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AND DESIRED OUTCOMES

Mitchell A. Jackson, MD
Lake Villa, Illinois

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Marc Safran, MD
A doctor doesn’t give a hospital its reputation.

A team of doctors do.

When the world demands the best, it looks to Wills Eye. With the nation’s highest clinical volume of annually referred patients, we’ve always been at the forefront of eye disease treatment. Our expertise and advanced capabilities are what defined the field in 1832, and continue to redefine it today.
In light of Dr. Williams’ column titled “Solo Practice in Ophthalmology: Resisting the Tides?” (Opinion, October), I want to encourage physicians to shape their futures despite the obstacles created by the following: Medicaid cost sharing with the federal government, uncertainty around the fate of individual insurance markets, looming MACRA and MIPS regulations, and more.

What happens when we take the reins. I invite you to imagine what is possible (and importantly, under our own control) when we shift our perception of health care reform and value-based care from externally imposed burdens to internally driven improvements. By focusing on your individual practice, you can solve your own unique challenges. There is plenty to do to improve your practice for intrinsic reasons, and fortunately many of these changes can also help you survive the transition from fee-for-service to value-based payments—for example, inefficiencies in your practice, uncertainty around the fate of individual insurance markets, looming MACRA and MIPS regulations, and more.

The 3 elements of improvement. The foundation for physician-directed practice improvements rests upon 3 pillars: autonomy, mastery, and purpose. Much has been written lately about these and “physician engagement with work”—and, yes, it is possible to use these concepts to find joy in our work. For example, when you problem-solve to eliminate inefficiencies in your practice, you can find pleasure in this exercise of autonomy. As your practice improves due to the solutions you found, you experience the element of mastery. Finally, a higher-performing practice allows the individual and organization to more effectively fulfill its purpose of helping others. Conversely, actions that do not feature these 3 principles lead to frustration and increase the risk of burnout.

Choose the best path for you. Both solo and group practice have their pros and cons; the choice boils down to how strongly you value autonomy. For some ophthalmologists, achieving mastery is found by working alone; for others, mastery can be facilitated through the advantages of a group practice.

At a minimum, we must continually evolve our clinical and surgical skills as well as basic business skills. At some point, however, we realize the importance of community and advocacy to achieve a higher purpose (the pillar of fulfillment): service to others. The Academy, state and subspecialty societies, and their advocacy groups exist to defend our professional autonomy, support our individual and collective efforts to achieve professional mastery, create vital bonds with like-minded professionals, and ultimately fulfill our purpose as healers.

Alan E. Kimura, MD, MPH
Denver

More on Low Vision

I read with interest “Low Vision Drivers: The Ophthalmologist’s Role and Responsibility” (Clinical Update, October), which quite thoroughly discusses the benefit that bioptic vision aids may offer to many individuals who would otherwise be unable to acquire a driver’s license, with the independence that this certification offers.

This remarkable visual/driving aid was brought to my attention in 1996. At that time, I evaluated a then-8-year-old boy who was found to have Stargardt disease, with his acuity eventually dropping to 20/200 in both eyes. With subsequent evaluation by C.J. Reed, OD, COMS, at the Judith A. Read Low Vision Services in Akron, Ohio, and fit with the then-available Ocutech VES II/6 × magnification, he has been able to continue successfully through college and obtain ongoing driving privileges.

A debt of gratitude needs to be given to William Feinbloom, OD, PhD, the “father of low vision care” in the United States, who introduced the concept of bioptic driving in this country. In 1932, at age 28, he used an astronomer’s telescope as a model to design a small 3 × power telescope that was small enough to be mounted in a spectacle frame, restoring one individual’s functional vision.

Later, in 1958, he introduced the concept of a bioptic telescopic system, which combined a prescription eyewear lens with a small mounted Galilean telescopic system. His system allowed the patient to change view from the telescope to the general prescription.

The website referenced below, with information from Richard L. Windsor, OD, is a most valuable resource, describing a number of up-to-date options that ophthalmologists/optometrists/low vision specialists may find useful, adding to EyeNet’s informative article.

Stuart M. Terman, MD
Cleveland

1 www.bioptichdwebsite.com
During the open microphone session at an Academy Young Ophthalmologist symposium, an ophthalmologist newly in practice, who was also a new father, asked, “How do I manage the tension between the demands of my job and the responsibility I feel to my son?”

I wanted to hug this young person. Finally, the well-known challenge of managing a young career and a young family has become a nongendered issue. In response to this challenge, some young ophthalmologists—both men and women—now ask about the possibility of practicing part time. But while they might wish to decrease work hours to accommodate other priorities, the concept of a part-time ophthalmologist is a flawed one.

There is no such thing as a part-time ophthalmologist.

Let me explain. A surprising number of physicians report working part time. In a compensation survey of nearly 20,000 physicians across 26 specialties, 22% of the women and 10% of the men report that they work fewer than 40 hours per week.¹ In ophthalmology, 24% of female and 15% of male ophthalmologists report working fewer than 40 hours each week. This trend might be increasing as dual professional career families become commonplace. Furthermore, we’re told that today’s young physicians tend to protect family and leisure time more than their older peers have and might be bolder about requesting a day off or protecting their weekends.

Yet no survey can capture the commitment that is required to be a physician. An ophthalmologist who chooses to work fewer hours for a period of time is still a completely committed physician. She might shorten her workday or compress the work week into fewer days, but she brings her training, her expertise, her experience, her compassion, and her wisdom to work when seeing patients. The “part-time” physician often maintains a regular call schedule and full malpractice coverage, and he is committed to continuous learning. The “part-time” ophthalmologist learns new techniques, innovates, and attends educational meetings. The “part-time” ophthalmologist is available for patients, emergencies, and advice to other physicians. In other words, the “part-time” ophthalmologist has a 100% commitment to the practice of ophthalmology.

Much has been written about Baby Boomers, for whom work is a moral imperative, and Gen Xers and Millennials, who reportedly want more work-life balance. This is an oversimplification of reality. For example, of the 15% of male ophthalmologists who work part time, I wonder how many are older physicians who immensely enjoy practice but now choose to work fewer hours and enjoy other activities. We value these physicians for their experience and their wisdom, and they ground us in a tradition of providing quality care, teaching colleagues, and continuing to learn. Likewise, we value the young ophthalmologists who might provide superb ophthalmic care and work fewer hours than their older peers did at the same career stage. And we recognize that many physicians who limit work hours early in their career increase their time commitment in later decades.

Traditionally, full-time work has been measured by how many hours a person works in the office. While this may be necessary for determining benefits, hours logged is hardly a meaningful measure of the value of a colleague. There are many metrics for valuing work, including RVUs, productivity, papers written, leadership roles, and teaching responsibilities. In my own practice, I’ve been impressed by the availability of my young colleagues to discuss a patient or provide advice at odd hours. Once, a colleague discussed a complex case with me, and at the end of the phone call I discovered that he was on a ski slope.

Some ophthalmologists who practice part time feel diminished by the choice and don’t like the label. Let’s acknowledge the 100% commitment to patient care and stop counting the hours. An ophthalmologist is “all in,” even if it’s not all the time.

There is no such thing as a part-time ophthalmologist.

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Sexual harassment allegations know no workplace boundaries. While most recent public cases involve the media and entertainment industries or government officials, other cases have touched nearly every type of organization and profession—including ophthalmology. This should not be surprising because sexual harassment frequently is driven by power differentials between the harasser and the victim, leading to feelings of vulnerability. Medicine is replete with such power relationships—between physician and staff; between professor and trainee; between senior and junior colleagues; and between physician and patient.

Harassment allegations run the gamut between single verbal episodes to patterns of frank sexual assault. The U.S. Equal Employment Opportunity Commission defines workplace sexual harassment in part as “unwelcome sexual advances or conduct of a sexual nature which … creates an intimidating, hostile, or offensive work environment.” How many times in our professional lives have we been a witness (or a party) to a crude joke, comments of a highly personal or sexual nature—or worse? How often is such behavior rationalized by statements like, “I’ve always been a big hugger” or “I’ve always been like that and she has never complained.” (Although I use “she,” sexual harassment may be male to female, female to male, female to female, or male to male.)

As many gray zones as have been recently illuminated (for example, “when is a hug appropriate?” and “what discussion subjects cross the line?”), the #MeToo movement has created a valuable teaching moment, forcing all of us—men and women—to rethink appropriateness and inclusiveness.

Implicit in the trust and respect we receive as physicians is our responsibility to create a safe and respectful professional environment. This includes zero tolerance for inappropriate behavior that might be interpreted as constituting harassment.

What is the Academy’s role? Every Academy member agrees to abide by the Code of Ethics and its Principles. The Principles describe “model standards of exemplary professional conduct for all Fellows or Members of the Academy.” Principle 2 states in part, “Ophthalmological services must be provided with compassion, respect for human dignity, honesty, and integrity.” This applies to all involved in the care process—colleagues, staff, patients, and families.

In the 30-plus years of the Academy’s Code of Ethics, there has never been an ethics challenge involving alleged sexual harassment or sexual misconduct involving patients, colleagues, or staff. However, surveys of female physicians in multiple specialties suggest that a large percentage of women ophthalmologists have personally experienced what they perceived to be sexual harassment—verbal and/or physical—from their physician colleagues. One study of 1,066 physicians revealed that 30% of women said they had directly experienced sexual harassment in their careers, versus 4% of men.1

Members and Fellows also deserve to understand how the Academy addresses this issue, the seriousness with which it is taken, the organizational culture we attempt to engender, and the processes we have in place to protect our staff, our volunteers, and our profession itself.

Every Academy staff member, without exception, must complete a sexual harassment training course every 2 years and acknowledge in writing familiarity with the Academy’s relevant policies. These policies acknowledge both organizational responsibility for compliance as well as individual responsibilities and reporting obligations for every employee. Any alleged incident is taken seriously, investigated thoroughly, and (if validated) is accompanied by disciplinary action—possibly including dismissal. Regardless of the investigation outcome, retaliation against an accuser is forbidden not only by Academy policy but also under the law.

We owe it to ourselves, our patients, all members of our professional team, and to ophthalmology itself to always exhibit exemplary behavior and to make all involved feel welcome, comfortable, and respected. The Academy as an organization similarly makes that pledge.

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Robert Wiggins, MD
Chair, Finance Committee and Treasurer
The Value of Education, and the Satisfaction of Giving Back

When I got the phone call from Dr. Parke inviting me to serve as Academy President-Elect in 2017 and Academy President in 2018, I was thrilled and humbled. I am very honored to serve as your president. A member for 30 years, I value the Academy, and I have worked on a great many projects and assumed many roles, from writing for *Focal Points* to serving on the Ethics Committee.

For my presidential term, I have several goals. One is technical: to influence improvement of the ability of ophthalmic equipment to communicate with the electronic medical record. We see equipment with great promise at our meetings, but, often, it can’t “talk” to the other systems that we use to care for patients. If we can promote a common language, as radiology has done, it would be a great accomplishment.

The second goal stems from a core value of mine. One of the mainstays of my career has been educating physicians in training, both at the University of Iowa and through the Academy. This is because I would not be where I am without very good teachers and mentors in my life. My first mentor was the physician who delivered me! He wrote letters of recommendation in my support for my applications to pharmacy school and medical school, and he influenced me to choose academics. I would never have seen numerous trainees mature into successful physicians or had my gratifying experiences at the Academy if it weren’t for the guidance, support, and encouragement of my mentors.

For this reason, I am excited about participating in a new collaborative program with the Association of University Professors of Ophthalmology (AUPO) to attract underrepresented minorities to the profession. We haven’t made significant gains in 30 years in recruiting professionals who reflect the populations that we serve. Part of the challenge is gaining the attention of these young students and securing mentors to guide them through the process. Then, the student needs to be prepared to be a competitive applicant. When competitive students with diverse experiences are in the classroom, this enhances everybody’s education.

Enhancing diversity within ophthalmology is part of giving back to the generations that follow us. Many of the younger generation are less color- or gender-based in their thinking, but efforts still must be made to change the professional landscape.

Giving back is vital—and a pleasure. As I progressed in my own positions, I discovered the joy that comes from seeing a student develop into a well-trained doctor, especially in terms of surgery. Another great pleasure about working with young people is that they constantly challenge you and keep you thinking. They bring excellent ideas—and we need to listen to them. Some of the biggest achievements we’ve seen come from physicians in training. For example, EyeRounds, our department’s online education forum, was originally presented by a resident who saw the vision of the Internet while we were all worrying about the book chapters we’d write. Now, EyeRounds is one of the most-visited ophthalmology websites around the world.

While much practical training and education is now online or increasingly done in simulation labs, the art of medicine can never be fully taught that way. Taking care of patients is passed on from doctor to doctor in real-life settings. Explaining how to alleviate a patient’s fears or how to deliver bad news cannot easily be taught from a book. It’s our role to be there for young ophthalmologists and share our experiences. Many practices recognize this and are asking to have trainees come to their offices for real-world exposure. That may be a bigger part of future training.

I am excited to step into this new role and hope to be seen as a president who values education and diversity and continually promotes the profession, but I can’t be successful without you. The Academy is great because of its many volunteers. If you have interests in education, diversity, technology, or other areas, let us know. Your involvement is welcome and necessary. Let’s get started!
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To avoid the potential for eye injury or contamination of the solution, patients should not touch the tip of the single-use container to their eye or to any surface.

Contact lenses should be removed prior to the administration of Xiidra and may be reinserted 15 minutes following administration.

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

For additional safety information, see accompanying Brief Summary of Safety Information and Full Prescribing Information on Xiidra-ECP.com.
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ADVERSE REACTIONS
Clinical Trials Experience
Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in clinical studies of a drug cannot be directly compared to rates in the clinical trials of another drug and may not reflect the rates observed in practice. In five clinical studies of dry eye disease conducted with lifitegrast ophthalmic solution, 1,401 patients received at least 1 dose of lifitegrast (1,287 of which received lifitegrast 5%). The majority of patients (84%) had ≤3 months of treatment exposure. 170 patients were exposed to lifitegrast for approximately 12 months. The majority of the treated patients were female (77%). The most common adverse reactions reported in 5-25% of patients were instillation site irritation, dysgeusia and reduced visual acuity. Other adverse reactions reported in 1% to 5% of the patients were blurred vision, conjunctival hyperemia, eye irritation, headache, increased lacrimation, eye discharge, eye discomfort, eye pruritus and sinusitis.

