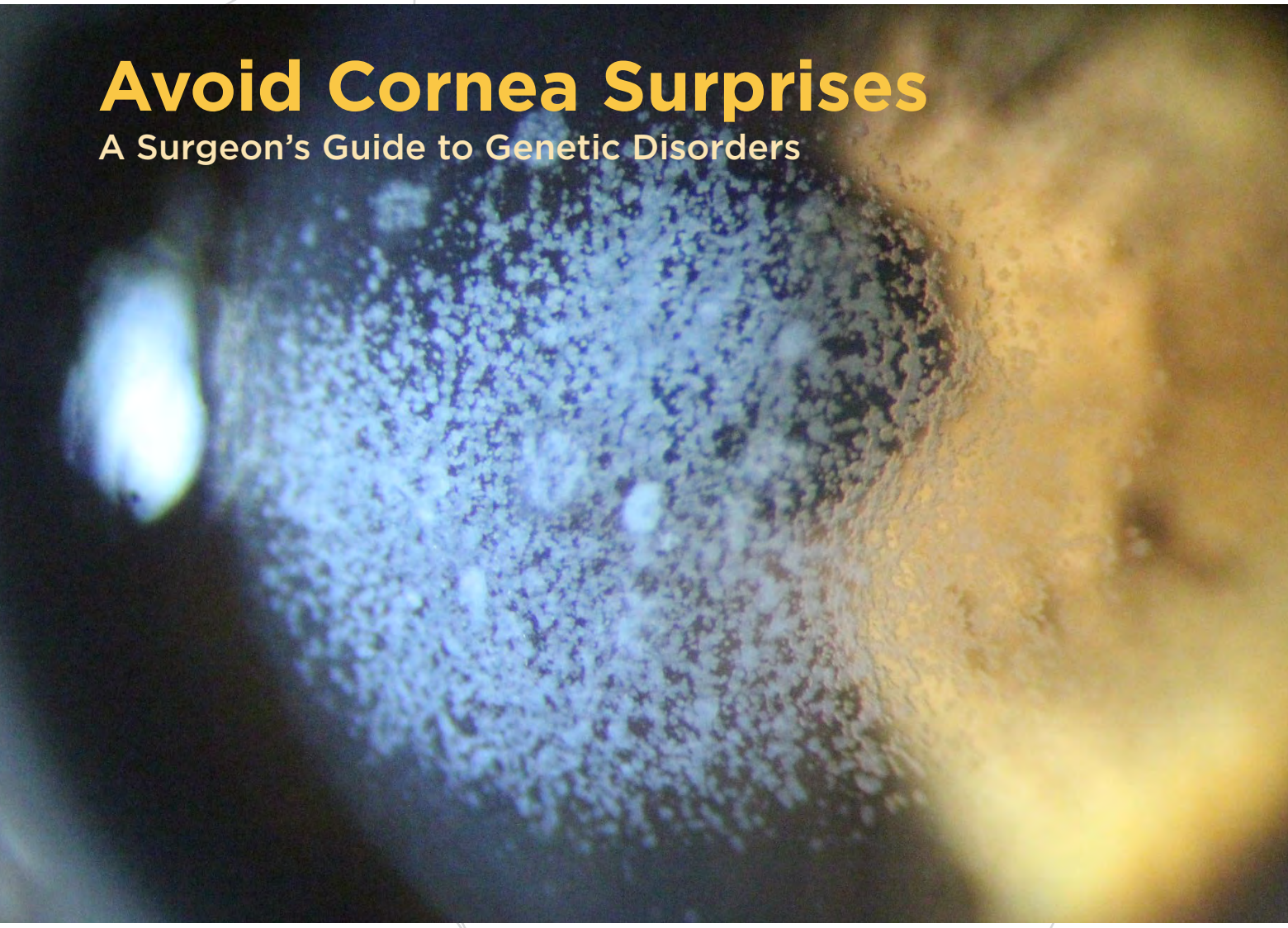
AMERICAN ACADEMY
OF OPHTHALMOLOGY®

EyeNet®

MAY 2020

Avoid Cornea Surprises

A Surgeon's Guide to Genetic Disorders



COVID-19 Pandemic
Telemedicine to the Forefront (p 25)
Ocular Tumor Triage and Care (p 29)
Plus: Editorials by Ruth Williams (p 10)
and David Parke (p 13)

MIPS 2020: The 64-Page Supplement
Keep This Reference at Your Desk

Protecting Sight. Empowering Lives.®

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

AAO 2020 VISION

Registration and Housing Open in June

June 17 (Academy and AAOE® members)
July 8 (Nonmembers)

No cancellation fee until August 12.

aao.org/registration
aao.org/hotels

See You in Las Vegas

AAO 2020 November 14 – 17
Subspecialty Day November 13 – 14
AAOE Program November 13 – 17
ASORN Nursing Program November 13 – 14

2020 Named Lectures Include:

Marshall M. Parks Lecture
Monte A. Del Monte, MD

Zimmerman Lecture
Patricia Chevez-Barrios, MD

Jones-Smolin Lecture
Thuy A. Doan, MD, PhD

Robert N. Shaffer Lecture
David S. Friedman, MD, PhD, MPH

Where All of Ophthalmology Meets®

aao.org/2020

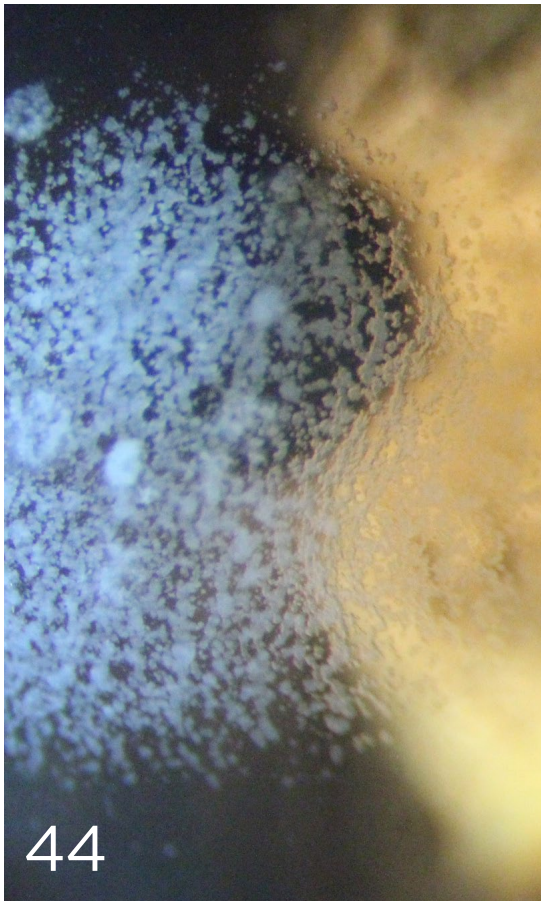
Protecting Sight. Empowering Lives.®

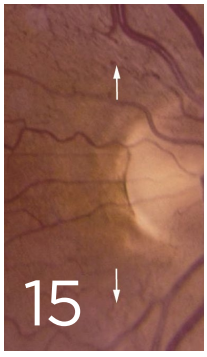
THE MOST ADVANCED CONTROL CENTER, AT YOUR FINGERTIPS

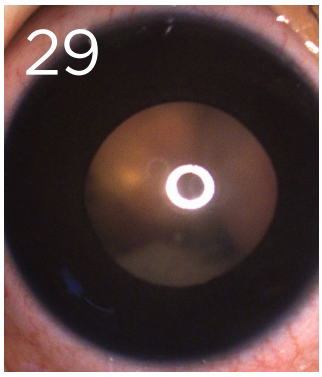
The CENTURION® Vision System with ACTIVE SENTRY® Handpiece is designed to establish an improved baseline of safety, consistency and control to cataract patients.

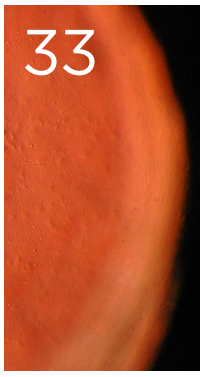
Alcon

Centurion®
Vision System With ACTIVE SENTRY®







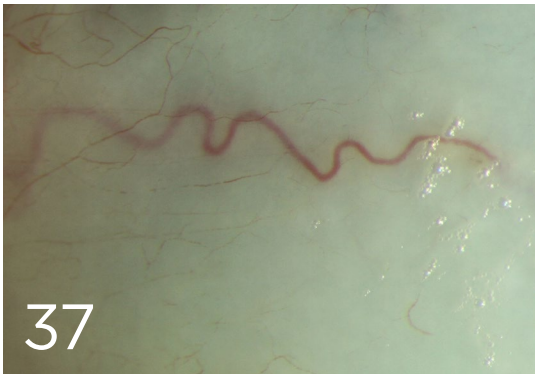


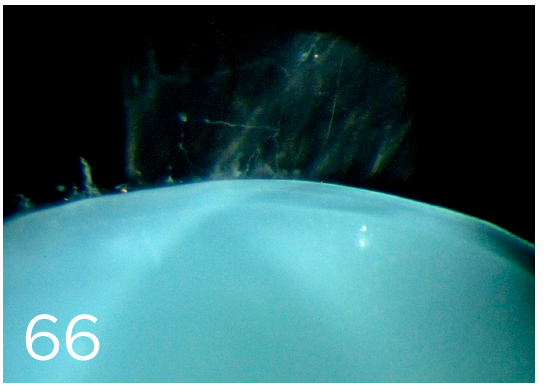
CONTENTS

MAY 2020
VOLUME 24 • NUMBER 5

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.





THANK YOU TO RETINA SPECIALISTS

and office staff for all you are doing amid the COVID-19 pandemic. We recognize your efforts and stand by you.

For more on Regeneron's scientific efforts to help address COVID-19, please visit our website: ***www.regeneron.com/covid19***

REGENERON®

777 Old Saw Mill River Road, Tarrytown, NY 10591 04/2020 OPH.20.04.0002

EDITORIAL BOARD

ACADEMY BOARD

Learn more about the Board *at aao.org/bot.*

EyeNet® MAGAZINE

David W. Parke II, MD
Editor-in-Chief

Ruth D. Williams, MD
Chief Medical Editor

Dale E. Fajardo, EdD, MBA
Publisher

Patty Ames
Executive Editor

Carey S. Ballard
Art Director / Production Manager

Chris McDonagh, Jean Shaw
Senior Editors

Miranda Smith
Associate Editor / Advertising Manager

Lori Baker-Schena, MBA, EdD; Leslie Burling; Peggy Denny; Miriam Karmel; Mike Mott; Linda Roach; Lynda Seminara; Annie Stuart; Rebecca Taylor; Gabrielle Weiner
Contributing Writers

Mark Mrvica, Kelly Miller
M.J. Mrvica Associates, Inc.
2 West Taunton Ave.,
Berlin, NJ 08009
856-768-9360
mjmrvica@mrvica.com
Advertising Sales

AMERICAN ACADEMY OF OPHTHALMOLOGY®
655 Beach St.
San Francisco, CA 94109
866-561-8558, 415-561-8500
aao.org

Governmental Affairs Division
20 F Street NW, Suite 400
Washington, DC 20001
202-737-6662

ARTICLE REVIEW PROCESS. Articles involving single-source medical and technical news are sent to quoted sources for verification of accuracy prior to publication. Quotes and other information in multisource articles are subject to confirmation by their respective sources. The chief medical editor and the executive editor review all news and feature articles and have sole discretion as to the acceptance and rejection of material and final authority as to revisions deemed necessary for publication.

DISCLOSURE KEY. Financial interests are indicated by the following abbreviations:
C = Consultant/Advisor
E = Employee
L = Speakers bureau
O = Equity owner
P = Patents/Royalty
S = Grant support
For definitions of each category, see aao.org/eyenet/disclosures.

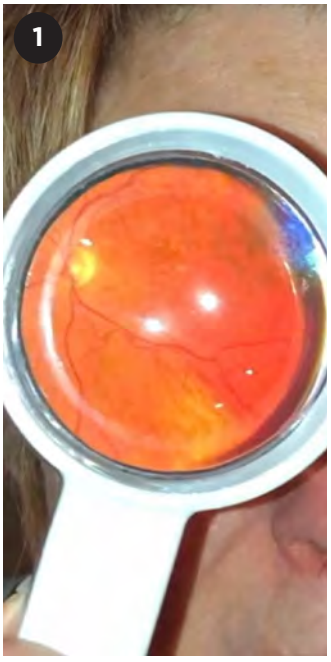
Letters

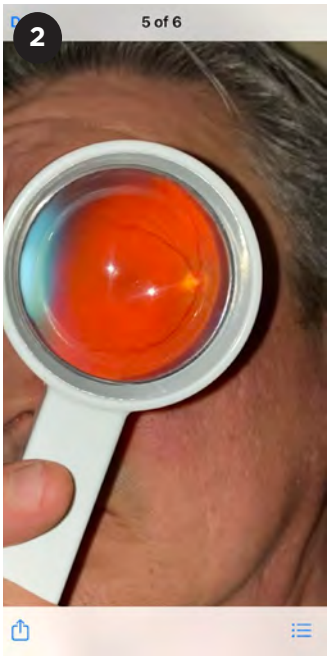
A Retina Telemedicine Technique

I really appreciate all the leadership and advice that the Academy and Dr. Parke have provided during the COVID-19 crisis.

I am an ophthalmologist and Academy member. Since I am in an increased risk group, I have limited my practice to telemedicine. I have developed a technique for patients to photograph their retina and optic nerve at home with just a smartphone and a $16 magnifier. The magnifier is a 20-D (6× magnification) low vision aid. This can be shipped to patients, and they can obtain a bottle of tropicamide for less than $10 (and have it delivered to them by a pharmacy). Therefore, the total cost with shipping for the magnifier and drops is approximately $30. This is invaluable for elderly patients or at-risk patients with macular degeneration who require monitoring by their ophthalmologist but are forced to stay home due to risk of contagion with COVID-19. It's also useful for the monitoring of other retinal diseases and glaucoma. As an illustration, here are two images: The first photo (Fig. 1) is a patient with macular drusen; she took the photo at home while I talked her through it from my house. The second photo (Fig. 2) is my retina, which I photographed myself at home. A video to elucidate the procedure is forthcoming.

Ira J. Salzman, MD
Syosset, N.Y.





WRITE TO US. Send your letters of 150 words or fewer to us at *EyeNet Magazine,* AAO, 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.)

Opinion

RUTH D. WILLIAMS, MD

Reflections During a Crisis

Ruth D. Williams, MD
Chief Medical Editor, EyeNet

As I write, the medical, financial, and administrative issues related to the SARS-Cov-2 pandemic are dominating our thoughts and our professional and personal lives. A magazine format isn't designed for the daily updates necessitated by a briskly evolving pandemic, but it is a great format for education, a summary of the evidence, discussions of clinical practice, and—most uniquely—reflection. I'm writing from my sofa during a multiday spell of being homebound except for seeing a few patients with urgent ophthalmic issues. I'll share a few observations about our ophthalmology community and some lessons learned during this challenging time.

First, the Academy has demonstrated extraordinary early leadership: Since Jan. 28, it has provided detailed information about the coronavirus. The Academy's COVID-19 webpages are updated daily and provide scientific material, current statistics, and practice recommendations. Examples of the latter have included information on triaging patients (those at both low and high risk of infection), postponing elective surgery, and disinfection protocols. Make sure you bookmark aao.org/coronavirus.

Clear communication is essential at this time. Our patients need guidance about whether to keep an appointment for an eye exam or a surgical procedure. Practices have responded to the pandemic by messaging patients in a variety of ways: through appointment reminders, call center staff, signs, our websites, and articles in local newspapers. Many of my partners personally called their patients to explain why an appointment was being rescheduled or, conversely, why it was necessary to keep an appointment. When I called a 60-year-old glaucoma patient, she said, "Thank you so much for telling me what I should do. I didn't know if my glaucoma checkup could wait until summer, and I'm glad you decided for me."

Our employees also crave constant communication. They need protocols, accurate scientific information, and protective equipment. Employees are worried, not only about their exposure risk, but also whether they will be able to continue working. Many of our hourly employees need every dollar for rent, groceries, and childcare. Being as clear as possible about paid time off and financial support goes a long way in diminishing anxiety. Most of all, our employees need to know that we are a team and that their employer cares about their physical, mental, and financial well-being. It helps to communicate daily, even when we don't know all the answers (which is usually).

I'm also reminded that ophthalmologist colleagues around the world are my friends. Talal Hrout, a comprehensive ophthalmologist in Amman, Jordan, and I have shared thoughts about which patients should be rescheduled. And on March 18—the day that David Parke announced the Academy's recommendation that U.S. ophthalmologists only see patients with urgent ophthalmic needs—several support mechanisms kicked into gear. For instance, the owners of several ophthalmology groups messaged one another about how to manage the finances of an extended shutdown. While one ophthalmologist was quarantined with a fever, awaiting the results of COVID testing, her ophthalmology friends checked on her every day. Sidney Gicheru led a discussion group for ophthalmologists on Facebook; a Google Group helped ophthalmologists share strategies and information; and on Instagram, several of you made me laugh with photos of your attempts to work at home with kids in the background. One person sent a daily text with a COVID-related joke or cartoon (yes, there is humor during crisis). At a time when I hardly see another person, I'm supported by a community of people who share similar challenges and values.

And I think of my ophthalmology partners at Wheaton Eye Clinic as my brothers and sisters. We've worked together for decades. We know one another's strengths and foibles. Our life's work—indeed, our purpose for living—is intertwined, along with our financial outlook. I'm not surprised by the dedication of my partners, but I'm inspired anew by it.

We talk about the ophthalmologist-led eye care team. In a time of crisis, ophthalmologists in private practice and academic departments are leading, yet again, with courage, thoughtfulness, and ahead-of-the-curve strategizing. You are my people.

oxervate™
(cenegermin-bkbj ophthalmic solution) 0.002% (20 mcg/mL)

The first FDA-approved pharmacologic treatment that targets the root pathogenesis of neurotrophic keratitis[1-3]

With OXERVATE, up to 72% of patients achieved complete corneal healing at 8 weeks*[1,4]

- Cenegermin-bkbj, the active ingredient in OXERVATE, is structurally identical to the human nerve growth factor (NGF) protein made in ocular tissues[5]
- NGF is an endogenous protein involved in the differentiation and maintenance of neurons, and acts through specific high-affinity (ie, TrkA) and low-affinity (ie, p75NTR) NGF receptors in the anterior segment of the eye to support corneal innervation and integrity.[1] Endogenous NGF is believed to support corneal integrity through 3 primary mechanisms (shown in preclinical models): corneal innervation, reflex tear secretion, and corneal epithelial cell proliferation and differentiation[3,6,7]

Explore the breakthrough therapy at Oxervate.com/HCP

Indication

OXERVATE is a recombinant human nerve growth factor indicated for the treatment of neurotrophic keratitis.

Important Safety Information

WARNINGS AND PRECAUTIONS

Patients should remove contact lenses before applying OXERVATE and wait 15 minutes after instillation of the dose before reinsertion.

ADVERSE REACTIONS

The most common adverse reaction in clinical trials that occurred more frequently with OXERVATE was eye pain (16% of patients). Other adverse reactions included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation, and increase in tears (1%-10% of patients).

For additional safety information, see accompanying Brief Summary of Safety Information on the adjacent page and full Prescribing Information on Oxervate.com/HCP.

*Complete corneal healing was defined as the absence of staining of the corneal lesion and no persistent staining in the rest of the cornea after 8 weeks of treatment. Based on results from the REPARO trial (Europe, NGF0212; N=156) and the US trial (NGF0214; N=48).[4,8]

References: 1. OXERVATE (cenegermin-bkbj) full prescribing information. Dompé. October 2019. **2.** FDA approves first drug for neurotrophic keratitis, a rare eye disease [FDA news release]. August 22, 2018. **3.** Mastropasqua L, Massaro-Giordano G, Nubile M, Sacchetti M. Understanding the pathogenesis of neurotrophic keratitis: the role of corneal nerves. *J Cell Physiol*. 2017;232:717-724. **4.** Bonini S, Lambiase A, Rama P, et al. Phase II randomized, double-masked, vehicle-controlled trial of recombinant human nerve growth factor for neurotrophic keratitis. *Ophthalmology*. 2018;125:1332-1343. **5.** Voelker R. New drug treats rare, debilitating neurotrophic keratitis. *JAMA*. 2018;320:1309. **6.** Müller LJ, Marfurt CF, Kruse F, Tervo TMT. Corneal nerves: structure, contents and function. *Exp Eye Res*. 2003;76:521-542. **7.** Sacchetti M, Lambiase A. Diagnosis and management of neurotrophic keratitis. *Clin Ophthalmol*. 2014;8:571-579. **8.** Center for Drug Evaluation and Research, US Food and Drug Administration. Oxervate (cenegermin-bkbj) BLA 761094. Medical Review(s). July 19, 2018. https://www.accessdata.fda.gov/drugsatfda_docs/nda/2018/761094Orig1s000TOC.cfm.

Dompé

US-OXE-1900180 01/20

oxervate™
(cenegermin-bkbj ophthalmic solution) 0.002% (20 mcg/mL)

Brief Summary of Safety

Consult the full Prescribing Information for complete product information.

INDICATIONS AND USAGE

OXERVATE™ (cenegermin-bkbj) ophthalmic solution 0.002% is indicated for the treatment of neurotrophic keratitis.

DOSAGE AND ADMINISTRATION

Contact lenses should be removed before applying OXERVATE and may be reinserted 15 minutes after administration.

If a dose is missed, treatment should be continued as normal, at the next scheduled administration.

If more than one topical ophthalmic product is being used, administer the eye drops at least 15 minutes apart to avoid diluting products. Administer OXERVATE 15 minutes prior to using any eye ointment, gel or other viscous eye drops.

Recommended Dosage and Dose Administration

Instill one drop of OXERVATE in the affected eye(s), 6 times a day at 2-hour intervals for eight weeks.

ADVERSE REACTIONS

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

In two clinical trials of patients with neurotrophic keratitis, a total of 101 patients received cenegermin-bkbj eye drops at 20 mcg/mL at a frequency of 6 times daily in the affected eye(s) for a duration of 8 weeks. The mean age of the population was 61 to 65 years of age (18 to 95). The majority of the treated patients were female (61%). The most common adverse reaction was eye pain following instillation which was reported in approximately 16% of patients. Other adverse reactions occurring in 1-10% of OXERVATE patients and more frequently than in the vehicle-treated patients included corneal deposits, foreign body sensation, ocular hyperemia, ocular inflammation and tearing.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary There are no data from the use of OXERVATE in pregnant women to inform any drug associated risks.

Administration of cenegermin-bkbj to pregnant rats or rabbits during the period of organogenesis did not produce adverse fetal effects at clinically relevant doses. In a pre- and postnatal development study, administration of cenegermin-bkbj to pregnant rats throughout gestation and lactation did not produce adverse effects in offspring at clinically relevant doses.

Animal Data

In embryofetal development studies, daily subcutaneous administration of cenegermin-bkbj to pregnant rats and rabbits throughout the period of organogenesis produced a slight increase in post-implantation loss at doses greater than or equal to 42 mcg/kg/day (267 times the MRHOD). A no observed adverse effect level (NOAEL) was not established for post-implantation loss in either species. In rats, hydrocephaly and ureter anomalies were each observed in one fetus at 267 mcg/kg/day (1709 times the MRHOD). In rabbits, cardiovascular malformations, including ventricular and atrial septal defects, enlarged heart and aortic arch dilation were each observed in one fetus at 83 mcg/kg/day (534 times the MRHOD). No fetal malformations were observed in rats and rabbits at doses of 133 mcg/kg/day and 42 mcg/kg/day, respectively. In a pre- and postnatal development study, daily subcutaneous administration of cenegermin-bkbj to pregnant rats during the period of organogenesis and lactation did not affect parturition and was not associated with adverse toxicity in offspring at doses up to 267 mcg/kg/day. In parental rats and rabbits, an immunogenic response to cenegermin-bkbj was observed. Given that cenegermin-bkbj is a heterologous protein in animals, this response may not be relevant to humans.

Lactation

There are no data on the presence of OXERVATE in human milk, the effects on breastfed infant, or the effects on milk production. The developmental and health benefits of breastfeeding should be considered, along with the mother's clinical need for OXERVATE, and any potential adverse effects on the breastfed infant from OXERVATE.

Pediatric Use

The safety and effectiveness of OXERVATE have been established in the pediatric population. Use of OXERVATE in this population is supported by evidence from adequate and well-controlled trials of OXERVATE in adults with additional safety data in pediatric patients from 2 years of age and older [*see Clinical Studies (14)*].

Geriatric Use

Of the total number of subjects in clinical studies of OXERVATE, 43.5 % were 65 years old and over. No overall differences in safety or effectiveness were observed between elderly and younger adult patients.

NONCLINICAL TOXICOLOGY

Carcinogenesis and Mutagenesis Animal studies have not been conducted to determine the carcinogenic and mutagenic potential of cenegermin-bkbj.

Impairment of fertility Daily subcutaneous administration of cenegermin-bkbj to male and female rats for at least 14 days prior to mating, and at least 18 days post-coitum had no effect on fertility parameters in male or female rats at doses up to 267 mcg/kg/day (1709 times the MRHOD). In general toxicology studies, subcutaneous and ocular administration of cenegermin-bkbj in females was associated with ovarian findings including persistent estrus, ovarian follicular cysts, atrophy/reduction of corpora lutea, and changes in ovarian weight at doses greater than or equal to 19 mcg/kg/day (119 times the MRHOD).

Dompé

Current Perspective

DAVID W. PARKE II, MD

Of Black Swans, TP, and Health Care

Nearly 2,000 years ago Roman poets wrote of black swans as mythical beings. When later discovered to exist in the wild, they became a metaphor for unanticipated events that capsize current social and economic assumptions and cause fundamental and disruptive change.

"Black swan events," as initially described by Taleb in his classic 2001 finance book *Fooled by Randomness,* have three primary attributes:

1. Each is rare and unexpected.
2. Each generates a massive impact that is broad in scope.
3. Each is rationalized in hindsight to have been predictable, if only certain observations and datasets had been appropriately valenced.

We are all experiencing a tragic global pandemic that some have described as a "once in a century event." Many assume that it was unpredictable while a few allege it was highly predictable. Some believe we'll see a similar event again before this century is up. Regardless, COVID-19 certainly fulfills the criteria for a black swan event.

