and ordered once for multiple future dates, a new result may be used in determining MDM level if it is analyzed in a subsequent encounter."

**Q. If an ophthalmologist reviews a test by a referring source on one date and then reviews that same test at a subsequent encounter, can that second review count as a data item?**

**A.** No. Each unique test performed by the referring source can be counted only once.

**Q. If the ophthalmologist orders a computed tomography (CT) scan and blood work, do they both count?**

**A.** Yes. The CT scan would contribute one data point and, depending on the individual CPT/HCPCS code(s), at least one more would be added for the blood work. With two data points, the exam would be considered to involve a "limited" level of data, which would help to support a "low complexity" level of MDM.

**Q. One way to meet the requirements of a moderate level of data review would be to have a "discussion of management or test interpretation with external physician/QHP*/appropriate source (not separately reported)." What does that mean?**

**AMA's response.** "Discussion requires an interactive exchange. The exchange must be direct and not through intermediaries such as clinical staff. Sending chart notes or written exchanges that are within progress notes does not qualify as an interactive exchange. The discussion does not need to be on the date of the encounter but is counted only once and only when it is used in the decision making of the encounter. It may be asynchronous (i.e., does not need to be in person), but it must be initiated and completed within a short time period (e.g., within a day or two)."

## MDM's Risk Component

MDM's risk component is defined as the "complications and/or morbidity or mortality of patient management."

**Q. The AMA gives several examples of scenarios that would be considered moderate risk. These include the "decision regarding minor surgery with identified patient or procedure risk factors" and the "decision regarding elective major surgery without identified risk factors." Are these determined by the global period of zero, 10, or 90 days of post-op care?**

**AMA's response.** "An elective procedure is typically planned in advance (e.g., scheduled for weeks later). An emergent procedure is typically performed immediately or with minimal delay. Both elective and emergent procedures may be minor or major." Note: For MDM purposes, the terms minor and major surgery are not determined by the global period.

* QHP = qualified health care professional.

**MORE ONLINE.** For further Q and A, see this article at aao.org/eyenet. For additional E/M resources, bookmark aao.org/em.

BY **SUE VICCHRILLI, COT, OCS, OCSR,** ACADEMY DIRECTOR OF CODING AND REIMBURSEMENT.

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# Your Voice Matters: Ensure Congress Hears It

When it seems no one is listening, OPHTHPAC®, the Academy's pro-ophthalmology political action committee, gives members a megaphone.

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For more information, visit **aao.org/ophthpac**.

# MIPS 2021—How to Boost Your Promoting Interoperability Score

Promoting interoperability (PI) is the electronic health record (EHR)–based performance category of the Merit-Based Incentive Payment System (MIPS). According to CMS, the PI measures are intended to promote electronic exchange of information and to increase patient engagement by allowing them to access details from their health records online.

**Many ophthalmic practices can improve their PI scores.** Low performance rates on the PI measures have meant that some practices have underperformed on the PI performance category. Last year, for example, fewer than half of those reporting MIPS via the IRIS Registry (aao.org/iris-registry) scored more than 80% for PI. This reduced their chance of avoiding a MIPS penalty and earning a bonus.

**Your PI performance period must start no later than Oct. 3.** Your PI score will be based on how you do during a performance period of 90 consecutive days during the current calendar year.

**Best not to wait until Oct. 3!** By starting your performance period earlier in the year, you will give yourself an opportunity for a do-over in case you run into problems. For example, your score for the Provide Patients Electronic Access to Their Health Information measure could be jeopardized if your patient portal goes offline for a few days.

**Make sure you understand how to perform (and document) the PI measures.** The Academy offers a detailed web page for each of the PI measures, including a measure description, definitions, and suggestions for documenting your performance. Academy and AAOE members can access these PI web pages at aao.org/medicare/promoting-interoperability/measures.

**Warning: Don't report PI twice.** You'll get a PI score of 0 if you submit conflicting data or conflicting attestation on PI measures. This could happen if, for example, you report PI twice—once via the IRIS Registry and again via your EHR vendor—and submit different information each time.

## Check Performance Rates

**For many PI measures, you are scored based on your performance rate.** The e-Prescribing measure, for example, can contribute up to 10 points to your PI score: If your performance rate is 100%, you would score 10 points. In calculating this point score, CMS typically rounds off to the nearest whole number—so a score of 84% would score 8 points, but a score of 86% would score 9 points. (Note: In an exception to that rounding rule for PI measures, CMS rounds up to 1 point rather than down to 0 points provided you have a numerator of at least 1.)

**Your performance rate is based on a numerator and a denominator.** For the e-Prescribing measure, for example, the denominator is the number of prescriptions written during the performance period for drugs that require prescriptions; the numerator is the number of those prescriptions that were generated and transmitted electronically using a certified EHR technology (CEHRT).

**You need a numerator of at least 1.** For any of PI's performance rate–based measures, you need a numerator of at least 1 to successfully report it.

**Run your PI reports ASAP.** Your EHR system should be able to run a report that calculates your performance rates for PI measures. If you haven't been running these reports throughout the year, you should do so as soon as possible to check your performance rates. If your numerator for a measure is 0, you will need time to work with your EHR vendor and your staff to determine how to attain the minimum numerator of 1.

## Provide Patients Electronic Access to Their Health Info

One area of underperformance involves the Provide Patients Electronic Access to Their Health Information measure. In some cases, practices had been providing patients with access to their medical information online but hadn't always been logging that, resulting in a discrepancy between their reported performance rate and their actual performance rate.

**Know your numerator and denominator.** The denominator for the Provide

BY **JOY WOODKE, COE, OCS, OCSR,** CODING AND PRACTICE MANAGEMENT EXECUTIVE, **JOHN WARD,** ACADEMY MANAGER OF CUSTOMER SERVICE, AND **CHRIS MCDONAGH,** *EYENET* SENIOR EDITOR.

Patients Electronic Access measure is the number of unique patients seen by the clinician during the PI performance period. The numerator is the number of those patients (or their patient-authorized representatives) who 1) received timely access to "view online, download, and transmit his or her health information" and 2) are able to access that information using "any application of their choice that is configured to meet the technical specifications of the Application Programing Interface (API)" in the practice's CEHRT. CMS defines "timely" as within four business days of the information being available to the clinician.

**When a patient is provided with online access, how is that recorded in the EHR?** Contact your EHR vendor and confirm how the EHR system captures the action of providing timely access. Some systems may require confirmation in the medical record or by completing a function in the integrated practice management system.

**How do you ensure that the EHR is updated each time a patient is provided with online access?** Develop the workflow to successfully log that you provided this access after every patient encounter. Next, test the protocol and review your PI reports.

**What does your EHR vendor offer?** You may be able to automatically offer patient access via a patient portal, but this functionality may require individual system setup. Ask your vendor whether this option is available.

**What if some patients don't want to view their information online?** Even if a patient opts out of receiving online access to personal medical information, he or she must still be included in the denominator for this measure. CMS states that you can include this patient in the numerator, provided that he or she is "provided all of the necessary information to subsequently access their information, obtain access through a patient-authorized representative, or otherwise opt-back-in without further follow-up action required by the clinician."

**When patients opt out, are staff taking these two steps?** When patients opt out of accessing their information online, be sure that staff are trained to update the EHR to indicate that the patient 1) opted out and 2) was instructed on how to access that online information if he or she later decides to opt in. Next, double-check that your EHR system is including such patients in the measure's denominator and, if applicable, in its numerator.

## Alert: CMS Changes Quality Benchmarks

On June 10, CMS published corrections to its benchmarks for almost all quality measures. Then, on June 30, CMS announced that it was suppressing Measures 1 and 117 for claims-based reporters The June 10 change impacts everyone; the June 30 change impacts those who report via Medicare Part B claims, but not those who report via the IRIS Registry.