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

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

Lactation
There are no data on the presence of lifitegrast in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to lifitegrast from ocular administration is low. The developmental and health benefits of breastfeeding should be considered, along with the mother’s clinical need for Xiidra and any potential adverse effects on the breastfed child from Xiidra.

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

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

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Carcinogenesis: Animal studies have not been conducted to determine the carcinogenic potential of lifitegrast. Mutagenesis: Lifitegrast was not mutagenic in the in vitro Ames assay. Lifitegrast was not clastogenic in the in vivo mouse micronucleus assay. In an in vitro chromosomal aberration assay using mammalian cells (Chinese hamster ovary cells), lifitegrast was positive at the highest concentration tested, without metabolic activation. Impairment of fertility: Lifitegrast administered at intravenous (IV) doses of up to 30 mg/kg/day (5400-fold the human plasma exposure at the recommended human ophthalmic dose (RHOD) of lifitegrast ophthalmic solution, 5%) had no effect on fertility and reproductive performance in male and female treated rats.

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NEURO-OPHTHALMOLOGY

Using the Visual System to Treat Multiple Sclerosis

MULTIPLE SCLEROSIS (MS) IS A DEGENERATIVE INFLAMMATORY DISEASE OF THE CENTRAL NERVOUS SYSTEM (CNS) INVOLVING DESTRUCTION OF MYELIN AND PROGRESSIVE NEUROAXONAL LOSS. TREATMENTS CAPABLE OF REMYELINATION ARE A MAJOR UNMET NEED FOR PATIENTS WITH THE DISEASE. HOWEVER, RESEARCHERS AT THE UNIVERSITY OF CALIFORNIA, SAN FRANCISCO (UCSF), MAY HAVE TAKEN A STEP TOWARD FILLING THAT NEED USING THE VISUAL SYSTEM AND THE OVER-THE-COUNTER ANTIHISTAMINE CLEMASTINE FUMARATE (CLARITIN).1

The study. For this double-blind randomized trial, known as ReBUILD, investigators included 50 patients with relapsing MS and chronic demyelinating optic neuropathy. Patients were randomized into 2 groups: The first received oral clemastine fumarate twice daily for 3 months and then placebo for 2 months, while the second received the placebo for 3 months and the active treatment for 2 months.

The primary outcome measure was shortening of P100 latency delay on full-field visual-evoked potentials. “Visual sensory dysfunction is the first symptom in up to 40% of patients with MS, and injury to the optic nerve is extraordinarily common,” said Ari J. Green, MD, at the UCSF Multiple Sclerosis Center. “It made sense for us to choose the visual pathway for investigation, especially because of the precision of clinical tests available for assessment.”

Possible remyelination? Patients in both groups experienced a reduction in latency delay while on the antihistamine treatment, demonstrating that the drug has a possible remyelinating effect, even after prolonged damage to the CNS.

To Dr. Green, this represents what he termed “a major breakthrough” for drug-induced repair in a chronic neurodegenerative condition. “To our knowledge, this is the first time that a drug has reversed the deficits caused by MS. We aren’t saying it’s a cure, but this is a step toward that direction.”

Importance to ophthalmologists. For Dr. Green, the ReBUILD study demonstrates the value of ophthalmology in treating MS, as there’s also preliminary evidence from the trial suggesting that drug-induced remyelination might extend to improved low-contrast letter acuity in patients with MS. But that might only be the beginning.

“We’ve been taught in the past that the retina and optic nerve are incapable of self-repair; however, we need to develop a more nuanced view acknowledging that there is some capacity for regeneration,” he said. Thus, he said, as clinicians wait for other promising treatments, including stem cell therapy, to bear fruit, “we should harness the eye’s own natural regenerative abilities, utilizing the processes that biology already provides us and manipulating them via specific medications.”

—Mike Mott


Relevant financial disclosures—Dr. Green: NIH: S; National Multiple Sclerosis Society: S; Rachleff Family: S; UCSF: S.
CATARACT

Assessing Retinal Redetachment Risk After Cataract Surgery

IN PATIENTS WHO HAVE HAD SCLERAL buckling surgery to repair a retinal detachment (RD), the risk of a redetachment remains low for up to 10 years after cataract surgery, a population-based Swedish study has found.

“One could easily think that these patients would have a significant increased risk of redetachment, especially considering that they have had 1 RD already. This study found, in contrast to that, a low risk of redetachment, 2.1%,” said Sara Forsell, MD, coauthor of the study.1

Study details. The researchers studied records on all patients who underwent surgery for primary repair of an RD at Norrlands University Hospital in Umeå, Sweden, during a 10-year period (N = 537).

The records showed that 145 of these patients subsequently had phacoemulsification surgery. Up to 10 years after the primary scleral buckling surgery, the cumulative rate of redetachment was 1%. The cumulative rate rose to 5% in the 10 years after cataract surgery, the researchers said. (In eyes with no prior detachment, the incidence of RD after cataract surgery is estimated to range between 0.6% and 1.7% in the first postoperative year, the researchers noted.)

Three redetachments (2.1%) occurred in the study cohort, taking place 2.4 years, 3.9 years, and 6.9 years after the cataract surgery. In all 3 cases, the retinas were successfully reattached with vitrectomy, and the final best-corrected visual acuity was

GLAUCOMA

Gene Editing for POAG Proves Successful in Mice

RESEARCHERS HAVE DEMONSTRATED THE FEASIBILITY of directly targeting and editing a gene mutation in the trabecular meshwork to treat the leading genetic cause of primary open-angle glaucoma (POAG).1 This novel approach delivers a one-two punch that both rescues cell function and prevents further glaucomatous damage—and it has implications for persons with mutations in the myocilin gene (MYOC), which have been reported in some 4% of POAG patients, most notably juveniles.

CRISPR to the rescue. “We found that reduction of myocilin gene and protein lowered intraocular pressure (IOP) and prevented vision loss in a mouse model of myocilin glaucoma,” said cell biologist Gulab Zode, PhD, at North Texas Eye Research Institute in Fort Worth, who conducted the study in collaboration with Val C. Sheffield, MD, PhD, at the University of Iowa in Iowa City.

The rescue mission deployed CRISPR-Cas9 technology, a biological cut-and-paste method that homes in on a gene defect, makes a double cut in the DNA, and then deletes, replaces, or repairs the damaged gene. For this study, the researchers used CRISPR (which stands for Clustered Regularly Interspaced Short Palindromic Repeats) to delete the MYOC gene in mice as well as in cultured trabecular meshwork (TM) cells and human donor eyes.

Building on earlier studies. Previously, the researchers found that mutant myocilin is not secreted into the aqueous humor. Instead, it accumulates in the endoplasmic reticulum (ER) of TM cells. ER stress leads to TM damage, resulting in increased outflow resistance and IOP elevation, Dr. Zode said. “We also found that normal myocilin is not required for regulation of IOP. Therefore, deleting the gene completely works in this case.”

Proof of concept. In the murine portion of this study, the researchers injected the MYOC gene intravitreally with the virus Ad5-crMYOC to halt expression of the mutant gene. In young asymptomatic mice, gene deletion prevented IOP elevation compared with controls. In older mice with MYOC ocular hypertension, treatment lowered pressure.

Treatment also significantly increased outflow facility, demonstrating that disruption of mutant MYOC also improves TM cell function in vivo.

Beyond mice. Although the study also demonstrated feasibility of human genome editing in cultured human eyes, additional research is needed before the treatment can be taken to the clinic, Dr. Zode said. “We hope that it translates in humans, but the main purpose was to demonstrate that genome editing is possible in vivo—and, especially, that human donor eyes can be used to study genome editing.”

—Miriam Karmel

1 Jain A et al. PNAS. 2017;114(42):11199-11204.

Relevant financial disclosures—Dr. Zode: NEI: S.
ONCOLOGY

First U.S. Guidelines for Retinoblastoma Screening

A PANEL OF OPHTHALMIC ONCOLOGISTS, pathologists, and geneticists has published the first set of U.S. screening guidelines for children at risk for retinoblastoma—the most common eye tumor affecting children.1

The goal. The team from the American Association of Ophthalmic Oncologists and Pathologists met over the course of 2 years to identify the key problems and clinical discrepancies in approaching “at-risk” patients—that is, children with a family history of retinoblastoma in a parent, sibling, or first- or second-degree relative. The published consensus report is a consolidation of how to proceed in different scenarios to initially identify and stratify disease risk. It’s at the discretion of the treating team to decide which approach is indicated once the diagnosis is made.

The recommendations. Highlights of the report include the following:

• All children with a family history of retinoblastoma should receive counseling and testing to clarify disease risk.

• The frequency of dilated fundus examination should be stratified on the basis of age and risk. Newborns at high risk, for example, require more frequent examination, every 2 to 4 weeks during their first 2 months of life. Newborns at intermediate or low risk should undergo monthly examination.

• Exam frequency declines as the child grows older, but screening for all at-risk patients should occur up to age 7. For asymptomatic children, no further screening is recommended after this time unless they are known to carry an RB1 mutation. These individuals should be followed indefinitely, every 1 to 2 years.

• All decisions regarding examination method should be discussed with the child’s family. Anesthesia is strongly recommended for any child unable to participate in a thorough in-office exam.

• Examiners should also be aware that tumor location can be age-specific. Newborns may present with tumors in the posterior pole; however, in children who are older at the time of disease development, the tumor may present peripherally.

Multispecialty support. The report has been endorsed by the Academy’s Quality of Care Secretariat as well as several medical organizations.

—Mike Mott


Relevant financial disclosures—Dr. Forsell: None.

Relevant financial disclosures—Dr. Chévez-Barrios: None.

Management Guidelines for Childhood Screening for Retinoblastoma Families

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**Journal Highlights**

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

### Ophthalmology

**Selected by Stephen D. McLeod, MD**

**Treat-and-Extend for Wet AMD Garners More Support**

*January 2018*

Monthly injections of ranibizumab can improve best-corrected visual acuity (BCVA) outcomes in patients with neovascular age-related macular degeneration (AMD), but the frequency of dosing can be inconvenient. Silva *et al.* compared monthly and treat-and-extend (T&E) protocols in patients with wet AMD and concluded that T&E was statistically noninferior and clinically comparable to monthly treatment for improving visual acuity.

This 12-month phase 3 trial was conducted at 90 centers in 18 countries. The main objective was to demonstrate noninferiority of ranibizumab T&E, as measured by change in BCVA from baseline to study endpoint.

Secondary outcome measures were safety, treatment exposure, and changes in retinal central subfield thickness (CSFT).

Patients ≥ 50 years of age (mean age, 75.2 years; 55.4% women; 91.8% white) with newly diagnosed wet AMD were assigned randomly to receive ranibizumab 0.5 mg either according to a T&E regimen (n = 323) or monthly (n = 327). Demographics and baseline ocular characteristics were similar for the study groups.

Approximately 90% of each group completed the study. At 12 months, the least-squares mean BCVA change from baseline reflected improvement of 6.2 letters with T&E and 8.1 letters with the monthly regimen (p < .001 for non-inferiority). Both groups had rapid gains in BCVA, primarily during the first 6 months, which continued throughout the study. Mean changes in CSFT were similar: 169.2 µm in the T&E group and 173.3 µm in the monthly group.

The mean number of ranibizumab injections was lower in the T&E group (8.7, vs. 11.1 for those treated monthly), as was the mean number of post-baseline visits (8.9 and 11.2, respectively). Types and rates of adverse events were similar.

The authors concluded that the T&E approach is not inferior to the monthly regimen. Advantages of T&E include treatment individualization, fewer injections, less-frequent visits, and lower costs.

### Using Art Observation to Improve Medical Students’ Ophthalmology Skills

*January 2018*

Although observation and description are crucial for practicing ophthalmology and other medical specialties, medical education does not include specific training in these areas. Gurwin *et al.* studied the effect of formal training in visual arts on the observation skills of medical students and found that just 6 sessions markedly improved the students’ skills.

This study included 36 first-year medical students who were assigned randomly (1:1) to receive either art education at the Philadelphia Museum of Art or a free membership to the museum. During a 3-month period, the training group participated in 6 customized 1.5-hour sessions. The art educators used the “Artful Thinking” approach, which emphasizes introspection and observation before interpretation.

Before and after the 3-month period, all participants underwent testing, which entailed writing descriptions of works of art, retinal pathology images, and external photographs that depicted eye diseases.

Reviewers graded each description according to an a priori rubric for the type of image presented. Descriptions of works of art were graded by museum educators, while those of retinal and external eye images were graded by 2 ophthalmologists and a fourth-year medical student.

The assessments showed that overall observational skills improved significantly in the training group, and results were similar for each image category. In a follow-up questionnaire, the students trained in art observation stated that they were applying their new knowl-
Predicting Vision-Related Disability for Patients With Glaucoma

January 2018

The results of visual field assessments and self-reported questionnaires can help physicians assess the overall degree of vision-related disability in patients with glaucoma. However, translating the findings from these tools into clinical practice can be challenging. To help classify and analyze changes that occur with glaucoma, Abe et al. developed a novel methodology, which demonstrated that the risk of disability is associated with disease severity at baseline and the rate of deterioration over time. In addition, their method also may help determine how aggressive the treatment must be to slow visual decline and avoid disability.

For this prospective observational study, vision-related quality of life (QoL) was assessed at baseline and the end of follow-up using portions of the 25-item National Eye Institute Visual Function Questionnaire (NEI VFQ-25). A latent transition analysis (LTA) model was used to characterize NEI VFQ-25 results and to evaluate the probability of disability occurrence during follow-up. Standard automated perimetry (SAP) was conducted at 6-month intervals, and mean sensitivity (MS) of the integrated binocular visual field was used to determine rates of change. Predictors of future disability that were investigated included baseline glaucoma severity and rate of visual field loss.

At baseline, 67 (28%) of 236 patients with glaucoma were categorized as disabled and 169 (72%) as nondisabled based on NEI VFQ-25 results. According to the LTA model, nondisabled participants had a 14.2% likelihood of transitioning to the disabled state during follow-up (mean, 4.3 years). Binocular MS data showed that visual field loss occurred nearly 4 times faster in patients who became disabled. With adjustments for age, baseline visual acuity, and follow-up duration, each 1-dB lower baseline binocular MS was associated with 34% higher odds of future disability. Each 0.5-dB/year faster rate of loss of binocular MS increased the risk of developing disability more than 3.5 times.