While viral pandemics in general have certainly been prophesied both in scientific literature and in popular cinema (such as the 2011 movie "Contagion"), the specifics of our current viral pandemic scenario were unforeseen. It is a black swan.

This black swan resulted in an acute and bothersome shortage of toilet paper (TP). While there was nothing specific to a pulmonary pandemic that should engender an acute rise in toilet paper use, past quasi-apocalyptic events were accompanied by hoarding behavior. In this case, it was toilet paper—to the point where sales exploded by 845% in mid-March as states announced various forms of lockdowns. And store shelves have stayed bare.

Why couldn't those shelves be quickly refilled and the TP Panic avoided? It comes down to basic TP economics. TP is a low margin product, and the tight supply chain is managed to be "just in time." While the average American uses 141 rolls per year, the supply chain diverts excess supply where it is needed most acutely. However, when everyone everywhere is purchasing a bit more, the system breaks down, shortages occur, and hoarding ensues.

So what do TP economics have to do with health care? They are both emblematic of the same core problems—tight margins, lack of surge capacity at either institutional or system levels, and globalized supply sourcing driven by economics and resulting in supply chain constraints. This is a version of the common aphorism "a chain is no stronger than its weakest link." Without redundancy or flexibility, the system is highly vulnerable to link failure—whether it is a unique manufacturing step for toilet paper or an essential drug, device, person, or facility needed to manage a pulmonary pandemic.

It may be one thing to pursue an economic strategy of supply constraints with toilet paper, but it is another thing entirely to do so with an entity as life-critical, economically-critical, and literally civilization-critical as is our health care infrastructure. Is it an ideally architected system that squeezes out surge capacity in the name of profitability? Is our drug supply chain ideally designed if unique molecules are sourced only outside of our borders and outside of our control or from a sole source? Is it wise to forego a central health care command and control structure equipped with regularly updated scenario-specific contingency plans and necessary statutory authority? What risks do we run by pursuing a provider compensation system that commoditizes health care and drives so much patient throughput and efficiency to achieve positive economic performance that we retain little or no surge flexibility?

David W. Parke II, MD
Academy CEO

A specific black swan event is a rare beast indeed. But, as a class, black swan events are not rare. And if we don't engineer our critical processes to account for them, we risk a recurrence of the cataclysmic disruption we now are enduring. Black swan events should and generally do force fundamental change. We need not only to recover effectively and rapidly from COVID-19 but also to thoughtfully consider what we can do at the strategic level to prepare for the next black swan—without treating health care like toilet paper and returning to squeezing out any excess capacity.

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

Ophthalmic Advisors Group

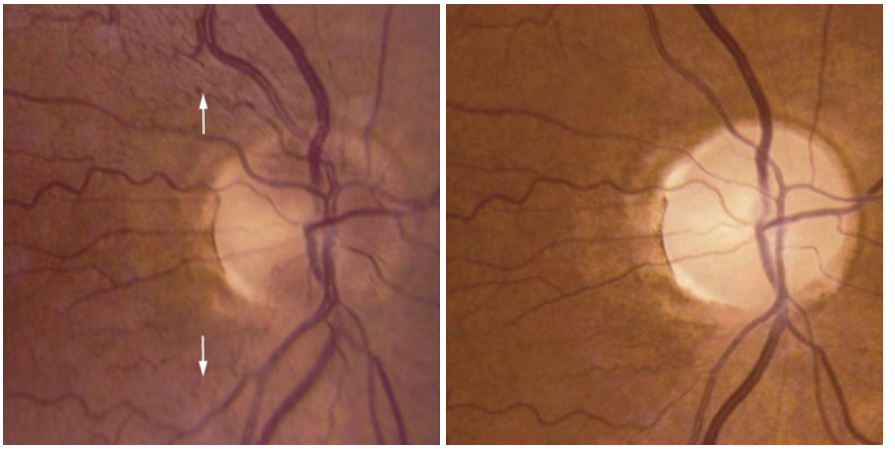
Personal Guidance. Practical Solutions.

Schedule coding and practice management consultations with Academy experts.

aao.org/consultation-services

News in Review

COMMENTARY AND PERSPECTIVE



LHON. *Genetic tests confirmed a point mutation in this patient with LHON. (Left) Arrows indicate peripapillary telangiectasias observed in the acute phase of vision loss. (Right) Several months later, the optic disc is diffusely pale.*

GENETICS

Outcomes of LHON Gene Therapy Elucidated

IN A PAIR OF STUDIES, A TEAM OF Chinese researchers has reported on long-term outcomes of gene therapy for Leber hereditary optic neuropathy (LHON)[1] and elucidated some factors that predispose patients to better visual outcomes following treatment.[2]

Study No. 1: Seven years of follow-up. In a small study of nine patients who underwent gene therapy for LHON, two-thirds continue to have persistent, significant gains in their best-corrected visual acuity (BCVA) after seven years (range, 75-90 months).[1]

The scientists found that the improvement in BCVA in these patients was ≥0.3 logMAR, equivalent to 15 letters on the EDTRS chart, said principal investigator Bin Li, MD, PhD, at the Huazhong University of Science and Technology and Tongji Hospital, both in Wuhan, China. In addition, no adverse outcomes were noted. "This demonstrates the long-term safety and efficacy of gene therapy," Dr. Li said.

Protocol and results. All patients received a single unilateral intravitreal injection of a recombinant adeno-associated virus serotype 2 (AAV2) carrying the *ND4* gene, which is mutated in most LHON cases.

Of the six patients who maintained clinically significant improvement in BCVA, the vision of two improved enough that one was admitted to a high school and the other, who gained 8 lines of BCVA, was able to travel to Beijing to obtain a job one year after treatment, Dr. Li said.

Study No. 2: A look at treatment response. In the second study,[2] the researchers reported on early treatment responses from a large prospective trial (149 subjects, including seven from Argentina). "On average, responders convert from legally blind to low vision, with a good percentage of patients reaching normal vision," Dr. Li said. "We will publish the full results soon, and we are actively investigating why some patients responded significantly better than the others."

The initial results in this study showed that about a third of the patients (28.9%) had significantly improved vision within three days of treatment, including significant improvement in acuity in some (18.8%) uninjected fellow eyes. These results confirm the promising findings from the smaller study, Dr. Li said.

The subjects who experienced such rapid acuity gains were the youngest patients and those who had the best vision before treatment, Dr. Li said. In addition, female participants had better responses to treatment than did their male counterparts, he said.

Need for additional investigation. Might patients benefit even more from a second injection? Dr. Li said his team is moving cautiously on this, because the first patient they treated received two injections and the visual outcome was poor.

"Years of research has made us realize that gene therapy is very different from small molecule and antibody drug treatment," Dr. Li said. "The specific mechanism of action may extend beyond the simple gene replacement concept, and much more needs to be explored in order to fully unveil and leverage this new modality of therapy."

An overview of the field. The Chinese group's studies, which began with preclinical work in 2008, are the longest-running trials so far to report on using a recombinant AAV vector to deliver a normal *ND4* mitochondrial gene to patients who have a mutant form of the gene. This mutation, G11778A, accounts for most cases of LHON and the severest disease.[3]

Another group, based at the University of Miami, reported in 2017 on using their own AAV vector containing the *ND4* gene on 14 LHON patients, nine of whom had been followed for at least 12 months.[4]

A third AAV vector for delivering the *ND4* gene is being investigated by European researchers on behalf of GenSight Biologics, which is based in Paris. The group has completed phase 1/2 clinical trials,[3] and a phase 3 trial is ongoing. —*Linda Roach*

1 Yuan J et al. *Ophthalmolology*. Published online Feb. 25, 2020.

2 Liu HL et al. *Acta Ophthalmol*. Published online Feb. 24, 2020.

3 Bouquet C et al. *JAMA Ophthalmol*. 2019;137(4): 399-406.

4 Guy J et al. *Ophthalmolology*. 2017;124(11): 1621-1634.

Relevant financial disclosures—Dr. Li: Wuhan Neurophth Biotechnology: S.

RETINA

Consider Early Tx for DME When VA Is Good

WATCHFUL WAITING, ACCEPTED AS proper management of patients with diabetic macular edema (DME) and good baseline visual acuity (VA), may not be the best approach in a select subset of patients.

In patients who have hyperreflective foci (HRF), a disorganization of the inner retina layers (DRIL), or a disruption of the ellipsoid zone (EZ) on spectral-domain optical coherence tomography (SD-OCT), early treatment may reduce the risk of future VA loss, German researchers reported.[1]

It appears that "there are patients with a higher risk for VA loss during observation than others," said Catharina Busch, MD, at University Hospital Leipzig in Leipzig, Germany. "We might have to consider that the conclusion we got from Protocol V and the OBTAIN studies—that close observation is proper management—does not apply for all patients. There might be patients in which an immediate treatment might provide better long-term results."

Clues from SD-OCT. The current findings are based on a subanalysis of OBTAIN, a 12-month retrospective cohort study that considered charts of 210 patients (249 eyes) with baseline VA equal to or worse than 20/25 and center-involving DME.[2]

For this secondary analysis, the researchers included observed eyes and eyes that received anti-VEGF treatment at baseline. They focused on the observed eyes (n = 147), of which 21% (n = 32) experienced VA loss of 10 or more letters during 12 months of follow-up. In the presence of one SD-OCT feature—HRF, DRIL, or EZ disruption—the odds of experiencing VA loss of

GLAUCOMA

Novel Contact Lens Sensor Passes First Hurdle

A NOVEL CONTACT LENS THAT MEASURES INTRA-ocular pressure (IOP) continuously over 24 hours, including during undisturbed sleep, proved accurate and reliable in a first in-human feasibility assessment.[1]

The noninvasive pressure-measuring contact lens (PMCL) measures IOP in mm Hg as well as ocular pulsation. (The latter's role in glaucoma pathogenesis remains controversial.)

"A 24-hour IOP curve could positively impact management of patients with glaucoma, especially those with functional/structural signs of progression despite apparently well-controlled IOP," said Kaweh Mansouri, MD, MPH, at the Montchoisi Clinic in Lausanne, Switzerland. The potential beneficiaries of 24-hour monitoring include at-risk subjects with IOP in normal range during office hours, unstable glaucoma patients showing glaucoma progression despite low target IOP, and patients with normal tension glaucoma, he said.

Proof of concept. The device includes a silicone contact lens, pressure sensor, antenna, and a telemetry microprocessor embedded in the lens. In this prospective nonrandomized trial, it was placed on the eyes of eight subjects—four with glaucoma and four without—shortly after IOP was measured by Goldmann applanation tonometry (GAT) and dynamic contour tonometry (DCT). The lens remained in place for 24 hours, after which researchers compared its IOP values to those obtained via GAT and DCT.

As measured by the sensor, the mean IOP difference was within 5 mm Hg in 75% of subjects measured with GAT and in 87.5% of subjects measured with DCT. The IOP difference was within the requested 5 mm Hg limits for new tonometers.

Subjects also took a water drinking test, which perturbs the aqueous fluid system and may promote a rise in IOP. In the test, the PMCL detected an average IOP increase of 2.43 mm Hg, compared to 1.85 mm Hg with DCT. (GAT was not used for this test.)

Need for improvement. After the sensor was removed, 75% of eyes had transient corneal erosions; of these, 33.3% were mild, 50% were moderate, and 16.7% were severe. All resolved with or without medication after a mean of 3.1 days. Patients rated PMCL tolerability somewhere in the middle, with a mean score of 55.5 on a scale from 0 (no discomfort) to 100 (severe).

The next step is to test a second-generation device, which was designed to enhance safety and tolerability and increase accuracy of the measurements, Dr. Mansouri said. —*Miriam Karmel*

1 Wasilewicz R et al. *Br J Ophthalmol*. Published online Feb. 19, 2020.

Relevant disclosures—Dr. Mansouri: Implandata: C; Sensimed: C.

at least 10 letters during observation increased 2.7- to 3.2-fold.

When all three features were present, the risk for future VA loss of 10 or more letters during observation increased up to 47% over baseline. When patients were treated immediately at baseline, the risk of future VA loss was reduced to 26% during follow-up.

The presence of subretinal fluid was not a factor.

More study needed. It should be noted that these findings did not reach statistical significance, perhaps due to the small sample size. Moreover, as with the original OBTAIN study, this was a retrospective evaluation.

But the findings suggest the need for further studies in bigger cohorts of patients to evaluate whether an immediate treatment in these high-risk patients is superior to observation or not, Dr. Busch said.

In the meantime, she suggested that clinicians consider the presence or absence of DRIL, HRF, and EZ disruption when deciding whether to treat immediately or closely observe. "Our study changed my personal awareness. If risk features are present, I adapt my control intervals and decide for treatment earlier." *—Miriam Karmel*

1 Busch C et al. *Acta Ophthalmol.* Published online March 1, 2020.

2 Busch C et al. *Acta Diabetol.* 2019;56(7):777-784.

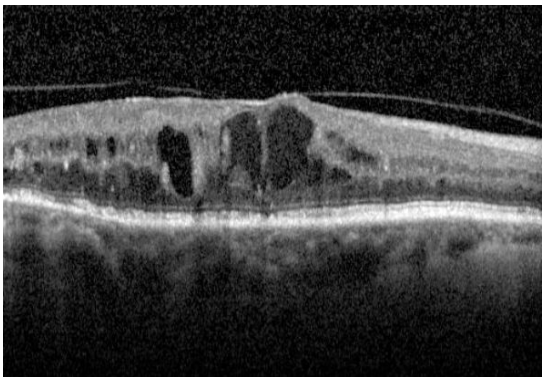
Relevant financial disclosures—Dr. Busch: None.

TELEMEDICINE

Cloud-Based Referral Platform Enables Rapid Triage

EACH MONTH, 22 INDIVIDUALS IN the United Kingdom lose vision because of hospital-initiated system delays, the Royal College of Ophthalmologists has estimated.[1] One potential solution to this dilemma: a cloud-based referral platform that was designed to improve communication between ophthalmologists and other providers and promote rapid triage.

The platform, developed by London-based Big Picture Medical, was put to the test in a pilot study involving three U.K. optometry offices and Moorfields Eye Hospital in London. The result: Of 103 patients initially classified into the referral pathway, 54 (52%) did not need to be referred to a specialist, 35 (34%) could be handled with a routine referral, and 14 (13.6%) needed urgent care.[2]



OCT MORPHOLOGY. *This patient had all three risk factors at baseline—DRIL, HRF, and EZ disruption.*

Catharina Busch, MD

For each case, it took the referring optometrist approximately 9 minutes to gather and send the pertinent clinical data—and it took the ophthalmologist an average of 3 minutes to review and triage the case.

Study rationale. "This study was the first of many steps taken to offer a more streamlined approach to eye care—a digital first encounter that may take the form of asynchronous telemedicine in a store-and-forward model—where a clinical history, eye scans, and visual fields may be reviewed remotely by a relevant specialist," said Dawn A. Sim, MBBS, FRCOphth, PhD, at Moorfields.

And while the study was conducted with referring optometrists, the platform could be put into place with general practitioners and urgent care facilities.

Well-suited to ophthalmology. The platform lends itself to "subspecialty areas with chronic diseases such as medical retina and glaucoma, which form a large proportion of outpatient consultations," Dr. Sim said.

In addition, it opens the door to synchronous telemedicine, she said, "in the form of video consultations with the patient at home or with doctors from the emergency department with the aid of a slit-lamp attachment." This could be useful for oculoplastic and strabismus patients, she said.

"Diagnostic drift" over time. The study has now been running for two years and currently includes nine optometry practices, Dr. Sim said. "The diagnostic drift of different eye conditions that were being referred demonstrates the efficacy of this shared learning [once it is] embedded into a referral workflow."

For example, she said, during the first year, most referrals were for suspected wet age-related macular degeneration. This shifted in the second year, when patients who had a wider variety and complexity of conditions were referred in.

Next steps. "Working with cloud-based telemedicine platforms has moved this field forward in ophthalmology" as the approaches aim to be "truly device-agnostic," Dr. Sim said. But while that represents improvement, real progress will depend upon electronic health records systems and major hardware vendors "opening their APIs and paying more than lip service to DICOM compliance," she said.

And a COVID-19 note. The current pandemic "has forced our hand in changing how we practice ophthalmology," Dr. Sim said. "In this digital age of high-definition eye scans, mobile devices, and high-speed networks, we must convince commissioners and insurers that specialist care does not always have to involve a slit-lamp exam."

—Jean Shaw

1 www.rcophth.ac.uk/wp-content/uploads/2019/01/RCOphth-A4-Census-Infographic.pdf. Accessed March 17, 2020.

2 Kern C et al. *Br J Ophthalmol.* 2020;104:312-317.

Relevant financial disclosures—Dr. Sim: Big Picture Eye Health: C.

See the financial disclosure key, page 8. **For full disclosures,** including category descriptions, view this News in Review at aao.org/eyenet.

SCIENCE IS JUST THE BEGINNING OF OUR INNOVATION.
LET'S PARTNER IN DOING MORE TO GIVE PEOPLE THE

VISION TO LIVE

Genentech
A Member of the Roche Group

Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Eyedrops After Cataract Surgery: Costs and Prescribing Patterns

May 2020

Zafar et al. looked at the costs and prescribing patterns for eyedrops after cataract surgery and estimated the savings of replacing brand drugs with generic or therapeutic options. They found that, in 2016, eyedrops were prescribed to 88% of Medicare patients who had cataract surgery. The total cost of these drugs exceeded $167 million during the study period, and brand products accounted for more than 75% of this amount. Substituting therapeutic or generic alternatives could have saved up to $118 million, said the authors.

For this retrospective cross-sectional study, the researchers evaluated Medicare Part D claims for patients who underwent cataract surgery in 2016. Outcomes were the cost of eyedrops used postoperatively, patient and physician factors linked to higher costs, and the potential savings of lower-cost options. For substitution, the most commonly prescribed generic medication in each drug class was used. For example, the authors considered generic ketorolac tromethamine as the alternative to nonsteroidal anti-inflammatory drugs (NSAIDs).

Of the 591,733 people who underwent cataract surgery that year, postoperative drops were prescribed for 520,688 (88%). Brand drugs accounted for 57.5% of the prescription volume and 76.5% of the total costs. Mean medication costs were $228 for those who underwent one operation and $324 for those who had two. The most commonly prescribed drugs were antibiotics (89%), steroids (86%), and NSAIDs (66%).

Results of the cost analysis showed that using generic and therapeutic alternatives could have saved as much as $118 million, or 70% of total costs. In regard to patient factors, higher drug costs were associated with being older, being female, and being black, Asian, or Hispanic.

Physician factors linked to higher costs included being female, practicing 10 or more years, and practicing in a metropolitan area.

The authors concluded that in the absence of clinical evidence favoring brand products, less expensive drugs offer a viable opportunity to improve the value and cost of care after cataract surgery. They acknowledged that studies are needed to compare the effects of different combinations of eyedrops to prevent such conditions as cystoid macular edema, rebound iritis, and dry eye syndrome.

Cost-Utility Analysis of Glaucoma Medication Adherence

May 2020

Could a personalized team-based approach to glaucoma management—including certified patient coaches—increase notoriously low medication adherence rates? If so, would such interventions be cost-effective from the societal perspective? **Newman-Casey et al.** modeled costs and time to blindness for patients with optimal versus poor adherence to glaucoma medication. They found that sticking to prescribed treatment regimens could improve quality of life years (QALYs), with just a small increase in lifetime health care costs.

In an earlier study, the authors suggested that a team-based approach might boost patients' adherence to a treatment plan. For this cost-utility analysis, they used Monte Carlo microsimulations with Markov tracking over one-year increments and a hypothetical cohort of patients. These theoretical patients all had mild glaucoma (less than –6 dB of mean deviation), were enrolled at 40 years of age, and continued until they turned 100 or had died. (Probability of death was based on U.S. Census data.)

At enrollment, the cohort's mean deviation was –1.4 ± –1.9 dB in the better eye and –4.3 ± –3.4 dB in the worse eye, reflecting baseline values of the U.K. Glaucoma Treatment Study, which also provided data for estimating

glaucoma progression and treatment effect on visual deficits. Adherence rates were derived from four-year U.S. claims data, and the probability of disease worsening each year (accumulated –0.8 dB loss) was based on the Glaucoma Laser Trial and the Tube Versus Trabeculectomy studies. Direct and indirect health costs were assessed at each "stage" of disease, as were societal costs from vision loss. Main outcomes were cost and QALYs of medication adherence.

After 10,000 iterations per strategy, the quickest progressions to blindness in one eye for consistently adherent and nonadherent patients were 23 and 19 years, respectively. Total health care costs (≤60 years after diagnosis) were $62,782 for adherent patients and $52,722 for those who did not adhere to their medication protocols. During the same period, nonadherent patients lost a mean of 0.34 QALY relative to adherent patients, yielding a cost-effectiveness ratio of $29,600 per QALY gained.

According to the authors, assuming a willingness to pay $50,000 per QALY gained, self-management counseling services that improve medication adherence would be highly cost-effective. They noted that more studies using national estimates of glaucoma are needed. *(Also see related commentary by Florent Aptel, MD, in the same issue.)*

Real-World Efficacy of Anti-VEGF Drugs for DME

May 2020

Although aflibercept and ranibizumab have shown efficacy in clinical trials of diabetic macular edema (DME), less is known about their benefit in clinical settings. To address this, **Bhandari et al.** analyzed registry data for patients with DME and found that both drugs were efficacious in treating the condition. Aflibercept produced slightly better anatomic outcomes, as well as greater visual improvement in patients with poorer baseline visual acuity (VA).

The observational Fight Retinal Blindness! registry was mined for data on patients with DME treated in various countries from Dec. 1, 2013, through June 1, 2018. Treatment choice (aflibercept or ranibizumab) and visit frequency were individualized for each patient by the practitioner. The main outcome was mean change in VA from baseline to month 12.

The sample included 383 treatment-naive eyes of 291 patients; initial treatment was aflibercept in 217 eyes and ranibizumab in 166. At baseline, the ranibizumab group was older (mean difference, +2.7 years), and the aflibercept group had lower mean VA (mean difference, –3.1 letters) and thicker maculae (mean difference, +26 µm); differences were not significant.

By 12 months, VA gains were similar for the study arms if baseline VA was ≥69 letters (Snellen 20/40 or better): 1.4 for aflibercept and 0.4 for ranibizumab ($p = .4$). However, more of the patients treated with aflibercept gained ≥10 letters. If mean baseline VA was ≤68 letters (20/50), VA gains were 10.6 and 7.6 letters for aflibercept and ranibizumab, respectively ($p < .01$).

Reduction in central subfield thickness (CST) was greater with aflibercept than ranibizumab, regardless of initial VA: At 20/40, CST reductions were –85 and –55 µm, respectively ($p < .01$); at 20/50 vision, reductions were –148 and –102 µm, respectively ($p < .02$).

The median number of injections during the year of treatment was eight for aflibercept and six for ranibizumab ($p = .13$). Few patients switched treatment, and the loss to follow-up was greater in the aflibercept group (21% vs. 9%; $p < .01$). Most switches were from ranibizumab to aflibercept.

The authors' observations are consistent with results of pivotal clinical trials and meta-analyses of these drugs. However, in this study, aflibercept led to greater visual gains in patients with poor baseline VA as well as larger CST reductions, which may be ascribed to more advanced disease at presentation, said the authors. They recommend longer-term observational studies of intravitreal therapy for DME.

—Summaries by Lynda Seminara

COVID-19 in the Journals: Selected Links

Ophthalmology

www.aaojournal.org/covid-19
www.ajo.com
www.jamanetwork.com/journals/jamaophthalmology

Publishers

www.elsevier.com/coronavirus-information.com
www.jamanetwork.com/journals/jama/pages/coronavirus-alert
www.nature.com

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Impact of Cataract Surgery on DME in VISTA and VIVID

May 2020

In a post hoc analysis of two phase 3 studies, **Moshfeghi et al.** set out to evaluate the impact of cataract surgery in patients who had been treated with anti-VEGF injections or laser for their diabetic macular edema (DME). They found that the incidence of cataract surgery was similar in both treatment groups—and that patients in both groups experienced improvements in best-corrected visual acuity (BCVA).

This secondary analysis was conducted in 54 patients (11 = laser treatment; 43 = intravitreal injections) who participated in the VISTA and VIVID trials and underwent cataract surgery during the initial study period. In these trials, more than 800 patients received aflibercept 2 mg every four weeks, aflibercept 2 mg every eight weeks after five monthly doses, or laser through 100 weeks.

Rescue treatment was also conducted during VISTA and VIVID, but those who received such treatment before cataract surgery were excluded from this follow-up study.

Main outcome measures for this secondary analysis were BCVA and central retinal thickness (CRT), as measured by spectral-domain optical coherence tomography. The results indicate that the cumulative incidence of cataract surgery did not depend on treatment group assignment ($p = 0.2174$).

With regard to pre- and post-op

BCVA and CRT, at the last study visit before cataract surgery, BCVA was 62.2 letters and CRT was 342 µm in the laser control patients, versus 56.9 letters and 301 µm in the aflibercept group. At the first visit following surgery, BCVA had improved to 73.5 letters in the laser cohort and to 67.2 letters in the aflibercept patients. In contrast, CRT worsened slightly after cataract surgery, with measurements of 364 µm in the laser group and 359 µm in the aflibercept group. —*Summary by Jean Shaw*

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Visual Impairment and Eye Disease in Chronic Kidney Disease

May 2020

As the worldwide prevalence of chronic kidney disease (CKD) increases, so have efforts to investigate the link between CKD and visual impairment (VI) and major eye diseases. In one of the first large studies to assess this issue in U.S. adults, **Zhu et al.** confirmed a significantly higher prevalence of VI and major eye diseases in participants with CKD than in those without the disorder, as well as links between CKD and VI and major eye diseases after adjustments for sex, smoking status, diabetes, hypertension, and other variables.

For this cross-sectional analysis, the researchers extracted data for noninstitutionalized, nationally representative U.S. civilians 40 years old and older from the National Health and Nutrition Survey (2005 to 2008). CKD was defined as estimated glomerular filtration rate <60 mL/min/1.73 m^2, and VI was defined as corrected visual acuity worse than 20/40 in the better eye. Data from questionnaires or retinal photographs were used to categorize major eye diseases, including any ocular disease (defined as presence of cataract surgery, age-related macular degeneration [AMD], glaucoma, or any retinopathy) and any objectively determined ocular disease (defined as AMD, glaucoma, or any retinopathy).