**Check that you're referencing the updated benchmarks.** It is important to check that you are using the most current versions of the *EyeNet* MIPS manual (aao.org/eyenet/mips-manual-2021) and *IRIS Registry Preparation Kit and User Guide* (aao.org/iris-registry/user-guide/getting-started).

**Watch for future alerts.** Check your email for *Washington Report Express* (Thursdays) and *Medicare Physician Payment Update* (first Saturday of the month). AAOE members also get *Practice Management Express* (Sundays).

## Direct Messaging for the Referral Loop Measures

The two Referral Loops measures involve the sending and receiving of health care summaries. This can be done in a HIPAA-compliant way via Direct messaging, which was developed by the Direct Project and uses an encryption standard for exchanging health information over the internet. To use Direct messaging, both the sender and recipient must have Direct addresses, which look similar to email addresses. If your EHR is a CEHRT, the vendor must offer you access to a Direct messaging service.

**Do you have a Direct address?** Practices can obtain Direct addresses from a variety of sources, including CEHRT vendors, State Health Information Exchange entities, regional and local Health Information Exchange entities, and Health Information System Providers.

**The National Plan and Provider Enumerator System (NPPES) has started to include Direct addresses in the NPI Registry.** NPPES is *trying* to make it easier to find the Direct addresses of other clinicians. Go to the NPI Registry's search page at https://npiregistry.cms.hhs.gov. Once you find the clinician who you are looking for, click his or her record, and then scroll down to "Health Information Exchange." *If* he or she has added a Direct address into the NPI registry, it will be listed here with "Direct Messaging Address" in the "Endpoint Type" column. However, few clinicians have added this information yet.

**How to update the NPPES directory.** If you do not know your exact electronic end point or Direct address, contact your EHR vendor for this information. Next, go to the NPPES website (https://nppes.cms.hhs.gov/#/) and update your provider profile. You can add your Direct address under the "Health Information Exchange" section. CMS provided a step-by-step guide to doing this in its *Medicare Learning Network*

### MORE RESOURCES

**Bookmark these resources.** To learn more about PI—including who can be excluded from it—visit aao.org/medicare/promoting-interoperability and aao.org/eyenet/mips-manual-2021.

**Use the *IRIS Registry Preparation Kit.*** Download it at aao.org/iris-registry/user-guide/getting-started.

**Share tips online.** AAOE members also can use the new listserv, AAOE-Talk (see page 62), to crowdsource MIPS solutions.

*Matters* bulletin.[1] If you already added this information, it is still worth visiting the directory to double-check that your practice's details are up to date. By making sure that the directory has your practice's correct Direct address(es) and electronic end point information, you can help your practice's clinicians succeed with PI's two Referral Loop measures.

**Contact your top referral sources.** Make sure referral sources are ready to meet the requirements of the Referral Loop measures. If, like most clinicians, their Direct addresses aren't yet listed in the NPPES NPI Registry, see if you can obtain that information directly from the practice.

## What About PI's New HIE Measure?

This year, PI's Health Information Exchange (HIE) objective gives you a choice of two measures. Either you can report (or claim exclusions for) the two Referral Loop measures or you can report the new HIE Bi-Directional Exchange measure. To earn all 40 points for the new measure, you must attest "yes" to these three statements:

- "I participate in an HIE in order to enable secure, bi-directional exchange to occur for every patient encounter, transition or referral, and record stored or maintained in the EHR during the performance period in accordance with applicable law and policy."
- "The HIE that I participate in is capable of exchanging information across a broad network of unaffiliated exchange partners including those using disparate EHRs, and does not engage in exclusionary behavior when determining exchange partners."
- "I use the functions of CEHRT to support bi-directional exchange with an HIE."

If you report "no" for one or more of these measures, you earn 0 points for the measure.

1 www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNMattersArticles/Downloads/MM11003.pdf. Accessed June 18, 2021.

## MORE AT AAO 2021

Visit aao.org/programsearch to explore this year's annual meeting and Subspecialty Day content.

**Get a MIPS update at this year's Medicare Forum.** Learn what's ahead with MIPS, as well as other coding and reimbursement changes that will impact your practice in 2022. **When:** Sunday, Nov. 14, 3:45-5:00 p.m. **Where:** New Orleans Theater AB.

**Learn more about EHRs.** EHR-related events include the following:

- **21st Century Cures Act: Interoperability, Information Blocking, and the ONC Health IT Certification Program Final Rule (253).** *Senior instructor; Jeffery Daigrepont.* **When:** Saturday, Nov. 13, 2:00-3:15 p.m. **Where:** Room 203.
- **What Every Ophthalmologist Must Know About Information Technology in 2021 (Sym11).** *Chairs: Aaron Y. Lee, MD, and Thomas Hwang, MD.* **When:** Saturday, Nov. 13, 2:00-3:15 p.m. **Where:** New Orleans Theater C.
- **Use and Misuse of Electronic Medical Records (460).** *Senior instructor: Kirk Mack, COE, COMT, CPC.* **When:** Sunday, Nov. 14, 3:45-5:00 p.m. **Where:** Room 215.
- **Artificial Intelligence: Demystification and Applications (246).** *Senior instructor: Sally Liu Baxter, MD.* **When:** Sunday, Nov. 14, 3:45-5:00 p.m. **Where:** Room 240.
- **What to Do (and Not Do) When Migrating Your PM or EHR (616).** *Senior instructor: Randall Marsden, BBA.* **When:** Monday, Nov. 15, 9:45-11:00 a.m. **Where:** Room 211.
- **The Ophthalmic Office for the Virtual World (Sym47V).** *Chairs: Louis R. Pasquale, MD, and James C. Tsai, MD, MBA.* **When:** On demand. **Where:** Virtual.

## Coming in the next EyeNet®

### Feature

**DEI** Diversifying the ophthalmology workforce: How to move from good intentions to intentional action.

### Clinical Update

**Cornea** Experts discuss cataract surgery in eyes with keratoconus or a corneal graft.

**Oculoplastics** As the use of antithrombotic drugs continues to rise, surgical planning is key. Tips on when to withhold medication, when to delay surgery, and more.

### Pearls

**Ocular Ischemic Syndrome** Timely diagnosis of OIS is necessary to reduce cardiovascular morbidity and mortality as well as to prevent permanent vision loss. What you need to know.

### Blink

Take a guess at the next issue's mystery image. Then find the article at aao.org/eyenet and report your diagnosis.

### For Your Convenience

These stories also will be available online at aao.org/eyenet.

# We are Here for you

OMIC understands the COVID-19 pandemic has severely impacted you both emotionally and financially.

We will recover but the effects on all of us will be felt for some time. Ultimately, we know that the resiliency of the ophthalmic community will help us pull through these challenging times.

Here is how we are helping.

## PREMIUM RETURNS

OMIC was one of the first carriers to announce financial assistance for policyholders due to the impact of COVID-19.

In April, 2020, we approved a special premium credit, which was effective for all insureds on May 1, 2020 and has now been applied to all policies.

On November 2, 2020, OMIC declared an additional dividend credit for physicians to be applied throughout 2021.

## COVID-19 RISK MANAGEMENT

OMIC created a COVID-19 page in March, 2020.

OMIC Policyholders requiring assistance should call OMIC's confidential Risk Management Hotline for COVID-19 questions and assistance at (800) 562-6642 and Press 4 or email riskmanagement@omic.com.

Resources currently available online:

COVID-19 Sample Patient Consent Documents

Risk Management Resources and Recommendations

OMIC News and Coverage Information

## More news and information at OMIC.com

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# Academy Notebook

NEWS • TIPS • RESOURCES

## WHAT'S HAPPENING

### The Academy Launches Initiative to Address Myopia Worldwide

The prevalence of myopia has been increasing and is a major cause of visual impairment globally. To address this issue, the Academy is working with organizations around the world to reduce the global burden from myopia by delaying myopia onset in children and reducing myopic progression in children and adolescents. The intent is to prevent the more severe consequences of higher levels of myopia.