—Summaries by Lynda Seminara

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Artificial Intelligence Predicts Visual Outcomes in Neovascular AMD

January 2018

Schmidt-Erfurth et al. set out to evaluate the ability of machine learning to predict functional outcomes in patients treated with ranibizumab for neovascular age-related macular degeneration (AMD).

They found that, according to their artificial intelligence (AI) algorithms, best-corrected visual acuity (BCVA) at month 3 was the strongest predictive factor of functional outcomes at the 1-year mark. In addition, they found that currently used morphological features were of limited value in predicting BCVA outcome.

For this post hoc analysis of a clinical trial database, the researchers evaluated data from 614 patients who participated in the HARBOR trial. (During HARBOR, patients received intravitreal injections of ranibizumab monthly or on a pro re nata basis for 12 months; in addition, they were evaluated monthly via spectral-domain optical coherence tomography [SD-OCT] imaging.) The researchers used AI algorithms to first correlate OCT parameters observed at baseline to the corresponding visual function at months 1, 2, and 3 and then to predict the patients’ final BCVA at 1 year.

They found that the correlation between predicted and final 12-month BCVA scores was loose at baseline—but by month 3, individual BCVA levels reached a solid predictive power for month 12.

However, fluid-based morphological features proved to be largely irrelevant for predicting therapeutic response, the researchers said.

The latter finding implies that classic exudative features—such as fluid within and underneath the retina—may be of limited value in explaining visual function in wet AMD and in providing individual patients with a visual prognosis, the authors said, and they added that this should prompt researchers to search for additional markers, such as a disruption of the external limiting membrane. —Summary by Jean Shaw
Neuroretinal rim loss and thinning of the retinal nerve fiber layer (RNFL) are hallmark features of glaucoma. As a result, eyes that deviate from the ISNT rule may need close monitoring for glaucoma—but research findings on the utility of this rule for establishing glaucoma are conflicting. Poon et al. sought to determine the percentage of normal eyes that follow the ISNT rule and found that, contrary to traditional teaching, the rule applies to less than 45% of rim assessments and RNFL measurements.

The authors’ cross-sectional study included 110 normal eyes (110 participants). Neuroretinal rim assessments were made from disc photographs, and measurements of RNFL thickness were obtained from spectral-domain optical coherence tomography. The main outcomes were the percentages of eyes that obeyed the ISNT rule and its variants.

The researchers found that the ISNT rule was valid for only 37% of rim assessments and RNFL measurements. For both types of assessments, variance of the nasal sector from the expected ISNT pattern was a major reason for deviation. Nasal rims were wider than inferior rims in 11% of subjects and wider than superior rims in 29%. Nasal rims were narrower than temporal rims in 15%. RNFL thickness was greater in the nasal quadrant than the temporal quadrant in 43%. Exclusion of the nasal quadrant from the ISNT rule significantly increased validity of the ISNT variants: 71% and 76% of disc photographs followed the IST rule and the IS rule, respectively. For RNFL thickness, 71% and 72% coincided with IST and IS rules, respectively.

As a result of these findings, the authors advocate use of IST and IS rules for distinguishing glaucomatous from nonglaucomatous eyes.

**Corneal Changes in Pregnancy Linked to Fluctuating Thyroid Hormone Levels**

Tabibian et al. documented corneal changes that occur during pregnancy and evaluated their association with simultaneous hormonal changes. They found that the changes they observed correlated with fluctuating thyroid hormone levels rather than altered estradiol levels.

This prospective single-center observational study involved 24 pregnant women (48 eyes). Biomechanical and topographic properties of the cornea were measured with the Ocular Response Analyzer (ORA) and a Scheimpflug imaging system at 4 time points: once during each trimester and 1 month after delivery. During the same 4 visits, the blood plasma level of estradiol (E2) was determined, as were thyroid hormone levels (TSH, T3t, T4t). One-way multivariate analysis of covariance was used to detect interactions between hormonal plasma levels and changes in corneal biomechanical/topographic parameters.

Biomechanical and topographic data for the 4 time points were comparable. Although the level of E2 did not affect corneal parameters, TSH levels affected the maximal keratometry and vertical keratometry readings as well as the index of height asymmetry (these results remained unchanged after excluding patients with hypothyroidism from the analysis). Moreover, differences in corneal biomechanical and topographic parameters were found in relation to T3t and T4t as well as the T3t/T4t ratio.

Further research is needed to determine the potential role of thyroid diseases in the development and progression of corneal disorders, the authors said.

—Summaries by Lynda Seminara

**Prevalence and Features of CPR-Type Diplopia in Epiretinal Membrane**

Veverka et al. sought to determine the prevalence of central-peripheral rivalry (CPR)–type diplopia among patients with epiretinal membrane (ERM) and to describe the common clinical features. They found that CPR-type diplopia is not uncommon in patients with ERM and is linked to greater severity of metamorphopsia.

This study included 31 adults with ERM treated at clinics specializing in retinal disease in addition to a retrospective cohort of 25 adults with ERM treated at strabismus clinics. Diplopia was established by patient history and responses to questionnaires. CPR type was defined as diplopia associated with evidence of retinal misregistration in the absence of other causes of diplopia. Visual acuity (VA) and ocular alignment findings were documented. Metamorphopsia was assessed qualitatively and quantitatively. Aniseikonia was determined by subjective description and the Awaya new aniseikonia test. Testing for retinal misregistration also was performed. Clinical findings of patients with and without CPR-type diplopia were compared to detect differentiating factors.
Among the group of 31 patients, the prevalence of any type of diplopia was 23% (n = 7) and that of CPR-type diplopia was 16% (n = 5). In the entire series of 56 patients, 12 (21%) had CPR-type diplopia, and 37 (66%) had no diplopia. The other 7 had another type of diplopia and were excluded from subsequent analyses.

Relative to patients who did not have CPR-type diplopia, those with the disorder had better VA in their worse eye (mean difference of –0.23; p = .003) and more severe quantitative metamorphopsia (mean M-score difference of 0.6; p = .01). Rates of aniseikonia misregistration were similar for those with and without the disorder.

Although results indicate that patients with CPR-type diplopia generally have better worse-eye acuity and more metamorphopsia than those without the disorder, individual variability is considerable. Coexistence of retinal misregistration and metamorphopsia appears necessary for the development of CPR-type diplopia, but many patients without this diplopia may exhibit those features.

**Generational Differences in AMD Incidence**

*December 2017*

Cruickshanks et al. set out to determine whether the 5-year risk of AMD is changing as longevity increases and found that the risk has declined over time.

For their assessment, the authors obtained longitudinal data from 2 Beaver Dam eye studies in which the 5-year incidence of AMD was measured. A total of 4,819 participants (baseline mean age, 54 years) were at risk for AMD based on findings from the fundus images obtained at baseline. Fundus images were graded for AMD using the Wisconsin age-related maculopathy grading system, and AMD incidence was determined from 5-year follow-up results.

AMD was identified by the presence of pure geographic atrophy, exudative macular degeneration, any type of drusen with pigmented abnormalities, or soft indistinct drusen without pigmentary abnormalities.

The 5-year incidence of AMD, adjusted for age and sex, was 8.8% for those born from 1901-1924, 3% for those born from 1925-1945, 1% for those born 1946-1964, and 0.3% for those born 1965-1984.

Each generation was > 60% less likely to experience AMD than the preceding generation, and this association remained significant after adjusting for age, sex, smoking status, education level, amount of exercise, selected lipid levels, and high-sensitivity C-reactive protein levels, and use/nonuse of non-steroidal anti-inflammatory drugs, statins, and multivitamins.

Although the 5-year risk of AMD declined throughout the 20th century, factors responsible for the decline were not apparent from this study. However, the results do suggest that modifiable factors contribute to the etiology of AMD and that the current epidemic of AMD among the oldest generation may diminish with time. Prospective epidemiologic studies are warranted to confirm the findings. *(Also see related commentary in the same issue by Raphael R. Goldacre, MSc, and Tiaran D.L. Keenan, PhD.)*

**Does Cornea Preservation Time Affect DSAEK Success?**

*December 2017*

Although donor corneas can be preserved in FDA-approved solutions for up to 14 days, many surgeons will not use cornea tissue that has been preserved for more than 7 days. To examine the effect of preservation time on graft success, Rosenwasser et al. compared 3-year outcomes of Descemet stripping automated endothelial keratoplasty (DSAEK) among corneas preserved for varying periods. They found that preservation time of < 12 days was linked to better success rates.

This double-masked randomized trial was conducted at 40 U.S. clinical sites (70 surgeons) from April 2012 to June 2017.

Eligible patients scheduled to undergo DSAEK for Fuchs endothelial corneal dystrophy (94.4% of participants) or pseudophakic or aphakic corneal edema received donor corneas preserved for ≤ 7 days (675 eyes) or 8-14 days (655 eyes). The median participant age was 70 years (range, 42-90 years), and 60.2% were female. Demographics of the study groups were similar.

The 3-year cumulative probability of graft success was 95.3% for donor corneas preserved for ≤ 7 days and 92.1% for those preserved 8-14 days. The upper limit of the 1-sided 95% confidence interval of this difference was 5.4%, which surpassed the noninferiority limit of 4% and was attributed to more primary donor failures in the group with longer preservation time (conditional probability of failure after the first month: 3.1% vs. 2.4%).

A secondary analysis showed that the likelihood of graft success decreased as preservation time increased. The success rate was lower for a period of 12-14 days (89.3%) than for ≤ 4 days (96.5%), 5-7 days (94.9%), or 8-11 days (93.8%).

The comparable success rates attained for corneas that had been preserved for up to 11 days should reassure surgeons. The high 3-year success rates with DSAEK for Fuchs dystrophy, regardless of preservation time, suggest that corneas that have been preserved for a longer time period can be used when necessary.

—Summaries by Lynda Seminara

**Other Journals**

Selected by Deepak P. Edward, MD

**Spironolactone Effective for Acute Central Serous Chorioretinopathy**

*British Journal of Ophthalmology* Published online Oct. 31, 2017

Previous studies have shown the promise of mineralocorticoid-receptor antagonists in the treatment of chronic or recurrent central serous chorioretinopathy (CSC). Building on this premise, Sun et al. studied the efficacy of oral spironolactone among patients with acute CSC and found that, compared with observation alone, the treatment was much more effective and resulted in fast absorption of subretinal fluid (SRF).
For this prospective trial, the authors evaluated 30 patients (30 eyes) with acute CSC. The patients were assigned randomly either to the treatment group (spironolactone 40 mg orally, twice daily for 2 months; n = 18) or to the control group (observation alone; n = 12). Main outcome measures were the proportion of eyes with complete resolution of SRF by 2 months and the changes in central macular thickness (CMT), SRF height, best-corrected visual acuity (BCVA), and subfoveal choroidal thickness (SFCT) during the same period.

By 2 months, complete resolution of SRF had occurred in 10 of the 18 treated eyes and in only 1 of the 12 control eyes. Both groups experienced a significant decline in mean CMT and mean SRF height (p < .05), with significant between-group differences apparent at 2 months (p < .05 and p < .05, respectively). Mean BCVA improved in both groups by 2 months (p < .05). In the treatment group, mean SFCT decreased significantly, from 502.50 ± 87.38 µm at baseline to 427.44 ± 74.37 µm at 2 months (p < .01), whereas the change from baseline in the control group was not significant. Spironolactone did not produce any adverse effects in this study, perhaps because of the short duration of treatment.

Due to the multifactorial nature of CSC, the mineralocorticoid receptor may play a role in some patients but not others. Findings of this study may help to guide early intervention for acute CSC. In addition, the authors suggested that patients with CSC be given a medication guide to treatment of the disease.

Retinal Scanning May Help Detect Alzheimer Disease in Living Patients

JCI Insight 2017;2(16):e93621

Retinal examination may be a noninvasive method of detecting Alzheimer disease (AD). The retinas of deceased patients with AD exhibit myriad retinal pathologies, including the hallmark amyloid-β (Aβ) protein. Koronyo et al., in a proof-of-concept study, demonstrated that such evidence also exists in the retinas of living patients. According to the retinal amyloid index (RAI) developed by the investigators, index scores were more than twice as high for patients with AD than in cognitively normal controls.

The authors first examined the burden, distribution, cellular layer, and structure of retinal Aβ plaques in donor tissue (eyes and brain) of patients with definitive AD (n = 23) and cognitively normal controls (n = 14). An amyloid probe curcumin formulation was derived from histologic findings, and a protocol for retinal amyloid imaging was established and applied to living patients (10 with AD, 6 healthy controls).

Histologic examination showed that patients with AD had classic and neuritic-like Aβ deposits, with increased retinal Aβ42 plaques (4.7-fold; p = .0063) and neuronal loss (p = .0023) relative to matched controls. The retinal Aβ plaque presentation mirrored brain pathology, particularly in the primary visual cortex. Retinal deposits often were associated with blood vessels and occurred in hot-spot peripheral regions of the superior quadrant and innermost layer of the retina. Transmission electron microscopy showed the assembly of retinal Aβ into protofibrils and fibrils.

The authors then demonstrated the ability to image retinal amyloid deposits with solid-lipid curcumin and a modified scanning laser ophthalmoscope in living patients. A fully automated calculation of the RAI, a quantitative measure of increased curcumin fluorescence, was devised. Analysis of RAI scores showed that scores for patients with AD were 2.1 times higher than those of controls.

The geometric distribution and increased burden of retinal amyloid pathology in AD, coupled with the feasibility to noninvasively detect retinal amyloid deposits in living patients, may lead to a practical approach for large-scale diagnosis and monitoring of AD. Such imaging technology may prove to be sensitive and inexpensive for screening people at risk for AD.

—Summaries by Lynda Seminara
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Primary iris cysts originate in the iris pigment epithelium or iris stroma, and secondary iris cysts are stimulated by outside factors. Most of these cysts are quite rare, but some can cause visual problems, requiring treatment. In addition, differential diagnosis is crucial to rule out more serious problems, mainly malignancies.

Types of Iris Cysts
Although iris cysts are relatively rare, the following are more commonly seen.

Iris pigment epithelium cysts. The most common type of iris cyst, iris pigment epithelium cysts tend to show up on routine examinations because they are asymptomatic and rarely cause visual problems, said Prithvi Mruthyunjaya, MD, MHS, at Stanford University in Palo Alto, California. Although these cysts are typically referred to the ocular oncologist as a single iris mass of unknown origin, he said, they are often multifocal and bilateral.