The analysis included 5,518 participants (mean age, 56.9 years). Of these, 839 had CKD. VI was much more common in those with CKD (7.7% vs. 1.1% without CKD; $p < .001$), and the risk of major eye diseases was up to five times higher in the CKD group. After adjustment for multiple confounding variables, participants with CKD had 1.65- to 2.34-fold higher odds of VI (odds ratio [OR], 2.01), any ocular disease (OR, 1.65), any objectively determined ocular disease (OR, 1.52), any retinopathy (OR, 1.70), and diabetic retinopathy (OR, 2.34). The ORs for cataract surgery, AMD, and glaucoma were not significant. Stratification by diabetes status showed that CKD was linked to VI in patients with diabetes and to any ocular disease in patients without diabetes.

The authors speculated that the relationships between CKD and VI and major eye disease observed in their study reflect common risk profiles (such as age, diabetes, hypertension, or obesity) and pathogenesis (such as atherosclerosis, oxidative stress, or inflammation). They suggested that further research on the pathogenesis of eye and renal disease could lead to development of viable treatments for both. Meanwhile, they stressed the importance of early ophthalmic screening of patients with CKD.

Algorithm for Assessing and Treating Microbial Keratitis

May 2020

To guide early management of corneal ulcers, **Ung et al.** devised a modified version of the 1-2-3-Rule, which they termed 1-2-3-ACT (for 1-2-3 Assessment, Culture, Treatment). They found that 1-2-3-ACT lessened the need for culturing after initial deferral in cases with borderline microbial keratitis (MK) and reduced unnecessary cultures among the least severe cases. In turn, this lowered costs.

This retrospective study involved patients with MK treated during two periods: group I (2013 to 2015) had clinician-led decision-making, while those in group II (2016 to 2018) were managed per 1-2-3-ACT.

The original 1-2-3-Rule has three parameters for performing corneal cultures: 1) ≥1 cell within the anterior chamber; 2) infiltrate ≥2 mm; and 3) infiltrate edge within 3 mm of the cornea center. To capture atypical bacterial, fungal, and *Acanthamoeba* infections, the authors added "and/or ≥2 adjacent lesions" to the second criterion. Patients who met at least one criterion received fortified antibiotic therapy. The main study outcome was any vision-threatening complication.

The primary analysis set included 665 patients in group I and 767 in group II. A vision-threatening complication developed in 12.9% of group I (median follow-up, 67 days) and in 11.2% of group II (median follow-up, 60 days) ($p = .51$). No meaningful differences in complication rates were found among patients who met zero, two, or three parameters. However, for those with just one parameter, it was more common in group II to culture at presentation (67.7% vs. 54.6% for group I; $p = .006$) and to start fortified antibiotics at that time (53.9% vs. 29.7% for group I; $p < .001$). The number of vision-threatening complications also was significantly lower in group II (1.8% vs. 9.7% for group I; $p = .001$). Among patients who did not undergo culture at presentation, culturing was later required for 5.1% of group II and 13.4% of group I ($p = .001$). The proportion of patients who had tissue sampling despite not satisfying any criterion was lower in group II (8.5% vs. 23.9%; $p < .001$).

Multiple logistic regression showed that all three 1-2-3-ACT criteria were strongly and independently associated with clinical outcome, even in a bootstrapped cohort of 10,000 theoretical patients, indicating that the model may be viable for various clinical settings.

The findings support tissue culturing and antibiotic use at presentation if a corneal ulcer meets at least two of the 1-2-3-ACT criteria. Judging disease severity can be challenging in patients who have just one criterion, said the authors; they emphasized that early aggressive treatment of borderline cases should reduce the risk of vision-threatening complications.

—*Summaries by Lynda Seminara*

JAMA Ophthalmology

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

Waterless Scrub Techniques May Curb Costs

April 2020

Although some health organizations recommend alcohol-based hand scrubbing as presurgical antisepsis, water-based scrub techniques are still common at some hospitals and other surgical facilities. **Javitt et al.** looked at the potential cost savings of a switch to waterless scrub for a large ophthalmic surgical center. They found that omitting water from the presurgical hand-sanitation process could save millions of dollars each year for modern health care facilities, while conserving valuable resources.

For this study, the authors tested the flow rate of industry-standard scrub sinks by running water for the time recommended by the World Health Organization, and the water produced was collected and weighed. This procedure was performed three times at each OR scrub sink, and the mean value was calculated. In addition, the authors reviewed cost data. Main outcome measures were the quantity of water used during aqueous scrubbing and the cost differences between alcohol- and water-based scrubs per OR per year.

The average water consumption was found to be 15.9 L in a two-minute period. Hence, substituting alcohol-based scrubs could save 61,631 L of water per OR each year, for a yearly savings of $277 in water costs. For each OR, the annual cost of alcohol-based surgical scrub was $1,083 less than that of aqueous soap applied from wall-mounted dispensers and $271 less than the price of soap-infused scrub brushes. Overall, adopting a waterless scrub technique could save $280,000 to $348,000 annually for each OR.

The researchers pointed out that the savings in water alone is "eclipsed by savings in supplies as well as staff and facilities resources" and noted that they hope that this study's findings may improve environmental and financial awareness in health care institutions.

Simulated Heading of Soccer Ball Impairs Neuro-Ophthalmologic Function

April 2020

The oculomotor system is sensitive to brain trauma, but the neuro-ophthalmologic response to subconcussive trauma is unclear. Using the King-Devick test (KDT) and oculomotor function as measured by the near point of convergence, **Nowak et al.** studied the impact of such injuries on ophthalmologic function and found that they indeed affect neuro-ophthalmologic function, at least in the short term.

For this randomized trial, adult soccer players were assigned to a heading group or a kicking group (controls). The heading group executed 10 head maneuvers with a soccer ball traveling at 25 mph. The kicking group followed a similar protocol but had foot contact with the ball rather than head contact. The authors used a triaxial accelerometer to assess head accelerations. Measurements of KDT speed, KDT error, and near point of convergence were taken at baseline (before heading or kicking) as well as 0, 2, and 24 hours after heading or kicking. The main outcome measure was the group-by-time interaction of KDT speed at hour 0 after heading or kicking. Secondary outcomes included KDT speed at 2 and 24 hours after ball contact, KDT error, and near point of convergence.

Of the 78 athletes (male and female) enrolled in the study, 11 withdrew voluntarily. The mean age of the remaining 67 participants was 20.6 years; 36 were in the heading group and 31 in the kicking group. The mean (standard deviation) peak linear acceleration and peak rotational acceleration per impact in the heading group were 33.2 (6.8) g and 3.6 (1.4) krad/s^2, respectively. As expected, soccer kicking did not produce a detectable level of head acceleration. Both groups showed improvement in KDT speed (heading group: −1.2 [p = .03], −1.3 [p = .05], and −3.2 seconds [p < .001] at 0, 2, and 24 hours, respectively; kicking group −3.3, −4.1, and −5.2 [all p < .001] seconds at 0, 2, and 24 hours, respectively). The kicking group performed KDT faster than the heading group at 0 hours (−2.2; p = .001), 2 hours (−2.8 seconds; p < .001), and 24 hours (−2.0 seconds; p = .007).

The authors concluded that the neural circuitry linking cognitive and oculomotor function seems vulnerable to acute subconcussive head. They added that further research may determine whether parameters used in this study could help in detecting subconcussive injury. *(Also see related commentary by Nita Bhat, MD, Shruthi Harish Bindiganavile, MD, and Andrew G. Lee, MD, in the same issue.)*

IOLs in Infants and Long-Term Visual Outcomes

April 2020

Does implantation of an IOL enhance long-term visual outcomes for infants who undergo unilateral cataract surgery? **Lambert et al.** performed a randomized study to address this question. Their findings showed that roughly 10 years following surgery, best-corrected visual acuity (BCVA) was no better if an IOL had been used as opposed to leaving the eye aphakic and correcting it later with a contact lens.

This multicenter randomized study included 114 infants with unilateral congenital cataract who had cataract surgery between 1 and 6 months of age, with or without primary implantation of an IOL. Visual outcomes were evaluated when the patients were 10.5 years of age. The primary outcome measure was BCVA according to the electronic testing protocol of the Early Treatment Diabetic Retinopathy Study.

Among the final analysis set of 110 patients, BCVA was excellent (logMAR 0.30 [Snellen 20/40] or better) in 22% of IOL-treated eyes and 27% of aphakic eyes. However, BCVA was inadequate (logMAR 1.00 [Snellen 20/200] or worse) in 44% of both groups. Results were similar in shorter-term studies of the same patients, at ages 12 months and 4.5 years.

The median BCVA for IOL-treated eyes was 0.89 (Snellen equivalent, 20/159; interquartile range [IQR], 0.38-1.38) and for aphakic eyes was 0.86 (Snellen equivalent, 20/145; IQR, 0.30-1.46). Although the difference between

groups was small, the estimate was imprecise (99% confidence interval, –0.54-0.47 for difference in medians).

Originally, the authors had hypothesized that BCVA would be better in the IOL group since those infants would have had at least partial correction at all times. Because they found no visual benefit, coupled with the fact that IOL-treated eyes are more likely to have visual axis opacity and require additional surgery, the authors no longer recommend routine use of IOLs for infants who require cataract surgery.

In summary, IOL implantation at the time of cataract surgery is neither beneficial nor detrimental to visual outcomes, the authors said. Based on the longitudinal consistency of results for these patients, the authors expect the visual outcomes to continue into adulthood, barring ocular injury or disease. The extent to which the findings may apply to less-experienced surgeons, or to patients whose families cannot afford contact lenses, should be factored into treatment decisions. *(Also see related commentary by Michael X. Repka, MD, MBA, in the same issue.)*

—Summaries by Lynda Seminara

Other Journals

Selected by Prem S. Subramanian, MD, PhD

Using AI to Differentiate Glaucomatous and Compressive Optic Neuropathy

British Journal of Ophthalmology
Published online Feb. 25, 2020

Lee et al. evaluated whether a novel deep learning (DL) classifier could discriminate between glaucomatous optic neuropathy (GON) and compressive optic neuropathy (CON). They found that their transfer learning–trained model accurately distinguished GON from CON and outperformed clinical diagnostic parameters.

The researchers' DL model uses ganglion cell–inner plexiform layer (GCIPL) and retinal nerve fiber layer (RNFL) maps obtained via spectral-domain optical coherence tomography (SD-OCT). For this study, they recruited their study population from a Korean database. Bottleneck features from four images were integrated and used as training data for the classifier's deep neural network. Area under the curve (AUC) was calculated to validate and compare the performance of the DL classifier with that of standard diagnostic parameters, such as SD-OCT thickness profiles.

Overall, 80 patients with GON and 54 patients with CON were included, along with 80 and 81 SD-OCT image sets, respectively. Baseline characteristics were similar for the study groups. When discriminating GON from CON, the DL classifier achieved AUC of 0.990, sensitivity of 97.9%, and specificity of 92.6%. Moreover, it significantly outperformed conventional diagnostic parameters: temporal raphe sign (AUC, 0.804), superonasal GCIPL thickness (AUC, 0.815), and superior GCIPL thickness (AUC, 0.776); all $p < .001$. Assessment of heat maps—derived from RNFL deviation maps that highlighted OCT areas for which the DL algorithm was the best predictor—indicated that the model used clinically important information to interpret the images.

According to the authors, the DL classifier's discrimination of GON from CON, even if the clinical diagnosis was unclear, supports its potential to augment diagnostic accuracy and objectivity in ophthalmology. With additional training and a larger dataset, the DL model could be helpful when visual field defect patterns are equivocal.

Do Certain Dietary Fats Protect Against AMD?

Investigative Ophthalmology & Visual Science
2020;61(2):20.

Although the etiology of age-related macular degeneration (AMD) is believed to be multifactorial, evidence suggests that a poor diet and high cholesterol levels play a role in disease development and progression. Dietary fat consumption also has been implicated, but concordance is lacking on the specific type of fat. **Roh et al.** looked more closely at dietary fat intake and found a link between AMD and high consumption of trans fat. Monounsaturated and polyunsaturated fatty acids (MUFA and PUFA) appeared to have a protective effect.

Participants in this cross-sectional study were at least 50 years old and had AMD based on color fundus photography. A U.S. cohort was recruited from January 2015 to July 2016, and Portuguese participants were recruited from a population-based study. A similar control group had no evidence of AMD. Patients completed a questionnaire to determine their energy intake of trans fat, saturated fat, MUFA, and PUFA during the preceding year.

The final analysis included 483 participants. Of these, 97 (20.1%) were controls, 90 (18.6%) presented with early AMD, 201 (41.6%) had intermediate AMD, and 95 (19.7%) presented with late AMD. Mean age was significantly higher for those with AMD, but otherwise the two groups were similar.

After multivariate adjustments, higher consumption of trans fat was found to correlate with AMD (odds ratio [OR], 2.36; $p = .0156$). In contrast, higher intake of PUFA and MUFA was inversely associated with AMD (OR, 0.25 [$p = .0063$] and 0.24 [$p < .0001$], respectively). No association was found for saturated fat. The analysis by stage showed that higher trans fat intake was common with intermediate AMD (OR, 2.26; $p = .0228$), but higher intake of PUFA and MUFA appeared protective of intermediate disease (OR, 0.2 [$p = .0013$] and 0.17 [$p < .0001$], respectively) as well as advanced disease (OR, 0.13 [$p = .02$] and 0.26 [$p = .004$], respectively). Omega-6 PUFA trended toward reducing the risk of intermediate AMD (OR, 0.30; $p = .0165$). The inverse relationship between MUFA and AMD was significant only for the Portuguese subset; this may reflect the composition of the Portuguese diet.

In addition to providing data on the various stages of AMD, this study showed that high intake of trans fat correlates with the presence of AMD, whereas PUFA and MUFA appear to offer protection. Omega-6 PUFA also seemed beneficial, but the authors urged more research into this relationship.

—Summaries by Lynda Seminara

Make every second count with high-performance OCT.

ZEISS CIRRUS 6000

At 100,000 scans per second, ZEISS CIRRUS 6000 is the next-generation OCT delivering high-speed image capture with wider field of view and HD imaging detail.

Maximize patient throughput with **performance OCT, proven analytics and patient-first design.**

zeiss.com/CIRRUS6000

ZEISS

Seeing beyond

EN_31_030_0087I CIR.11579 Contact a local representative for regulatory status and approved labeling.

COVID-19 Moves Telemedicine to the Forefront

Until recently, Michael A. Kipp, MD, rarely thought much about the need for a telemedicine program in his practice. That changed on Wednesday, March 18, when the Academy recommended that ophthalmologists cease providing any treatment other than urgent or emergent care.

Rapid Response

Dr. Kipp, a pediatric ophthalmologist, and his colleagues at the Wheaton Eye Clinic in Wheaton, Illinois, immediately started evaluating their schedules, assessing which patients needed to be seen and which could be rescheduled.

From idea to implementation. Two days after the Academy's alert, Dr. Kipp —after reading numerous professional social media posts and emails about the potential of telemedicine—suggested that the practice implement a teleophthalmology program. Shortly thereafter, he was appointed head of the practice's new Telemedicine Committee, which by Saturday morning had developed a game plan for approval by the board of directors. By the following Wednesday, Dr. Kipp had created comprehensive worksheets on navigating Medicare's recent section 1135 telemedicine waiver and coding different patient scenarios. He developed new coding and billing documentation for the practice using guidelines from the Academy (see "Resources for Getting Started," next page) and the American Association for Pediatric Ophthalmology and Strabismus.

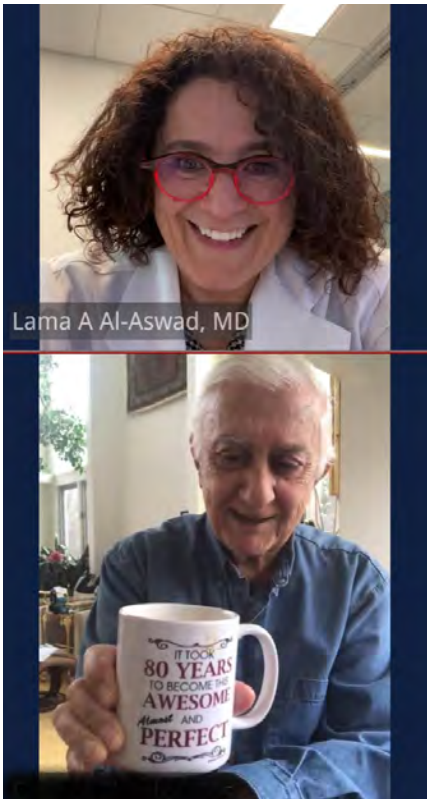
"None of the 32 doctors in our practice was familiar with telemedicine," Dr. Kipp said. "We truly started from ground zero. In less than a week, with tremendous guidance from the Academy and subspecialty societies, we had created a telemedicine program."

A variety of virtual visits. In the first week, Dr. Kipp conducted five telemedicine visits for various conditions, among them a 2-year-old who was checked for strabismus.

"The mother was worried about her child developing a lazy eye," Dr. Kipp said. "She also is an emergency room nurse who had been exposed to patients with COVID-19, so I preferred not to bring her into the office. I was pleased that we were able to obtain a fairly compliant evaluation on the video screen and that I could determine that there was no obvious lazy eye problem. As a result, I felt that we could safely wait a month or two before having her child fully evaluated in the office."

A Technology Whose Time Has Come

For glaucoma specialist Lama A. Al-Aswad, MD, MPH, at NYU Langone Health in New York City, this shift to telemedicine is welcome and long overdue. Well before the COVID-19 outbreak, Dr. Al-Aswad was running teleophthalmology projects in an effort to reach more patients who lacked direct access to ophthalmologists.



A VIRTUAL VISIT. *Dr. Al-Aswad and an 82-year-old patient use the Epic Haiku mobile app that was developed collaboratively by NYU and Epic.*

Valuable in mobile screenings. Her passion for glaucoma prevention in high-risk populations inspired a study in which 8,547 individuals were screened on the streets of New York through telemedicine techniques using mobile equipment.[1] Among the screened individuals, 2,118 (25%) were

BY LORI BAKER-SCHENA, MBA, EDD, CONTRIBUTING WRITER, INTERVIEWING **LAMA A. AL-ASWAD, MD, MPH, MALIK Y. KAHOOK, MD,** AND **MICHAEL A. KIPP, MD.**

deemed glaucoma suspects; and 52% of those who were followed up were confirmed to have the disease.

More recently, Dr. Al-Aswad developed a mobile screening program in New York City that offered free screenings for glaucoma, cataracts, macular degeneration, and diabetic retinopathy. The program, which used a telemedicine van and a secure data-capturing system, was able to obtain visual fields, anterior and posterior segment optical coherence tomography (OCT) images, and fundus photographs. The data were shared immediately with an offsite physician, followed by a teleconference with the patient to discuss the results and next steps. In addition, Dr. Al-Aswad piloted the first teleophthalmology kiosk in 2019 to screen for the four leading causes of blindness in New York City.

Benefits and impediments. An advocate for telemedicine, Dr. Al-Aswad observed that recent advances in technology and artificial intelligence could help address the incidence of disease underdiagnosis and the predicted shortage of physicians in the future. Both ophthalmology and health care at large could benefit from finding ways to care for patients apart from the traditional office setting.

However, the widespread adoption of telemedicine had been stymied by government regulations involving the lack of codes for telemedicine, the inability to practice telemedicine across state lines, and strict HIPAA restrictions. The arrival of COVID-19 has—at least for now—changed that.

Changes in Response to COVID-19

CMS eases access. On March 6, 2020, the Centers for Medicare & Medicaid Services (CMS) broadened access to Medicare telehealth services under the section 1135 waiver authority and Coronavirus Preparedness and Response Supplemental Appropriations Act.[2] Under the new policies, Medicare can pay for telehealth visits whether the patient is in a health care facility or at home when seen. If a patient has Medicare Advantage or commercial insurance, the visit may include a co-pay, co-insurance, or deductible or be considered a noncovered service. It's important to make patients aware of this potential cost.

More e-communication platforms allowed. Dr. Kipp added that the Department of Health and Human Services has loosened its requirements regarding HIPAA-compliant platforms during the pandemic. This allows physicians to use their discretion in communicating with patients through non–public-facing platforms such as Skype, Zoom, Doxy.me, and Google Hangouts.[3] Notably, the doctor may conduct video visits from his/her home.

"While these interfaces have limited capabilities—for example, you can't do a retina exam at this time—at least in my field we can identify lazy eye, follow vision problems, track patching progress, and look at lesions on the eyelid or red eye," Dr. Kipp said. "There are several printable eye charts that allow patients to check their visual acuity at home and apps with near-vision eye charts that patients can download. These tools can help in conducting a virtual examination by teleconference."

Challenges for Setting Up a Telemedicine Program

"My main advice when creating a telemedicine program is to bring in every resource you can find," Dr. Kipp said. "The Academy is an excellent source of information [see "Resources for Getting Started"]. Also, reach out to your colleagues. Without a doubt, we can learn from each other."

In addition to Academy resources, Malik Y. Kahook, MD, at the University of Colorado School of Medicine in Aurora, sought information from health care facilities across the country that use the Epic electronic health record (EHR) system to learn how they implemented virtual health for ophthalmic care.

"While we brought together a small internal group that could gather, analyze, and disseminate this information with the rest of our department, our health care system [UC Health] was proactive in educating our attending doctors through Zoom meetings on how to start a virtual health visit and how to document and bill for each encounter," Dr. Kahook noted.

"It took 10 days to train 1,000 surgeons to use virtual health across

Resources for Getting Started

The Academy's coronavirus hub page, aao.org/coronavirus, has a link to practice management resources from the American Academy of Ophthalmic Executives, aao.org/practice-management/resources/coronavirus-resources. Here you will find links with lots of information, including the following:

Telemedicine Considerations Tip Sheet
aao.org/practice-management/article/coronavirus-telemedicine-telehealth-considerations
Includes advice on getting started, a checklist for when and how to conduct a telemedicine session, Medicare telehealth FAQs, and more.

Telehealth Resources
aao.org/practice-management/telehealth
A road map to all Academy-produced resources designed to help practices safely and smoothly transition to telehealth environments.

Coding for Phone Calls, Internet, and Telehealth Consultations
aao.org/practice-management/news-detail/coding-phone-calls-internet-telehealth-consult
Recorded overviews of telemedicine options; clinical vignettes for 99202, 99212, and 99213; checklists, at-a-glance information, and more.

Cybersecurity
aao.org/practice-management/cybersecurity
Hackers are taking advantage of the COVID-19 pandemic's increased burden on the health care system. How to protect your practice and patients.

our system, and it took our department around the same time to get the majority of our faculty trained on the basics of shifting our practices toward virtual care when possible," he added.

Consistent terminology. One key to communicating both within our department as well as with colleagues across the globe is knowing what each of the telemedicine terms mean, said Dr. Kahook. Specifically, while his department uses the broad term virtual health to mean any type of communication (phone, video, email, text) used in caring for a patients or answering health questions, "telemedicine" is more focused on the phone or video conferencing with a patient. "There are many other terms that we are learning as we go along," he added.

Patient selection. A challenge with starting a telemedicine program is determining which patients and conditions are most amenable to virtual health. Dr. Kahook and his colleagues asked each of the department's service leaders to identify patient categories that would benefit from video-based visits. For example, red eye, post-op blepharoplasty checks, conjunctivitis symptoms, and questions about medication use can easily be moved to virtual health. In contrast, glaucoma visits requiring IOP measurement and visual field testing are not as appropriate for virtual visits.

Education for rapid deployment. Another challenge has been finding resources that provide clear and concise educational information that the faculty and department can rapidly adopt and deploy in their practice. "We often have had to create our own path and are documenting each workflow and standard operating procedure so that we can share with other Epic users," Dr. Kahook said. "My colleague Cara Capitena-Young championed much of this work, and we are open to sharing all that we are producing."

Putting Telemedicine Into Practice

Early in the COVID-19 outbreak, Dr. Al-Aswad realized that telemedicine would be an optimal way to take care of many patients. "I want to applaud NYU, which had been doing virtual urgent care in its emergency department for a few years," she said. By mid-March, NYU had rolled out telemedicine protocols to all departments. She said, "Prior to this, we had created telemedicine protocols specific for each subspecialty in the department and criteria for face-to-face visits."

ONSITE VIRTUAL HEALTH. *The patient (not pictured) checks in and is escorted, along with her husband, to the exam room. The tech, in a nearby room, talks with the husband, who is the family historian, by phone. The tech will enter the room to perform necessary testing with as little talking as possible.*

Glaucoma. "We are looking at glaucoma patients, and this is not optimal as of right now in terms of checking pressure," she continued. "But what we can do is check on the patients, look at the front of their eyes, and check vision and Amsler grid when needed. We are currently developing an app to better evaluate our patients remotely and are sending those patients who require close monitoring an iCare tonometer to measure their pressure at home."

Retina. Retina also has telemedicine challenges, and some retina specialists are finding creative solutions. (See Letters, p. 9.)

Age is no limit. Dr. Al-Aswad dispels the perception that older patients do not have the tech skills to participate in telemedicine visits. On one recent day, she had virtual visits with an 85-year-old woman and an 82-year-old man and was amazed at how savvy they were. "We must not assume that older patients cannot handle telemedicine visits. They will surprise you."

Be aware of the patient's overall health. Dr. Al-Aswad added, "The most important piece of advice I can give is to approach telemedicine as a physician first, and then as an ophthalmologist—especially while we are coping with this pandemic. Taking a thorough history is of vital importance, not only for ophthalmic conditions but also to determine patients' overall health and ascertain whether they have other conditions that may need to be addressed."

Conducting a Video Visit

Physical Environment

- Private, quiet, professional space; no clutter.
- Ensure that background noise, such as traffic, pets, and other sounds that may be heard in your environment, is not audible during the visit. Close any doors and shut windows.
- Sit in front of a simple background.

Attire

- Business casual attire with solid color shirts and blouses.
- Avoid stripes, checks, and patterns as they can create visual distraction for your patients.
- Avoid sparkling jewelry, which may be reflective on camera.

Devices

- Make sure all devices have a full charge and/or are plugged in before starting the visit.
- Set up headset, if using one.
- Close out of all other programs.

Punctuality

- Aim to see patient on time and be aware of the scheduled start and end times.

Planning Ahead

Dr. Kahook said that he is planning how to manage the backlog of patients caused by cancellation of all nonurgent appointments.