**Accomplishments.** An Academy task force, bringing together clinicians and scientists from around the globe, recently completed a yearlong investigation into the science of myopia. This team developed a white paper published in *Ophthalmology*[1] to help guide the Academy's strategic and tactical implementation in fighting myopia.

**Goals.** The Academy will focus on four major areas:

**Education.** The Academy will provide educational resources to inform ophthalmologists and other eye care providers, patients and their families, policy makers, and the public about the growing burden imposed by myopia. It will also provide scientific evaluation of effective interventions.

**Research.** The Academy will foster communication and collaboration between researchers, academic centers, and other health care organizations to share learnings and advance research on novel interventions.

**Public health.** The Academy will support the development and dissemination of public health initiatives to implement safe and effective approaches to delay myopia onset and reduce myopic progression in children and adolescents.

**Advocacy.** The Academy will promote the appropriate access to technologies for control of or reduction of myopia progression.

**Sponsors.** The Academy's initiative is supported by sponsors, including Nevakar and CooperVision, that have each committed $125,000 to fight myopia over the next five years.

**Learn more** at aao.org/myopia-resources.

1 Modjtahedi BS et al. for the Academy's Task Force on Myopia. *Ophthalmology*. 2021;128(6): 816-826.

***CONGRESS' AUGUST RECESS.*** *Members of Congress are home for the August recess, and your elected official is available to meet with constituents like you. It is imperative that ophthalmologists use the August recess to let lawmakers know how pending policies could affect eye care in their communities. Above, OphthPAC Committee member, S. Anna Kao, MD, (right) poses with Rep. Drew Ferguson, DMD, (R-GA.). For tips on getting started, visit aao.org/local.*

### Available Now: *BCSC* Social Determinants of Health Chapter

The new Social Determinants of Health (SDOH) chapter, which will be included in the *2022–2023 Basic and Clinical Science Course* (*BCSC*) in June 2022, is available now as a downloadable PDF on the Academy's Diversity, Equity, and Inclusion web page. This important addition (Chapter 17) is part of the minor revision of Section 1 (General Medicine), but the Academy has published it online ahead of print to make it accessible to all members as soon as possible. The chapter presents an evolving, high-level overview of social determinants of health. Key points include:

- SDOH are major drivers of health disparities;
- addressing SDOH will "create social, physical, and economic environments that promote attaining the full potential for health and well-being for all" (Healthy People 2030, an initiative by the U.S. Department of Health and Human Services);

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• minority ethnicity, lower educational attainment, lower income, and lack of insurance are all associated with greater visual impairment in the United States; and
• ophthalmologists should assess the impact of SDOH as part of every patient encounter and should address SDOH in their treatment of patients.

This initial chapter serves as a preview to the full-length version that will be included in the *2023–2024 BCSC* major revision.

**Download the chapter** under "Academy Publications and Articles" at aao.org/diversity-equity-and-inclusion.

## YO Committee Earns 2021 Special Recognition Award

The 2021 Special Recognition Award (SRA) will be awarded to the members of the Academy's Young Ophthalmologist (YO) Committee. YO Committee Chair **Janice C. Law, MD,** will accept the award at AAO 2021 this November in New Orleans on behalf of the YO Committee and its three subcommittees (*YO Info* Editorial Board, YO Advocacy Subcommittee, and YO International Subcommittee).

**SRA.** The Academy's SRA is presented to an individual or organization for outstanding service in a specific effort or cause that improves the quality of eye care. The Academy president has the honor of selecting the recipient of this award. "I joined the YO Committee in 1997," Academy President **Tamara R. Fountain, MD,** said. "We were seven people tasked with putting on a three-hour course geared to young ophthalmologists. From those nascent beginnings, the YO program has expanded to an entire membership division overseen by Gail Schmidt and Neeshah Azam. By recognizing the value of this young demographic, the YO program is investing in the Academy's future."

**YO Committee.** Since its inception, the YO Committee and its subcommittees have brought a significant voice and more effective representation to the newest Academy members—the potential future leaders of the profession. Highlights of these efforts include the following:

**Newsletters.** Developed by and for YOs, the monthly e-newsletter *YO Info* goes out to 7,000 global YOs. It provides clinical pearls, practice management advice and resources, highlights of YOs engaging in advocacy to protect quality patient eye care, and features on unique efforts by international YOs. Other *YO Info* publications include an annual print issue, *YO Info Resident Edition,* dedicated to incoming residents; a newsletter for those just finishing practice titled *YO Info Graduate Edition;* and an edition highlighting international efforts, *YO Info International.* You also can view *YO Info* stories at aao.org/young-ophthalmologists/yo-info.

**The Advocacy Ambassador Program.** An Academy program implemented in collaboration with ophthalmic state and subspecialty societies, the Advocacy Ambassador Program was designed to engage residents and fellowship trainees in advocacy. At the federal level, this includes participation in Congressional Advocacy Day and the LEAP Forward program, a Mid-Year Forum session designed specifically for residents and fellows to network with active leaders in ophthalmology. At the state level, advocacy efforts happen in concert with state ophthalmology societies.

**Educational programs.** The YO Committee has collaborated with YO leaders from the European Society of Ophthalmology, the Asia-Pacific Academy of Ophthalmology, and the Pan-American Association of Ophthalmology to create joint educational programs at the Academy's annual meeting as well international meetings.

**Learn more** about the YO Committee at aao.org/young-ophthalmologists/grow-in-leadership.

# FOR THE RECORD

## Board Nominees

In accordance with Academy bylaws, notice is hereby given of the following nominations for elected board positions on the 2022 board. These nominations were made by the Academy Board of Trustees in June. If elected, the following individuals will begin their terms on Jan. 1, 2022.

**President-Elect**
Daniel J. Briceland, MD

**Senior Secretary for Clinical Education**
Christopher J. Rapuano, MD

**Trustees-at-Large**
Purnima S. Patel, MD

**Council Chair**
Thomas A. Graul, MD

**Council Vice Chair**
Prem Subramanian, MD, PhD

**Board appointments.** During the June Board of Trustees meeting, the following individuals were appointed to the 2022 Board of Trustees and will begin their terms on Jan. 1, 2022.

**Foundation Advisory Board Chair**
Gregory L. Skuta, MD

**International Trustee-at-Large**
Iqbal (Ike) Ahmed, MD. Ontario, Canada

**Nomination procedures for the Academy Board.** Elections to fill the five open elected positions on the 2022 Board of Trustees will take place by ballot after the Nov. 12, 2021, Annual Business Meeting. To nominate a candidate by petition, submit a written petition to the Academy's CEO no later than Sept. 13. The petition must be signed by at least 50 voting Academy members and fellows.

**To suggest a nominee for the 2023 board,** watch for the call for nominations, which will be published in the January 2022 *EyeNet.*

**To read the rules in full,** visit aao.org/about/governance/bylaws/article5.

## Annual Business Meeting Is on a Friday

Notice is hereby given that the Annual Business Meeting of the American Academy of Ophthalmology will be held Friday, Nov. 12, 2021, in the Great Hall at the Ernest N. Morial Convention Center in New Orleans from 5:00 to 6:30 p.m., as part of the Opening Session.

## Notice of Membership Termination

At its February 2021 meeting, the Academy's Board of Trustees determined that **Jeffrey N. Weiss, MD,** of Parkland, Florida, violated the Academy's Code of Ethics Rule 3 on Research and Innovation and Rule 13 on Communications to the Public. Dr. Weiss' Academy membership has been terminated. Academy Fel-

lows or Members whose membership is terminated as a Code of Ethics sanction may not reapply for membership in any class. The Board of Trustees' determination was upheld on appeal.