Located underneath the iris, these cysts push the iris forward, creating a dome-shaped surface, said Zélia M. Corrêa, MD, PhD, at the University of Cincinnati. They may be midzonal, right in the middle of the iris leaflet, but also can be located at the inner or outer edges of the iris, near the pupil or ciliary body, potentially making them a diagnostic challenge. In some cases, these cysts may also detach from the iris and float freely in the anterior chamber or vitreous. They are translucent with speckles of light brown and are usually benign, said Dr. Mruthyunjaya.

Stromal cysts. Arising from the front part of the iris, stromal cysts tend to be translucent-white and can more readily deform the structure of the iris itself than iris pigment epithelium cysts do, said Dr. Mruthyunjaya. “This cyst can be confused for an iris melanoma, especially if it is strongly pigmented, making it look like a nodule.”

Epithelial downgrowth cysts. Following trauma—from either surgery or injury—epithelial cells may be transmitted from the outside of the eye to the inside, or cells inside the eye may transdifferentiate into epithelial cells, said Michael E. Snyder, MD, at Cincinnati Eye Institute.

“When surface epithelial cells get inside the eye, they do not behave nicely,” he said. “If they start forming an iris cyst, they are unlikely to cause immediate sight-impairing complications as long as they remain encased. But if they break or start growing into important structures of the eye, they can, rarely, cause fairly profound vision loss and sometimes loss of the eyeball itself.” In children younger than age 10, he added, these cysts can cover the pupil space, leading to amblyopia.

Because they grow toward the inside of the eye, Dr. Corrêa prefers to call them epithelial ingrowth—rather than downgrowth—cysts. “Although they may start developing years after the initial trauma,” she said, “they are very aggressive and can grow quickly, almost
Confounding a Cyst Diagnosis

“I want to be able to properly identify the location and origins of a cyst,” said Dr. Mruthyunjaya. “That will involve a thorough history; complete examination, including a gonioscopy and examination of the anterior segment; and imaging. Sometimes looking at both eyes also provides clues about the etiology of the cyst.”

In the case of a suspected downgrowth cyst, he added, confirming etiology might also involve looking for surgical wounds or previous operative notes.

Don’t overlook history. “Curious and peculiar stories have underscored the importance of history-taking for me,” said Dr. Corrêa. She recounted the story of a civil engineer who felt “a slight snag” in his eye while overseeing the paving of a road. A tiny piece of gravel had lodged in his iris, but it didn’t raise red flags until months later when his vision became blurry from a developing cyst. Complicating matters, said Dr. Corrêa, the cyst looked like a tumor because the gravel was dark in color.

Dr. Snyder mentioned another instance in which history-taking is critical: Ask patients if they have traveled to other parts of the world where parasites are endemic; they may have experienced a parasitic infection. “Parasites that travel to the eye, such as Cycstercus cellulosae, can cause cysts that can be quite dangerous. If you inadvertently open the cyst and expose the parasite to the eye, it can die, causing a significant inflammatory response.”

Other questions to ask. Dr. Corrêa counsels colleagues to take time to talk with the patient and ask questions like these: How long have you been aware of the cyst? How long has it been since your last ophthalmology visit? What kind of exam did you receive? Did you have your pupils dilated?

If a cyst appears suddenly, said Dr. Mruthyunjaya, it’s worth asking whether the patient is on prostaglandin analogs, which can affect cyst size. Alert the doctor in charge of monitoring the eyedrops, especially if the cyst has become quite large.

Imaging. To rule out other problems and diagnose an iris cyst, ophthalmologists may use either anterior segment OCT or high-resolution ultrasound biomicroscopy (UBM), said Dr. Corrêa. “As long as you scan the whole cyst and have a good enough image of the lesion, you’re in great shape,” she said, adding that each diagnostic modality has its advantages.

Advantages of OCT. Anterior segment OCT may identify small cystic structures, giving early confirmation of diagnosis. However, it does have limitations. For example, in patients with dark irides, the OCT signal may become attenuated, said Dr. Mruthyunjaya. Also, the pigmentation or size of the cyst may prevent ideal resolution, he said. “But I’ve been impressed with the ability to penetrate even small cysts,” he said, adding that repeatedly scanning the same area also provides a useful way to follow up on a cyst’s growth over time. OCT also has the advantage of no contact with the patient’s eye, said Dr. Corrêa, which can be especially helpful for younger patients.

Although Dr. Mruthyunjaya finds OCT helpful in imaging peripheral cysts, Dr. Corrêa warned that it may not be possible to see the full extent of these cysts with OCT, especially if they are large.

Advantages of ultrasound. High-resolution ultrasound of the anterior segment provides a very good view, allowing you to visualize thin walls and hollow cavities, indicating a fluid-filled cyst, versus the solid nature of a malignancy, said Dr. Snyder. In addition to looking at the quadrant of the suspected cyst, Dr. Mruthyunjaya’s initial evaluation involves a scanning protocol around the peripheral part of the iris and ciliary body—as well as the other eye. “It’s striking how often you will find tiny cysts in multiple locations that weren’t detected clinically.”

Dr. Corrêa also uses UBM for surgical planning. “It’s easier to turn the probe around and get a feel for the extent of the cyst and consistency of the tissue.” Those who lack experience with UBM should consider referring this out, she said.

What’s next? If you see a lesion with a solid component, you might confirm this with magnetic resonance imaging, said Dr. Corrêa, and even biopsy for confirmation of malignancy.
When Treatment Is Needed
In most cases, Dr. Corrêa simply observes iris pigment epithelial and stromal cysts.

Conditions dictate choices. However, said Dr. Corrêa, treatment may be needed if there are other problems such as increasing eye pressure or multiple cysts occluding the angle. Consider other conditions as well, said Dr. Mruthyunjaya: Is there an incomplete wound involved in epithelial downgrowth that you need to address? What is the size of the cyst and its velocity of growth? Is it intermittently leaking and causing inflammation? Is it rubbing against ocular structures such as the lens or the cornea, causing secondary problems?

Treat it like a tumor? Dr. Snyder said it is most effective to treat epithelial downgrowth cysts as though they are tumors, as they cause unrestricted growth of cells where they don’t belong. “Sometimes, treatment’s one and done,” said Dr. Mruthyunjaya, “but sometimes it requires multiple attempts at controlling the cyst. In other cases, reduction is good enough. Regardless, you need to watch them closely.”

What to consider beforehand. You can use a variety of options to treat epithelial downgrowth cysts. “But whatever you do with these cysts,” said Dr. Corrêa, “you must remove every little bit of abnormal epithelium from the anterior chamber, or the cyst may recur, proliferate rapidly, and cause a lot of damage inside the eye.” Before any procedure, ensure that imaging has revealed the full extent, size, and location of the cyst, she said, so you can approach it the right way.

Excision. To cause less collateral damage, Dr. Mruthyunjaya prefers excising these cysts when they are small. Dr. Snyder recommends a partial lamellar iridocorneal trabeculectomy—removing the internal eye wall and the areas the cyst is touching—to avoid rupturing or breaking the wall of the cyst. “If this procedure creates a serious iris defect,” he said, “it often causes glare or light sensitivity. If it is not possible to surgically close the area that’s been removed, an artificial iris may be needed.”

Drainage and injection. Dr. Corrêa also likes to treat ingrowth cysts by using a needle to drain the cyst, inject alcohol inside it, and then deflate the cyst. “In case there is any sign of residual epithelium on the surface of the iris, I use an endolaser probe to treat the area and make sure any epithelial cells are destroyed.”

To minimize the chances of leaving cells behind, Dr. Mruthyunjaya recommended avoiding going through the open aqueous humor and anterior chamber. “Try to go through the back or more peripheral part of the cyst. Consequently, if there’s anything that’s being released when you pull in and out of the eye, it’s coming right out of the eye with your needle.”

Dr. Mruthyunjaya also uses fluorescein eye stain to make sure the alcohol is contained within the cyst and not accidentally instilled into the anterior chamber, where it can be very toxic. Filling the eye with Healon viscoelastic also acts as a diffusion barrier for the alcohol, he said, but the viscoelastic must be thoroughly removed after the procedure.

Cryotherapy. Following drainage and injection, Dr. Mruthyunjaya then uses cryotherapy at the edge of the track by the limbus to sterilize any cells that may be remaining. Sometimes it is possible to freeze an entire cyst if it is tiny and located peripherally, right at the edge of the cornea at the limbus, added Dr. Snyder.

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Outer Retinal Tubulation: Sign of Neurodegeneration

If you use high-resolution imaging to guide treatment of retinal diseases, the most important thing to know about outer retinal tubulation (ORT) structures is that they commonly appear in cross-sectional images as features that look somewhat like intraretinal cysts—but aren’t.

The tubular structures in ORT-affected eyes appear on high-resolution, spectral-domain ocular coherence tomography (SD-OCT) B-scans as well-defined circular or ovoid areas of hyporeflectivity, surrounded by a hyperreflective band, said K. Bailey Freund, MD, who coauthored the first clinical description of ORT.

“If you did not know that these lesions existed, particularly if you were using the older time-domain OCT devices, you could easily confuse them with cysts or subretinal fluid,” said Dr. Freund, who practices in New York City. “And if you were using a treatment regimen that was guided by presence or absence of fluid, you could end up giving intravitreal injections to an eye that really didn’t need them.”

**Many Roads Lead to ORT**

Despite this narrow clinical utility, ORT has garnered increasing attention over the last several years because of the realization that tubulations in the outer nuclear layer represent a common neurodegenerative pathway in a variety of retinal diseases. These include neovascular age-related macular degeneration (AMD); geographic atrophy (GA) secondary to AMD and other disorders; inherited retinal diseases, particularly choroideremia; and mitochondrial diseases.

**Prognostic value.** In all of these conditions, the presence of ORT structures indicates disorganized outer retinal layers, irreversible photoreceptor damage, and a worse visual prognosis, Dr. Freund said. “Most people would consider ORT a sign that, at least in that one particular area of the macula, you’re not going to be able to recover visual function,” he said.

A better understanding of the ORT process eventually might yield clues about how to stop photoreceptors from dying, said Glenn J. Jaffe, MD, at Duke Eye Center in Durham, North Carolina. In treatment trials, a biomarker like ORT might prove valuable for excluding prospective participants unlikely to regain vision, he said.

“The hope would be that we could help preserve people’s vision if we can prevent the degeneration of the photoreceptors,” Dr. Jaffe said. “Whether it’s with a neurotrophic agent or some other type of treatment, we are becoming more aware that we need to be able to prevent the loss of the photoreceptors in these diseases.”

**RETINA CLINICAL UPDATE**

BY LINDA ROACH, CONTRIBUTING WRITER. INTERVIEWING CHRISTINE A. CURCIO, PHD, K. BAILEY FREUND, MD, AND GLENN J. JAFFE, MD.
Clues from CATT. Dr. Jaffe said he became interested in ORT because of what he observed during the Comparison Age-related Macular Degeneration Treatment Trials (CATT). “We were the OCT reading center for CATT, and while we were looking at the images I started to notice that ORT [structures] were becoming more frequent as the study went on. So we looked at the percentages and found that by 5 years, about 1 in 5 patients had this characteristic appearance,” Dr. Jaffe said.

Genesis of Tubulation
The tubules characteristic of ORT are the retina’s heroic yet last-ditch attempt to protect localized areas of macular cone photoreceptors from the failure of the underlying retinal pigment epithelium (RPE), said Christine A. Curcio, PhD, at the University of Alabama at Birmingham.

“What ORT lesions have in common with each other is that the RPE is dying or is gone. These are responses of retina cells to the extreme stress of this detachment,” Dr. Curcio said.

In 1996, her research group published the first histological descriptions of photoreceptors surviving in mysterious interconnected tubes in the maculas of eyes with neovascular AMD. It wasn’t until 2009 that Dr. Freund and his colleagues, using SD-OCT images, published the first clinically oriented paper about “a peculiar outer retinal morphologic change occurring in a variety of advanced degenerative retinal disorders.”

Since those publications, Drs. Curcio and Freund have worked together to correlate high-resolution histopathology in donor eyes with eye-tracked OCT images of living eyes, in order to understand the ORT process.

Gliosis implicated. Their overall conclusion: Tubulation is a protective gliotic response—ultimately futile—triggered by activated Müller cells, Dr. Curcio said. “The Müller cells are trying to take care of the remaining photoreceptor cells. They are protecting them from the failure of the RPE and all the problems in the RPE/Bruch membrane complex.”

Dr. Freund agreed. “It’s the Müller cells that are driving this process, and in the very late stage of tubulation you only have Müller cells and no surviving cones,” he said.

Rolling up the photoreceptors. As described recently by Dolz-Marco et al., ORT occurs when the external limiting membrane (ELM), which is normally a thin horizontal reflective line made by Müller cells and photoreceptors, begins “circling the wagons.” The ELM descends toward Bruch membrane and gradually begins scrolling the at-risk photoreceptors into a tubular structure. Depending on the stage of development, the outer band can appear in cross-section as flat, J-shaped, or partially (or fully) curved back on itself.

Both the inner and outer segments of the scrolled photoreceptors initially point radially into the lumen delineated by the ELM, and these can be seen clinically as a reflective fringe around the hyporeflective lumen (dark on the OCT).

As ORT progresses, the lumen becomes uniformly hyporeflective as the outer segments degenerate and the inner segments are pulled back across the ELM. Remnants of the numerous mitochondria in the inner segments migrate into the cell body of the degenerating cells, accounting for the reflectivity of the outer band of ORT.

In their study of 38 eyes with pre-existing ORT, Dolz-Marco et al. found that the mean time for new tubules to form was 14.9 months.2 It is unknown how long the end-stage ORT lesions persist in the retina, but in clinical experience they commonly are stable through at least 3 years of follow-up.

Serpentine patterns on OCT. En face OCT scans of ORT-affected maculas reveal the tubules snaking in various patterns across the retina. “A branching or pseudodendritic pattern is observed mainly in association with neovascularization, whereas a singular tube may line the border of GA. Interestingly, analysis of ORT over time has shown fluctuations in ORT volume in cross-sectional SD-OCT scans, even while the ORT footprint seen with en face imaging remains constant,” Dolz-Marco et al. wrote.

What about GA? In a subgroup of affected patients in the Geographic Atrophy Treatment Evaluation (GATE) trial, ORT was present in 65% of eyes in the atrophic region and in 26% of eyes in the junctional zone. But there is disagreement over what this means, Dr. Jaffe said.