Satellite clinics. With the hospital disrupted by COVID-19, he is considering satellite clinics. "We will schedule several patients to get IOP checks, along with visual fields and OCT if needed, with our technicians taking the lead in performing these duties.

"This will be followed by a virtual health visit with a doctor to review IOP and testing among patients who span a wide geographic area," he said. "This will work best for patients who are very stable and were due for routine six- to 12-month visits. For all patients who require more intensive care, we will need to find times for them to come in for more traditional visits with the treating physicians."

New procedures. Another workflow that Dr. Kahook's department has adopted to protect technicians and physicians is called "onsite virtual health." It can be used at any type of facility. Once the patient is checked in, the visit proceeds as follows:

1. The patient is escorted to the room by a technician and the door is closed.
2. The technician goes to the tech station and calls the patient's cell phone to ask the rooming questions, note the history of the present illness, and discuss other points as appropriate.
3. The technician enters the room to perform necessary testing and exits the room with as little talking as possible.
4. The doctor can talk to the patient and conduct the history by phone before entering and performing the exam.
5. The discharge instructions can be given over the phone as well.

"This practice workflow minimizes face-to-face time and allows for efficient documentation," Dr. Kahook explained. "The visit is billed as usual without using telemedicine codes. We will likely continue this workflow for all patients with potential communicable diseases beyond the time of COVID-19."

Future Directions

For Dr. Kahook and his department, the transition to telemedicine, while a major undertaking, has brought a high level of cooperation and camaraderie. "I have found all of my partners to be proactive, hardworking, and very helpful in this entire process," he said. "We have had very little pushback because everybody understands that a change in practice patterns is both necessary and here to stay for the long term." He predicted that virtual health will continue to play a major role in ophthalmology across all subspecialties and practice locations "even after COVID-19 has been vanquished."

Dr. Al-Aswad called the adoption of telemedicine in response to the COVID-19 pandemic a "game-changer" for clinicians around the world. "More and more technology will become available to better reach patients in the comfort of their homes, and this will become a large part of how we practice medicine in the future," she said.

Beyond that, Dr. Al-Aswad envisions a time when teleophthalmology, in combination with artificial intelligence and centralized data management, will promote maximum efficiency and effectiveness in the practice of ophthalmology.

Pearls for Implementing Telemedicine

As a physician on the front lines of implementing a telemedicine program, Dr. Kahook shared his pearls as of April 1. Reflecting on the rapidly changing nature of the pandemic, Dr. Kahook said that, within two more weeks, "I promise the list will be three times as long."

1. Find resources to read and digest quickly.
2. Contact others who are using the same EHR system and who adopted virtual health before you did so you can learn from their successes and mistakes.
3. Start with basic phone call visits and transition into video visits while learning the processes.
4. Simplify billing workflows for the physician and have billing teams to support these efforts. Doctors should not be expected to be billing experts for these complex situations.
5. Identify virtual health superusers who can support the team. In Dr. Kahook's department, the superusers group includes two or three physicians and four or five administrative/technical staff. Billing supervisors are also needed to support the entire enterprise in the early days of implementation.
6. Continue to take notes and update the team weekly about new learning and any glitches in the system.

1 Al-Aswad LA et al. *Cogent Medicine.* Published August 2017. https://doi.org/10.1080/2331205X.2017.1367059.

2 www.cms.gov/newsroom/fact-sheets/medicare-telemedicine-health-care-provider-fact-sheet.

3 www.hhs.gov/hipaa/for-professionals/special-topics/emergency-preparedness/notification-enforcement-discretion-telehealth/index.html.

Dr. Al-Aswad is professor of ophthalmology, vice chair for innovation, and director of Teleophthalmology, Artificial Intelligence, and Innovations at NYU Langone Health in New York City. *Financial disclosures: Aerie: C; Globechek: O; Topcon: L,S; Verily: C; Zeiss: S.*

Dr. Kahook is professor of ophthalmology and The Slater Family Endowed Chair in Ophthalmology at the University of Colorado School of Medicine and vice chair of translational research, chief of the Glaucoma Service, and codirector of the glaucoma fellowship at the University of Colorado Sue Anschutz-Rodgers Eye Center in Aurora, Colo. *Financial disclosures: Alcon: P; Aurea Medical: O,P; Equinox: O; Fluent Ophthalmics: O,P; Ivantis: O; Johnson and Johnson Vision: P; New World Medical: P; ShapeTech: O,P; SpyGlass Ophthalmics: O,P.*

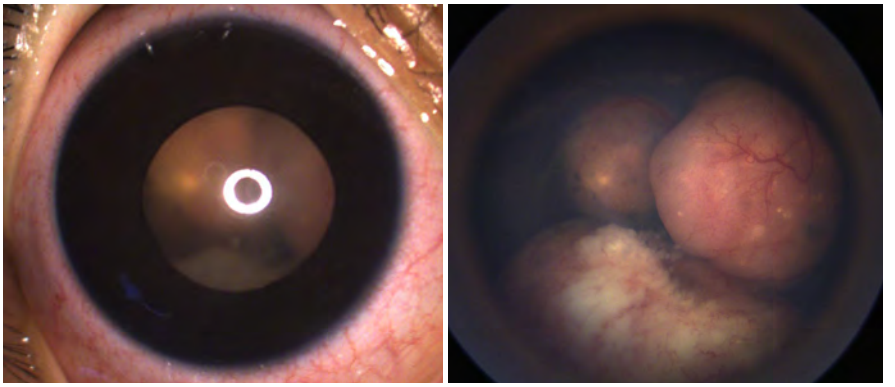
Dr. Kipp is a pediatric ophthalmologist practicing at the Wheaton Eye Clinic in Wheaton, Ill. *Financial disclosures: Wheaton Eye Clinic: O; Dupage Eye Surgery Center: O; 2015 Realty: O; Naperville Raymond Realty: O; Northwestern Medicine at Central Dupage Hospital: C.*

COVID-19 Pandemic: Ocular Tumor Triage and Care

Because of the growing COVID-19 pandemic, on March 18, the Academy recommended that ophthalmologists provide only urgent or emergent care. In this environment, ocular oncologists face unique challenges. "Some of the tumors we treat are potentially fatal," said Zélia Maria Corrêa, MD, PhD, at Johns Hopkins University in Baltimore. "But many of our patients are also immunocompromised from cancer treatment, which increases their risk of contracting COVID-19."

Triage. "How long can we delay evaluation and treatment, especially when we don't know how the crisis will pan out? And what about the 'invisible casualties' that might result from denying or delaying care if we fail to prioritize correctly?" she asked.

To provide a snapshot of the approaches in the field, J. William Harbour, MD, at the Bascom Palmer Eye Institute in Miami, surveyed 25 members of the Collaborative Ocular Oncology Group (COOG).[1] "We hope the survey provides insights about real-world practice patterns at a time when evidence is limited," said Dr. Harbour, "to help build consensus for a subspecialty that's small in numbers but is treating complex, rare conditions." This *EyeNet* article reflects the practices of the majority in the COOG survey and adds commentary from three of the group's members.



RETINOBLASTOMA. *Telemedicine can be challenging in ocular oncology, especially for intraocular tumors that cannot be easily photographed remotely with a smartphone. For example, it was clear from this external photo that there was an abnormal pupillary reflex (left), but it was not possible without EUA with indirect ophthalmoscopy to confirm that this abnormality was caused by a retinoblastoma (right).*

Practice During Pandemic: Evolving and Variable

"We're all trying to do what's best for our patients, but every hospital or university system is addressing these challenges in different ways," said Prithvi Mruthyunjaya, MD, MHS, at Stanford University Medical Center in Palo Alto, California. The challenges are evolving and differ from one region to another, he said. "Clinic capacity, staffing, and imaging expertise may all be moving targets affecting when patients can be seen," he said. "We are all getting used to 'pre-rounding' to assess urgency and disease severity for our established patients and learning as much as possible about our new patients so we can postpone as many visits as possible."

Decisions will be based, in part, on the extent and acuity of disease, as well as the availability of personal protective equipment (PPE), supplies, and staff, said Dr. Harbour. "With limited resources," added Dr. Mruthyunjaya, "we don't want to tax the system if other patients have higher priority."

However, it's important to ensure that urgent patients aren't unnecessarily delayed due to fear of infection, he said. Rather than faxing or mailing in referral requests as is typically done, it's advisable for ophthalmologists seeing new patients with a suspected ocular tumor to contact an ocular oncologist and properly "hand off" coordination of care. This may also provide an opportunity to initiate additional testing locally, said Dr. Mruthyunjaya.

Contingency plans. There's also the ever-present elephant in the room: If

BY ANNIE STUART, CONTRIBUTING WRITER, INTERVIEWING **ZÉLIA MARIA CORRÊA, MD, PHD, J. WILLIAM HARBOUR, MD,** AND **PRITHVI MRUTHYUNJAYA, MD, MHS.**

the ocular oncologist gets sick, what to do? "We may be able to offer telemedicine if we aren't hospitalized," said Dr. Corrêa. "But it's a good time to think about a contingency plan. When dealing with ocular tumors, you need a backup or two in case patients need to be seen and you're not able to do it."

Pediatric Patients

One of the biggest challenges during the pandemic is that children must come in with their parents, said Dr. Mruthyunjaya. "If the child's mother is under isolation or is COVID-19–positive, your institution may set rules to protect the OR team and other staff. That may impact when children are seen, and care may be delayed beyond what is ideal."

"And, if a child is sick or has a fever," said Dr. Harbour, "many institutions may now require testing for COVID-19 before admission to the hospital, even for cases considered urgent." For example, Johns Hopkins currently has a strict policy of only one family member accompanying a minor, said Dr. Corrêa, and this family member is also screened and tested for COVID-19 before walking into the OR pre-op area.

"All my recommendations are based on the assumption of healthy, nonexposed children," said Dr. Mruthyunjaya. "But there will be scenarios where children need to be treated, even though they are at higher risk. That's where conversations with the entire OR team—and maybe even an ethics consult—may be needed."

Retinoblastoma. Retinoblastoma cases are the most challenging for ocular oncologists right now, said Dr. Harbour. "Most other ocular tumors will not threaten the survival of the patient if there is a delay in care of a month or two, but with retinoblastoma, such a delay could be life-threatening." These cases also require exams under anesthesia (EUA), which necessitates intubation, a procedure that increases risk of spreading COVID-19 to health care workers, he said.

Children with suspicion for retinoblastoma. "I still see any child with a suspicion of retinoblastoma as quickly as possible, regardless of age," said Dr. Corrêa. "I also obtain an MRI of the brain and orbits within a week or so to look for optic nerve invasion, orbital extension, and intracranial involvement."

New patients and active disease. Nearly 100% of COOG survey respondents would manage new patients and patients with active disease within the last three months as per their normal protocols. "If the child's eye has any other abnormalities such as proptosis or pain, then it is more of an emergency," said Dr. Corrêa.

Follow-up visits. Dr. Mruthyunjaya is prioritizing—often in concert with systemic treatment—cases that have had intervention in the past three months. "I'm trying to keep them under the same follow-up plan as previously, which is typically every three- to four-week EUAs and any necessary treatment."

Of survey respondents, 60% would delay EUAs or office visits for a few weeks in patients who have previously stable disease (e.g., no prior treatments or changes for more than three months). Factors such as age or laterality would not change their management decisions, according to the survey. "Regardless, we are all keeping close track of these patients," said Dr. Mruthyunjaya. "We don't want to 'forget' any of these kids or lose them to scheduling neglect."

A change in treatment protocol? "Normally, we can save most eyes with unilateral retinoblastoma using intra-arterial or intravenous chemotherapy," said Dr. Corrêa. "During the pandemic, however, I would tend to promptly enucleate if I think the child has very limited visual potential. We don't know how long this crisis will last or how reliably the child would be able to return for frequent follow-up exams and treatment. I would rather keep the child healthy and lose the eye."

Dr. Mruthyunjaya agrees that difficult decisions may be required. "But they are rarely made in isolation and should include a multidisciplinary discussion with the pediatric oncologist or a virtual tumor board, when available," he said.

Benign tumors. Benign ocular

Candidates for Telemedicine

Because rules about the use of telemedicine have been relaxed for COVID-19, ocular oncologists are seeing patients remotely. "Although I may not be able to see the fundus during a telemedicine visit, by carefully taking a history and going over the symptoms, I feel I can gauge a lot of what is going on with the patient," said Dr. Corrêa. Dr. Mruthyunjaya noted, "Documenting phone calls and telemedicine encounters in the medical record is essential."

Ocular surface tumors. Because they are on the external surface of the eye and do not progress rapidly, ocular surface tumors such as conjunctival melanoma, conjunctival squamous cell carcinoma, and conjunctival lymphoma are great candidates for telemedicine—whether through an official telemedicine encounter or the patient emailing you photos, said Dr. Harbour.

Other types of tumors. Telemedicine can also be helpful when assessing symptoms in patients with intraocular tumors, said Dr. Harbour. "You may be able to defer the initial in-person exam if patients don't have visual loss or other symptoms."

Get patients on video and ask how their vision is doing, advised Dr. Corrêa. "Ask them to write down the smallest letter they can see and show it to you on video. This gives a rough idea of who needs to be coming in within the next month or so, and it can be reassuring to the patient."

To avoid unnecessary visits, you may be able to screen most benign tumors before the patient comes into the clinic, said Dr. Mruthyunjaya. "Let's be clear, families coming into health care facilities increase the risk of exposure, and we don't know the full extent of how children respond to this virus. Minimizing exposure for both families and clinic staff can help keep everyone safe."

For more about how to get started with telemedicine, see Clinical Update, page 25, and aao.org/practice-management/telehealth.

tumors can include hemangiomas, osteomas, and hamartomas, some of which may occur in the setting of systemic syndromes such as Sturge-Weber, neurofibromatosis types 1 and 2, and other conditions.

Remote assessment. "Many of these patients are good candidates for telemedicine in the short term," said Dr. Harbour. "Usually these tumors are not life threatening, and only rarely is prompt intervention required." (See "Candidates for Telemedicine," p. 30.)

"It is even more important to get as much information as you can by talking to the referring physician, reading all prior clinic notes, and looking at any old imaging studies like photos or OCT," said Dr. Mruthyunjaya. "Reviewing this information with the family via phone or video visit may allow you to offer your opinion and expected treatment course. More importantly, you can reassure them that you will still care for their child, but the safest thing might be to cautiously delay their evaluation for the time being."

New patients and follow-up. "With suspected benign tumors that you have not previously evaluated yourself, the concern is always whether or not the referring doctor got the right diagnosis," said Dr. Harbour. Still, most ocular oncologists would delay the initial evaluation by one to four weeks and follow-up visits by more than four weeks. However, if visual symptoms are present, most would see the patient sooner.

Where a definitive diagnosis is not yet established, Dr. Mruthyunjaya would consider an office visit. "It could be something malignant if you haven't checked." If no images are available that are clearly consistent with a benign condition like a retinal astrocytic hamartoma, Dr. Corrêa would still consider bringing the patient in promptly to rule out a retinoblastoma.

Adult Patients

In the case of adult ocular tumors, said Dr. Harbour, most ocular oncologists fortunately have a colleague such as a retina specialist who can provide backup to manage patients, at least temporarily.

Uveal melanoma. Uveal melanoma occurs mainly in patients over age 60, said Dr. Harbour. Ocular treatment usually involves plaque brachytherapy or enucleation. "There's no evidence that delaying treatment for a month or two alters survival, he said, "but you don't want to wait six months."

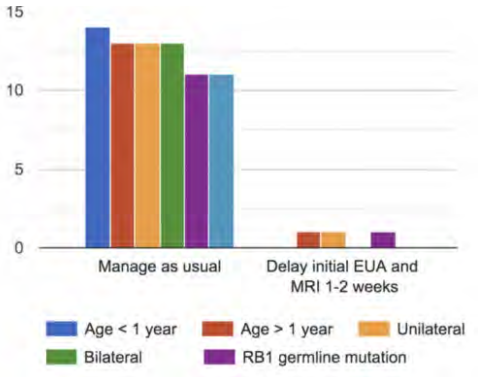
New patients. "For new patients, these are anxious times, and they want to be seen," said Dr. Mruthyunjaya. "But telemedicine may be an excellent first step. Prior to scheduling an office visit, try to look at photographs, clinical notes, imaging, or other available information. This may allow you to determine that the case does not require immediate treatment." If a delay is reasonable, outline your rationale to the referring physician and patient, he said, and ask the patient to report any changes in symptoms.

"I do my best to see patients expeditiously—within one to two weeks—if they have extraocular extension or neovascularization with pain, or neovascular glaucoma," said Dr. Corrêa.

Follow-up visits. It's important to customize follow-up for each patient, said Dr. Mruthyunjaya. One issue is patients undergoing regular intravitreal injections of anti-VEGF medications for radiation complications. "At least for now, many of us are continuing to do these injections, but they can most likely be safely delayed by four to eight weeks since this is a chronic process," said Dr. Harbour. If the patient has immune or pulmonary compromise, most survey respondents recommended delaying injections for four weeks or more. "This is something doctors need to evaluate on a case-by-case basis," added Dr. Corrêa.

High-risk choroidal nevus. "We see a lot of these patients with suspicious choroidal nevi who have borderline clinical features between a benign nevus and a small malignant melanoma," said Dr. Harbour. "In recent years, there has been an increased tendency to treat

How are you prioritizing the timing of initial EUA for patients with newly suspected unilateral or bilateral retinoblastoma?



RETINOBLASTOMA. *Respondents to the COOG survey provided their practice patterns under the pandemic. Be sure to view full survey results at https://castlebiosciences.com/wp-content/uploads/2020/03/COOG-Consensus-COVID19_Results_2020-03-26.pdf.*

Patients With COVID-19

How would you deal with a patient who has tested positive for COVID-19? "Except for the very young kids, I would usually prioritize systemic treatment and wait to treat the ocular tumor later," said Dr. Corrêa.

Dr. Mruthyunjaya has one COVID-19-positive patient who needs an enucleation. "Even though I have full assurances that I can perform the surgery any time I want, I'm looking across the entire system," he said. "I don't want to tax the use of PPE or unnecessarily expose hospital staff. Ophthalmologists, scrub nurses, anesthesiologists, PACU nurses—everyone is a vital link in the chain. If any link needs to get pulled due to exposure, the whole chain gets weakened." After a long discussion with the medical oncologist and others in ophthalmology, anesthesia, and surgery, Dr. Mruthyunjaya is delaying the patient's surgery by a few weeks while carefully watching his status. "It's a great example of multidisciplinary decision-making that went to the highest levels for just one patient—and it's appropriate at this time."

these patients more promptly, hoping to reduce their risk of metastasis," he said, "but this an unproven theoretical assumption."

There's no evidence that waiting for three months to recheck them for tumor growth increases the risk of metastasis, he said. "As a result, I am currently managing most of these patients more conservatively for now, having them come back in two to three months unless growth has already been documented."

Intraocular metastasis to the eye. Most survey respondents would promptly see new patients with suspected intraocular metastasis from a systemic cancer. However, there are other considerations in this decision process.

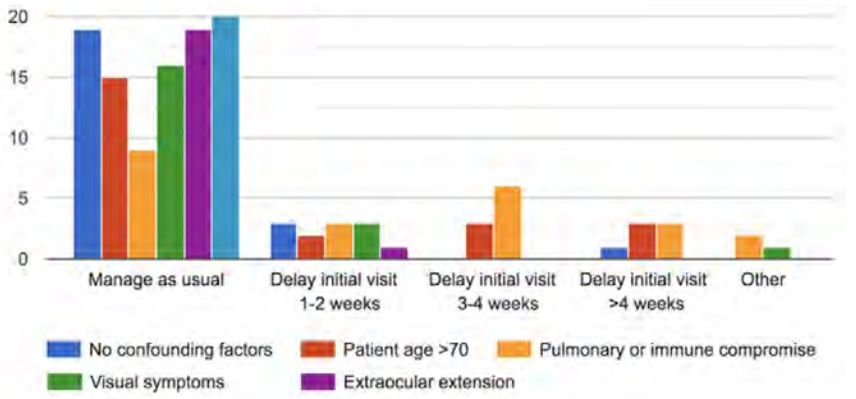
"Patients who have metastasis to the eye may have been on systemic chemotherapy, immunotherapy, or targeted molecular therapy," said Dr. Harbour, and may be immunocompromised from their treatment. "We should use the greatest of care with these patients," said Dr. Mruthyunjaya.

"Although we occasionally use external beam radiation, laser, or other types of treatment," said Dr. Harbour, "most of these patients won't require ongoing regular eye treatment. We often wait a few months to see if the eye tumors respond to systemic therapy before considering ocular treatment."

Vitreoretinal lymphoma. Frequently involving both the brain and eyes, this highly lethal type of lymphoma may be first diagnosed by ophthalmologists, said Dr. Harbour. Most of these patients are over the age of 65, and they usually receive systemic chemotherapy.

New patients. Most COOG survey respondents would see new patients promptly for initial evaluation of suspected vitreoretinal lymphoma—especially patients with blurred vision or floaters. One challenge of this type of lymphoma is that it may share visual symptoms and clinical features with benign conditions, said Dr. Mruthyunjaya. Although a diagnostic vitrectomy is often required for diagnosis, these patients could first get nonsurgical evaluations including blood tests to rule out simulating conditions, MRI, or lumbar puncture, he said. "These tests may take a few weeks to coordinate, which is still appropriate for the patient."

How are you prioritizing initial clinic visits in patients with newly suspected or diagnosed uveal melanoma?



UVEAL MELANOMA. *The COOG survey found that most respondents would manage most new uveal melanoma patients according to normal protocols.*

Follow-up visits. Most patients typically receive external beam radiation or intravitreal chemotherapy injections to treat the eyes, said Dr. Harbour. "At this point, I am more likely to convert patients receiving intravitreal injections to external beam radiation therapy," said Dr. Corrêa. "Bringing them into the office every four weeks for injections, especially if they're immunocompromised, is not worth the risk." If an institution has challenges getting patients in promptly for radiotherapy, she would advise continuing injections until the patient can be treated by radiation oncology.

1 https://castlebiosciences.com/wp-content/uploads/2020/03/COOG-Consensus-COVID19_Results_2020-03-26.pdf.

Dr. Corrêa is director of ocular oncology and echography services at the Wilmer Eye Institute and professor of oncology and ophthalmology at Johns Hopkins University in Baltimore. *Relevant financial disclosures: None.*

Dr. Harbour is director of ocular oncology and vice chairman of translational research at Bascom Palmer Eye Institute, and associate director of basic science at Sylvester Comprehensive Center in Miami. *Relevant financial disclosures: None.*

Dr. Mruthyunjaya is director of ocular oncology and vitreoretinal surgery fellowship at the Byers Eye Institute and associate professor of ophthalmology at Stanford University Medical Center in Palo Alto, Calif. *Relevant financial disclosures: None.*

For full disclosures, view this article at aao.org/eyenet.

Other COVID-19 Resources

Coronavirus and Eye Care
aao.org/coronavirus
The Academy's coverage of and resources for the COVID-19 pandemic.

List of Urgent and Emergent Procedures
- Guidance from the American Association of Ophthalmic Oncologists and Pathologists can be found at aaoop.org/corona-virus/
- A multisubspecialty list can be found at aao.org/headline/list-of-urgent-emergent-ophthalmic-procedures

Collaborative Ocular Oncology Group Survey: Management of Ocular Oncology Patients During the COVID-19 Pandemic
https://castlebiosciences.com/wp-content/uploads/2020/03/COOG-Consensus-COVID19_Results_2020-03-26.pdf
The results of the COOG survey discussed in this article. (PDF, 21 MB)

Evaluation and Management of Fuchs Dystrophy

Fuchs dystrophy is a slow, progressive degeneration of the corneal endothelium, leading to stromal edema. The edema can cause symptoms such as blurry vision, eye pain, and light sensitivity. Signs and symptoms can begin to appear in the fourth decade of life, although the typical onset is between the fifth and seventh decades. In developed nations, Fuchs dystrophy is one of the most common indications for corneal transplantation.[1]

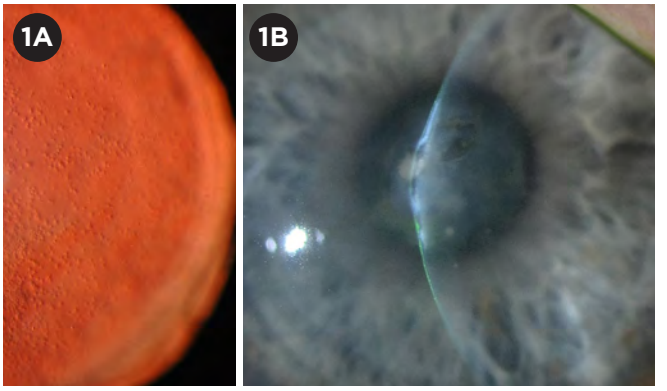
Genetics

Fuchs dystrophy is inherited in an autosomal dominant pattern, with a strong predilection for women (3:1 ratio); evidence also suggests a higher prevalence in white populations. The disorder's genetic basis and pathophysiology are multifactorial, with recent studies illuminating various contributing genes.

One of these genes, *COL8A2*, is responsible for the α2 subtype of collagen VIIIA, and a point mutation in this gene is responsible for altering a key component of Descemet membrane in the early-onset subtype of Fuchs.[1,2] The *SLC4A11* gene, associated with a late-onset Fuchs subtype, encodes for the densely populated endothelial membrane borate pump (transportation of water and ammonia), responsible for maintaining deturgescence. The *TCF4* gene encodes for the E2-2 protein, which belongs to a family of transcription factors responsible for cell growth and differentiation. Other associated genes include *ZEB1, AGBL1, KANK4, LAMC1, ATP1B1, LOXHD1,* and *DMPK*.[1,2]

Diagnosis

The diagnosis of Fuchs is made primarily based on a comprehensive exam, as there is no definitive diagnostic test. A careful slit-lamp exam, including retroillumination, can identify central guttae (excrescences in Descemet membrane; Fig. 1A). The guttae may spread peripherally and may coalesce, forming a beaten metal appearance. Edema may appear as a fine gray haze (best seen with sclerotic scatter), and it may progress to fine vertical wrinkles (striae), overt Descemet folds, and microcystic epithelial edema and bullae (Fig. 1B). A pachymeter may be useful in identifying corneal edema, particularly if baseline pachymetry is available for the patient. Specular microscopy can also be used to determine the number and quality of endothelial cells (Fig. 2).