## TAKE NOTICE

### What Will You Leave for the Next Generation?

When you remember the Academy with a future gift, you support the education of future ophthalmologists. Learn about the 1896 Legacy Society and the convenient ways to give, from wills and living trusts to donor advised funds and charitable gift annuities.

**Read more** at aao.org/planmylegacy.

### Volunteer: Eye Exams for Underserved Populations

Did you know that you can give back to your community without leaving your office and with little time commitment?

You can do so by volunteering with EyeCare America, a program that helps seniors who have not had a medical eye exam in three or more years, and those at increased risk for glaucoma.

**Get started** at aao.org/volunteering, then choose "Connect." (This is just one of many Academy volunteer opportunities.)

### Volunteer: Clinical Currency Review

Would you like to help the Academy maintain its educational material? Sign up to do a clinical currency review. The Academy publishes a variety of books, online cases, podcasts, and more. These materials periodically require review for clinical currency.

To review, you must have no financial relationships with industry and have experience formally teaching, managing, or collaborating with the publication's target audience.

**Get started** at aao.org/volunteering, then choose "Review." (This is just one of many Academy volunteer opportunities.)

### Ask the Ethicist: Patient's Service Animal in the Office

***Q:*** *I have a patient who wants to bring his emotional support animal to his office visits. He is now scheduled for surgery and wants his dog in the OR when he goes to sleep and wakes up. We feel that this puts him and other patients at risk. How should I handle this?*

**A:** The Americans with Disabilities Act (ADA) of 1990 prohibits discrimination based on disability (physical or mental). However, because emotional support animals have not been trained to perform a specific job or task, they do not qualify as service animals under the ADA. Even if they did qualify, the ADA does not require entities, such as

D.C. REPORT

## Academy Urges CMS to Ban Step Therapy in Medicare Advantage Plans

Today, most Medicare Advantage plans have some step therapy rules for Part B drugs. These rules require that patients first try a less expensive treatment before trying a more expensive one. As a result, step therapy may delay or disrupt timely access to care and can negatively affect patients' health outcomes. In 2021, the Academy's advocacy agenda includes efforts to reverse step therapy rules.

**Recent history of step therapy rules.** Medicare Advantage plans had been banned from imposing step therapy. This changed under the last administration: In 2018, CMS removed the ban with certain conditions. When the Academy questioned the legal standing for the new policy, CMS went through the proper rule-making process to protect plans that imposed step therapy. Under a new final rule, step therapy was limited to new administrations of a Part B drug with a 365-day look-back period beginning in 2020.

Although CMS included some patient safeguards in the final policy, they are not enough.

**Legal issues surrounding step therapy.** At the Academy's virtual 2021 Mid-Year Forum in April, speakers explored the legal issues surrounding step therapy requirements. Paul Rudolf, MD, JD, an internist and a partner at the law firm Arnold & Porter, said that step therapy use by Medicare Advantage plans is "contrary to the statutory requirement that Medicare Advantage plans cover all items and services that are covered by the original fee-for-service Medicare program."

**What the Academy is doing about it.** The Academy has spearheaded robust efforts to challenge CMS' inappropriate step therapy requirements and protect patients.

In April, the Academy—joined by more than 55 patient, physician, and health care groups—launched an advocacy campaign to reverse the rule. The Academy urged the Biden administration to immediately reinstate the ban and to lower medication costs.

In its letter to the U.S. Department of Health and Human Services and CMS, the Academy stressed that "while a drug or therapy might be generally considered appropriate for a condition, individual patient issues, such as the presence of comorbidities, potential drug-drug interactions, or patient intolerances, may necessitate the selection of an alternative drug as the first course of treatment."

**Next steps on banning step therapy.** After receiving the letter, CMS agreed to meet with Academy leaders to discuss documented patient stories. The Academy is optimistic that the Biden administration, which has rolled back several Trump-era policies, will give the rule a second look.

If CMS agrees to reinstate the step therapy ban, it would likely do so by executive order or annual rulemaking.

ophthalmology practices, to modify or change policies, practices, or procedures if doing so would "fundamentally alter" the nature of the services provided to the public. The ADA does not override legitimate safety requirements such as public health rules that prohibit dogs in swimming pools or the need for sterility in a health care environment. Thus, if admitting service animals would fundamentally alter the nature of a service or program, such as a surgery center, the animals may be prohibited. Moreover, the ADA requires that the service animal be under the handler's control at all times, which would be impossible if the handler is undergoing surgery.

Principles 1 and 7 of the AAO Code of Ethics state that when faced with an ethical dilemma, the ophthalmologist is responsible for assuring that the best interests of patients are served. Resolving ethical dilemmas may require you to make choices limiting one patient's behavior to protect others.

As some state or local governments have laws that allow people to take emotional support animals into public places, you may wish to check with your local government agencies to find out about these laws. And from a liability perspective, you can visit OMIC's service animal page (www.omic.com/do-you-have-a-service-animal-policy).

**To read the Code of Ethics,** visit aao.org/ethics-detail/code-of-ethics.

**To submit a question,** email ethics@aao.org.

### OMIC Tip: How Effective Is Your Missed Appointment Protocol?

When patients routinely miss appointments, not only do they place their own health at risk, but also they increase your risk of a claim due to a missed or delayed diagnosis. These no-shows also have multiple costs for your practice, from lost revenue and time spent rescheduling appointments to the lost opportunity of using that appointment for another patient. In the current climate of catching up on deferred care and surgeries postponed due to the pandemic, missed appointments have even greater impacts.

An effective missed appointment protocol begins far in advance of the appointment itself. Decide on the method of communication that you will use to remind patients of their appointments. Whether your system is manual, automated, or a hybrid of the two, it should be customized to suit your patients in order to increase the probability of success. When patients register with your practice for the first time, or return for an appointment, take the opportunity to note if they prefer appointment reminders by text, email, or telephone. Keep the reminders brief and be clear about what action the patient needs to take to confirm or reschedule the appointment. These appointment reminders are also an opportunity to reinforce current safety precautions in your office.

When patients do miss appointments, it is imperative that your staff knows what information to collect, so that you can review no-shows and cancellations and determine next steps. This is a medical decision that cannot be delegated.

Page 5 of OMIC's Noncompliance Toolkit provides a sample strategy for managing missed appointments. See it at www.omic.com/how-effective-is-your-missed-appointment-protocol.

*OMIC offers professional liability insurance exclusively to Academy members, their employees, and their practices.*

## ACADEMY RESOURCES

### Got New Clinicians? Notify the IRIS Registry by Sept. 1

Has a new clinician joined your practice or has an existing clinician become newly eligible for the Merit-Based Incentive Payment System (MIPS)? If you are using your electronic health record (EHR) system to report MIPS quality data via the IRIS Registry, make sure you haven't left any clinicians out during the 2021 MIPS performance year: Notify FIGmd, which is an IRIS Registry vendor, as soon as you can and no later than Sept. 1. Make sure that you include the clinician's National Provider Identifier and, if the person is an ophthalmologist, his or her Academy member ID.

**How do you contact FIGmd?** For instructions on submitting a help desk ticket, you can visit aao.org/iris-registry/user-guide/submit-help-desk-ticket.

### By Aug. 31, Submit Your Plan for an ABO/IRIS Registry Improvement Project

Is your electronic health record (EHR) system integrated with the IRIS Registry? If so, you can use data from your IRIS Registry dashboard to design an improvement project that can earn you credit for both American Board of Ophthalmology (ABO) Continuing Certification and the Merit-Based Incentive Payment System (MIPS). For the 2021 MIPS performance year, this project would count as a medium-weighted improvement activity—but you must submit your plan to the ABO no later than Aug. 31.