“It’s a little bit unclear” as to how well the presence of ORT predicts GA progression, he said. “In one of the publications that we’ve done, we found that it was associated with more rapid progression. But at least one other group [led by SriniVas Sadda, MD, at the University of Southern California] has reported not seeing that.”

Attention to the different stages of ORT, which were not appreciated at the time of these prior studies, might help solve this discrepancy in future studies, Dr. Freund’s group suggested.
Diagnosis and Management of Central Retinal Vein Occlusion

Retinal vein occlusion (RVO) has a prevalence of 0.5%, making it the second-most common retinal vascular disorder after diabetic retinopathy. RVO is classified according to the anatomic level of the occlusion, with 3 major distinct entities:

- Central retinal vein occlusion (CRVO): occlusion of the central retinal vein at the level of, or posterior to, the lamina cribrosa (Fig. 1)
- Hemiretinal vein occlusion (HRVO): occlusion at the disc, involving either the superior or inferior hemiretina
- Branch retinal vein occlusion (BRVO): occlusion of a tributary vein, typically at the site of an arteriovenous crossing; thought to be caused by compression from an overlying atherosclerotic arteriole

This article will focus on diagnosis and management of the first entity, CRVO.

Risk Factors
Systemic disorders. Systemic risk factors for CRVO include increasing age, diabetes mellitus, and hypertension. In selected cases, hypercoagulable states, including hyperhomocysteinemia and factor V Leiden mutation, or local vessel factors such as vasculitis are also associated with increased risk of CRVO. The literature also contains case reports of many other systemic conditions possibly associated with the development of CRVO.

Ocular conditions. Open-angle glaucoma is a major ocular risk factor for CRVO.

In addition, individuals with CRVO in 1 eye are at higher risk of developing CRVO in the fellow eye. In the Central Vein Occlusion Study (CVOS), 4% of patients presented with bilateral CRVO at study enrollment, and a further 5% had evidence of previous CRVO in the fellow eye at baseline. In the remaining subjects, 1.4% developed CRVO in the fellow eye during 3 years of follow-up.

Other ocular risk factors include retrobulbar external compression of the central retinal vein, as occurs in thyroid orbitopathy, or compression by intraorbital space-occupying lesions.

Clinical Presentation
Patients with CRVO typically present with a history of unilateral acute, painless visual loss. Visual impairment may be severe, ranging from better than 20/40 to worse than 20/200. A relative afferent pupillary defect may be present in the affected eye.

Fundus findings. Dilated fundus examination reveals unilateral disc swelling with peripapillary intraretinal hemorrhages, dilated tortuous veins, and intraretinal dot, blot, and flame hemorrhages in all quadrants, resulting in the classic “blood and thunder” fundus appearance (Fig. 1). The macula may be edematous.

In less severe cases, disc swelling may be absent. In subacute or late presentations in which disc swelling has resolved (with or without collateral vessel formation), the flame-shaped hemorrhages clear first, leaving deeper dot/blot hemorrhages that may be difficult to distinguish from a severe microangiopathic retinopathy such as diabetic retinopathy (Fig. 2). Fluorescein angiography (FA) may help to confirm the diagnosis of CRVO.

Other key aspects. As part of the examination, the clinician should note the intraocular pressure and cup-to-disc ratio, which may suggest concurrent glaucoma, as well as any sequelae, such as rubeosis iridis. Undilated gonioscopic examination is important to rule out neovascularization of the angles.

Types of CRVO
Clinically, CRVO may be divided into 2 major subtypes: ischemic and nonischemic.
**Ischemic.** The CVOS investigators defined ischemic CRVO as evidence of more than 10 disc areas of capillary nonperfusion on 7-field fundus FA (although investigators are reassessing this definition in light of recent advances in widefield angiography).

Ischemic CRVO may be identified by the following characteristics:
- Poor visual acuity (>90% had VA of <20/200)
- Presence of a relative afferent pupillary defect in the affected eye
- Presence of extensive dark, deep intraretinal hemorrhages
- Presence of multiple cotton-wool spots
- Greater than 10 disc areas of retinal capillary nonperfusion on 7-field FA
- Reduced b-wave amplitude, reduced b:a ratio, and prolonged b-wave implicit time on electroretinography

In ischemic CRVO, visual acuity remains poor, often decreasing further over time. Causes of visual loss include chronic macular edema, macular ischemia, peripheral/global ischemia with secondary vitreous hemorrhage, and neovascular glaucoma.

Approximately 23% of eyes with ischemic CRVO develop iris neovascularization over 15 months; in the CVOS, 44% of eyes that presented with vision worse than 20/200 subsequently developed iris neovascularization. Some patients may develop retinal neovascularization.

**Nonischemic.** In the CVOS, 34% of eyes that initially presented with nonischemic CRVO underwent conversion to an ischemic perfusion status over 3 years; conversion is heralded by rapid visual deterioration in the affected eye. Sudden decrease in visual acuity

in a patient with existing nonischemic CRVO should, therefore, prompt further assessment for development of ischemic CRVO.

Of the eyes that remained nonischemic, approximately 30% showed resolution of macular edema within 15 months. Occurrence of subsequent neovascular complications is rare in nonischemic eyes.

**Workup**
A thorough initial workup can provide useful information to guide clinical decision making.

**Optical coherence tomography.** OCT is useful to confirm and quantify the severity of macular edema, assess the integrity of the ellipsoid zone/photoceptor layers, and monitor response to treatment. In clinical practice, OCT measurements often guide treatment decisions.

**Fluorescein angiography.** Features of CRVO on FA include delayed arm-to-retina time, prolonged arteriovenous transit time (markedly so in ischemic CRVO), late staining along vessel walls, capillary dropout with pruning of the vessels in areas of ischemia, and late leakage in a petaloid pattern in the presence of macular edema (Fig. 3).

Clinically, FA allows evaluation of the extent of capillary nonperfusion and the degree of macular ischemia and enables differentiation between collateral vessels and new vessels.

**Systemic.** Systemic evaluation is often performed in patients with CRVO and is directed by the patient’s age, coexisting risk factors, and medical history. Assessment should be performed in conjunction with an internist, as patients with RVO may be at higher risk of cardiovascular disease and cerebrovascular accidents.

There are no clear guidelines on systemic testing, but it generally begins with a dilated fundoscopic examination in clinic, along with a detailed medical history to identify risk factors; further assessment includes blood pressure and serum glucose, complete blood count, and erythrocyte sedimentation rate. In young patients without clear risk factors, additional testing should be considered to exclude a hematologic or vasculitic etiology.

**Treatment**
All patients should optimize control of systemic risk factors, with the help of their internist. Management of the ocular manifestations may be divided into the following areas.

**Macular edema.** Both laser and medical therapies have been used in the treatment of macular edema.

**Laser.** Studies assessing grid-pattern laser photocoagulation for treatment of macular edema in CRVO showed anatomic improvement without improvement in visual acuity. Anti–vascular endothelial growth factor. Intravitreal anti-VEGF therapy is currently the gold standard of treatment for macular edema associated
FLUORESCEN FINDINGS. FA at 4 time points shows (3A) masking from intraretinal hemorrhages, (3B) delayed arteriovenous transit time, (3C) leakage at the swollen optic disc, and (3D) late staining of the vessel walls.

with CRVO. There is increasing evidence that anti-VEGF therapy results in lower risk of visual loss, higher rates of visual gains, greater reduction in central retinal thickness, and reduced risk of progression to iris neovascularization.

For example, the CRUISE study reported that intravitreal ranibizumab significantly improved best-corrected visual acuity (BCVA) at 6 and 12 months compared with sham injections. In the open-label extension HORIZON trial, the eyes initially treated with sham and subsequently treated with ranibizumab showed improvement in BCVA but did not catch up to the visual outcomes attained by the group that received ranibizumab at enrollment. This finding suggests that delaying treatment for macular edema has adverse effects on visual outcomes.

Aflibercept, a VEGF-trap molecule, has also been shown to improve BCVA compared with sham and laser treatment in the COPERNICUS and GALILEO trials.

More recently, SCORE2, a randomized noninferiority trial including eyes with CRVO or HRVO, demonstrated that bevacizumab was noninferior to aflibercept in terms of visual acuity gain at month 6 compared to baseline (mean improvement of 18.6 vs. 18.9 ETDRS letters, respectively).3

Corticosteroids. Corticosteroids reduce retinal capillary permeability and inhibit the expression and metabolic pathway of VEGF. The SCORE-CRVO trial demonstrated that intravitreal triamcinolone acetonide was superior to observation for visual loss associated with CRVO–related macular edema. The GENEVA trial evaluated the use of a sustained-release intravitreal dexamethasone implant (Ozurdex) and demonstrated improvements in visual acuity and macular thickness compared with both sham and laser-treated groups.

More recently, the Clinical Efficacy and Safety of Ranibizumab Versus Dexamethasone for Central Retinal Vein Occlusion (COMRADE C) trial compared intravitreal ranibizumab 0.5 mg (monthly for at least 3 months, followed by as-needed dosing) to a single injection of Ozurdex. This trial reported similar efficacy between ranibizumab and Ozurdex but found a higher incidence of adverse effects in the group receiving Ozurdex.

Retinal ischemia. Current evidence recommends regular monitoring of patients with ischemic CRVO for development of iris or angle neovascularization, for which panretinal laser photocoagulation (PRP) remains the mainstay of treatment.

There is currently no evidence to recommend prophylactic treatment prior to the development of new vessels. However, in circumstances where regular follow-up is impractical and the degree of ischemia is severe (high risk of progression to neovascularization), prophylactic PRP may be appropriate.

Anti-VEGF agents are antiangiogenic and may be useful adjuncts to PRP in the management of patients with CRVO and associated anterior segment neovascularization, particularly when the view of the fundus is not sufficiently clear to permit adequate PRP.

Venous outflow. A number of alternative therapies focused on improving retinal blood flow have been described. These include the use of antiplatelet agents (e.g., ticlopidine),4 hemodilution,5 and thrombolytic agents delivered systemically, intravitreally, or directly into a retinal vein during pars plana vitrectomy.

Techniques to alleviate a possible compartment syndrome, with optic nerve sheath decompression through an orbital approach or radial optic neurectomy via a pars plana approach, have been tried. However, these are no longer used because of their limited benefit and significant risks.

Creation of a laser chorioretinal venous anastomosis (L-CRA) to bypass the occluded central retinal vein has been reported to be beneficial in nonischemic CRVO, with improvement in visual acuity and reduced rates of ischemic progression, but less so in eyes with the ischemic type of disease. The failure of anastomosis was most likely due to endothelial cell damage secondary to ischemia.7


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The Case of Aches and Pains and Blurry Vision

Becky Brown*, a 28-year-old Caucasian woman, was doing well until about 2 weeks prior to presentation, when she felt as if she had the flu, complete with headaches and joint pain. A few days later, she noted that her eyes were red, painful, and highly sensitive to light. Her vision was also becoming blurred. Very worried about her symptoms, Ms. Brown sought medical help.

We Get a Look
Prior to evaluation by our vitreoretinal service, Ms. Brown had been treated by a primary care provider with oral methylprednisolone. By the time she came to our clinic, her arthralgia had resolved with steroid treatment, but her headaches and blurred vision persisted. She did not have any other significant ocular or medical history.

**Exam findings.** On presentation, Ms. Brown’s visual acuity was 20/40 in the right eye and 20/80 in the left eye. Intraocular pressure was 13 mm Hg in each eye. Her pupils were equal, round, and reactive, with no afferent pupillary defect. She had full ocular motility bilaterally.

We observed conjunctival injection in both eyes. Slit-lamp exam showed fine, diffuse keratic precipitates, as well as 2+ cells and fibrin in the anterior chamber. Trace anterior vitreous cells were also noted.

**Fundus lesions.** Dilated fundus exam revealed optic disc hyperemia with obscured borders. Multiple creamy, yellow-white placoid lesions were visible in the posterior pole adjacent to the superior and inferior arcades, with extension into the central macula. The lesions appeared to be at the level of deep retina and the retinal pigment epithelium (Fig. 1). The peripheral retina appeared normal.

**Imaging.** To augment the exam findings, we obtained the following imaging studies.

**Optical coherence tomography.** OCT demonstrated multiple hyper-reflective discrete areas at the level of
the outer nuclear layer and ellipsoid band, with attenuation of the normal retinal architecture (Fig. 2; see also online Figs. 2A-2D).

**Fundus autofluorescence.** FAF showed diffuse areas of hyperfluorescence corresponding to the lesions in the posterior pole and some mottled areas of hypofluorescence (see online Fig. 3).

**Fluorescein angiography.** FA revealed hypofluorescence or blockage corresponding to areas of the lesions in the early phase, followed by hyperfluorescence in the late phase consistent with staining (Fig. 3A; see also online Fig. 4).

**Indocyanine green angiography.** ICGA disclosed confluent areas of hypofluorescence in the posterior pole and midperiphery in both the early and late stages. On ICGA, the lesions were found to be more numerous than what was apparent on examination or FA, especially in the midperiphery (Fig. 3B; see also online Fig. 4).

**Making the Diagnosis**

Based on the history, exam, and imaging findings, our working diagnosis was acute posterior multifocal placoid pigment epitheliopathy (APMPPE). The creamy, yellow-white placoid retinal lesions we noted in Ms. Brown are characteristic funduscopic findings; similarly, the early-phase blockage or hypofluorescence followed by diffuse late staining in the same areas are typical of APMPPE.

However, her fundus appearance also raised the possibility of serpiginous choroiditis or serpiginous-like choroidopathy associated with tuberculosis. Thus, we ordered a Quantiferon-TB Gold test, which was negative, ruling out the alternative diagnosis.

**Discussion**

APMPPE, one of the white dot syndromes, was first described by Gass in 1968. It is an acute-onset bilateral disease with characteristic findings of multiple yellow-white patches of chorioretinal inflammation in the posterior pole. The mean age of onset is 27 years, with 85% of cases occurring in patients 16 to 40 years of age. APMPPE is considered to be rare, and the true incidence and prevalence are unknown.

**Pathogenesis.** Although the etiology of APMPPE is unclear, up to one-third of patients experience a viral prodrome before the onset of ocular symptoms. The pathogenesis is thought to be obstruction of choriocapillary lobules, possibly as an inflammatory reaction to a viral infection. Alternatively, APMPPE may be a primary disease of the retinal pigment epithelium itself.