SLIT-LAMP PHOTOS. *Eyes with Fuchs demonstrating (1A) cornea guttae highlighted with retroillumination and (1B) severe central bullous keratopathy (microcystic edema and bullae) and stromal fibrosis.*

Staging. Endothelial degeneration progresses slowly over the course of 10 to 30 years and can be clinically categorized by three stages of symptoms and signs.

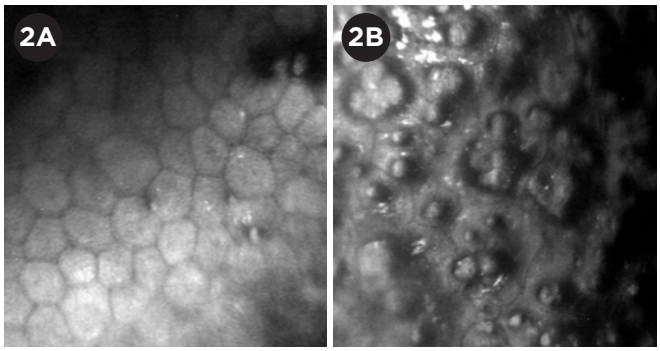
- The initial stage is characterized by the presence of central guttae. Often asymptomatic at this stage, guttae can lead to symptomatic glare from higher-order aberrations and backscatter.
- The second stage is marked by the accumulation of fluid in the stroma and epithelium, producing blurry vision, halos around lights, and eye pain. Symptoms may be worse in the morning as a result of decreased evaporation of corneal fluid when the eyes are closed during sleep.
- The final stage is marked by loss in visual acuity (VA) and is remarkable for the development of avascular subepithelial fibrous scarring between the epithelium and Bowman membrane (best viewed with tangential illumination), peripheral superficial corneal neovascularization, and a reduction in edema.

WRITTEN BY **ALEX IM, BS, ALBERT Y. CHEUNG, MD,** AND **ELIZABETH YEU, MD.** EDITED BY BENNIE H. JENG, MD.

David Heidemann, MD.

Treatment

Medical therapy. In the early course of the disease, medical management aims to remove excess fluid from the cornea by using topical hypertonic saline ointment/solutions (e.g., 5% sodium chloride), dehydrating the cornea with a blow dryer in the morning or throughout the day (at low heat and kept at an arm's distance to avoid burning/damage), and reducing intraocular pressure. Bandage contact lenses may decrease symptoms from painful bullae or prevent recurrent erosions.



SPECULAR MICROSCOPY FINDINGS. *(2A) Polymegethism and occasional guttae compared with (2B) severe polymegethism and significant guttae.*

Keratoplasty. Surgery (see table below) is indicated when symptoms warrant intervention, often when there is a decrease in VA or discomfort from epithelial edema or erosions.

PK vs EK. Historically, penetrating keratoplasty (PK, full-thickness keratoplasty) was a common treatment. PK is now reserved for corneas with combined pathologies such as Fuchs in the setting of symptomatic anterior corneal scarring, stromal dystrophy, or keratoconus.

The currently preferred approach for symptomatic Fuchs is partial-thickness endothelial keratoplasty (EK), which selectively replaces the dysfunctional corneal endothelium. These procedures include Descemet stripping automated endothelial keratoplasty (DSAEK) and Descemet membrane endothelial keratoplasty (DMEK; Fig. 3).

Compared with traditional PK, EK has the advantages of superior visual outcomes, faster recovery, fewer intraoperative and suture-related complications, lower graft rejection and failure rates, and greater tectonic integrity. Reviewing long-term outcomes in Fuchs eyes, Woo et al. found that PK had worse graft survival rates (73.5%) than DMEK (98.7%) or conventional DSAEK (96.2%).[3] Additionally, PK had a higher graft rejection rate (14.1%) than DMEK (1.7%) or conventional DSAEK (5.0%).

DMEK. Series reported in the literature[4-6] show that DMEK provides an average best-corrected VA (BCVA) of 20/25 in 50% to 80% of Fuchs and pseudophakic bullous keratopathy cases at six months. DMEK achieves 20/20 or better in at least 40%, although Fuchs eyes tend to attain better results.

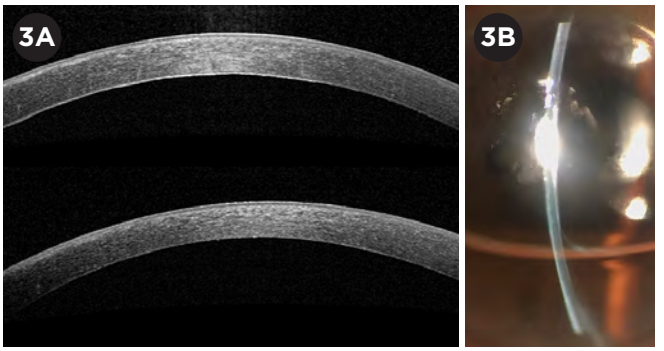
The DETECT trial showed that DMEK yields superior visual results compared with ultrathin DSAEK and has similar endothelial and complication outcomes.[7] Despite the superior clinical outcomes of DMEK (better BCVA, faster visual recovery, decreased rejection rates), DSAEK is still performed more commonly in the United States. This is because DMEK has a steeper learning curve and higher postoperative graft dehiscence rate.

Surgical Treatments

Procedure	Abbreviation	What Is It?	Thickness of Graft Tissue
Penetrating keratoplasty	PK	Full-thickness replacement of the patient's cornea with a donor corneal graft	Full thickness
Descemet stripping automated endothelial keratoplasty	DSAEK	Selective removal of the patient's Descemet membrane and endothelium followed by transplantation of a donor graft composed of corneal stroma (variable thickness), Descemet membrane, and endothelium	100-200 µm
Ultrathin Descemet stripping automated endothelial keratoplasty	UT-DSAEK		50-100 µm
Nanothin Descemet stripping automated endothelial keratoplasty	NT-DSAEK		≤50 µm
Descemet membrane endothelial keratoplasty	DMEK	Selective removal of the patient's Descemet membrane and endothelium followed by transplantation of a donor graft composed of Descemet membrane and endothelium	10-15 µm
Descemetorrhexis without endothelial keratoplasty/Descemet stripping only	DWEK/DSO	Selective removal of the patient's Descemet membrane and endothelium; no subsequent donor graft transplantation	No graft tissue

Albert Y. Cheung, MD

Advanced DSAEK. Thinner DSAEK grafts in the ultrathin (50-100 µm) and, more recently, nanothin range (≤50 µm) have shown promising results that are close, if not comparable, to DMEK in terms of BCVA (53% achieving 20/20 at five years for ultrathin, and 57% achieving 20/20 at one year for nanothin in certain series).[8,9] Although DMEK still allows for quicker visual recovery than the new DSAEK approaches, ultrathin and nanothin DSAEK provide EK surgeons with a viable alternative that affords the same comfort and predictability as conventional DSAEK. Intraoperatively, the tissue behaves similarly in eyes with complex anterior segment anatomy as it does for routine Fuchs cases.



BEFORE AND AFTER. *Anterior segment OCT of Fuchs eye (3A, top) before and (3A, bottom) one week after DMEK surgery. Note the cornea edema with visible folds, thickened Descemet, and guttae in the top image. The cornea is appreciably thinner in the bottom image; it is also impossible to detect the graft, as it is an anatomic replacement. (3B) Slit-lamp photograph one day after DMEK surgery with a 60% gas fill shows that the cornea has already thinned.*

DWEK/DSO. Certain Fuchs patients may benefit from descemetorhexis without endothelial keratoplasty (DWEK), also known as Descemet stripping only (DSO). These are patients with symptomatic central guttae or edema and clear peripheral cornea with an endothelial cell count (ECC) of at least 1,000 cells/mm^2. In this technique, the central 4 mm of Descemet and endothelium is removed by means of descemetorhexis. Resolution of central corneal edema occurs through migration and regeneration of peripheral endothelial cells after a mean of three months.

While reported clearance rates range from 63% to 100%, the use of ripasudil, a topical rho-associated protein kinase (ROCK) inhibitor, may improve endothelial proliferation and corneal clearance.[10] DSO eliminates graft complications, rejection, and the need for long-term postoperative corticosteroids.

However, because experience is limited with this procedure compared to the others, careful patient selection is important. DSO may be rescued with a DMEK surgery if the cornea fails to clear.

Other Procedures

For Fuchs patients with corneal edema and recurrent erosions who are not candidates for keratoplasty, anterior stromal micropuncture may be applied in focal areas of painful bullae. This technique can also be used after EK for residual bullae (i.e., in the areas of bare stroma if there is a mismatch between the descemetorhexis and the EK graft).

Another option for treating bullous keratopathy may be corneal cross-linking, which can improve symptoms, vision, and/or pachymetry in certain cases.[11] Although improvement can be seen in the first month, regression may occur over the ensuing months.

EK With Cataract Surgery

In Fuchs patients with a visually significant cataract, cataract surgery can be performed alone, at the same time as EK, or in a staged process based on which pathology (cornea or cataract) is more symptomatic or which order the ophthalmologist is most comfortable with. When the cataract appears to account for the visual decrease, cataract surgery may be considered earlier when there is more endothelial reserve. An ECC less than 1,000 cells/mm^2 or corneal thickness greater than 640 µm should raise concern about the possibility of corneal decompensation with intraocular surgery.[12]

Cataract technique and lenses. During cataract surgery in Fuchs, an effort should be made to replenish dispersive ophthalmic viscosurgical devices (OVDs) during nuclear disassembly to give continued protection to the endothelium. Femtosecond laser may decrease the phacoemulsification energy needed and the subsequent endothelial damage.

Hydrophilic IOLs should be avoided, as they can develop hydroxyapatite deposition from the gas or air fill if an EK is needed in the future. Multifocal IOLs should also be avoided in Fuchs because of their diffractive optics and reduced image quality. In patients who are expected to undergo EK in the future, the surgeon may select the IOL power for postsurgical myopia to compensate for EK-induced hyperopia.

Combined surgery. For combined cataract surgery and EK, the surgeon should adjust the paracentesis sites for the EK (postoperatively, a superior paracentesis allows for selective gas removal, while an inferior paracentesis allows for aqueous removal). A smaller anterior capsulorrhexis (~4.5 mm) will minimize anterior displacement of the IOL during the anterior chamber shallowing and filling that occurs during EK. A cohesive OVD is utilized to ensure complete removal, and phacoemulsification can be performed above the iris plane to protect the posterior capsule without concern for the endothelium. IOL power selection should account for the expected hyperopic shift of approximately 0.50 to 0.75 D for DMEK and 1.00 to 1.25 D for DSAEK. Eyes with greater corneal edema (thicker central pachymetry) as well as flatter and more oblate posterior corneal surfaces may have greater-than-expected hyperopic shifts.

Future Options

Kinoshita and colleagues have published results of a clinical trial using cultured human corneal endothelial cells (CECs) supplemented with a ROCK inhibitor in eyes with endothelial disease, including Fuchs.[13] After mechanical removal of abnormal extracellular matrix on the Descemet

Albert Y. Cheung, MD

membrane, the cultured CECs were injected into the anterior chamber, and the patients were positioned face down for three hours. Results were promising, with an increase in CEC density, decrease in pachymetry, and clearing of the cornea by 24 weeks; at two years, corneal transparency was maintained, and no serious adverse events were noted.

Conclusion

Fuchs dystrophy is an endothelial degeneration that results in progressive stromal edema. Endothelial keratoplasty (DSAEK, DMEK) currently remains the preferred treatment for symptomatic Fuchs; however, newer surgical techniques such as DSO may benefit specific patients. Future advances with cultured human CECs eventually may change the treatment paradigm.

1 Nanda GG, Alone DP. *Mol Vis.* 2019;25:295-310.
2 Sarnicola C et al. *Eye Contact Lens* 2019;45(1):1-10.
3 Woo JH et al. *Am J Ophthalmol.* 2019;207:288-303.
4 Trindade BLC, Eliazar GC. *Clin Ophthalmol.* 2019;13:1549-1557.
5 Guerra FP et al. *Ophthalmology.* 2011;118(12):2368-2373.
6 Rodriguez-Calvo-de-Mora M et al. *Ophthalmology.* 2015;122(3):464-470.
7 Chamberlain W et al. *Ophthalmology.* 2019;126(1):19-26.
8 Madi S et al. *Cornea.* 2019;38(9):1192-1197.
9 Kurji KH et al. *Cornea.* 2018;37(10):1226-1231.
10 Garcerant D et al. *Curr Opin Ophthalmol.* 2019;30(4):275-285.
11 Ucakhan OO, Saglik A. *Case Rep Med.* 2014;463905.
12 American Academy of Ophthalmology. Cataract/Anterior Segment Panel. *Cataract in the Adult Eye Preferred Practice Pattern.* aao.org/preferred-practice-pattern/cataract-in-adult-eye-ppp-2016.
13 Kinoshita S et al. *N Engl J Med.* 2018;378:995-1003.

Mr. Im is a second-year medical student at Eastern Virginia Medical School (EVMS) in Norfolk, Va. **Drs. Cheung** and **Yeu** are cornea specialists at Virginia Eye Consultants/CVP in Norfolk and are on faculty at EVMS' Department of Ophthalmology. *Relevant financial disclosures: None.*
For full disclosures, see this article at aao.org/eyenet.

The Case of a Teen With Nyctalopia

Jennie Davis,* a 15-year-old with a history of cystic fibrosis, had been experiencing progressive decreased vision and difficulty with her night vision in both eyes for almost three years.

After seeing her primary care physician, she was referred to our clinic for evaluation.

We Get a Look

When we examined Jennie, her best-corrected visual acuity was 20/40 in her right eye and 20/50 in her left. In both eyes, intraocular pressure was normal, and color vision was 11/11 in each eye on testing with Ishihara plates. The anterior segment exam was notable for areas of dryness and early foamy plaques on the conjunctiva bilaterally (Fig. 1).

The dilated ophthalmoscopic exam showed a normal-appearing optic nerve and macula in both eyes, but both retinas had innumerable yellow-white punctate deposits which appeared deep to the retina and were more pronounced in the periphery (Fig. 2).

Further Investigations

We further reviewed Jennie's medical and surgical history. It included cystic fibrosis–related pancreatic insufficiency, for which she was receiving standard enzymatic replacement therapy. As a neonate, she had developed meconium ileus, which necessitated multiple bowel resections, resulting in short gut syndrome. Two years prior to our evaluation, she had received a liver transplant for unspecified liver disease. Her clinical course was complicated by low-level chronic rejection.

The yellow-white deposits in Jennie's peripheral retina raised concerns for a fleck retina syndrome. Macular optical coherence tomography (OCT) was performed, showing multiple subretinal deposits with photoreceptor disruption (Fig. 3). Electroretinography (ERG) demonstrated a decreased scotopic response (Fig. 4).

Differential Diagnosis

The differential diagnosis of nyctalopia includes common disorders such as uncorrected myopia, cataract, and glaucoma.

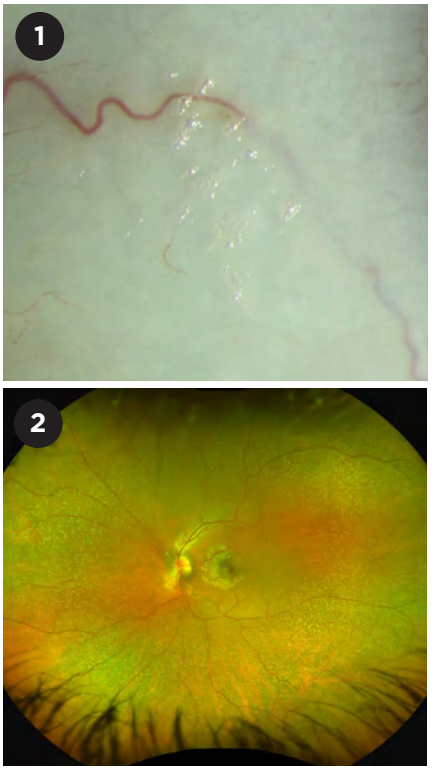
Congenital or genetic conditions can also be implicated. These include retinitis pigmentosa, congenital stationary night blindness, Oguchi disease, choroideremia, gyrate atrophy, or ocular albinism.

Other acquired causes of nyctalopia include vitamin A deficiency, zinc deficiency, medications such as thioridazine or chloroquine, siderosis, or a history of panretinal photocoagulation.

Our Diagnosis

Given the findings of xerosis and fleck retinopathy, in combination with Jennie's history of cystic fibrosis with pancreatic insufficiency and short gut syndrome, we placed vitamin A deficiency at the top of our differential.

We obtained serum vitamin A levels, which measured <5 µg/dL (the reference range for individuals who are 13-17 years old is 14.4-97.7 µg/dL), confirming the diagnosis of vitamin A deficiency.



WE GET A LOOK. *(1) When we performed the slit-lamp examination, plaques of foamy spots were visible on both conjunctivas. (2) The dilated ophthalmoscopic exam was noteworthy for numerous yellow-white dots in both retinas, particularly in the periphery.*

BY **JOHN DEANS, MD, KATHY WHITFIELD, MD, ALICE YANG ZHANG, MD,** AND **KENNETH L. COHEN, MD.** EDITED BY INGRID U. SCOTT, MD, MPH.

Debra Cantrell, OCT-C, COA

Discussion

Vitamin A consists of a group of lipid-soluble compounds known as retinoic acids. Along with the other fat-soluble vitamins D, E, and K, vitamin A must be acquired through the diet or supplementation. These compounds undergo emulsification by bile salts in the duodenum and absorption in the ileum before being stored in the liver or adipose tissue.

Vitamin A has essential functions in phototransduction, cellular differentiation, epithelial maintenance, and immunity. Although vitamin A deficiency is commonly associated with malnutrition, our patient's case highlights the fact that this condition is not confined to developing nations. Rather, it can occur in any patient with liver, gallbladder, pancreatic, or small-bowel pathology that impairs vitamin A absorption, despite an adequate dietary intake.

Etiology and Epidemiology

Vitamin A deficiency is the leading cause of preventable childhood blindness worldwide. The World Health Organization estimated that in 2013, the deficiency affected approximately one-third of children aged 6-59 months, with higher rates in sub-Saharan Africa (48%) and South Asia (44%).[1]

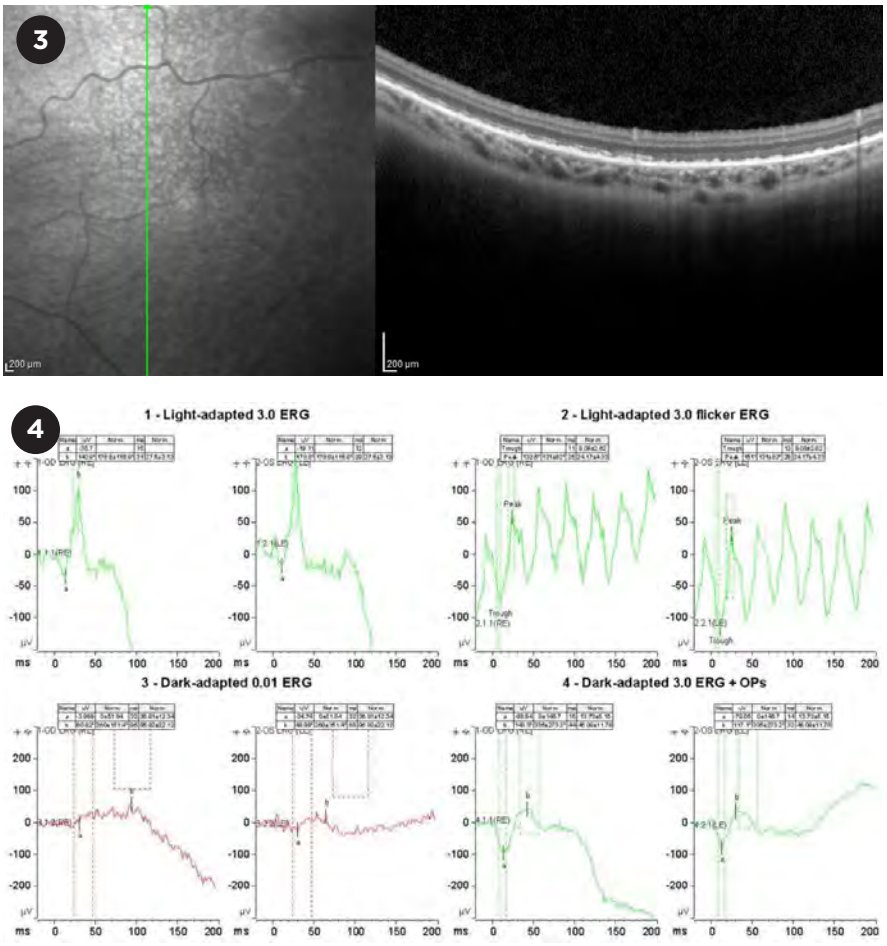
In the developed world, vitamin A deficiency is much rarer but may occur in fat malabsorption conditions such as cystic fibrosis, celiac disease, primary biliary cirrhosis, small-bowel Crohn's disease, and short gut syndrome, as well as after bariatric surgery. It may also be seen with hepatic cirrhosis, most commonly due to alcoholism, and in patients following severely restricted diets by choice or as a result of mental health conditions.

What the Ophthalmologist Should Look For

Nyctalopia is the earliest and most common symptom of vitamin A deficiency. This occurs due to an insufficient supply of the chromophore 11-cis retinal, which is a derivative of vitamin A and a necessary constituent of the visual pigment rhodopsin.

The next ophthalmic manifestation is conjunctival and corneal xerosis. In the absence of vitamin A, which has vital functions in epithelial maturation, there is a loss of mucin-secreting conjunctival goblet cells. This will result in tear film disruption and dryness. Bitot's spots are a classic associated finding (see the foamy spots in Fig. 1). These triangular patches of xerosed conjunctiva represent areas of squamous metaplasia with overlying keratin debris mixed with *Corynebacterium xerosis*. The gas that is produced by this bacterium accounts for the foamy appearance of these lesions.

Finally, vitamin A deficiency can cause a fleck retinopathy, as shown in Figs. 2 and 3. The cause and composition of these small, white peripheral subretinal dots is not yet known, but they may represent areas of photoreceptor damage or lipofuscin accumulation.[2]



FURTHER INVESTIGATIONS. *When developing our differential, we ordered OCT and an ERG. (3) Macular OCT reveals subretinal deposits and photoreceptor disruption. (4) ERG tracings demonstrate a decreased scotopic response.*

Complications

The xerophthalmia associated with vitamin A deficiency represents a spectrum of disease. The earliest findings of conjunctival dryness with Bitot's spots and corneal punctate epithelial erosions may progress to peripheral corneal ulcers or keratomalacia with full-thickness liquefactive necrosis of the cornea. Blindness may result from scar formation and/or corneal decompensation.

Confirming the Diagnosis

Vitamin A deficiency is a clinical diagnosis; however, additional testing may be beneficial for confirmation. For adults, a serum vitamin A level of <30 µg/dL is suggestive but not diagnostic, as serum levels do not fully reflect hepatic vitamin A stores and may be depressed in protein-deficiency states.[1,3] Retinol-binding protein (RBP) levels may also be measured. The reference

Sean Grout, OCT-C; Debra Cantrell, OCT-C, COA; Rona Lyn Esquejo-Leon, BS

range is 30 to 75 mg/L, and a serum retinol:RBP ratio of <0.8 suggests vitamin A deficiency. Conjunctival impression cytology may be considered; histology shows squamous metaplasia of the conjunctival epithelium and goblet cell loss. Further evaluation of nyctalopia or xerophthalmic fundus may also include ERG, OCT, fluorescein angiography, and visual fields.

Treatment

Vitamin A deficiency is treated with high-dose oral or intramuscular vitamin A supplementation. Dose adjustments are required for infants and pregnant women.[4] Topical retinoic acid (0.1%) may serve as adjunctive therapy in cases of xerosis, as healing may be delayed several days from the start of systemic therapy. Nyctalopia improves or resolves within 48 hours of treatment, and retinopathy has been shown to resolve within eight months.[2]

Our Patient's Course

Jennie was referred to the nutritional services department. She was initially treated with a beta carotene–based supplement. However, this treatment did not improve her symptoms or vitamin A levels, which suggested that she could not convert beta carotene to retinol in her gut because of prior bowel resections. Therefore, her therapy was changed to retinyl palmitate, a preformed type of vitamin A. Because zinc is a necessary cofactor of RBP, she was started on zinc supplementation as well.

With the above regimen, Jennie's serum vitamin A recovered to a normal level of 17.0 µg/dL. Her nyctalopia resolved, as did her yellow-white deposits. We performed OCT and found that her macula had normalized, but the patient did not return for repeat ERG.

Conclusion

Vitamin A deficiency is the leading preventable cause of childhood blindness worldwide, but it can also occur in the developed world in patients with fat malabsorption or liver disease.[5] Ophthalmic manifestations include night blindness, xerophthalmia, and retinopathy. Treatment is oral or intramuscular vitamin A supplementation.

*Patient name is fictitious.

1 https://data.unicef.org/topic/nutrition/vitamin-a-deficiency. Accessed March 11, 2020.
2 Chow CC, Mieler WF. *Retin Cases Brief Rep.* 2014;8(3):164-166.
3 Krishna U et al. *EyeNet.* 2016;20(12)35-36. aao.org/eyenet/article/management-of-bitot-s-spots. Accessed Feb. 13, 2020.
4 World Health Organization. Vitamin A supplements: a guide to their use in the treatment and prevention of vitamin A deficiency and xerophthalmia. 2nd ed. 1997. www.who.int/nutrition/publications/micronutrients/vitamin_a_deficiency/9241545062/en/. Accessed Feb. 13, 2020.
5 McLaughlin S et al. *Eye* (Lond). 2014;28(5):621-623.

Dr. Deans is chief resident of ophthalmology; **Dr. Whitfield** and **Dr. Zhang** are both assistant professors of ophthalmology; and **Dr. Cohen** is the Sterling A. Barrett Distinguished Professor Ophthalmology. All four are at the University of North Carolina at Chapel Hill. *Financial disclosures: None.*

FIRST AND ONLY
FDA-APPROVED TREATMENT FOR THYROID EYE DISEASE

IT'S TIME FOR A BREAKTHROUGH
IT'S TIME FOR TEPEZZA

TEPEZZA is proven to[1-4]:

- Decrease proptosis[1]
- Improve diplopia[1]
- Reduce orbital pain, redness, and swelling[2,3]
- Improve functional vision and patient appearance[2,3]

...in patients with Thyroid Eye Disease (TED), without concomitant steroids (vs placebo at Week 24).[2-4]

Learn more at TEDbreakthrough.com

INDICATION

TEPEZZA is indicated for the treatment of Thyroid Eye Disease.