**Learn more** at aao.org/iris-registry/maintenance-of-certification and https://abop.org/IRIS.

### NEW Practice Management Online Community

The American Academy of Ophthalmic Executives (AAOE) has replaced its popular email group list with a new online community for resource sharing and networking. The new AAOE-Talk provides administrators, office managers, and managing physicians a place to openly exchange ideas and discuss the business issues facing modern ophthalmic practices. Use this exclusive AAOE member benefit to get answers to your questions about coding, human resources, financial management, and other practice management issues.

**Learn more** at aao.org/aaoe-talk.

### Meet Your Practice's Payer Requirements in the Exam Lane

*Ultimate Documentation Compliance Training for Scribes and Technicians* is a comprehensive on-demand course that will significantly improve your team's ability to document patient encounters correctly, satisfy payer requirements, and effectively shield your practice from audits and recoupments.

**Learn more** at aao.org/techtraining.

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Keep your skills and knowledge on the cutting edge. Academy members get exclusive access to *EyeNet® Magazine* and *Ophthalmology®* journal, plus thousands of curated instructional videos, self-assessment questions, simulators and courses on the Ophthalmic News and Education (ONE®) Network.

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DRY EYELAND™

# Journey to a world

## WHERE A LOSS OF TEAR FILM HOMEOSTASIS LEADS TO DRY EYE[1]

When it comes to dry eye disease and the loss of tear film homeostasis, there's a broader integrated system that needs exploring. We call it Dry Eyeland.[2,3]

**Come travel this anatomical landscape, where:**

- Loss of tear film homeostasis is the unifying characteristic of all dry eye[1]
- The parasympathetic nervous system plays a major role in tear film homeostasis[2]
- The lacrimal functional unit (LFU) is far more than just the lacrimal gland[3]

**Allow us to be your guide to dry eye—visit DryEyeland.com to see the sights.**

**Because a whole world awaits beyond the ocular surface.**

OYSTER POINT™

**References: 1.** Craig JP, Nelson JD, Azar DT, et al. *Ocul Surf.* 2017;15(4):802-812. **2.** Efron N, Jones L, Bron AJ, et al. *Invest Ophthalmol Vis Sci.* 2013;54(11):TFOS98-TFOS122. **3.** *Ocul Surf.* 2007;5(2):75-92.

# Destination AAO 2021

GET READY FOR NEW ORLEANS • PART 3 OF 6

***2021 ORBITAL GALA MASQUERADE.*** *Reconnect with your colleagues at the 18th annual Orbital Gala at the House of Blues in New Orleans on Sunday, Nov. 14. Join the cocktail party and swap stories. Bid on items including vacations, ophthalmic equipment, wine, and conversations with legends. Celebrate David J. Noonan (third from the left), former Academy deputy executive vice president, for his numerous contributions to ophthalmology (aao.org/tribute). Purchase tickets now for the live event or register for the virtual event at aao.org/gala.*

## BEAT THE CLOCK

### AAO 2021: Less Than Four Months Away

Take in four days of intensive education at AAO 2021: Hear new perspectives, learn clinical pearls, and improve your practice. AAO 2021 will be held at the Ernest N. Morial Convention Center in New Orleans from Friday, Nov. 12, to Monday, Nov. 15, and is concurrent with Subspecialty Day meetings, which will take place on Friday, Nov. 12, and Saturday, Nov. 13.

**Don't wait.** Early registration for AAO 2021 ends Aug. 19, so plan your trip to New Orleans before the price increases. Book your preferred hotel room now, and start reviewing the program before labs sell out. See below for more details, and check this section of *EyeNet* each month for event highlights and important notices.

## REGISTRATION

### Register Now: Fees Increase Aug. 19 and Sept. 30

Register today for AAO 2021, Subspecialty Day meetings, and the half-day AAOE coding sessions. On Aug. 19 and Sept. 30, registration fees for specific registration categories and ticket fees increase.

**New—Your AAO 2021 registration includes access to instruction courses.** Your registration for AAO 2021 in New Orleans includes the opening and closing sessions, all instruction courses, clinical sessions, Skills Transfer lectures, videos, papers, and poster presentations. It also provides access to AAO 2021 Virtual, which includes highlights from New Orleans and additional on-demand–only content developed for the virtual meeting.

**Some events still require tickets.** The AAOE Practice Management Master Classes and Skills Transfer labs require the purchase of individual tickets. And Subspecialty Day and Friday AAOE Coding Sessions require separate registration.

**Pick up your badge at the convention center.** When you register for the in-person meeting you will pick up your badge in New Orleans, starting Thursday, Nov. 11. Bring your mobile device or a printout of your confirmation email to Registration, Halls D and E, Level 1 of the Ernest N. Morial Convention Center. Scan the barcode or type your name or ID number into the computer to print your badge. Photo ID will be required. Badges will not be mailed.

**Find more information,** including pricing, at aao.org/registration.

### Can't Make It to New Orleans? Register for AAO 2021 Virtual

Your AAO 2021 Virtual registration fee includes access to 1) selected sessions streamed live from New Orleans (which will also be recorded to view later), 2) sessions recorded at the meeting and placed in the virtual meeting to view on-demand, 3) special on-demand–only content developed exclusively for the virtual meeting, and 4) videos and poster discussions. You can also earn up to 50 AMA PRA Category 1 Credits.

Register separately for the Subspecialty Day virtual meeting by day.

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Registration includes content from all Subspecialty Day sessions on that day, streamed live from New Orleans and available later on demand; detailed course syllabi online; and the opportunity to earn 12 AMA PRA Category 1 credits per day.

**Find more information** at aao.org/registration.

## Book Hotel Rooms

The Academy has negotiated the lowest price for annual meeting hotel rooms (see map, page 68). When you book your hotel room with the Academy's official hotel reservation provider, Expovision, you can also earn all of your hotel loyalty points.

**New!** When you reserve your hotel room, you will no longer be charged a deposit upon booking. You can use your credit card information to guarantee your reservation, and the hotel will charge your card approximately two to three weeks prior to arrival.

**Beware of fraud!** Be sure to reserve hotel rooms only through the Academy's official housing provider, Expovision.

**Book online.** Visit aao.org/hotels for reservations. Reserving a room online is the quickest way to secure a hotel, and you receive immediate confirmation.

**Book by phone or email.** Agents at Expovision can assist you from Monday through Friday, 8:30 a.m.-5:30 p.m. EST. Call 866-774-0487 (toll-free from the United States and Canada) or email aaohotels@expovision.com.

# PROGRAM & ACTIVITIES

## Earn CME Credits in Person or Online

For AAO 2021 the Academy has re-created the meeting to include options to learn and to earn CME credits both in New Orleans and through the virtual meeting. Choose the learning experience that works best for your schedule. You'll have the opportunity to earn a maximum of 50 AMA PRA Category 1 Credits for attending the in-person meeting in New Orleans and/or viewing AAO 2021 Virtual content online.

## Build Your Schedule

Start planning which sessions to attend by viewing course listings and abstracts online with the Program Search. Look up information by presenter, keyword, or event number. Hit the Filter button to search the program by topic (e.g., "Cataract"), event type (e.g., "Symposium"), endorsements (e.g., "Endorsed by the Young Ophthalmologist Committee"), or credit type (e.g., "Eligible for Pain Management Credit").

**Find more information** at aao.org/programsearch.

## Skills Transfer Program

Refine your surgical skills with hands-on learning opportunities. Skills Transfer courses are included with your registration. Skills Transfer labs are ticketed events, which must be purchased separately.

Two new in-person Skills Transfer labs will be available at the annual meeting:

- Mastering Childhood Glaucoma Surgical Techniques (event code Lab-146A), directed by Alana L. Grajewski, MD, and
- Corneal Neurotization Techniques (Lab135A), directed by Ilya M. Leyngold, MD.