**Systemic symptoms and complications.** APMPPE is a vasculitis that is often accompanied by a viral prodrome, and systemic manifestations may include headaches, flulike symptoms, erythema nodosum, arthralgias, and myalgias.

Neurologic symptoms such as headaches, transient aphasia, paresthesias, and muscular weakness may be associated with cerebral vasculitis and require further evaluation. Thomas et al. reviewed 18 patients diagnosed with APMPPE; of these, 11 patients (61%) had neurologic symptoms, with the most common being headache (9 patients). Stroke due to cerebral vasculitis was the most severe complication.

Although there is no sexual predilection for APMPPE per se, the majority of cerebral vasculitis cases occur in men.

**What About Our Patient’s Headaches?**

Ms. Brown’s symptoms of headaches along with ocular findings consistent with APMPPE were concerning for cerebral vasculitis, and we recommended urgent neurology consultation. She underwent extensive testing with neuroimaging, including conventional and computed tomography angiography, which did not demonstrate any evidence of cerebral vasculitis.

**Further studies.** Examination of her cerebrospinal fluid (CSF) found no evidence of herpes simplex virus, varicella-zoster virus, or cytomegalovirus infection.

Direct antigen testing of the CSF was also performed, and the results were negative for *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Neisseria meningitidis*.

In addition, the following laboratory studies were ordered as part of her neurology evaluation: rapid plasma reagin (RPR) and fluorescent treponemal antibody absorption (FTA-ABS) tests for syphilis, Quantiferon-TB Gold, and Lyme disease antibody testing. All were negative.

**Treatment**

APMPPE is typically a self-limited condition. No particular therapy has proved to be beneficial, although some patients with severe ocular inflammation or signs and symptoms of cerebral vasculitis are treated with systemic corticosteroids.

The chorioretinal lesions may begin to resolve in 1 to 2 weeks even without treatment. Visual prognosis is usually good, and patients can expect improvement in visual acuity in the long term;
however, visual recovery is often incomplete.³

Our patient’s course. Ms. Brown was started on topical prednisolone acetate 6 times per day and atropine twice a day for the anterior chamber inflammation.

Treatment with systemic corticosteroids was deferred until she completed evaluation for cerebral vasculitis, which was negative. We decided to initiate treatment with systemic steroids because of Ms. Brown’s persistent ocular inflammation and lack of visual improvement. She was treated with a course of 60 mg of oral prednisone daily for 10 days, which was then tapered weekly over 4 weeks.

Follow-up
After 1 month of treatment, Ms. Brown’s visual acuity had improved to 20/20 in the right eye and 20/40 in the left eye. Fundus exam showed pigmentary changes in area of the yellow-white placoid lesions (see online Fig. 5), which were better seen by FAF. The lesions, as seen on OCT, improved with restoration of near-normal retinal architecture (see online Fig. 6).

*Patient name is fictitious.


Dr. Chaleff is a first-year transitional resident, Dr. Patel is a second-year ophthalmology resident, and Dr. Bhaleeya is a professor of ophthalmology; all are at the University of South Florida Eye Institute, Morsani College of Medicine, in Tampa. Relevant financial disclosures: None.
Volunteer ophthalmologists are ramping up the fight against eye disease by building capacity in communities around the world. Here’s how you can help.

By Mike Mott, Contributing Writer

Volunteering abroad is undergoing a sea change. Gone are the days of simply flying overseas to an under-resourced community, performing hundreds of cataract surgeries, and returning home to your practice. Most communities now have their own health systems in place with local physicians who can perform procedures at a lower cost than in the past.

Rethinking the Rationale
Instead of “delivering care,” the buzzword in medical volunteerism is now “building capacity.”

Magnify your impact. “Given the cataract backlog in the world today, we are more than 100 years from eradicating this cause of blindness if we simply rely on delivery of care,” said Jeff H. Pettey, MD, at the University of Utah in Salt Lake City. “Yes, performing cataract surgeries will impact individuals, but it pales in comparison to the overall impact you’ll have if you build capacity in an individual, a practice, and a country.”

Build local partnerships. How is this done? By partnering with individuals and groups to improve education and training. By procuring equipment and connecting communities to local resources. By bringing local physicians to international meetings and uniting them with their ophthalmic societies. “It’s about substituting single-episode surgical care with impact that functions 365 days a year,” said Dr. Pettey. “We as volunteers transfer our skills to a community and empower a population because it’s the members of that community who are best able to care for one another.”

And the more boots on the ground the better. Here’s how you can play a role in the leading edge of global ophthalmology.

Why They Do It
Volunteering is a uniquely individual experience, as each community has distinct needs with its own rewards and challenges. At the same time, each volunteer brings his or her own motivations.

STRABISMUS. Dr. Safran, shown with a young boy who had strabismus surgery that was provided via Healing the Children in Guayaquil, Ecuador.
Marc Safran, MD, who practices in Liverpool, N.Y., has volunteered in Bolivia, Ecuador, India, and Vietnam. Doing work overseas allows him to reconnect with the core of why he originally went into medicine. “It’s a throwback to providing medical care to needy people in a free and unencumbered way,” said Dr. Safran, “without electronic health records, MIPS, MACRA, and all of the bureaucratic hassles we now face at home.”

For Mitchell V. Brinks, MD, MPH, the motivation to volunteer overseas in areas like Cambodia, Guatemala, and Myanmar stems from the power of human connection. “It’s a pretty special feeling to know you have friends and a sense of home in another part of the world,” said Dr. Brinks, at Oregon Health & Science University’s Casey Eye Institute in Portland. “Cataract surgery, for example, can open the door to do so much good in so little time. And to have that access to the inside of a community? That’s pretty rare. But we as ophthalmologists have the key—it’s sitting right in our hands.”

**BUILDING CAPACITY.** Today’s No. 1 goal is to help build programs that will continue long after the volunteer returns home. Friendships—as the one between Dr. Brinks (left) and Benjamin D. Siatu’u, MD, who practices in Pago Pago, American Samoa—are a bonus.

**Become a Better Clinician**

Volunteering might mean different things to different ophthalmologists, but all agree on one thing: Whether you are a resident, a young ophthalmologist new to practice, or a seasoned vet, the skills you learn doing mission work will have a significant impact on your practice at home.

**Sharpen your skills.** “There might not be a better way to hone your skills as an ophthalmologist,” said Dr. Pettey. “You’ll be faced with the most complicated cases and forced to make important decisions in incredibly difficult environments. Afterwards, little will faze you. You return more focused and more capable of making difficult decisions on the fly. When done right, you return a better surgeon.”

You’ll also see the natural progression of diseases in a way that’s just not part of most ophthalmologists’ day-to-day experience in the United States. During his travels, Dr. Safran has witnessed child after child with advanced strabismus, which could have been easily corrected if eyeglasses were available. “Seeing the natural path of uncorrected disease gives you a genuine appreciation of its true nature and severity,” he said. “Whether it’s amblyopia, congenital cataract, or ptosis, I’ve gained a better appreciation for biology in a way that’s not possible in the normal U.S. clinic, where we have more early interventions [available].”

**Deepen connections with patients.** Not only can volunteering abroad make you a better surgeon, but it also will teach you how to build better physician-patient relationships. “By having the opportunity to work with people from different cultures and backgrounds, I’m building a skill set that translates to a lot of different scenarios domestically,” said resident Travis Redd, MD, MPH, at the Casey Eye Institute.

Andreas K. Lauer, MD, also at the Casey Eye Institute, agreed. “In my experience, it’s been really helpful to learn more about other cultures firsthand so that when I return home, I can interact more meaningfully with patients from diverse backgrounds. If I can tell a patient, ‘Hey, I recently visited your country,’ there’s automatically a better connection.”

**Gain greater perspective.** In addition to giving you a broader and deeper perspective on another culture, working abroad can also give you a new perspective on your own practice. “Volunteering gives you a window like no other into how commercialized and money-oriented medicine has become here in the United States,” said Dr. Brinks. “Many times, we as physicians buy into the earnings and the patient volume as our metrics of success. We can take it too seriously. Getting out of the clinic and setting foot in another world can help you build another model of professional satisfaction. It can make ophthalmology a truly enjoyable, long-term endeavor.”

For Dr. Redd, his mission work as a resident has made him rethink the role of public health in the practice of ophthalmology. “Going overseas to places like Uganda and Ethiopia reminds me to think about medicine in a different way when I return home. It’s more than just, how am I going to treat someone? It’s, how are my patients getting to the exam room? What hoops do they have to jump through? How can I better recruit my patients and better serve my local community?”

**Getting Started**

There are several ways to approach volunteering abroad, depending on your career stage.

**Residents.** For ophthalmologists still in training, many U.S. residency programs have integrated overseas experiences into their educational program. And some of them will help subsidize a resident’s travel expenses and other costs. For example, the International Ophthalmology Program at the Casey Eye Institute allows ophthalmology residents to travel internationally to areas like Fiji to learn low-cost alternative surgical skills, such as manual small-incision cataract surgery, for
treating patients in underserved communities.

**Fellows.** A small but growing number of institutions around the United States have also created global ophthalmology fellowships to help young ophthalmologists put their training at home into practice abroad. These include the following:

- Dean McGee Eye Institute’s Global Eye Care Fellowship (University of Oklahoma)
- Emory Eye Center’s Global Ophthalmology Fellowship (Emory University)
- Moran Eye Center’s Moran International Ophthalmology Fellowship (University of Utah)
- Truhlsen Eye Institute’s Prevention of Global Blindness Fellowship (University of Nebraska)
- Wills Eye Center for Academic Global Ophthalmology Fellowship (Wills Eye Hospital)

**Midcareer and older physicians.** More established ophthalmologists may want to consider volunteering through a charitable or nonprofit organization. Groups like Orbis International (www.orbis.org), the Seva Foundation (www.seva.org), and the Himalayan Cataract Project (www.cureblindness.org), for example, serve close to 100 countries and train thousands of medical professionals a year in how to build self-sustaining programs for preserving and restoring vision. For such a trip, most ophthalmologists can expect to take a hit on the income they’d normally bring in from their own practices, but some of these organizations might be able to offset a portion of the costs, including travel and lodging.

**Developing a Plan**

Regardless of the route you take to get involved, prospective volunteers will want to heed the following expert advice when exploring their opportunities.

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**Before You Go**

Once the path is clear and you’ve decided on your journey, you’ll want to make sure you follow a standard to-do list:

- **Get your passport ready.** The minute you decide you are going somewhere, check the official country website and figure out what you need (e.g., passport and visa) to enter the country. Plan ahead; the materials can take months to acquire.
- **Make sure you’re licensed.** You’ll head out overseas with the best of intentions. But if you aren’t legally approved by the host country’s government to perform surgery in your host country, you’ll be heading back home sooner than expected.
- **Get your vaccines.** This is essential. Some countries may even require proof of immunization prior to entry.
- **Purchase evacuation insurance.** You don’t want to become acutely ill and stranded in a foreign country that lacks proper resources. In addition to purchasing health insurance when traveling abroad, you should obtain evacuation insurance. This service will provide a jet or helicopter to extricate you from the direst of circumstances.
- **Register with the appropriate U.S. consulate.** You shouldn’t expect any danger when you are working overseas, but you’ll want to make sure the U.S. State Department knows where you are in case of catastrophe, natural disaster, or political unrest.
- **Learn the language.** Doing your homework about the local language and cultural makeup will be tremendously helpful down the road. You don’t need to be fluent, but learning simple terms like “thank you” and “good evening” will ingratiate you with hosts and patients.

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EyeCare America program (aao.org/eyecare-america/volunteerophthalmologists). The program helps medically underserved seniors and those who are at increased risk for glaucoma receive eye care through dedicated volunteer ophthalmologists. Once an ophthalmologist enrolls as a volunteer, eligible patients are matched online to the nearest volunteer by zip code.

Find a mentor. Dr. Pettey’s experience echoes that of Dr. Lawrence. Before taking his experience overseas, he started volunteering locally in a homeless clinic in Salt Lake City. And he is adamant about the importance of mentors. Under the guidance of Drs. Randy Olson, Alan Crandall, and Geoff Tabin at the Moran Eye Center, he learned how to translate the skills he was developing at home into the ability to provide high-quality care abroad.

“Good mentors really are the doorway to involvement,” Dr. Pettey said. “As a young ophthalmologist, you don’t have a clinical skill set that translates to the developing world. The cataracts you’ll encounter, for example, are the most difficult cases you’ve seen. It takes mentors who can build that clinical capacity in you before you can really get to work in a different country.”

Even for the most seasoned physician, a good mentor can prevent you from becoming a burden, added Dr. Brinks. “You’re not sleeping well, you have jet lag, you might have a bug, everything is difficult,” he said. “Unless you have someone alongside you who’s gone through it before, you’ll have to relearn their same mistakes on patients who are in dire need. So even for the smartest ophthalmologist out there who has the best of intentions, there’s just too much to learn on the ground to think you can do it by yourself the first try.”

Go with a group that has experience. Your first impressions of your mission site will be vital, so find an experienced organization to join. “Inspiration is your fuel when you’re volunteering abroad,” said Dr. Brinks. “And it’s delicate. You don’t want a traumatic experience to destroy it. So, research the location and go with a group that reflects your own values, because once you go overseas, the regulations and standards of care that you are accustomed to are all gone. The only things you have to guide you are the values and principles of the people you surround yourself with.”

Consider long-term impact. Finally, be sure the organization has a plan for long-term follow-up care, Dr. Redd added. “Many new volunteers think they’ll just pop into an outreach camp, work for a few days, and then return home. That might sound appealing, but you can do more harm than good in the long run if the organization has no plan for follow-up care and has no foundation built up for referral networks to help patients after you leave.” You have a duty to these patients to volunteer with a responsible organization, he said.

The Academy’s GO Guide

“The best way to get started,” said Dr. Pettey, “And to really prep my residents, I send them to the Academy’s Global Ophthalmology (GO) Guide.”

The guide provides members-in-training with a listing of fellowships and observerships available as well as online CME courses for all physicians who want to work overseas. Topics include the following:

• “Starting in Global Ophthalmology: Mentorship, Funding, and the Work-Home Balance”
• “Assessing Outcomes in Global Health Programs”
• “So You Want to Work Overseas?”

You can use the GO Guide to find region-based treatment and management information on a variety of disease topics; multimedia clips pertaining to global ophthalmology; and an Academy pamphlet, “Before You Go,” in which veteran physicians discuss how to make lasting changes around the world.