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

Infusion Reactions: TEPEZZA may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with TEPEZZA. Reported infusion reactions have usually been mild or moderate in severity. Signs and symptoms may include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache, and muscular pain. Infusion reactions may occur during an infusion or within 1.5 hours after an infusion. In patients who experience an infusion reaction, consideration should be given to premedicating with an antihistamine, antipyretic, or corticosteroid and/or administering all subsequent infusions at a slower infusion rate.

Preexisting Inflammatory Bowel Disease: TEPEZZA may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of TEPEZZA.

References: 1. TEPEZZA (teprotumumab-trbw) [prescribing information] Horizon. **2.** Douglas RS, Kahaly GJ, Patel A, et al. Teprotumumab for the treatment of active thyroid eye disease. *N Engl J Med*. 2020;382(4):341-352. **3.** Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med*. 2017;376(18):1748-1761. **4.** Smith TJ, Kahaly GJ, Ezra DG, et al. Teprotumumab for thyroid-associated ophthalmopathy. *N Engl J Med*. 2017;376(18)(suppl):1748-1761. https://www.nejm.org/doi/suppl/10.1056/NEJMoa1614949/suppl_file/nejmoa1614949_appendix.pdf.

TEPEZZA™
teprotumumab-trbw

Significantly greater proptosis responder rate* (Study 2)[1,2]

TEPEZZA **83%** (TEPEZZA (n=41))

vs

Placebo **10%** (Placebo (n=42))

P<0.001 at Week 24

*Both the safety and efficacy of TEPEZZA were evaluated in 2 randomized, double-masked, placebo-controlled clinical trials (Studies 1 and 2) consisting of 171 patients with TED (84 were randomized to TEPEZZA and 87 to placebo). The primary endpoint in Studies 1 and 2 was proptosis responder rate, defined as having a ≥2-mm reduction from baseline in proptosis in the study eye at Week 24 without deterioration (≥2-mm increase in proptosis) in the non-study eye.[1]

Hyperglycemia: Increased blood glucose or hyperglycemia may occur in patients treated with TEPEZZA. In clinical trials, 10% of patients (two-thirds of whom had preexisting diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be managed with medications for glycemic control, if necessary. Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with TEPEZZA. Patients with preexisting diabetes should be under appropriate glycemic control before receiving TEPEZZA.

Adverse Reactions

The most common adverse reactions (incidence ≥5% and greater than placebo) are muscle spasm, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache, and dry skin.

Please see Brief Summary of Prescribing Information for TEPEZZA on following page.

HORIZON

TEPEZZA™
teprotumumab-trbw

For injection, for intravenous use

Brief Summary - Please see the TEPEZZA package insert for full prescribing information.

INDICATIONS AND USAGE

TEPEZZA is indicated for the treatment of Thyroid Eye Disease.

WARNINGS AND PRECAUTIONS

Infusion Reactions

TEPEZZA may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with TEPEZZA. Signs and symptoms of infusion-related reactions include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache and muscular pain. Infusion reactions may occur during any of the infusions or within 1.5 hours after an infusion. Reported infusion reactions are usually mild or moderate in severity and can usually be successfully managed with corticosteroids and antihistamines. In patients who experience an infusion reaction, consideration should be given to pre-medicating with an antihistamine, antipyretic, corticosteroid and/or administering all subsequent infusions at a slower infusion rate.

Exacerbation of Preexisting Inflammatory Bowel Disease

TEPEZZA may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of TEPEZZA.

Hyperglycemia

Hyperglycemia or increased blood glucose may occur in patients treated with TEPEZZA. In clinical trials, 10% of patients (two-thirds of whom had preexisting diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be controlled with medications for glycemic control, if necessary.

Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with TEPEZZA. Patients with preexisting diabetes should be under appropriate glycemic control before receiving TEPEZZA.

ADVERSE REACTIONS

The following clinically significant adverse reactions are described elsewhere in the labeling:

- Infusion Reactions [see Warnings and Precautions]
- Exacerbation of Inflammatory Bowel Disease [see Warnings and Precautions]
- Hyperglycemia [see Warnings and Precautions]

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.

The safety of TEPEZZA was evaluated in two randomized, double-masked, placebo-controlled clinical studies (Study 1 [NCT:01868997] and Study 2 [NCT:03298867]) consisting of 170 patients with Thyroid Eye Disease (84 received TEPEZZA and 86 received placebo). Patients were treated with TEPEZZA (10 mg/kg for first infusion and 20 mg/kg for the remaining 7 infusions) or placebo given as an intravenous infusion every 3 weeks for a total of 8 infusions. The majority of patients completed 8 infusions (89% of TEPEZZA patients and 93% of placebo patients).

The most common adverse reactions (≥5%) that occurred at greater incidence in the TEPEZZA group than in the control group during the treatment period of Studies 1 and 2 are summarized in Table 1.

Table 1. Adverse Reactions Occurring in 5% or More of Patients Treated with TEPEZZA and Greater Incidence than Placebo

Adverse Reactions	TEPEZZA N=84 N (%)	Placebo N=86 N (%)
Muscle spasms	21 (25%)	6 (7%)
Nausea	14 (17%)	8 (9%)
Alopecia	11 (13%)	7 (8%)
Diarrhea	10 (12%)	7 (8%)
Fatigue[a]	10 (12%)	6 (7%)
Hyperglycemia[b]	8 (10%)	1 (1%)
Hearing impairment[c]	8 (10%)	0
Dysgeusia	7 (8%)	0
Headache	7 (8%)	6 (7%)
Dry skin	7 (8%)	0

a - Fatigue includes asthenia
b - Hyperglycemia includes blood glucose increase
c - Hearing impairment (includes deafness, eustachian tube dysfunction, hyperacusis, hypoacusis and autophony)

Immunogenicity

As with all therapeutic proteins, there is potential for immunogenicity. The detection of antibody formation is highly dependent on the sensitivity and specificity of the assay.

In a placebo-controlled study with TEPEZZA, 1 of 42 patients treated with placebo had detectable levels of antidrug antibodies in serum. In the same study, none of the 41 patients treated with TEPEZZA had detectable levels of antidrug antibodies in serum.

USE IN SPECIFIC POPULATIONS

Pregnancy

Risk Summary

Based on findings in animals and its mechanism of action inhibiting insulin-like growth factor-1 receptor (IGF-1R), TEPEZZA may cause fetal harm when administered to a pregnant woman. Adequate and well-controlled studies with TEPEZZA have not been conducted in pregnant women. There is insufficient data with TEPEZZA use in pregnant women to inform any drug associated risks for adverse developmental outcomes. In utero teprotumumab exposure in cynomolgus monkeys dosed once weekly with teprotumumab throughout pregnancy resulted in external and skeletal abnormalities. Teprotumumab exposure may lead to an increase in fetal loss [see Data]. Therefore, TEPEZZA should not be used in pregnancy, and appropriate forms of contraception should be implemented prior to initiation, during treatment and for 6 months following the last dose of TEPEZZA.

If the patient becomes pregnant during treatment, TEPEZZA should be discontinued and the patient advised of the potential risk to the fetus.

The background rate of major birth defects and miscarriage is unknown for the indicated population. In the U.S. general population, the estimated background risks of major birth defects and miscarriage in clinically recognized pregnancies are 2-4% and 15-20%, respectively.

Data

Animal Data

In an abridged pilot embryofetal development study, seven pregnant cynomolgus monkeys were dosed intravenously at one dose level of teprotumumab, 75 mg/kg (2.8-fold the maximum recommended human dose [MRHD] based on AUC) once weekly from gestation day 20 through the end of gestation. The incidence of abortion was higher for the teprotumumab treated group compared to the control group. Teprotumumab caused decreased fetal growth during pregnancy, decreased fetal size and weight at caesarean section, decreased placental weight and size, and decreased amniotic fluid volume. Multiple external and skeletal abnormalities were observed in each exposed fetus, including: misshapen cranium, closely set eyes, micrognathia, pointing and narrowing of the nose, and ossification abnormalities of skull bones, sternebrae, carpals, tarsals and teeth. The test dose, 75 mg/kg of teprotumumab, was the maternal no observed adverse effect level (NOAEL).

Based on mechanism of action inhibiting IGF-1R, postnatal exposure to teprotumumab may cause harm.

Lactation

Risk Summary

There is no information regarding the presence of TEPEZZA in human milk, the effects on the breastfed infant or the effects on milk production.

Females and Males of Reproductive Potential

Contraception

Females

Based on its mechanism of action inhibiting IGF-1R, TEPEZZA may cause fetal harm when administered to a pregnant woman (see Use in Specific Populations). Advise females of reproductive potential to use effective contraception prior to initiation, during treatment with TEPEZZA and for 6 months after the last dose of TEPEZZA.

Pediatric Use

Safety and effectiveness have not been established in pediatric patients.

Geriatric Use

Of the 171 patients in the two randomized trials, 15% were 65 years of age or older; the number of patients 65 years or older was similar between treatment groups. No overall differences in efficacy or safety were observed between patients 65 years or older and younger patients (less than 65 years of age).

OVERDOSAGE

No information is available for patients who have received an overdosage.

PATIENT COUNSELING INFORMATION

Embryo-Fetal Toxicity

Advise females of reproductive potential that TEPEZZA can cause harm to a fetus and to inform their healthcare provider of a known or suspected pregnancy.

Educate and counsel females of reproductive potential about the need to use effective contraception prior to initiation, during treatment with TEPEZZA and for 6 months after the last dose of TEPEZZA.

Infusion-Related Reactions

Advise patients that TEPEZZA may cause infusion reactions that can occur at any time. Instruct patients to recognize the signs and symptoms of infusion reaction and to contact their healthcare provider immediately for signs or symptoms of potential infusion-related reactions.

Exacerbation of Inflammatory Bowel Disease

Advise patients on the risk of inflammatory bowel disease (IBD) and to seek medical advice immediately if they experience diarrhea, with or without blood or rectal bleeding, associated with abdominal pain or cramping/colic, urgency, tenesmus or incontinence.

Hyperglycemia

Advise patients on the risk of hyperglycemia and, if diabetic, discuss with healthcare provider to adjust glycemic control medications as appropriate. Encourage compliance with glycemic control.

Manufactured by:
Horizon Therapeutics Ireland DAC
Dublin, Ireland
U.S. License No. 2022

Distributed by:
Horizon Therapeutics USA, Inc.
Lake Forest, IL 60045

HORIZON

6 reasons to switch to OMIC

EXPERIENCE
OMIC has defended far more ophthalmic claims than any other carrier. OMIC's knowledge and familiarity with regard to litigation targeting ophthalmology is unmatched in the industry.

EXPERTISE
OMIC is the only malpractice carrier offering comprehensive ophthalmic-specific education for physicians and their employees with resources designed to help minimize claims and lawsuits.

DEFENSE
OMIC has settled 25% fewer of the claims reported to us than our multi-specialty competitors and OMIC's average indemnity payment is 27% lower than the industry.

PERFORMANCE
OMIC is A (Excellent) rated by A.M. Best and has outperformed multi-specialty carriers in almost all financial benchmarks, including operating, combined and premium-to-surplus ratios.

BENEFITS
OMIC provides 17 regulatory and cyber coverage benefits in the standard malpractice policy at no additional premium.

DIVIDENDS
OMIC's operating advantage has made possible significantly higher policyholder dividends, averaging a 20.8% return per year during the most recent 5-year period compared to 6.6% for multi-specialty malpractice carriers.

OPHTHALMIC MUTUAL INSURANCE COMPANY

A Risk Retention Group of the
American Academy of Ophthalmology

Request a quote today!

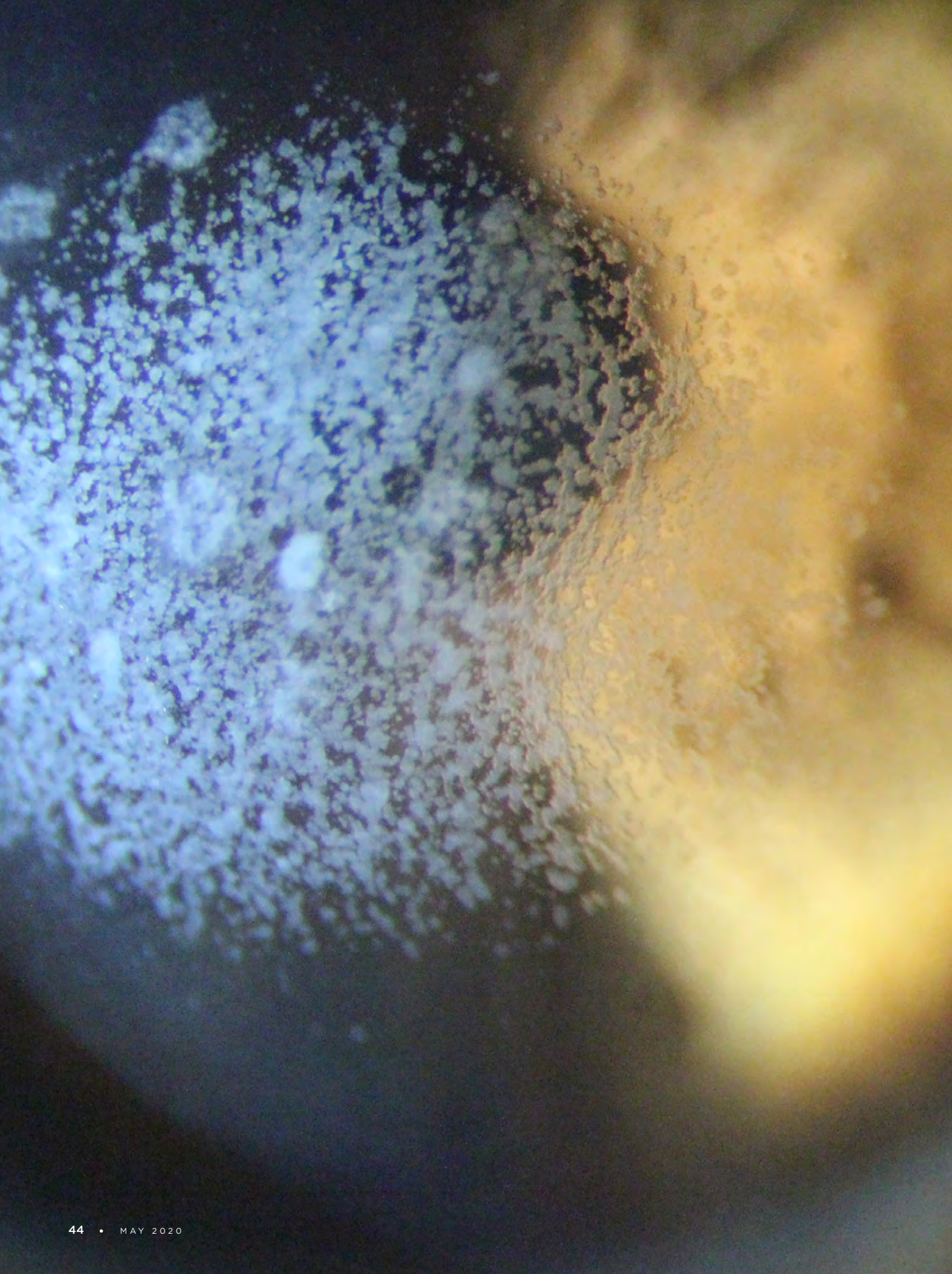
Learn more at OMIC.com

Quick Quote:	OMIC.com/request-a-quote
Find Your Rep:	OMIC.com/about-omic/meet-omic
Resources:	OMIC.com/risk-management

Contact us:

800.562.6642

OMICPage MyOMIC



Genetic Disorders of the Cornea: Preventing Surgical Surprises

Notoriously difficult to identify, genetic disorders of the cornea—many of which are rare—can mystify even the most experienced surgeon.

By Annie Stuart, Contributing Writer

No ophthalmologist has experience with all corneal dystrophies—let alone all the genetic disorders of the cornea, said Jayne S. Weiss, MD, at Louisiana State University in New Orleans. Consequently, these disorders may be challenging to diagnose at first.

"Before you operate on a patient with a corneal dystrophy, you really need to understand it," said Dr. Weiss. It's important to appreciate the depth and location of the disease and to realize that surgery may exacerbate the condition in an atypical way, she said.

What steps should a surgeon take? If you suspect a hereditary condition, said Dr. Weiss, you might take photos of the patient's cornea and send the pictures to a specialist who has more familiarity with these types of diseases.

Another approach is to turn to the International Classification of Corneal Dystrophies–Edition 2 (IC3D2),[1] available for free at the Cornea Society website (www.corneasociety.org/publications/ic3d), she said. There, you can find approximately a page of information about each type of dystrophy with clinical photos and findings as well as background on genetics.

© Eung Kweon Kim, MD, PhD

GCD2. *Exacerbated GCD2 after LASIK.*

To provide a sense of some of the challenges involved, five cornea experts discuss examples of corneal dystrophies and other genetic corneal disorders that can lead to surgical surprises—and what you can do to avoid operating in the dark.

Brittle Cornea Syndrome: A Big Risk for Rupture

Brittle cornea syndrome (BCS) is an autosomal recessive connective tissue disorder that causes severe corneal thinning and carries an increased risk for spontaneous perforation or rupture from minimal trauma.[2]

BCS is a more accurate name for a group of conditions that previously were labeled keratoglobus and that are sometimes mistakenly lumped in with keratoconus—both also characterized by corneas that are abnormally thin, said Deborah S. Jacobs, MD, at Harvard Medical School in Boston. "As we got a better understanding of the molecular abnormalities involved and the genetic commonalities," said Dr. Jacobs, "it became clear that many of these syndromal disorders were linked—and are better classified as brittle cornea syndrome."

Diagnosing BCS. Presenting early in life, BCS tends to create a pattern of bilateral thinning from limbus to limbus, said Dr. Jacobs. She added that

tomography, rather than topography, can be helpful with diagnosis. In addition, the sclera appears blue because it is so thin that you can see the choroid through it, said Ken K. Nischal, MD, FRCOphth, at the University of Pittsburgh Medical Center Children's Hospital of Pittsburgh.

"If you see a thin cornea that looks like it is protruding, stop and ask yourself, 'Could this be BCS?'" said Dr. Nischal. Because both parents could carry one mutated gene without manifesting abnormalities clinically, you have to do genetic testing to confirm the diagnosis, he said.

Risks of BCS. With brittle corneas as thin as 200 µm, children with BCS can easily experience a rupture of the eye with only minimal trauma, said Dr. Nischal. He described children under his care who had experienced ruptures—one whose eye was hit by a paper ball and another with a pen, and another who accidentally poked herself in the eye.

Surgical precautions. With such fragility, the eye behaves atypically on the operating table, said Dr. Jacobs. "The tissue is floppier, so it's like suturing butter. Because it's hard to seal wounds, the eye leaks post-op and is often prone to infection and rupture."

Dr. Nischal offers two surgical precautions: "First, when making an incision in the eye, make it smaller than you want because the incision will expand," he said. "For example, if you want a 20-gauge entry, use a 25-gauge needle."

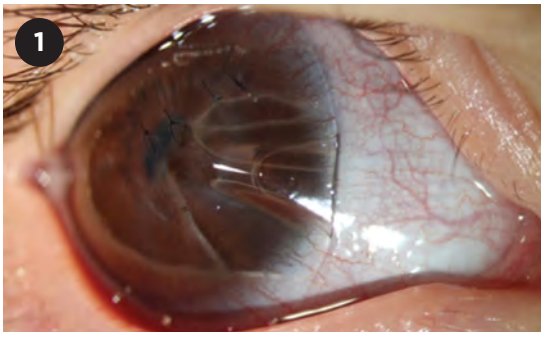
Second, reduce pressure in the eye. Because the cornea is thin and there is no rigidity at the limbus, pressure will always read low, even though it is actually high, he said. "I invariably start these children on glaucoma medication to make sure they don't get a spontaneous rupture because of high pressure. Also, by reducing the pressure in the eye, you allow the cornea to be a little thicker."

What about CXL? Corneal cross-linking (CXL) is used to prevent further thinning in keratoconus, so the question has arisen: Should it ever be used in children with BCS? Dr. Nischal would never consider it. There is a report of a single case that was successful,[3] said Dr. Jacobs, adding that penetrating surgery tends to not go well. "Surgeons need to get better at identifying who to cross-link, who to operate on, and who to offer more creative techniques," she said. (For a cautionary case report about atypical keratoconus, view this article at aao.org/eyenet.)

Corneal grafts. An option for everyday protection of the eyes is to place an overlay graft, said Dr. Nischal. This involves removing the epithelium from the host and placing a donor Descemet and endothelium overlay graft from limbus to limbus.

"Beforehand, you should perform a paracentesis to lower the pressure in the eye," he said. "That way, the tissues will appose each other when you suture on the overlay." In many cases, added Dr. Nischal, it's necessary to insert a tube shunt to manage eye pressure.

Sometimes an overlay graft may allow you to later do a full-thickness corneal transplant to improve vision, added Dr. Jacobs.



BRITTLE CORNEA SYNDROME. *Spontaneous corneal perforation in a child with BCS. To repair it, four corneal sutures were placed and the eye was covered with a contact lens.*

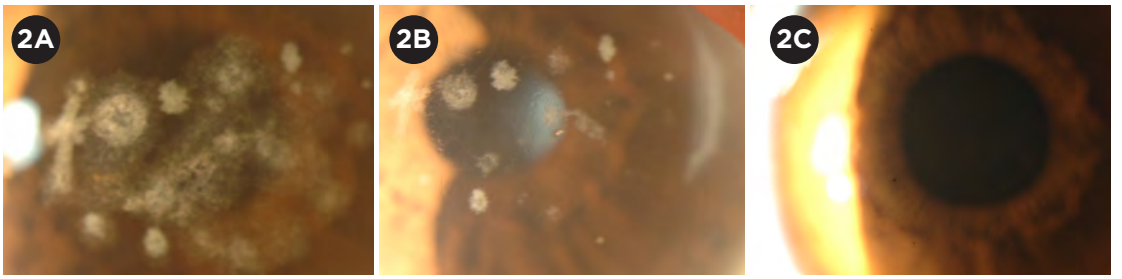
Granular Corneal Dystrophy, Type 2: An Evolving Presentation

Granular corneal dystrophy, type 2 (GCD2) is a rare autosomal dominant genetic disorder caused by a mutation in the *TGFBI* gene. Although *TGFBI* dystrophies affect multiple layers of the cornea, irregularly shaped but well-demarcated granular deposits appear mainly in the superficial central corneal stroma in GCD2, leading to progressive visual impairment.

Presentation in children. Early cases of GCD2 may show up as an unimpressive subepithelial opacity, said Dr. Weiss, and look very different from full-blown disease. This is why having an understanding of early disease is important.

"In children, a *TGFBI*-related dystrophy will often present like dry eye or Thygeson superficial punctate keratitis," said Dr. Nischal. "If you have made that diagnosis in a child and treatment is not working as expected—but you see discrete spots within a localized faint hazy cornea—have a low threshold of suspicion for GCD2." However, added Eung Kweon Kim, MD, PhD, it's important to realize that these signs may not show up in a heterozygote who is age 8 or younger.[4,5]

Diagnosis. A slit-lamp exam and/or gene test can help diagnose the condition, said Dr. Kim, at Yonsei University in Seoul, South Korea. "First look at the cornea through the slit lamp," he said, but recognize that GCD2 shares a similar morphology with other genetic conditions. "That's why genetic testing is sometimes needed to confirm the diagnosis and is especially recommended before



GCD2. *A 67-year-old woman with (2A) granular deposits, linear lesion (latticelike lesion), and diffuse haze; (2B) after some granular deposits were removed. (2C) A 23-year-old genetically heterozygote woman with no deposits.*

refractive surgery when deposits are not visible."

Dr. Kim said that a test called AvaGen (Avellino; about $300) examines more than 70 mutations of the *TGFBI* gene for corneal dystrophies in addition to testing 1,000+ variants for keratoconus.[6]

Dr. Kim also uses an OCT scan of the cornea to measure the thickness of deposits before performing phototherapeutic keratectomy or lamellar keratoplasty.

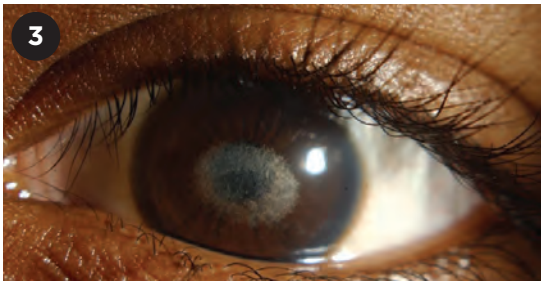
Surgical contraindications. "Do not perform surgery through the central cornea," said Dr. Kim. "This can exacerbate the deposits in GCD2 after procedures such as photorefractive keratectomy, LASIK, and LASEK."

"Cutting a flap during a LASIK procedure, for example, will cause the GCD2 to progress and opacities to worsen," said Dr. Weiss. Many deposits occur along the interface between the posterior surface of the flap and the surface of the remaining posterior stroma, said Dr. Kim. "If you discover GCD2 during a LASIK procedure, do not go forward with LASIK on the second cornea."

Other types of surgery. If LASIK has been performed, phototherapeutic keratectomy (PTK) may improve corneal transparency and visual acuity.[7] "It is better to amputate a LASIK flap than to preserve it," said Dr. Kim.

It is also sometimes possible to postpone a keratoplasty by performing PTK on these patients, he said. PTK may be used judiciously to reduce the visually significant stromal haze, added Dr. Weiss. "However, with repeated PTK, eventually kerotoplasty may be required. Therefore, it's important to understand what the laser can and cannot do, and not to promise the patient too much." For example, after PTK, there can be delayed healing at the superficial cornea, where the previously deeply located deposits remain and are finally exposed to the ablated surface, said Dr. Kim. And you are more likely to end up with more scarring after PTK than you would with a different type of mutation, added Dr. Nischal.