For the first time, the Academy is providing an on-demand–only Skills Transfer lab in the virtual meeting:

- Deep Sclerectomy: Unveiling the Pearls (Lab150V), directed by Ahmed M. Abdelrahman, MD.

## Save the Dates: *EyeNet* Corporate Lunches

Be sure to leave room in your schedule for *EyeNet*'s free corporate educational lunches from 12:45-1:45 p.m., Nov. 13-15. Located onsite in the Ernest N. Morial Convention Center, these non-CME symposia are developed independently by industry—they are not affiliated with the official program of AAO 2021 or Subspecialty Day. Complimentary boxed meals are available on a first-come, first-served basis, with lunch pickup beginning at 12:15 p.m. Please note, by attending, you may be subject to reporting under the Physician Payment Sunshine Act and you consent to share your contact data, inclusive of National Provider Identifier, with the corporate partner.

## Don't Miss Diversity, Equity, and Inclusion Events at AAO 2021

The Academy has committed to nurturing an inclusive ophthalmologist community that meets the eye care needs of a diverse patient population. In keeping with that commitment, several Diversity, Equity, and Inclusion events are offered at AAO 2021.

Highlights include the following:

**FRIDAY, NOV. 12.**

- **Diversity, Equity, and Inclusion in Retina (event code Ret03).** *Presenter: Julia A. Haller, MD.* This presentation takes place as part of Retina Subspecialty Day and requires separate registration. **When:** 9:36-9:42 a.m. (as part of Section II: Public Health, Education, and Business of Retina, 9:06-9:52 a.m.). **Where:** The Great Hall.

**SATURDAY, NOV. 13.**

- **Diversity and Inclusion in the Ophthalmic Practice (272).** *Senior instructor: Patricia Morris, MBA, COE.* Diversity cannot be created overnight. It requires a leadership dedicated to increasing cultural awareness and inclusion. It requires coworkers who are willing to take the time to learn about each other. It means being willing to identify and address personal biases. And it means boldly opening up to discomfort for the greater good of patients. This course suggests strategies to overcome bias and achieve inclusion. **When:** 3:45-5:00 p.m. **Where:** Room 211.

**SUNDAY, NOV. 14.**

- **Diversity Task Force Researching Eye Health Care Equity Amidst Workforce Disparity (Sym23).** *Chairs: Anne Louise Coleman, MD, PhD, and Angela R. Elam, MD.* The epidemiology of the major eye diseases and their impact on vision demonstrates significant variation by ethnicity and socioeconomic status in the United States. Similarly, the access to and availability of eye care is different in communities across the country. Projections indicate that without changes in the present approach, visual impairment—including that due to refractive error—will increase by 2050. This symposium provides insights into the current state of, and possible actions to improve, visual health disparities, access to care, the

relationship of workforce diversity to disparities, and the needs for education of the public, patients, and the profession. A framework for present and future action to utilize data sources, including the IRIS Registry, to measure and continuously improve access to quality eye care is key. **When:** 11:30 a.m.-12:45 p.m. **Where:** New Orleans Theater C.

- **Employee Recruitment and Retention Strategies That Champion Diversity (463).** *Senior instructor: Aimee Greeter.* This interactive presentation 1) focuses on actionable strategies to champion diversity and inclusion in both physician and nonphysician employee and executive selection and retention, 2) relays firsthand examples from diverse health care constituents about what equitable opportunities, sponsorship, and promotion have meant for their careers and how they now apply their lessons learned, and 3) discusses employment laws and compliance with applicable employment laws while recruiting employees from diverse backgrounds. **When:** 3:45-5:00 p.m. **Where:** Room 214.

**MONDAY, NOV. 15.**

- **Diversity, Equity, and Inclusion: Perspectives From Ophthalmology Leadership (Sym39).** *Chairs: Usiwoma E. Abugo, MD, and Nikisha Q. Richards, MD.* Ophthalmology departments remain among the least diverse clinical departments at U.S. medical schools, and the profession must address this lack of diversity among ophthalmologists and their support staff. This symposium brings together ophthalmology chairs, residency program directors, and other leaders in a roundtable. *Cosponsored by the National Medical Association (NMA) Ophthalmology Section.* **When:** 11:30 a.m.-12:45 p.m. **Where:** Room 243.
- **Achieving Health Equity in Glaucoma Care (Sym42).** *Chair: Yvonne Ou, MD.* Growing evidence demonstrates the unequal impact of COVID-19 on ethnic minorities, including Black and Latinx Americans. Unfortunately, the burden of glaucoma in the United States also reflects the disproportionate impact of glaucoma on ethnic minorities. As such, is it imperative that ophthalmologists and eye care providers understand the impact of social determinants of health, recognize inequities in care, strive to follow best practices in medical education and clinical guidelines of care, and learn about innovative and nontraditional models of care delivery. *Cosponsored by Prevent Blindness.* **When:** 2:00-3:15 p.m. **Where:** Room 243.

## 2021 AWARDS

### Special Awards

Individuals who are honored with these Special Awards for both 2020 and 2021 will attend the annual meeting in New Orleans as guests of Academy President **Tamara R. Fountain, MD,** and they will be formally recognized during the Opening Session, which will take place on Friday, Nov. 12, 5:00-6:30 p.m.

#### LAUREATE AWARD

The Academy's highest honor, this award recognizes individuals who have made exceptional contributions to the betterment of eye care, leading to the prevention of blindness and restoration of sight worldwide.

George B. Bartley, MD (2020)
Michael T. Trese, MD (2021)

#### GUESTS OF HONOR

This award recognizes individuals chosen by the president for their contributions to ophthalmology.

Paul P. Lee, MD, JD
Don Liu, MD
Terri L. Young, MD, MBA

#### DISTINGUISHED SERVICE AWARD

This award recognizes individuals or organizations for ongoing notable service to ophthalmology and the Academy.

Paul A. Sieving, MD, PhD (2020)
Jane Aguirre (2021)

#### SPECIAL RECOGNITION AWARD

This award recognizes individuals or organizations for outstanding service in a specific effort or cause that improves the quality of eye care.

American College of Surgeons (2020)
Young Ophthalmologist (YO) Committee (2021)

#### OUTSTANDING HUMANITARIAN SERVICE AWARD

This award recognizes Academy members for outstanding humanitarian efforts through their participation in charitable activities, care of the indigent, and involvement in community service performed above and beyond the typical duties of an ophthalmologist.

Steve A. Arshinoff, MD (2020)
John H. Kempen, MD (2020)
David H. Cherwek, MD (2021)
Bradley K. Ferris, MD (2021)

#### OUTSTANDING ADVOCATE AWARD

This award recognizes Academy members for their participation in advocacy-related efforts at the state and/or federal level.

Thomas L. Steinemann, MD (2020)
Dorothy M. Moore, MD (2021)

#### INTERNATIONAL BLINDNESS PREVENTION AWARD

This Award recognizes an individual who has made significant contributions to reducing blindness and/or restoring sight worldwide.

Larry Schwab, MD (2020-2021)

## SUBSPECIALTY DAY

### Program Directors Preview: Retina and Cornea Lineup

This month, program directors from Retina and Cornea Subspecialty Day meetings preview some of this year's highlights.