Prospective volunteers will also want to check out the Academy’s “Advisory Opinion on Ethical Issues in Global Ophthalmology.” It covers the challenges involved in international ophthalmic care, including how ophthalmologists can maintain professionalism and high clinical standards while practicing abroad.

For more information about the GO Guide, visit aao.org/global-ophthalmology-guide. To read the Academy’s Advisory Opinion as well as other ethics-related material, visit aao.org/clinical-education/redmond-ethics-center and click on “Global Ophthalmology.”
On the Ground
No matter how long you prepare for your work overseas, there are certain things that only experience can teach when you touch down on the ground.

Don’t be the hero. “As a resident or new volunteer in a foreign country, keep in mind that you are first a guest,” said Dr. Lauer. “So be respectful of the host because the host has a lot of responsibility. There’s a cost to them to ensure that the visit achieves the aim. If you go over there thinking that you’re going to run the show, you won’t be welcomed back.”

It’s also important to remember that your surgical skills or station in life should never dictate how you interact with the people you meet on the ground. “Fifteen years ago, physicians in the developing world didn’t have great access to the internet,” Dr. Safran said. “Times have changed, and now an ophthalmologist from the furthest reaches of the globe might very likely be a better surgeon than you. So, treat every person you meet—physicians, nurses, patients, community members—as a fellow human citizen.”

Don’t undercut the local economy. “This is something very important that I’ve learned from decades of volunteering abroad,” said Dr. Lawrence. “Where I work in Peru, for example, I used to bring donated [glasses] frames to a local school. But a mother of one of the students is an optician in the community. Why would I give away my glasses? What better thing could I do to help them? This is a prime example of understanding the local economy.”

Understand your limits. Perhaps the most important caveat is to set realistic expectations of yourself, the experts said. For a resident, this might mean that you simply go as a student rather than a practitioner. But even the most experienced ophthalmologist will still want to be cognizant of his or her comfort zone. Clinics overseas might be saving up the most difficult cases for someone like you. But if it involves something that you wouldn’t normally do or involves compromising on your own safety or the safety of your patients, you should know when to say “no” and defer to someone else.

“Most of the patients you’ll see are going to be blind, and they will need a lot of care,” said Dr. Brinks. Arriving at your destination “with an undefined desire to help isn’t a sophisticated strategy. People try to work themselves to death. They’ll do things they’re not ready to do, and then there’s nobody to help fix the problem afterwards. So be safe, be calm, and be humble.”

An Unmet Need
According to the World Health Organization, almost 90% of the world’s visually impaired live in low-income countries. And in these areas, treatable cataracts are the leading cause of blindness. It’s therefore no surprise that mission work to provide cataract surgery is the leading intervention for ophthalmologists. But there are also millions of others suffering from other diseases, such as glaucoma, who require ophthalmology’s attention. And this is where new recruits play a vital role.

“Manual small-incision cataract surgery is definitely an amazing type of intervention to prevent blindness,” said Dr. Lauer. “It has the ‘wow’ factor. But as we get more sophisticated about doing international missions, building capacity, and investing in public health, we need to expand our focus and find new volunteers to tackle these other conditions. It’s going to be a challenge, but if we can help these patients collectively, we really will be making the world a better place.”

**SUPERIOR EFFICACY AND STEROID-SPARING SUSTAINED REMISSION\(^1\)**

**INDICATION**
ACTEMRA is indicated for the treatment of giant cell arteritis (GCA) in adult patients.

**IMPORTANT SAFETY INFORMATION**

**BOXED WARNING: RISK OF SERIOUS INFECTIONS**
Patients treated with ACTEMRA are at increased risk for developing serious infections that may lead to hospitalization or death, including tuberculosis (TB), bacterial, invasive fungal, viral, or other opportunistic infections. If a serious infection develops, interrupt ACTEMRA until the infection is controlled.

Reported infections include:
- Active tuberculosis, which may present with pulmonary or extrapulmonary disease. Patients should be tested for latent tuberculosis before ACTEMRA use and during therapy. Treatment for latent infection should be initiated prior to ACTEMRA use.
- Invasive fungal infections, including candidiasis, aspergillosis, and pneumocystis. Patients with invasive fungal infections may present with disseminated, rather than localized, disease.
- Bacterial, viral and other infections due to opportunistic pathogens.

The risks and benefits of treatment with ACTEMRA should be carefully considered prior to initiating therapy in patients with chronic or recurrent infection.

Patients should be closely monitored for the development of signs and symptoms of infection during and after treatment with ACTEMRA, including the possible development of tuberculosis in patients who tested negative for latent tuberculosis infection prior to initiating therapy.

**CONTRAINDICATION**
ACTEMRA is contraindicated in patients with known hypersensitivity to ACTEMRA.

**WARNINGS AND PRECAUTIONS**

**Gastrointestinal Perforation:** Events of gastrointestinal (GI) perforation have been reported in clinical trials, primarily as complications of diverticulitis in RA patients. Use ACTEMRA with caution in patients who may be at increased risk for GI perforation. Promptly evaluate patients presenting with new-onset abdominal symptoms for early identification of GI perforation.

**Laboratory Parameters:** Laboratory monitoring is recommended due to potential consequences of treatment-related laboratory abnormalities in neutrophils, platelets, lipids, and liver function tests. Dosage modifications may be required.

**Neutropenia:** Treatment with ACTEMRA was associated with a higher incidence of neutropenia. It is not recommended to initiate ACTEMRA treatment in patients with a low neutrophil count i.e., absolute neutrophil count (ANC) less than 2000 per mm\(^3\). In patients who develop an ANC less than 500 per mm\(^3\) treatment is not recommended.

**Thrombocytopenia:** Treatment with ACTEMRA was associated with a reduction in platelet counts. It is not recommended to initiate ACTEMRA in patients with a platelet count below 100,000 per mm\(^3\). In patients who develop a platelet count less than 50,000 per mm\(^3\), treatment is not recommended.

**Elevated Liver Enzymes:** Treatment with ACTEMRA was associated with a higher incidence of transaminase elevations. These elevations did not result in apparent permanent or clinically evident hepatic injury in clinical trials. Increased frequency and magnitude of these elevations was observed when potentially hepatotoxic drugs (e.g., methotrexate) were used in combination with ACTEMRA.

- It is not recommended to initiate ACTEMRA treatment in patients with elevated transaminases ALT or AST >1.5x ULN. In patients who develop elevated ALT or AST >5x ULN, treatment is not recommended.

**Lipid Abnormalities:** Treatment with ACTEMRA was associated with increases in lipid parameters such as total cholesterol, triglycerides, LDL cholesterol, and/or HDL cholesterol.

**Immunosuppression:** The impact of treatment with ACTEMRA on the development of malignancies is not known, but malignancies were observed in clinical studies with ACTEMRA. ACTEMRA is an immunosuppressant, and treatment with immunosuppressants may result in an increased risk of malignancies.

**Hypersensitivity Reactions:** Hypersensitivity reactions, including anaphylaxis, have been reported in association with ACTEMRA. For ACTEMRA subcutaneous injection, advise patients to seek immediate medical attention if they experience any symptoms of a hypersensitivity reaction. If anaphylaxis or other hypersensitivity reaction occurs, stop administration of ACTEMRA immediately and discontinue ACTEMRA permanently. Do not administer ACTEMRA to patients with known hypersensitivity to ACTEMRA.

**Demyelinating Disorders:** The impact of treatment with ACTEMRA on demyelinating disorders is not known, but multiple sclerosis and chronic inflammatory demyelinating polyneuropathy were reported rarely in clinical studies. Monitor patients for signs and symptoms of demyelinating disorders. Prescribers should exercise caution in considering the use of ACTEMRA for the treatment of GCA in patients who may be at increased risk of demyelinating disorders.
In the ACTEMRA + Steroid* Taper Arms, More Patients Experienced Sustained Remission at 52 Weeks vs Placebo + Steroid Taper Arms

Sustained Remission at 52 Weeks: ITT Population

<table>
<thead>
<tr>
<th></th>
<th>Primary Endpoint</th>
<th>Key Secondary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACTEMRA QW + 26w</td>
<td>56%</td>
<td>56%</td>
</tr>
<tr>
<td>steroid taper 26w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=100</td>
<td></td>
<td></td>
</tr>
<tr>
<td>placebo + 26w</td>
<td>14%</td>
<td>17.6%</td>
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<tr>
<td>steroid taper 26w</td>
<td></td>
<td></td>
</tr>
<tr>
<td>n=50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ACTEMRA QW + 26w</td>
<td>53.1%</td>
<td>53.1%</td>
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<tr>
<td>steroid taper 26w</td>
<td></td>
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<tr>
<td>n=100</td>
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<td>placebo + 26w</td>
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<tr>
<td>steroid taper 26w</td>
<td></td>
<td></td>
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<tr>
<td>n=51</td>
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</tbody>
</table>

Most patients in the ACTEMRA arms were steroid free from Week 26 through Week 52.

The most commonly reported adverse reactions were nasopharyngitis, headache, and peripheral edema.

GIACTA was a randomized, double-blind, multicenter study in patients with active GCA. Patients (N=251) were randomized to one of four treatment arms. Two SC doses of ACTEMRA (162 mg QW and 162 mg Q2W) were compared to two different placebo control groups (pre-specified prednisone-taper regimen over 26 weeks and 52 weeks) randomized 2:1:1:1.

GIANT CELL ARTERITIS (GCA)

In the Phase III clinical trial, the most common adverse events (>20% of patients treated with ACTEMRA-SC) during the 52-week study were:

<table>
<thead>
<tr>
<th>Adverse Event</th>
<th>PR0 + 26 weeks prednisone taper (%)</th>
<th>PR0 + 52 weeks prednisone taper (%)</th>
<th>TCZ 162 mg SC Q2W + 26 weeks prednisone taper (%)</th>
<th>TCZ 162 mg SC Q2W + 26 weeks prednisone taper (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Headache</td>
<td>32.0</td>
<td>23.5</td>
<td>27.0</td>
<td>20.4</td>
</tr>
<tr>
<td>Nasopharyngitis</td>
<td>18.0</td>
<td>25.5</td>
<td>29.0</td>
<td>24.5</td>
</tr>
<tr>
<td>Peripheral Edema</td>
<td>16.0</td>
<td>11.8</td>
<td>16.0</td>
<td>24.5</td>
</tr>
<tr>
<td>Dizziness</td>
<td>12.0</td>
<td>15.7</td>
<td>6.0</td>
<td>20.4</td>
</tr>
</tbody>
</table>

The overall safety profile observed in the ACTEMRA treatment groups was generally consistent with the known safety profile of ACTEMRA. There was an overall higher incidence of infections in GCA patients relative to RA patients.

Infections: The rate of infections was 200.2 per 100 patient-years in the ACTEMRA SC weekly group and 160.2 per 100 patient-years in the ACTEMRA SC every other week group, as compared to 156.0 per 100 patient-years in the placebo + 26 week prednisone taper and 210.2 per 100 patient-years in the placebo + 52 week taper groups.

The rate of serious infections was 9.7 per 100 patient-years in the ACTEMRA SC weekly group and 4.4 per 100 patient-years in the ACTEMRA SC every other week group, as compared to 4.2 per 100 patient-years in the placebo + 26 week prednisone taper and 12.5 per 100 patient-years in the placebo + 52 week prednisone taper groups.

The most common types of infections across all treatment groups were nasopharyngitis, upper respiratory tract infection, bronchitis, and urinary tract infection.

Injection-Site Reactions: The frequency of injection-site reactions was 6% (6/100) in the ACTEMRA SC weekly group, and 14% (7/49) in the ACTEMRA SC every other week group, as compared to 10% (5/50) in the placebo + 26 week prednisone taper and 2% (1/51) in the placebo + 52 week taper groups. No injection site reaction was reported as a serious adverse event or required treatment discontinuation.

DRUG INTERACTIONS

In GCA patients, no effect of concomitant corticosteroid on ACTEMRA exposure was observed.

Cytochrome P450s in the liver are down-regulated by infection and inflammation stimuli including cytokines such as IL-6. Exercise caution when coadministering ACTEMRA with CYP3A4 substrate drugs where decrease in effectiveness is undesirable, e.g., oral contraceptives, lovastatin, atorvastatin, etc.

USE IN PREGNANCY

There is a pregnancy exposure registry that monitors pregnancy outcomes in women exposed to ACTEMRA during pregnancy. Physicians are encouraged to register patients and pregnant women are encouraged to register themselves by calling 1-877-311-8972.

The limited available data with ACTEMRA in pregnant women are not sufficient to determine whether there is a drug-associated risk for major birth defects and miscarriage.

You may report side effects to the FDA at (800) FDA-1088 or www.fda.gov/medwatch. You may also report side effects to Genentech at (888) 835-2555.

Please see following brief summary of Prescribing Information, including Boxed WARNING, for additional important safety information.


Q2W=every-other-week dose; QW=every-week dose.

*Prednisone.
Treatment-related reduction in platelets was not associated with serious bleeding events in clinical trials [see Adverse Reactions (6.1, 6.2)].

It is recommended that treatment in patients with a platelet count below 100,000 per mm³. In patients who develop a platelet count less than 50,000 per mm³ treatment is not recommended.

- Monitor platelets 4 to 8 weeks after start of therapy and every 3 months thereafter.

For recommended modifications based on platelet counts see [Dosage and Administration (2.8)].

Elevated Liver Enzymes Treatment with ACTEMRA was associated with a higher incidence of elevated liver enzymes. These elevations did not result in apparent permanent or clinically evident hepatic injury in clinical trials [see Adverse Reactions (6.1, 6.2)]. Increased frequency and magnitude of these elevations was observed when potentially hepatotoxic drugs (e.g., MTX) were used in combination with ACTEMRA.

Liver enzymes include:
- Aspartate transaminase (AST), alanine transaminase (ALT), alkaline phosphatase, total bilirubin, and creatinine.

In patients who have received ACTEMRA 8 mg per kg monotherapy without elevations in transaminases experienced elevation in AST to above 10x ULN and elevation in ALT to above 16x ULN when MTX was initiated in combination with ACTEMRA. Transaminases returned to normal in both treatment groups, but patients whose ALT and AST were continued.

It is recommended to initiate ACTEMRA treatment in patients with elevated transaminases ALT or AST greater than 5x ULN. In patients who develop elevated ALT or AST greater than 5x ULN treatment is not recommended.

- Monitor ALT and AST levels 4 to 8 weeks after start of therapy and every 3 months thereafter.