DALK. Because the endothelial layer is always normal in GCD2, a relatively deep anterior lamellar keratoplasty (DALK) is better than a penetrating keratoplasty, said Dr. Kim. Also consider DALK instead of PTK for this particular mutation, said Dr. Nischal. "To prevent scarring after a corneal transplant, consider removing sutures sooner than you normally would."



SCHNYDER CORNEAL DYSTROPHY. *Corneal crystals in a girl with Schnyder corneal dystrophy.*

Schnyder Corneal Dystrophy: Crystals May Not Be Present

Schnyder corneal dystrophy is an autosomal dominant eye disease leading to abnormal deposits of cholesterol and phospholipids in the cornea (Fig. 3). It has always been classified as a stromal dystrophy. However, Dr. Weiss has surgically removed the cornea and found lipid deposits not only throughout the stroma, but also in the base of the epithelium and in some endothelial cells.

Although the disease used to be called Schnyder crystalline corneal dystrophy (SCCD), only about half the people with the condition have crystals, which are superficial underneath the epithelium, said Dr. Weiss. "In the past, those without crystals never got diagnosed," she said, explaining that this prompted creation of the IC3D to initiate a name change for the disease.

"The disease is poorly understood by most ophthalmologists," said Dr. Weiss, "but it's critical to know how and where it occurs to manage it surgically the right way."

Signs of Schnyder. All Schnyder patients develop a front-to-back opacification of the cornea with time, said Dr. Weiss. Characteristic findings based on age are as follows:

- Age 23 or younger: All have a central opacity and/or central subepithelial crystals.
- Between about ages 23 and 38: Patients also develop the arcus lipoides at the corneal periphery.
- Older than about 38: A formerly clear area between the central opacity or crystals and the peripheral arcus becomes cloudy—more so at the center and periphery. Patients may also have decreased corneal sensation, said Dr. Weiss.

Diagnosis. If you simply examine the patient straight on, sometimes the whole cornea looks hazy, said Dr. Weiss. However, it can help to dilate the pupil and use retroillumination at the edge of the cornea. This will highlight opacification at the center and periphery, revealing a less-opacified, donut-shaped area in between.

"If you know what you are looking for, Schnyder is as obvious as the day is long," said Dr. Weiss. "If you don't, genetic testing may be a good idea. Also, ask if anyone in the family has had cloudy corneas. This can help you make the diagnosis."

Cholesterol testing. Although it's not diagnostic, cholesterol testing is a good precaution to take before surgery, said Dr. Nischal. "In adults, I would advise both a lipid screen and an examination to confirm that arteries are healthy."

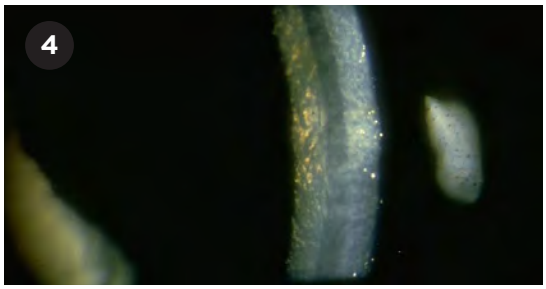
Dr. Weiss suggests that both affected and unaffected members of Schnyder pedigrees obtain serum lipid testing because of increased prevalence of hyperlipidemia in these families.

Surgery. Addressing disease surgically includes:

- **Removing crystals.** "If crystals are in the visual axis, often the ophthalmologist's focus is to remove them, which can be done with PTK," said Dr. Weiss. "But if you are not familiar with the other feature of Schnyder—the opacification of the cornea from front to back—you may be surprised, and the patient may be disappointed to find that vision remains poor even after crystals have been removed."
- **Addressing opacification.** When central opacification is significant, said Dr. Weiss, it may prompt a discussion: Do you do a DALK, taking out the majority of the cornea and leaving the endothelium? Or do you do a full-thickness corneal transplant? Helping to inform this decision is the knowledge that any dystrophy can recur over time, moving from the periphery to the center, she said.

Fuchs Dystrophy: Preventing Progression, Ensuring a Better Outcome

In contrast to other dystrophies, Fuchs is an abnormality of the corneal endothelium, leading to corneal decompensation, said Dr. Weiss. "It's important to distinguish between patients who just have corneal guttae and those who have a family history or who progress from corneal guttae to corneal edema, which is Fuchs."



FUCHS DYSTROPHY. *Corneal guttae in a Fuchs patient.*

Surgeons can successfully treat Fuchs with replacement of the corneal endothelium—the most common reason for this type of surgery in the United States, said Kathryn Colby, MD, PhD, at the University of Chicago. However, there are key steps to ensure better outcomes for Fuchs patients undergoing either cataract surgery or corneal replacement.

Cataract surgery. Fuchs is more common and more easily identified than other types of genetic diseases of the cornea, said Dr. Jacobs. "However, if you don't recognize it before you perform cataract surgery, you may speed progression of the disease."

Cataract surgery is more challenging in patients with Fuchs dystrophy, said Dr. Colby. "The corneal guttae impair the view into the eye, the Descemet membrane is prone to detaching during surgery, and corneal edema is common after surgery, slowing visual recovery." During cataract surgery, be careful with the endothelium and Descemet membrane, consider near-clear incision to reduce endothelial cell loss, and be parsimonious with phaco power, said Dr. Colby.

Preop considerations. Advice for better outcomes after cataract surgery includes:

- **Tomography.** A recent paper in *Ophthalmology*[8] shows that tomography can identify several features that may put patients at greater risk of progression after cataract surgery, said Dr. Colby. These features include loss of regular isopachs, nasal displacement of the thinnest point, and posterior surface depression. The researchers found that when two or three tomographic features of subclinical edema are present—versus none or only one—there was a several fold–increased risk of disease progression over a median of five years. "Before this paper came out, I relied on the thickness of the cornea, which wasn't the best measure due to baseline variability in the general population," Dr. Colby said. Now, however, she relies on tomographic features to assess prognosis in Fuchs patients. "If they have no features, they are unlikely to need a corneal transplant after cataract

surgery. If they have one feature, they are at intermediate risk of needing a transplant. If they have two or three features, they are at higher risk."

In addition to tomography, specular microscopy and endothelial cell count may be helpful in preparing physicians and counseling patients, added Dr. Jacobs.

- **IOL selection.** Because the eye must have perfect optics to produce good results, Dr. Colby suggests exercising extreme caution about putting a multifocal lens in a Fuchs patient. She's seen cases in which the cataract surgeon didn't notice that the patient had Fuchs and put in an expensive multifocal. Besides being unhappy about the cost and outcome, she said, patients sometimes ask, "Did the cataract surgery cause my Fuchs?"

Corneal replacement. There are a few options.

- **Corneal transplantation.** "All evidence suggests that Descemet membrane endothelial keratoplasty (DMEK) provides the quickest visual recovery," said Dr. Colby. "People achieve almost the same level of vision with a Descemet stripping endothelial keratoplasty (DSEK), but visual recovery is quicker with DMEK." However, in 2018, nearly two-thirds of all EKs were DSEK, she said, likely because DMEK is more technically demanding. (See "Evaluation and Management of Fuchs Dystrophy," page 33 for more Fuchs surgeries.)
- **Descemet stripping only (DSO).** Six years ago, Dr. Colby performed her first deliberate Descemet stripping only (DSO) procedure. This involves removing the Descemet membrane and endothelium and allowing the peripheral endothelium to grow back and rejuvenate the cornea.

Rho kinase (ROCK) inhibitors have been used as an adjunct therapy for DSO. Preliminary evidence suggests that they help increase the final endothelial cell count and speed the healing process, said Dr. Colby. Although ripasudil eyedrops are not FDA approved for use in endothelial rejuvenation, patients can order them online for use postoperatively. It's a ROCK inhibitor approved in Japan as a glaucoma treatment, she said. There has also been some off-label usage of topical netarsudil, currently approved in the United States for treatment of glaucoma, to promote endothelial rejuvenation, she said.

However, Dr. Colby cautions ophthalmologists that online patient communities are recommending use of ROCK inhibitors without removal or destruction of the endothelium. "From a scientific standpoint, this makes no sense," she said. "The cells of the endothelium are contact inhibited. Once they touch each other, they stop moving around. Unless you physically get rid of some of the cells—either by freezing or removal—the healthier peripheral cells will not be able to migrate because there is nowhere for them to go."

1 Weiss JS et al. *Cornea*. 2015;34(2):117-159.
2 Wright E et al. *Orphanet J Rare Dis*. 2013;68:1-11.
3 Kaufmann C et al. *Cornea*. 2015;34(10):1326-1328.
4 Hong JP et al. *Cornea*. 2011;30(7):729-738.
5 Kim SW et al. *Cornea*. 2011;30(8):848-854.
6 Avellino: "New Avagen Genetic Test." www.avellino.com/en/products/avagen-test.
7 Jun J et al. *J Refract Surg*. 2018;34(2):132-139.
8 Patel SV et al. *Ophthalmology*. 2020;127(3):315-323.

MEET THE EXPERTS

KATHRYN A. COLBY, MD, PHD Louis Block professor and chair of ophthalmology and visual science at the University of Chicago. *Relevant financial disclosures: None.*

DEBORAH S. JACOBS, MD Director of the ocular surface imaging center at Massachusetts Eye and Ear in Boston. She is also a part-time associate professor of ophthalmology at Harvard Medical School. *Relevant financial disclosures: None.*

EUNG KWEON KIM, MD, PHD Professor of ophthalmology at Yonsei University College of Medicine in Seoul, South Korea. *Relevant financial disclosures: Avellino Lab, USA: C.*

KEN K. NISCHAL, MD, FRCOPHTH Chief of pediatric ophthalmology, strabismus, and adult motility at the University of Pittsburgh Medical Center (UPMC) Children's Hospital of Pittsburgh and medical director of UPMC Children's telemedicine program. Dr. Nischal is also director of pediatric program development at the UPMC Eye Center and professor of ophthalmology at UPMC in Pittsburgh. *Relevant financial disclosures: None.*

JAYNE S. WEISS, MD Chair of ophthalmology and professor of ophthalmology, pathology, and pharmacology at Louisiana State University (LSU) in New Orleans. She is also chief medical officer at LSU Healthcare Network, associate dean of clinical affairs at LSU Medical School, and director of LSU Eye Center of Excellence. *Relevant financial disclosures: None.*

See disclosure key, page 8. **For full disclosures,** view this article at aao.org/eyenet.

START WITH THE POWER OF

EYLEA®
(aflibercept) Injection
For Intravitreal Injection

As Demonstrated in Phase 3 Clinical Trials[1]

IMPORTANT SAFETY INFORMATION AND INDICATIONS

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.

REGENERON

777 Old Saw Mill River Road, Tarrytown, NY 10591

TRUST ≈8 YEARS of Extensive Clinical Experience and the Integrity of Data From Large, Well-Controlled Trials[1]

EYLEA IS THE

#1

PRESCRIBED anti-VEGF FDA approved for Wet AMD, DME, and MEfRVO*

*IBM Truven MarketScan data: Number of injections administered from Q4 2017 through Q3 2018; data on file.

AN ESTIMATED

≈9

MILLION doses administered to ≈790,000 eyes since launch (and counting)[2]

ACROSS ALL APPROVED INDICATIONS

8

PHASE 3 CLINICAL TRIALS including more than 3000 EYLEA–treated patients[1]

START WITH EYLEA
Visit HCP.EYLEA.us to see our data.

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.

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).

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

anti-VEGF = anti–vascular endothelial growth factor; AMD = Age-related Macular Degeneration; DME = Diabetic Macular Edema; MEfRVO = Macular Edema following Retinal Vein Occlusion.

References: 1. EYLEA® (aflibercept) Injection full U.S. Prescribing Information. Regeneron Pharmaceuticals, Inc. August 2019. **2.** Data on file. Regeneron Pharmaceuticals, Inc.

11/2019
EYL.19.10.0044

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:

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 CRVO in 2 clinical studies (COPERNICUS and GALILEO) and 91 patients following 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.19.07.0306

Modifier –62: How to Determine Whether You Can Bill for Cosurgery

The Office of Inspector General (OIG) recently announced that it would investigate how practices are using modifier –62, which represents cosurgery. Make sure your practice is using it appropriately.

Cosurgery 101

The OIG, in its March 2020 work item, outlined the key features of cosurgery.

What is cosurgery? Cosurgery occurs when "the individual skills of two surgeons are necessary to perform a specific surgical procedure or distinct parts of a surgical procedure (or procedures) simultaneously on the same patient during the same operative session." However, billing for cosurgery isn't an option for all CPT codes.

Use modifier –62. Each surgeon "should report the specific procedure(s) by billing the same procedure code(s)" with modifier –62.

Reimbursement. "By appending modifier –62 to the procedure code(s), the fee schedule amount applicable to the payment for each cosurgeon is 62.5% of the global surgery fee schedule amount." So in total, CMS would pay 125% of the usual fee.

Scope of audit. The OIG plans "to audit a sample of claim line items—specifically where different physicians billed for the same cosurgery procedure code, for the same beneficiary, on the same date of service."

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

You Can Append –62 to Some CPT Codes, But Not Others

How do you know that cosurgery is even an option for a specific CPT code?

First, go to the Physician Fee Schedule Search, which is at www.cms.gov/apps/physician-fee-schedule.

Set the search parameters. In the "HCPCS Code" field, enter the CPT code of the procedure, select "2020," "Payment Policy Indicators," and "All Modifiers," and click "Submit."

Check the cosurgery column. A successful search will populate a chart for the CPT code that you submitted. See which of these three numerals is in the chart's "Cosurg" column:

- 0—cosurgeons not permitted for the procedure
- 1—cosurgeons could be paid (supporting documentation is required to establish the medical necessity of two surgeons for the procedure)
- 9—cosurgery concept doesn't apply to the procedure

Coding Tips

Cosurgeons can be of the same specialty. Years ago, the CPT had noted that cosurgeons are "usually of different specialties," but that was deleted in 1999.

Not for surgical assistants. If you are billing for an assistant-at-surgery, use modifier –80 or –82, not –62.

EXTRA **MORE ONLINE.** For more on cosurgery, see this article at aao.org/eyenet.

Cosurgery for the Eye

The "Eye and Ocular Adnexa" section of the Current Procedural Terminology (CPT) includes scores of codes. Currently, if you were to use the CMS Physician Fee Schedule Search for those codes, you would find that 102 of them have a cosurgery indicator of 1. This means that two cosurgeons can each use modifier –62 to bill for the same procedure. These codes are as follows: 65091, 65093, 65103, 65105, 65110, 65112, 65114, 65125, 65130, 65175, 65265, 65273, 65290, 65710, 65730, 65750, 65755, 65756, 65780, 65781, 65782, 65850, 65865, 65870, 65875, 65920, 65930, 66150, 66160, 66170, 66172, 66174, 66175, 66180, 66220, 66225, 66500, 66680, 66852, 66920, 66940, 66985, 66986, 66999, 67005, 67010, 67015, 67025, 67027, 67030, 67036, 67039, 67040, 67041, 67042, 67043, 67107, 67108, 67112, 67113, 67120, 67121, 67250, 67255, 67299, 67312, 67318, 67331, 67332, 67334, 67335, 67343, 67399, 67400, 67412, 67414, 67420, 67440, 67445, 67450, 67550, 67570, 67599, 67902, 67903, 67904, 67950, 67971, 67973, 67974, 67999, 68320, 68325, 68335, 68362, 68399, 68525, 68540, 68720, 68745, 68750, and 68899.

To see which of the "Eye and Ocular Adnexa" CPT codes have a cosurgery indicator of 0 or 9, see this article at aao.org/eyenet.

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

Only Academy Members Get Full Access to the #1 Resource for Innovative Ophthalmic Education

Keep your skills and knowledge on the cutting edge with the Academy's **Ophthalmic News and Education (ONE®) Network**. Enjoy exclusive on-demand access to 14 journals — including *EyeNet® Magazine* and *Ophthalmology®* — and the most relevant curated content, including thousands of instructional videos, self-assessment questions, simulators and courses.

Renew your membership and activate the most valuable benefits in our profession. aao.org/benefits

Protecting Sight. Empowering Lives.®

Vital Signs: Use Benchmarking to Monitor Your Practice's Health

In medicine, benchmarks are frequently used by physicians to accurately gauge the vital signs of their patients and properly treat them when the situation dictates it.

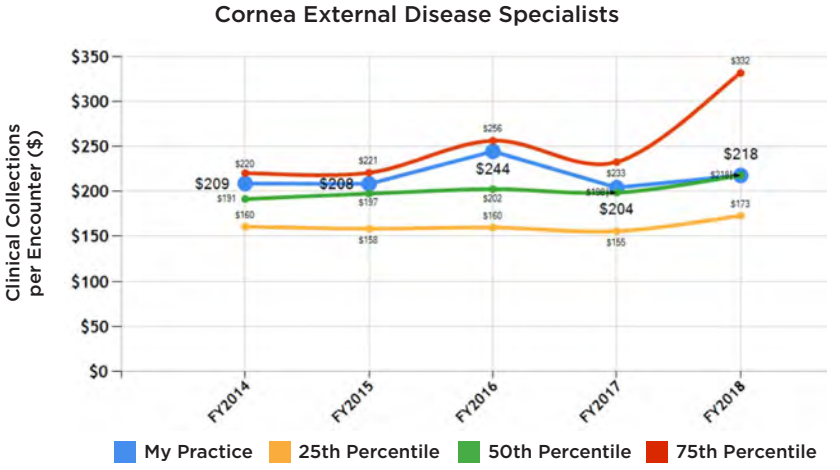
Similarly, practice management benchmarks can help you monitor the vitals of your ophthalmology practice and inform a treatment plan when areas of your business don't fall within normal limits.

Know the Vital Signs of Practice Management

The Academy, in conjunction with the American Academy of Ophthalmic Executives (AAOE), provides a benchmarking tool called AcadeMetrics. Its ophthalmology-specific benchmarks enable practices to compare their financial and patient flow indicators—in other words, their vital signs—against similar practices.

AcadeMetrics has 78 benchmarks. You can use AcadeMetrics to monitor dozens of metrics, including the following:

- **Overhead ratio,** which judges how efficient a practice is in converting collections into cash for the owners
- **Physician productivity ratios by subspecialty,** which gauge whether a practice's providers are seeing a typical number of patients and generating normal revenues
- **Employee productivity ratios,** which help you to understand whether the staffing levels are appropriate in various areas of the practice
- **Accounts receivable ratios,** which monitor billing staff's effectiveness in collecting money owed to the practice
- **Optical ratios,** which analyze the profitability of a practice's optical operations (if it has an optical shop)



GAIN SOME PERSPECTIVE. *Compare your numbers on dozens of metrics—such as collections data (shown above)—against benchmarks based on similar practices.*

An ophthalmology-specific resource. Many of the 78 benchmarks are unique to the AcadeMetrics and are not published anywhere else. They will provide focused insight into your practice's health.

Benchmarking Your Practice With AcadeMetrics

To access the benchmarks, you must first share your data. The resulting benchmarks and comparative reports will be available only to the practices that complete at least 50% of the AcadeMetrics Survey; the data won't be available for purchase by nonparticipants.

To access the benchmarks, fill out the survey. Each spring, ophthalmology practices start entering their data from the previous fiscal year into the AcadeMetrics Survey. This year, practices could start entering their data in mid-April and must finish doing so by July 31.

New to AcadeMetrics? New practices can register at https://academetrics.aao.org/academetrics_signup.aspx.

Already using AcadeMetrics? Past AcadeMetrics Survey participants don't need to sign up again; they can use the same login that they used in previous years at https://academetrics.aao.org/.

Make the most of AcadeMetrics. Once you submit your data, you will be

WRITTEN BY **DIXON DAVIS, MBA, MHA, ELIZABETH CIFERS, MBA, MSW, CHC, CPC,** AND **DEREK A. PREECE, MBA.**

able to start comparing your practice's performance against the latest benchmarks. By participating in the AcadeMetrics Survey, you'll be able to access detailed comparison reports that will help identify the specific strengths and weaknesses of your practice.

Maintain the data's integrity. When you fill out the survey, it's essential to enter the data accurately, as poor data diminish the value of the benchmarking information.

Your data are confidential. Other AcadeMetrics participants will not see your data. Identifiers specific to your practice will be stripped from the final dataset, and the reporting tools will only display datasets that include a sample size with a minimum of 10 participant submissions. (This minimum applies to both complete aggregated datasets and any filtered dataset.)

What does it cost? AcadeMetrics is free for Academy and AAOE members.

Benchmarking in Action: An Example

Knowing your key benchmarking figures and how they compare to similar practices is important in identifying issues, as shown in this hypothetical example.

The problem. The owners of ABC Eye Care felt they were making less-than-average income for ophthalmologists.

Identifying the cause. By comparing their practice data to the AcadeMetrics benchmarking data, they learned that their overhead ratio was too high. It also showed the leading cause of the high overhead ratio was that the physicians were generating collections well below the 25th percentile for their subspecialties. (Overhead ratio = total operating costs ÷ total collections.)

Identifying a problem is the first step in solving it. Since no comparative benchmarking had been done in the practice before, none of the physicians realized that they were bringing in much less revenue than their peers. And since they were unaware of the primary cause of their reduced income, they hadn't taken appropriate steps to address it. Consequently, their below-average revenue had prevented them from doing several important things, such as investing in the equipment needed to keep up to date and ensuring that their staff pay rates were competitive with the market.

Benchmarking helps you to uncover problems early and limit the damage. As with silent medical conditions such as undetected hypertension, pernicious problems can, unknown to you, exist within your practice if you aren't checking its vital signs. On the other hand, knowing your AcadeMetrics benchmarking numbers can help you to discover and address such problems early. This can prevent a silent impairment that could show up years later, sometimes in irreversible ways, perhaps jeopardizing the financial health of your practice.

Maintaining Practice Health

Be proactive by participating in the AcadeMetrics Survey. Comparing these data to your own performance will allow you to identify any underlying issues in your practice and properly address them in a timely manner. The future health and success of your practice depend on it.

For more information, visit aao.org/academetrics.

Mr. Davis is a principal and senior consultant, **Ms. Cifers** is a senior consultant, and **Mr. Preece** is a former executive consultant. All are with BSM Consulting, headquartered in Incline Village, Nev. Mr. Davis currently assists Academy staff with the AcadeMetrics benchmarking survey. *Financial disclosures: None.*

What About Clinical Benchmarking?

Sign up for Verana Practice Insights. In 2017, the Academy partnered with Verana Health to accelerate the analysis of deidentified data in the IRIS Registry (Intelligent Research in Sight). As part of that partnership, Verana Health has developed Verana Practice Insights to make data analytic tools available—at no charge—to U.S. Academy members who have integrated their electronic health record (EHR) system with the IRIS Registry (aao.org/iris-registry).

What are your cataract metrics? The first four metrics developed by Verana Health relate to cataract surgery (diagnoses, visual acuity before and after surgery, Nd:YAG capsulotomies, and endophthalmitis). You can review your data based on yearlong, quarterly, or customized date ranges.

Coming soon: Retina and other subspecialties. Verana Health will soon add metrics for other subspecialties on Verana Practice Insights, starting with retina.

Define the future of clinical benchmarking. Verana Health seeks to support you as you navigate the many changes caused by the COVID-19 pandemic. Share your thoughts on what insights would be valuable as you move forward. Email support@veranahealth.com to participate in a feedback session.

How to sign up. Complete the form at www.veranahealth.com/verana-practice-insights-signup. You will need your 10-digit National Provider Identifier (NPI). After Verana Health verifies that your data are accurate and complete, they will email you with your account information.

What About COVID-19?

Financial challenges. In recent years, ophthalmology practices have been buffeted by a series of financial threats. These include cuts in payment for cataract surgery and a threatened overhaul of E/M payments that could short-change surgical specialties. Now, they're facing the dire disruption caused by the COVID-19.

Bookmark the AAOE's coronavirus page. Go to aao.org/coronavirus and click on "Practice Management."

The importance of benchmarking. Knowing your practice's past strengths and weaknesses will help you navigate the current crisis.

Academy Notebook

NEWS • TIPS • RESOURCES

WHAT'S HAPPENING

Coronavirus Resource: A Popular Resource

On Jan. 28, the Academy launched a coronavirus alert web page. Primarily intended for ophthalmologists, the page—updated frequently and covering statistics, the latest evidence, protocols for seeing patients, and links to resources—received almost 32,000 views within the first week. At press time two months later, aao.org/coronavirus had become a landing site for a series of subpages, which together had more than a million views. The successful launch of the well-used educational resource page can be attributed to its authors: **James Chodosh, MD, MPH,** with assistance from **Gary N. Holland, MD,** and **Steven Yeh, MD.**

Please note: In response to the pandemic, the aao.org/coronavirus pages are being updated rapidly, providing links for ophthalmologists, the public, and practice managers.

Watch the Iowa Primaries

Academy member and Iowa state senator **Mariannette J. Miller-Meeks, MD,** is running for Congress in Iowa's open 2nd District seat. As of press time, the Iowa primary is scheduled for June 2.

In 2008, 2010, and 2014, Dr. Miller-Meeks ran unsuccessfully against Rep. David Loebsack, the incumbent, who is retiring this year. She rebounded from those losses, winning a state senate seat in 2018 by running as an avowed advocate for patient-centered health care. She highlighted her background in eye care during discussions with voters in her district. She previously served as head of Iowa's state health department.

RUNNING FOR CONGRESS. *On her website (millermeeks2020.com), Dr. Miller-Meeks, who is running for a House seat from Iowa, introduces herself, talks about her stances on various issues, and shares press releases.*

Dr. Miller-Meeks would provide an immediate, valuable medical perspective for health care issues facing Congress. As a leader in the Iowa state senate, she was instrumental in stopping legislation that would have expanded the optometric surgical scope.

She's not the only Academy member seeking a congressional seat in 2020. Academy Board Trustee-at-Large and Air Force Veteran **William S. Clifford, MD,** is running for Kansas' open 1st District seat in September. Visit Dr. Clifford's website (cliffordforcongress.com) for more on his campaign.

TAKE NOTICE

2020 MIPS: June 1 Deadline for EHR-Based Reporting

The IRIS Registry can streamline your reporting for the Merit-Based Incentive Payment System (MIPS) if you meet the deadlines.

Report quality measures using automated data extraction. The least burdensome way to report MIPS quality measures is by integrating your electronic health record (EHR) system with the IRIS Registry.