**View the schedules** at aao.org/programsearch.

#### RETINA 2021: EMERGING EVEN STRONGER

**Program Directors:** Mark W. Johnson, MD, and Srinivas R. Sadda, MD.

**When:** Friday, Nov. 12 (8:00 a.m.-4:00 p.m.), and Saturday, Nov. 13 (8:00 a.m.-5:30 p.m.)

The Retina Subspecialty Day program will celebrate the emergence from a life-altering pandemic with several exciting enhancements to the traditional powerhouse program and faculty. In the opening session, faculty speakers and panelists will focus on complex and challenging vitreoretinal

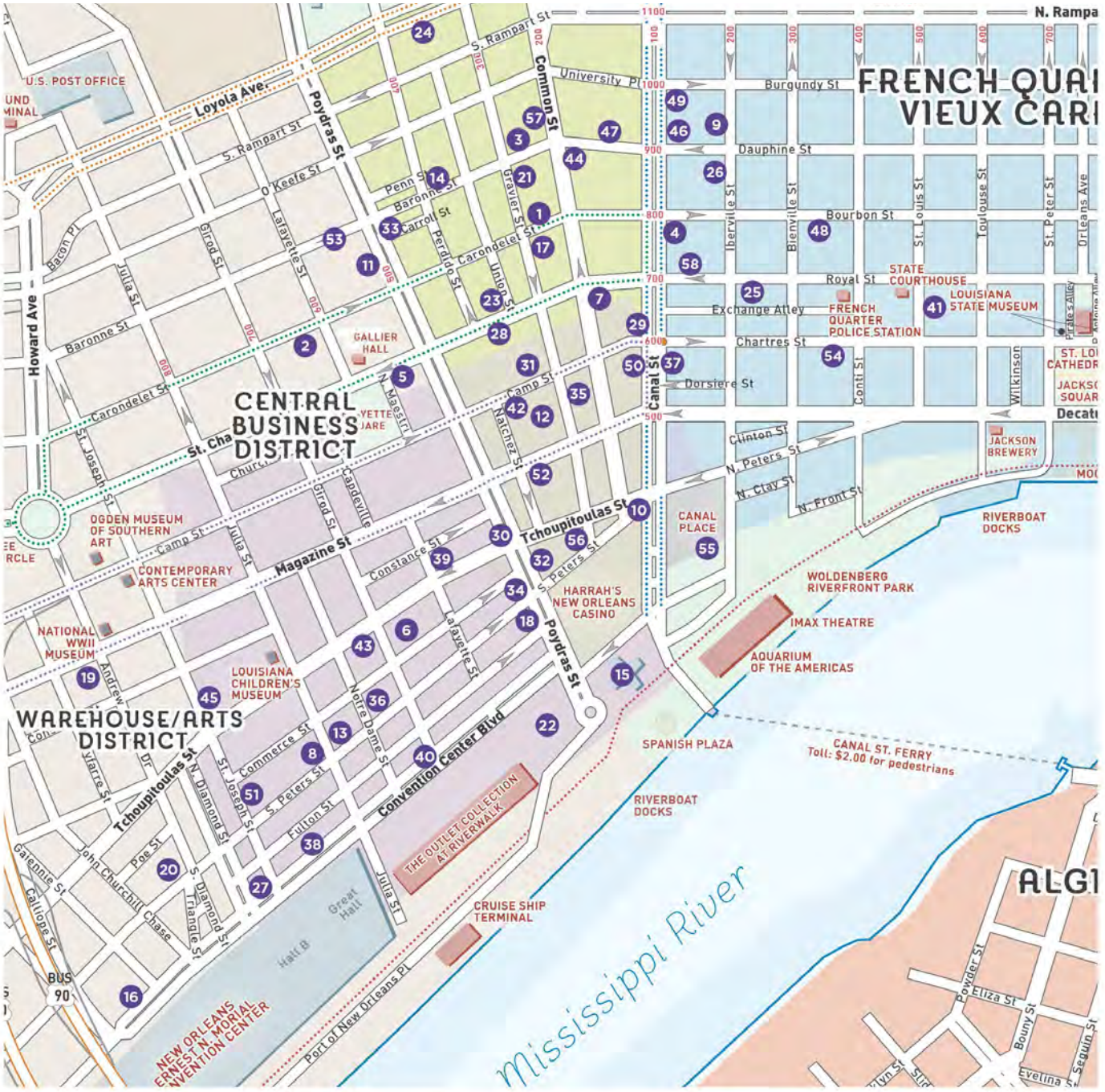
surgical conditions and techniques. The Business of Retina session has been expanded to include talks on retina-related issues in public health, education, and diversity and equity. And a minisymposium on fascinating new concepts in central serous retinopathy and pachychoroid disease will highlight the Medical Retina session.

Sessions on artificial intelligence and gene- and cell-based therapies have been expanded to keep us informed about the rapid changes in these fields. And the final Surgical Videos session has been expanded to include both surgical complications and cool surgical cases. Making return appearances this year are the ever-popular My Best Medical Retina Cases, the Charles L. Schepens Lecture, the Retina Debates, OCT Diagnoses You Don't Want to

## OFFICIAL AAO 2021 HOTELS

**Reserve a hotel room for AAO 2021 today.** Visit aao.org/hotel for reservations, an interactive map, and information on hotel amenities and availability.

**Beware of scams.** Fraudulent companies pretending to be associated with the Academy and AAO 2021 may appear in web searches or contact you via email.



Miss, First-Time Results of Clinical Trials, and Late-Breaking Developments. Finally, audience members will be thoroughly updated and energized with talks and panel discussions covering the full spectrum of topics in medical and surgical retina, oncology, uveitis, pediatric retina, and retinal imaging. This year's fantastic face-to-face program will truly serve as the one-stop shopping destination for continuing education in retina.

*Retina Subspecialty Day is organized in conjunction with the American Society of Retina Specialists, the Macula Society, the Retina Society, and Club Jules Gonin.*

Only book hotel rooms and registration through the Academy's website and official housing provider, Expovision. If you are ever in doubt, email meetings@aao.org or call 1-415-561-8500 to confirm.

| # | HOTEL |
|---|---|
| 1 | AC Hotel New Orleans French Quarter |
| 2 | Ace Hotel New Orleans |
| 3 | Aloft New Orleans Downtown |
| 4 | Astor Crowne Plaza New Orleans French Quarter |
| 5 | Blake Hotel New Orleans |
| 6 | Cambria Hotel New Orleans Downtown Warehouse District |
| 7 | Courtyard New Orleans Downtown |
| 8 | Courtyard New Orleans Convention Center |
| 9 | Courtyard New Orleans French Quarter/Iberville |
| 10 | DoubleTree by Hilton Hotel |
| 11 | Drury Plaza Hotel |
| 12 | Eliza Jane, Unbound by Hyatt |
| 13 | Embassy Suites by Hilton |
| 14 | Fairfield Inn & Suites New Orleans |
| 15 | Four Seasons Hotel New Orleans |
| 16 | Hampton Inn & Suites New Orleans Convention Center |
| 17 | Hampton Inn & Suites |
| 18 | Harrah's New Orleans |
| 19 | Higgins Hotel |
| 20 | Hilton Garden Inn/Convention Center |
| 21 | Hilton Garden Inn/French Quarter, CBD |
| 22 | Hilton New Orleans Riverside |
| 23 | Hilton New Orleans St. Charles Ave. |
| 24 | Holiday Inn New Orleans/Superdome |
| 25 | Hotel Monteleone |
| 26 | Hyatt Centric French Quarter |
| 27 | Hyatt Place/Convention Center |
| 28 | InterContinental New Orleans |
| 29 | JW Marriott New Orleans |

| # | HOTEL |
|---|---|
| 30 | Kimpton Hotel Fontenot |
| 31 | La Quinta Inn & Suites/Downtown |
| 32 | Le Meridien New Orleans |
| 33 | Le Pavillon Hotel |
| 34 | Loews New Orleans Hotel |
| 35 | Magnolia New Orleans |
| 36 | Mercantile Hotel New Orleans |
| 37 | New Orleans Marriott |
| 38 | New Orleans Marriott/Warehouse Arts District |
| 39 | Old No. 77 Hotel |
| 40 | Omni Riverfront Hotel |
| 41 | Omni Royal Orleans |
| 42 | Q&C HotelBar New Orleans, Autograph Collection |
| 43 | Renaissance New Orleans Arts/ Warehouse District Hotel |
| 44 | Renaissance New Orleans Pere Marquette/French Quarter |
| 45 | Sonesta ES Suites/Convention Center |
| 46 | Ritz-Carlton New Orleans |
| 47 | Roosevelt New Orleans |
| 48 | Royal Sonesta New Orleans |
| 49 | Saint Hotel |
| 50 | Sheraton New Orleans |
| 51 | SpringHill Suites/Convention Center |
| 52 | St. James Hotel |
| 53 | Virgin Hotels New Orleans |
| 54 | W New Orleans/French Quarter |
| 55 | Westin New Orleans |
| 56 | Windsor Court Hotel |
| 57 | Wyndham Garden Baronne Plaza New Orleans |
| 58 | Wyndham New Orleans/French Quarter |