June 1 deadline for getting started with IRIS Registry–EHR integration. If you haven't yet integrated your EHR system with the IRIS Registry, you must sign up or—if you signed up last year but didn't integrate—notify the IRIS Registry staff by June 1 that you plan to integrate this year. You must complete the integration process by Aug. 1.

The IRIS Registry is a one-stop shop for MIPS reporting. You also can use

the IRIS Registry web portal to manually attest to promoting interoperability (PI) measures and improvement activities, and—if you aren't able to report quality via IRIS Registry–EHR integration—manually enter data for quality measures. If you are new to the IRIS Registry, you will need to sign up for manual reporting by Oct. 31.

Review this year's improvement activities. Some improvement activities that were available for last year have been discontinued, but many more have been made available for reporting via the IRIS Registry. For detailed descriptions of each of those activities, visit aao.org/medicare/improvement-activities.

For more information on using the Academy's IRIS Registry for MIPS, go to aao.org/iris-registry/medicare-reporting.

Volunteer Opportunity: Become a Congressional Advocate

With health care in flux as the COVID-19 pandemic continues, it is more important than ever for ophthalmologists to have relationships with their lawmakers to help educate them on how patients and practices are being impacted. Participate in the Academy's Congressional Advocacy Program and help to make sure that patients have timely access to care and that practices have relief from regulatory burdens such as prior authorization requirements. Help to ensure that practices also get immediate access to the financial assistance and other resources they need as Congress responds to this crisis.

Become an effective physician advocate. With assistance from the Academy, you'll develop relationships with lawmakers to represent the Academy's key priorities. As a Congressional Advocate, you will communicate with members of Congress and congressional staff. Join this national network of ophthalmologists, which has the power to influence Congress' actions to support patients and physician practices during this difficult time.

Get started. To sign up, visit aao.org/member-services/volunteer/advocate/be-congressional-advocate.

More on volunteering. Learn about dozens of Academy volunteering opportunites at aao.org/volunteering.

Follow @AAOjournal for the Latest Articles

Use Twitter to stay up to date on new research, including the latest on COVID-19, from *Ophthalmology, Ophthalmology Retina,* and *Ophthalmology Glaucoma.* Content is posted daily and includes articles in press, "Pictures & Perspectives," editorials, and new issue alerts.

Follow @AAOjournal at twitter.com/AAOjournal.

Interested in an Externship?

Are you interested in an externship opportunity with a leading refractive, cataract, cornea, or lens-based surgeon? The International Society of Refractive Surgery (ISRS) is now offering its members a chance to bolster their clinical knowledge in imaging technology, diagnostic devices, and various surgical platforms by learning alongside colleagues through the ISRS Externship Program.

These training opportunities are offered by leading ISRS members in Africa, Asia, Europe, Latin America, and the Middle East, and they last between two weeks and three months. Stipends are available to help cover expenses such as airfare, transportation, lodging, and meals.

Atanas Y. Bogoev, MD, recently finished a one-month ISRS externship program in Germany. "I am extremely grateful to Prof. Burkhard Dick and ISRS for the opportunity to enhance both my clinical and theoretical knowledge in the field of ophthalmology," he said. Dr. Bogoev is an ophthalmology resident at the Vision Eye Clinic in Sofia, Bulgaria.

ON LOCATION. *H. Burkhard Dick, MD (left), with Dr. Bogoev (right), during his ISRS externship at the University Hospital in Bochum, Germany.*

Learn more and apply at isrs.org/externships. Fall applications are open now and are due by Aug. 19.

List a Training Opportunity

The Academy's Global Directory of Training Opportunities is an online resource for ophthalmologists seeking a training experience outside their country, and it's the best way for institutions or practices to reach the broadest pool of candidates. If you have a fellowship or observership that accepts ophthalmologists outside your country, list your opportunities in this free directory—it only takes two or three minutes to post.

1. Visit aao.org/gdto-submission.
2. Click "Submit a Training Opportunity."
3. Log in (this step will save you time later).
4. Enter opportunity information.

For more information, visit aao.org/training-opportunities.

OMIC Tip: Leaving a Practice

Ophthalmologists leave practices for a variety of reasons, including illness, retirement, changes in employment status, and personal or family needs.

Before departure, the individual ophthalmologist and the practice need to take steps to promote continuity of care, prevent allegations of abandonment, and ensure that all involved ophthalmologists have access to the medical records in the event that the patient's care is ever called into question. At the same time, both parties must take into consideration the terms of their contracts and the requirements of state and federal law.

It's important to prepare your exit strategy early and make an effort to limit the likelihood of lawsuits. Download the "OMIC Leaving Practice Toolkit" PDF at omic.com/leaving-practice-toolkit to help with this often difficult transition.

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

MEMBERS AT LARGE

2020 Ellis Island Medal of Honor

Jim Mazzo, Academy Foundation Board Member and Global President of Ophthalmic Devices with Carl Zeiss Meditec, has been chosen to receive the 2020 Ellis Island Medal of Honor.

The Ellis Island Honors Society awards the medal to those who have shown an outstanding commitment to serving the United States professionally, culturally, or civically. Past Ellis Island Medalists include U.S. presidents and Nobel Prize winners.

2020 Migel Medal Winner

The Migel Medal, from the American Foundation for the Blind, honors professionals and volunteers whose dedication and achievements improve the lives of those who are blind or visually impaired. **Michael J. Schermer, MD,** is the 2020 recipient in the volunteer category.

Dr. Schermer has served the Sacramento Society for the Blind for four decades, established "A Party for the Senses" at the California State Fair for individuals who are blind or visually impaired, assisted in developing a division for blind runners in the Sacramento Marathon, helped raise $45 million for construction of a new vision care center at the University of California at Davis, and has volunteered abroad through SEE International and the World Eye Foundation.

ACADEMY RESOURCES

Keep Up With Current Retina/Vitreous Practices

All seven Academy *Preferred Practice Pattern* guidelines (*PPP*s) for retina/vitreous were recently updated, including "Age-Related Macular Degeneration" and "Retinal Vein Occlusions." The *PPP*s are based on the best available scientific data as interpreted by panels of experts.

View all *PPP*s at aao.org/ppp.

D.C. REPORT

Academy Funds Efforts to Reverse E/M Reimbursement Change

The Academy has provided financial support to a sweeping effort by the country's top surgical specialties to fight drastic cuts to surgery reimbursements scheduled to begin in January 2021.

Investing major funds into a cross-specialty campaign. The Academy Board of Trustees voted to commit several hundred thousand dollars to the effort to reverse the Centers for Medicare & Medicaid Services' (CMS) plan. The campaign, led by the American College of Surgeons, targets lawmakers, regulators, and the public this year.

"The Academy and the American College of Surgeons have worked together since last summer to implement this program," said Academy CEO David W. Parke II, MD. "Even during tough times with COVID-19 it is critical that we invest reserve funds to restore some of the cuts to surgical payments that will have massive impacts on our members. This sort of investment is what reserves are for."

The Academy has already met with some federal agencies and lawmakers in Congress to persuade them that CMS' proposed plans would be devastating to patients and to ophthalmologists. The Academy is pulling out all the stops to convince key lawmakers, including those on the Energy and Commerce, Finance, and Ways and Means committees, that the cuts will hurt surgical services, which ultimately will adversely affect their constituents.

Background. The Medicare physician payment system is budget-neutral, which means that as the value of some services increases or new services are added to the system, the values of other services are reduced. Unless CMS changes course, two future policies related to a boost in evaluation and management (E/M) payments will result in drastic payments cuts for surgical and specialty services starting in January 2021.

Free! Key AAOE Resources Open to All Academy Members

In these uncertain times, the American Academy of Ophthalmic Executives (AAOE), the Academy's practice management affiliate, has made some of its membership benefits available to every Academy member for free through July 31.

One particularly valuable benefit is the Practice Management Resource Library (aao.org/aaoe-resources), which offers free access to a myriad of resources including online coding courses and new practice management webinars to assist practices dealing with the pandemic.

Explore the other newly opened resources at aao.org/practice-management/resources/coronavirus-resources.

Drive Your Practice Success With Benchmarking

The Academy/AAOE AcadeMetrics practice management benchmarking survey opened April 15 and closes July 31, so act quickly to benefit from this valuable tool.

Enter your 2019 practice management data by the deadline and use the AcadeMetrics benchmarking tool throughout the year to compare your financial data to that of similar practices. Get valuable insight into optimal staffing levels, number of satellite offices, and more.

Find out more about these free member tools at aao.org/practice-management/analytics.

Complete the benchmarking survey by July 31, 2020, to be eligible to win a $200 gift card.

Santen

A Clear Vision For Life™

WORKING TO EMPOWER A NEW ERA OF GLAUCOMA SURGICAL DEVICE INNOVATION

We're dedicated to advancing proactive glaucoma surgery by working toward more predictable and sustainable outcomes

PREDICTABILITY

- A minimally invasive device would help mitigate trauma and expedite recovery[1]
- Subconjunctival drainage is a proven method to achieve target IOP[2]

SUSTAINABILITY

- Device design could help maximize outflow while minimizing hypotony[3,4]
- Biocompatible material that resists degradation could help deliver more-sustainable benefits[3]

Hear from your peers and register for more information at
AdvancingGlaucomaSurgery.com

References: 1. Chan JE, Netland PA. EX-PRESS Glaucoma Filtration Device: efficacy, safety, and predictability. *Med Devices (Auckl).* 2015;8:381-388. **2.** Lee RMH, Bouremel Y, Eames I, Brocchini S, Kaw PT. The implications of an ab interno versus ab externo surgical approach on outflow resistance of a subconjunctival drainage device for intraocular pressure control. *Transl Vis Sci Technol.* 2019;8(3):58. **3.** Amoozgar B, Wei X, Lee JH, et al. A novel flexible microfluidic meshwork to reduce fibrosis in glaucoma surgery. *PLoS One.* 2017;12(3):e0172556. **4.** Agrawal P, Bradshaw SE. Systematic literature review of clinical and economic outcomes of micro-invasive glaucoma surgery (MIGS) in primary open-angle glaucoma. *Ophthalmol Ther.* 2018;7(1):49-73.

Destination AAO 2020

GET READY FOR LAS VEGAS • PART 1 OF 6

WELCOME

Looking Forward to Las Vegas

Now is the time to start preparing for the Academy's annual meeting, the year's best opportunity to learn from leaders in the field, discuss current topics in medicine, connect with colleagues, and explore the city.

What about COVID-19? Of course, given the current crisis, the Academy is actively monitoring developments and soliciting input from public health authorities, as the health and safety of meeting participants and attendees is of utmost importance. At this time, AAO 2020 is still scheduled for November as planned. The Academy looks forward to the passing of this pandemic and a visionary meeting in Las Vegas.

When to be there. AAO 2020 runs Nov. 14-17 and is preceded by Subspecialty Day meetings, held Nov. 13-14. You can also attend the American Academy of Ophthalmic Executives (AAOE) Practice Management Program Nov. 13-17, and the American Society of Ophthalmic Registered Nurses (ASORN) Program Nov. 13-14.

How to prepare. Over the next six months, this Destination AAO 2020 section will guide you through deadlines, preview the scientific program, and highlight key events.

AMERICAN ACADEMY OF OPHTHALMOLOGY®

SKILLS TRANSFER LABS. *The Skills Transfer labs are an important opportunity for physicians to learn the most up-to-date techniques. Tickets, available for members starting June 17, are required for Skills Transfer labs.*

REGISTRATION

New! June—Not April—for AAO 2020 Registration and Hotel Booking

The Academy has announced that AAO 2020 registration and hotel reservations will now open **June 17** for members and July 8 for nonmembers.

In the meantime, avoid scams. Several fraudulent companies pretending to be associated with the Academy and AAO 2020 may appear in web searches or may have already contacted you via email.

Learn how to spot a fraud, visit aao.org/registration#fraud.

WHAT'S TO COME

Dr. Jeng's Insider Perspective

Bennie H. Jeng, MD, is serving his first year as the Chair of the Annual Meeting Program Committee. Here, Dr. Jeng gives a preview of what's to come in Las Vegas.

Q: What's new for AAO 2020?

A: There is increased emphasis on making courses and materials more interactive. Especially with the newer generation of attendees, we're finding that they're learning more through engagement than by sitting in a lecture, and we want to be sure the Academy is providing that. We're going to have more of the interactive poster sessions to promote more discussion and small group learning.

Q: What kind of trends have you seen in association meetings?

A: In general, meetings are getting bigger, and the Academy is no exception. Some of the feedback that we have been getting—at least from newer attendees—is that there are so many excellent sessions to choose from that it can be a challenge to decide what's a priority. With this in mind, the Mobile Meeting Guide is constantly being improved to offer a better navigation experience.

The Academy meeting is also a convener of all the different subspecial-

ties. People have plenty of choices, and that's something that a lot of the other meetings don't really offer.

Q: What are some of the most exciting course topics being planned?

DR. JENG: *"Artificial intelligence is becoming hotter and hotter."*

A: One of the new developments that I'm particularly interested in is the Light Adjustable Lens course on the cataract front. In cornea, one of the most popular courses will be Top 10 Hot Corneal Surgical Tips for 2020. The Academy has been doing this every year for many years, but we're always updating it with new material. This year, I expect that's going to be very interesting because cornea is still very much changing.

Q: If you could take just one instruction course or symposium at this meeting, what would it be and why?

A: Because I'm a cornea person, I'm looking forward to the Cornea Society symposium that's called Cornea in 2020 and Beyond. But in terms of a topic that I think everyone should follow, artificial intelligence is becoming hotter and hotter. There will be symposia and various courses, as well as lots of original papers, throughout the meeting on the topic. For attendees, whatever their specialty is, they should take some time to see something about artificial intelligence because it's coming, and it's going to change the way we do things.

Q: What is the best memory or experience you've had with this meeting?

A: My best memory is the first time I was invited to speak at Subspecialty Day. It was such an honor to be asked, and it was a great experience. It included a big panel discussion that I thought was very useful, and I got a lot of good feedback.

Q: What's the No. 1 extracurricular activity you're looking forward to in Las Vegas?

A: I do really like the hubbub of everything going on in the city, and there's a lot to do in Las Vegas besides the casinos. I really enjoy getting together with friends and colleagues, so the alumni receptions are what I look forward to most, no matter the city.

BEAT THE CLOCK

Course Pass and Tickets: Buy Them Early

Registration for AAO 2020 gives you access to many types of sessions, including papers, Poster Theater presentations and Poster Discussions, conversation (and coffee) at the Academy Café, and other symposia. You also will get access to e-posters and videos on demand. For greater access, purchase the Academy Plus course pass.

Academy Plus. Academy Plus is a course pass that offers unlimited access to all Academy and AAOE instruction courses, including Skills Transfer didactic lectures. No need to plan or preselect courses. Pass holders can float among all available courses.

You can purchase the Academy Plus course pass when you register for AAO 2020 online. Academy Plus will also give you complimentary access to the annual meeting components of Meetings on Demand, a product that captures highlighted presentations recorded during the annual meeting.

Some events require tickets or separate registration. Tickets are required for Skills Transfer labs, some special meetings, and AAOE Practice Management Master Classes, among other sessions. (Note: Tickets are no longer printed. Your badge will be scanned to allow entry to these ticketed events.)

Tickets and the Academy Plus course pass will be available for purchase starting June 17 for members.

For more information, visit aao.org/registration.

PROGRAM

June 17: Access Full Program Information

The full, official program for AAO 2020—including Subspecialty Day schedules—will be online starting June 17.

You will be able to look up information by day, topic, type of event or course, special interest, or presenter. You don't have to log in or be a member to view program information, but you will need to log in to build a personal calendar and register.

Learn more at aao.org/program.

Attend Subspecialty Day 2020

Subspecialty Day meetings feature world-renowned ophthalmologists presenting the latest developments and pearls. Dates are as follows:

One-day meeting on Friday, Nov. 13:

- Refractive Surgery: Celebrating 2020

Two-day meeting on Friday, Nov. 13, and Saturday, Nov. 14:

- Retina: Vision for the Future

One-day meetings on Saturday, Nov. 14:

- Cornea: Seeing Clearly Into the Future
- Glaucoma: Winning Bets: Strategies in Glaucoma Care
- Ocular Oncology/Pathology: Collaboration Now More Than Ever
- Oculofacial Plastic Surgery: Back to the Basics With Tips and Tricks
- Pediatric Ophthalmology: The Only Game in Town
- Uveitis: Beating the Odds—How to Make Sure You Get a Full House When You're Dealt Uveitis

Subspecialty Day registration provides attendees the flexibility to float among meetings. One-day meeting registrants can attend any of the meetings taking place that day; two-day registrants are free to attend any Subspecialty Day presentation on Friday or Saturday. In addition, those registered for a Subspecialty Day meeting taking place on Saturday will have access on that day to the AAO 2020 Exhibition.

Meetings on Demand is compli-

SUBSPECIALTY DAY. *Internationally recognized ophthalmologists will present their findings and insights during eight Subspecialty Day meetings in Las Vegas.*

mentary. All Subspecialty Day meeting attendees receive access to the Meetings on Demand recordings from the Subspecialty Day programs.

Register. Online registration for Subspecialty Day meetings opens June 17 for members and July 8 for nonmembers.

Find more information at aao.org/subspecialty-day.

Boost Your Practice Recovery With the AAOE Practice Management Program

Many practices have been drastically affected by the COVID-19 pandemic and need solid strategies to recover from financial and operational setbacks. Engage with leaders and experts in ophthalmology to find solutions and new opportunities that you can implement immediately in your practice.

Attend the AAOE Program, Nov. 13-17. It includes a variety of courses, workshops, and roundtables, free for AAOE and Academy members. Choose from more than 70 instruction courses on leadership, practice optimization, risk management, coding, and more.

Admission to instruction courses is via the Academy Plus course pass, which must be purchased separately. For deeper immersion, attend three-hour Master Classes and intensive coding sessions (ticketed separately) on Friday and Saturday.

On June 17, watch for info to be posted at aao.org/aaoe.

TRAVEL

Plan Your Visit

Las Vegas is known for its many entertainment options, from gambling at the strip's iconic casinos to the unforgettable drive through the Valley of Fire State Park, less than an hour from the city. And for theater lovers, tickets are already available for several in-residence shows in November 2020, including "Le Rêve–The Dream," a performance that incorporates swimming, acrobatics, and fire at an intimate theater-in-the-round; Penn & Teller, the famous magicians; and "KÀ," a cinematic Cirque du Soleil production.

Learn more at aao.org/lasvegas.

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

Foundation

Join George B. Bartley, MD, and Lynn Bartley, in Supporting Academy Programs

Become a Leadership Council Donor

Make a bigger impact than you ever thought possible by giving to the American Academy of Ophthalmology Foundation at the Partners for Sight level ($1,000 – $2,499) or the Leadership Council level ($2,500+). Your support of Academy programs will help us educate more ophthalmologists and do even more good for patients worldwide.

Learn how your gift will make a difference at **aao.org/foundation/partners-for-sight**

"Giving back is an easy decision. While dues support the Academy's ongoing services, contributions to the Foundation allow the Academy to pursue new initiatives, from developing innovative education to building the Truhlsen-Marmor Museum of the Eye. Supporting the Foundation is a small token of our continuous gratitude."

DR. GEORGE AND LYNN BARTLEY
LEADERSHIP COUNCIL DONORS
ROCHESTER, MINN.

Protecting Sight. Empowering Lives.®

CONNECT WITH WORLD-CLASS EXPERTS IN REFRACTIVE AND CATARACT SURGERY

Only **ISRS members** have access to exclusive opportunities and programs to network with leading experts from 90+ countries and stay clinically up-to-date.

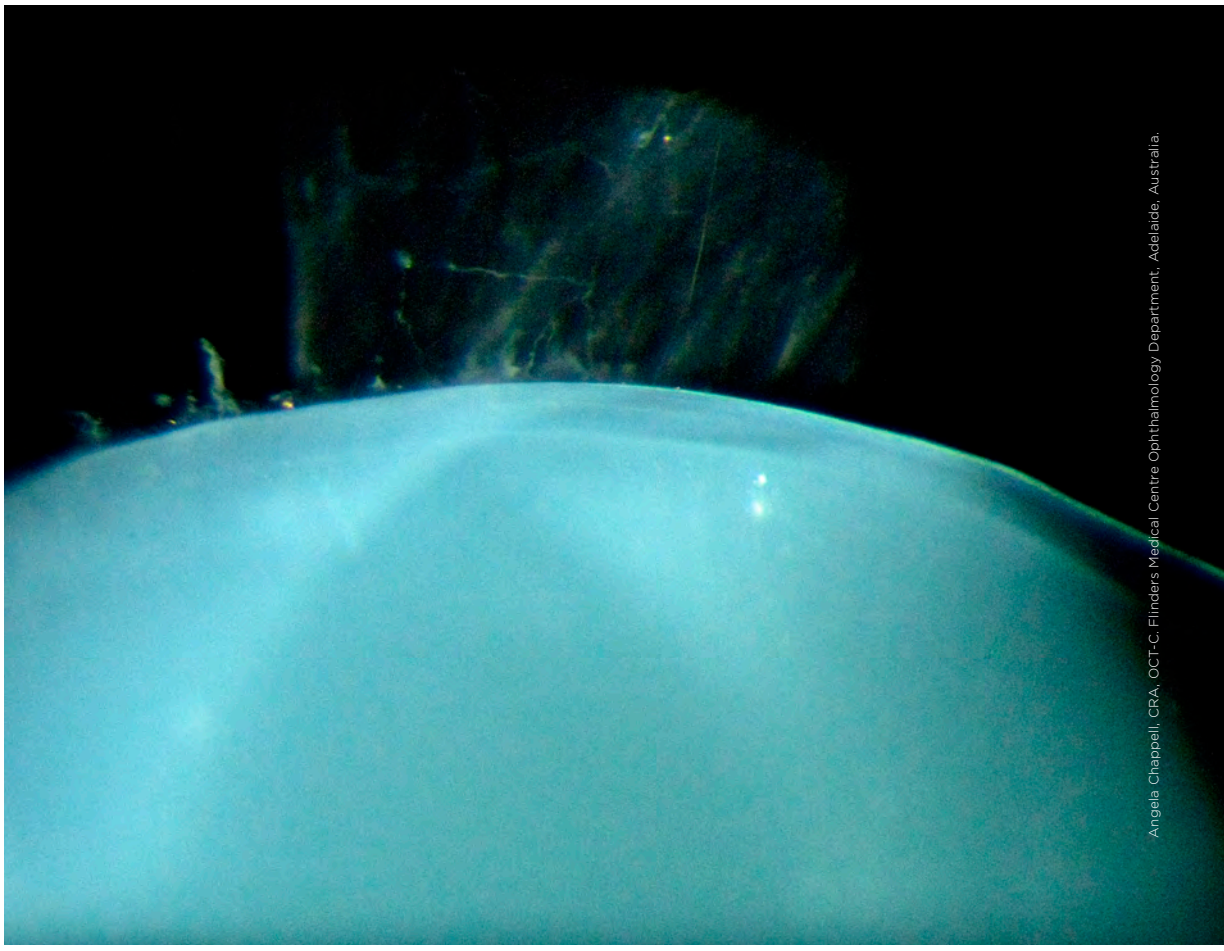
Visit **isrs.org/benefits** to learn more about your member benefits.

isrs.org/benefits

ISRS®
International Society of Refractive Surgery
A Partner of the American Academy of Ophthalmology

MYSTERY IMAGE

BLINK



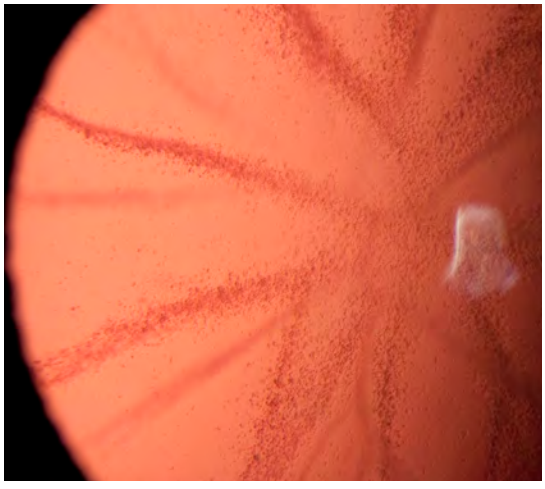
Angela Chappell, CRA, OCT-C, Flinders Medical Centre Ophthalmology Department, Adelaide, Australia.

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

LAST MONTH'S BLINK

Congenital Cataract

This patient is a member of a family that has congenital cataracts due to mutation in the *BFSP1* gene. The non–visually significant anterior and posterior sutural cataract appears in a configuration resembling the spokes of a bicycle wheel. The opacities are best seen in retroillumination during slit-lamp examination. None of the family members with such cataracts has impaired vision that requires surgical intervention.



WRITTEN BY **DEEPA TARANATH, MBBS, MS, FRANZCO.** PHOTO BY **ANGELA CHAPPELL, CRA, OCT-C.** BOTH ARE AT FLINDERS MEDICAL CENTRE OPHTHALMOLOGY DEPARTMENT, ADELAIDE, SOUTH AUSTRALIA, AUSTRALIA.

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

AAO 2020 VISION

Don't Miss *EyeNet*'s Meeting Coverage

Get the inside news on Subspecialty Day and AAO 2020.

MONTHLY PREVIEWS *Destination AAO 2020:* Deadlines, quick tips, and sneak peeks in the May-October issues of *EyeNet*.

THE MEETING NEWSPAPER *AAO 2020 News:* Subspecialty Day recommendations, named lecture previews, and more.

MAP AND LISTINGS *Exhibitor Guide:* Must-know exhibitor information.

BREAKING NEWS *AAO 2020 Daily:* Meeting news emailed nightly from Las Vegas.

Where All of Ophthalmology Meets®

aao.org/2020

Protecting Sight. Empowering Lives.®

GET THE ADVANTAGE OF SPEED

OPHTHALMOLOGY'S FASTEST EHR & PM ALL-IN-ONE SOLUTION

GUARANTEED TO INCREASE YOUR EFFICIENCY

and Bottom Line in less than ***90 days!***

Our ***Advantage SMART Practice***® EHR and practice management solution uses real-time data to make every part of your workflow faster.

EHR | PM | ASC | RCM | TELEHEALTH

MyEyeStore | OPTICAL | PATIENT ENGAGEMENT | ON-LINE BILL PAY | ON-LINE SCHEDULING | MIPS

WWW.COMPULINKADVANTAGE.COM/ONETAB | 805.716.8688

compulink