## CORNEA 2021: A CLEAR VISION FOR THE NEW DECADE

**Program Directors:** Sophie X. Deng, MD, PhD; Vishal Jhanji, MD; and Sonal S. Tuli, MD.

**When:** Saturday, Nov. 13 (8:00 a.m.-5:00 p.m.)

The 2021 Cornea Subspecialty Day will encompass a wide range of topics of interest to both cornea specialists and comprehensive ophthalmologists. The program will incorporate evidence-based information for the medical and surgical management of corneal and ocular surface diseases presented by experts in the field. To increase engagement of the audience, panel discussion will be complemented by case presentation and audience participation in each session.

The COVID-19 pandemic has changed how ophthalmologists practice. The beginning session is dedicated to the current understanding of SARS-CoV-2 and its impact on eye banking and corneal transplants.

Cataract surgery in the setting of corneal disease, management of complex anterior segment conditions, and ocular surface reconstruction are challenging even for experienced surgeons. Ocular surface diseases caused by dry eye and blepharitis are common conditions, but much has evolved in the diagnosis and management using new technology. The current best practices to manage these conditions and pearls of surgical techniques will be the highlights of several sessions.

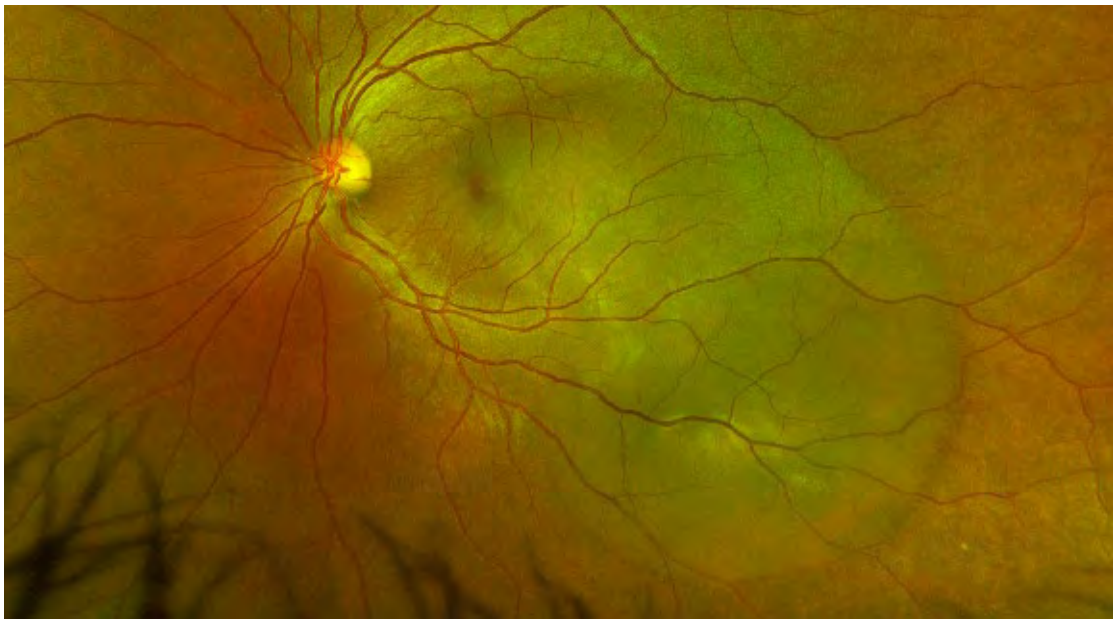
The techniques of corneal transplant continue to evolve. Lamellar keratoplasty in complex eyes is a focus of the keratoplasty session. The current status on xenotransplantation will also be presented.

Significant advances have been made in developing the next generation of therapies for corneal and ocular surface diseases. The day will conclude by introducing several exciting new therapies that could revolutionize the management of corneal diseases.

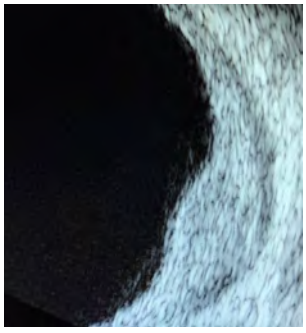
*Cornea Subspecialty Day is organized in conjunction with the Cornea Society.*

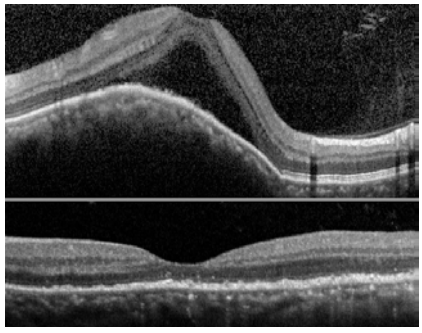
MYSTERY IMAGE

# BLINK



George Henry, CRA, PBT (ASCP), Wheaton Eye Clinic, Wheaton, Ill.



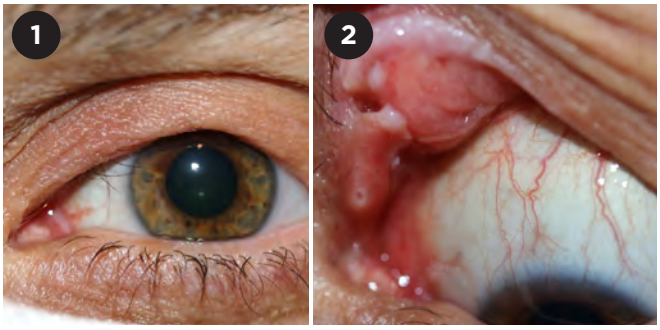


***WHAT IS THIS MONTH'S MYSTERY CONDITION?*** *Visit aao.org/eyenet to make your diagnosis in the comments.*

LAST MONTH'S BLINK

## Self-Harm During the Pandemic

A 40-year-old engineer on duloxetine for depression presented for evaluation of persistent left upper eyelid chalazion (Fig. 1). During the COVID-19 pandemic, she self-managed her chalazion by using sharp forceps to etch out her meibomian glands and denude any granulation tissue, which she believed were painful meibomian stones. She reported that although the act of picking at the eyelid was painful, it resulted in temporary but significant relief of the constant foreign body sensation.




Examination revealed eyelid retraction, madarosis, and effacement of the margin and meibomian gland structures with a full-thickness tarsal cleft (Fig. 2). Use of a scleral bandage contact lens broke her obsessive-compulsive cycle, allowing her eyelid to heal.

Ophthalmologists should have a heightened awareness for self-inflicted injury triggered by quarantine and isolation, especially in patients with preexisting psychiatric diagnoses. Detailed history taking continues to be of utmost importance, and comanagement with psychiatry should be considered in difficult cases.

WRITTEN BY **VICTOR D. LIOU, MD,** AND **NAHYOUNG G. LEE, MD.** PHOTOS BY DR. LEE. BOTH ARE AT MASSACHUSETTS EYE AND EAR, BOSTON.

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