When ACTEMRA-induced, other liver function tests such as bilirubin should be considered.

For recommended modifications based on transaminases see [Dosage and Administration (2.8)].

Lipid Abnormalities Treatment with ACTEMRA was associated with increases in lipid parameters such as total cholesterol, triglycerides, LDL cholesterol, and/or HDL cholesterol [see Adverse Reactions (6.1, 6.2)].

- Assess lipid parameters approximately 4 to 8 weeks following initiation of ACTEMRA therapy, then at approximately 24 week intervals.

- Management of hyperlipidemia may include drug guidelines [e.g., National Cholesterol Educational Program (NCEP)] for the management of hyperlipidemia.

5.4 Immunosuppression Treatment with ACTEMRA on the development of malignancies is not known but malignancies were observed in clinical studies [see Adverse Reactions (6.1)]. ACTEMRA is an immunosuppressant, and treatment with immunosuppressants may result in an increased risk of infection.

5.5 Hypersensitivity Reactions, Including Anaphylaxis Hypersensitivity reactions, including anaphylaxis, have been reported in association with ACTEMRA [see Adverse Reactions (6.6)] and anaphylactic events with a fatal outcome have been reported with intravenous ACTEMRA. Anaphylaxis and other hypersensitivity reactions that required treatment discontinuation were reported in 0.1% (6 out of 2644) of patients in the 6-month controlled trials of intravenous ACTEMRA. 0.2% (8 out of 4009) of patients in the 12-month controlled trials of intravenous ACTEMRA, and 0.5% (6 out of 1068) of patients in the 6-month controlled trials of subcutaneous ACTEMRA. Reaction that required treatment discontinuation included generalized erythema, rash, and urticaria. Injection site reactions were categorized separately [see Adverse Reactions (6.1)]. In the postmarketing setting, events of hypersensitivity reactions, including anaphylaxis and death have been reported in patients treated with a range of doses of intravenous ACTEMRA, including postmarketing reports from clinical trials and open-label studies. Anaphylaxis has been reported with intravenous ACTEMRA with and without premedication. Hypersensitivity, including anaphylaxis events, have occurred both with and without previous hypersensitivity reactions and as early as the first infusion of ACTEMRA [see Adverse Reactions (6.6)]. ACTEMRA for intravenous use should only be infused by health care professionals with access to treatment for anaphylaxis.

For ACTEMRA subcutaneous injection, advise patients to seek immediate medical attention if they experience any symptoms of a hypersensitivity reaction. If anaphylaxis or other hypersensitivity reaction occurs, stop administration of ACTEMRA immediately and discontinue permanently. Do not administer ACTEMRA to patients with known hypersensitivity to ACTEMRA [see Contraindications (4) and Adverse Reactions (6.6)].

5.6 Demyelinating Disorders Because ACTEMRA treatment with ACTEMRA on demyelinating disorders is not known, but multiple sclerosis and chronic inflammatory demyelinating polyneuropathy were rarely used in RA clinical studies. Monitor patients for signs and symptoms potentially indicative of demyelinating disorders. If suspected, treat with a course of corticosteroids and consider the use of ACTEMRA in patients in preexisting or recent onset demyelinating disorders.

5.7 Active Hepatic Disease and Hepatic Impairment Treatment with ACTEMRA is not recommended in patients with active hepatic disease or hepatic impairment [see Adverse Reactions (6.6), Use in Specific Populations (8.6)].

5.8 Vaccinations Avoid use of live vaccines concurrently with ACTEMRA as clinical safety has not been established. No data are available on the therapeutic efficacy of vaccines in ACTEMRA-treated patients. Use of live vaccines in patients receiving ACTEMRA is not recommended.

No data are available on the effectiveness of vaccination in patients receiving ACTEMRA. Before initiating ACTEMRA, advise patients of the need for immunization against seasonal and pandemic influenza, pneumococcal, and hepatitis B. Also advise patients to begin a course of immunization against other potentially relevant infections based on current vaccine guidelines and any recommendations they may have received.

6 ADVERSE REACTIONS Because clinical studies are conducted under widely varying conditions, adverse reaction rates observed in the clinical studies of another drug and may not predict the rates observed in a broader patient population in clinical practice.

6.1 Clinical Trials Experience in Rheumatoid Arthritis Patients Treated with Intraocular Methotrexate (ACTEMRA-I)

The ACTEMRA-I data in rheumatoid arthritis (RA) includes 5 double-blind, controlled, multicenter studies. In these studies, patients received doses of ACTEMRA-I 8 mg per kg monotherapy (228 patients), ACTEMRA-I 4 mg per kg in combination with DMARDs (including methotrexate) (1582 patients), or ACTEMRA-I 4 mg per kg in combination with methotrexate (774 patients). The total exposure population includes all patients in registration studies who received at least one dose of ACTEMRA-I. Of the 3577 patients in this population, 3577 received treatment for at least 6 months, 3309 for at least one year, 2954 received treatment for at least 2 years and 2189 for 3 years. All patients in these studies had moderately to severely active rheumatoid arthritis. The study population had a mean age of 52 years, 82% were female and 74% were Caucasian. The most commonly reported serious adverse reactions were serious infections [see Warnings and Precautions (5.1)].

The most commonly reported adverse reactions in controlled studies up to 24 weeks (occurring in at least 5% of patients treated with ACTEMRA-I monotherapy or in combination with ACTEMRA-I).

Injection, for intravenous use Injection, for subcutaneous use This is a brief summary. Before prescribing, please refer to the full Prescribing Information.
In the 24 week, controlled clinical studies, a total of 2876 patients have been tested for anti-tocilizumab antibodies. Forty-six patients (2%) developed positive anti-tocilizumab antibodies, of whom 5 had an associated, medically significant, hypersensitivity reaction leading to withdrawal. Thirty patients (1%) developed neutralizing antibodies. The data reflect the percentage of patients whose test results were positive for antibodies to tocilizumab in specific assays. The observed incidence of antibody positivity in an assay is highly dependent on several factors, including assay sensitivity and specificity, assay methodology, timing of sample collection, concurrent medication, and underlying disease. For these reasons, comparison of the incidence of antibodies to tocilizumab with the incidence of antibodies to other products may be misleading.

Malignancies: During the 24 week, controlled period of the studies, 15 malignancies were observed in patients receiving ACTEMRA-IV, compared to 8 malignancies in patients in the control groups. Exposure-adjusted incidence was similar in the ACTEMRA-IV groups (3.12 events per 100 patient-years) and in the placebo plus DMARD group (1.37 events per 100 patient-years). In the all-exposure population, the rate of malignancies remained consistent with the rate observed in the 24 week, controlled period (see Warnings and Precautions [5.4]).

Other Adverse Reactions: Adverse reactions occurring in 2% or more of patients on 4 or 8 mg per kg ACTEMRA-IV plus DMARD and at least 1% greater than that observed in patients on placebo plus DMARD are summarized in Table 2.

Table 2  Adverse Reactions Occurring in at Least 2% or More of Patients on 4 or 8 mg per kg ACTEMRA-IV plus DMARD and at Least 1% Greater Than That Observed in Patients on Placebo plus DMARD

<table>
<thead>
<tr>
<th>Preferred Term</th>
<th>N = 288 (%)</th>
<th>N = 284 (%)</th>
<th>N = 774 (%)</th>
<th>N = 1582 (%)</th>
<th>N = 1170 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Placebo plus DMARD</td>
<td>56</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>ACTEMRA-IV 8 mg per kg MONOTHERAPY</td>
<td>121</td>
<td>8</td>
<td>21</td>
<td>7</td>
<td>4</td>
</tr>
<tr>
<td>ACTEMRA-IV 4 mg per kg + DMARDs</td>
<td>121</td>
<td>8</td>
<td>21</td>
<td>7</td>
<td>4</td>
</tr>
</tbody>
</table>

*For a description of these studies, see Section 14, Clinical Studies.*

**Other infrequent and medically relevant adverse reactions occurring at an incidence less than 2% in rheumatoid arthritis patients treated with ACTEMRA-IV in controlled trials were:**

- Infections and Infestations: oral herpes simplex
- Gastrointestinal disorders: stomatitis, gastric ulcer
- Respiratory, thoracic, and mediastinal disorders: dyspnea, cough

**Elavated Liver Enzyme Abnormalities:** In the 24 week, controlled period of the studies I to V, increases in transaminases were generally not associated with clinical hepatitis. These elevations were not associated with clinically relevant increases in direct bilirubin, nor were they associated with clinical evidence of hepatic or hematopoietic insufficiency (see Warnings and Precautions [5.3]).
neutralizing antibodies. In SC-II, 1.6% (7/434) in the ACTEMRA-SC arm compared with 1.4% (3/217) in the placebo arm developed anti-tocilizumab antibodies; of these, 1.4% (6/434) in the ACTEMRA-SC arm and 0.5% (1/217) in the placebo arm also developed neutralizing antibodies. A total of 14/54 (26%) patients who received ACTEMRA-SC in the all exposure group have been tested for anti-tocilizumab antibodies. Thirteen patients (0.9%) developed anti-tocilizumab antibodies, and, of these, 12 patients (0.8%) developed neutralizing antibodies. The rate is consistent with previous intravenous experience. No correlation of antibody development with treatment duration, events or loss of clinical response was observed.

Laboratory Abnormalities
Neutropenia During routine laboratory monitoring in the 6-month controlled clinical trials, a decrease in neutrophils ≤ 1 x 10^9/L occurred in 2.9% and 3.7% of patients receiving ACTEMRA-SC weekly and every other week, respectively. There was no clear relationship between decreases in neutrophils below 1 x 10^9/L and the occurrence of serious infections.

Thrombocytopenia During routine laboratory monitoring in the 6-month controlled clinical trials, none of the patients had a decrease in platelet count ≤ 50,000/mm³.

Elevated Liver Enzymes During routine laboratory monitoring in the 6-month controlled clinical trials, ALT and AST were increased in 6.5% and 4.1% of patients, respectively, receiving ACTEMRA-SC weekly and 3.4% and 0.7% receiving ACTEMRA SC every other week.

Lipid Parameters Elevations During routine laboratory monitoring in the ACTEMRA-SC 6-month clinical trials, 19% of patients dosed weekly and 19.6% of patients dosed every other week and 10.2% of patients receiving tocilizumab experienced increases in total cholesterol > 6.2 mmol/L (240 mg/dL), with 9%, 10.4% and 5.1% experiencing a significant increase in LDL to 4.1 mmol/L (160 mg/dL) receiving ACTEMRA-SC weekly, every other week and placebo, respectively.

6.3 Clinical Trials Experience in Giant Cell Arteritis Patients Treated with Subcutaneous ACTEMRA (ACTEMRA-SC)
The safety of subcutaneous ACTEMRA (tocilizumab) has been studied in one Phase III study (WA28119) with 251 GCA patients. The total patient years duration in the ACTEMRA GCA exposure population was 105 patient years during the double-blind and placebo-controlled phase of the study. The overall safety profile observed in the ACTEMRA treatment groups was generally consistent with the known safety profile of ACTEMRA. There was an overall higher frequency of adverse events in the patients treated with ACTEMRA-SC compared to placebo. 20.8% of patients treated with ACTEMRA-SC were seen for at least one serious adverse event compared to 15.4% in placebo. In the ACTEMRA treatment group, 50% of patients had at least one serious adverse event compared to 36.7% in placebo.

Avoid use of live vaccines concurrently with ACTEMRA [see Warnings and Precautions (5.8)].

Patient Counseling
Inform patients that some patients who have been treated with ACTEMRA have had serious side effects such as positive HBV and HCV serology [see Warnings and Precautions (6.7)].

8.2 Lactation
The safety and efficacy of ACTEMRA have not been studied in patients with hepatic impairment, including patients with Child-Pugh class C disease with positive HBV and HCV serology [see Warnings and Precautions (6.7)].

8.3 Renal Impairment
No dose adjustment is required in patients with mild or moderate renal impairment. ACTEMRA has not been studied in patients with severe renal impairment [see Clinical Pharmacology (12.3)].

10 OVERDOSAGE
There are limited data available on overdoses with ACTEMRA. One case of accidental overdose was reported in a patient in whom ACTEMRA was infused at a dose of 40 mg per kg. No adverse drug reactions were observed. No serious adverse drug reactions were observed in healthy volunteers who received single doses of up to 28 mg per kg. In case of an overdose, it is recommended that the patient be monitored for signs and symptoms of adverse reactions. Patients who develop adverse drug reactions should receive appropriate symptomatic treatment.

17 PATIENT COUNSELLING INFORMATION
See FDA-approved patient labeling (Medication Guide).

Patient Counseling
Advise patients of the potential benefits and risks of ACTEMRA. Physicians should instruct their patients to read the Medication Guide before starting ACTEMRA therapy. In case of an overdose, it is recommended that the patient be monitored for signs and symptoms of adverse reactions. Patients who develop adverse drug reactions should receive appropriate symptomatic treatment.

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It’s not a matter of if but when a third-party payer sends you a request for records. And when that day arrives, having a written protocol in place will help to ease your angst. Here’s how to get started.

**Be Audit Ready: Create Written Protocol**

Use the protocol below as a starting point, and customize it to fit your practice.

**You receive a request for records.** What do you do next?

1. **Do not toss the envelope.** It shows the postmark date. The letter inside may be dated much earlier than the date when you received the request.

2. **Determine the type of audit or investigation.** The government has assigned auditing duties to several types of organization, each with its own type of audit. These include the following:
   - CERT: Comprehensive Error Rate Testing
   - OIG: Office of Inspector General investigation
   - RA and RAC: Recovery Audit (RA) and Recovery Audit Contractor (RAC)
   - SMRC: Supplemental Medical Review Contractor
   - TPE: Targeted Probe and Educate
   - ZPIC: Zone Program Integrity Contractor

   The mechanics of the audit may vary, depending on which type of audit is performed.

**Two Real-Life Scenarios**

**Scenario 1: The dutiful but ill-informed staff member.** A staff member opens the mail and finds an audit request for 40 charts. In an effort to be helpful, he compiles what he perceives to be the appropriate documentation. He submits it without telling the physician.

   The audit results are not favorable, and a substantial refund is requested. Now the employee needs to plan for an appeal or a refund and must tell the physician. If the refund is not made within the allotted time frame, future payments will be withheld until the recoupment is paid in full. This can have some awkward repercussions. Suppose, for instance, the physician’s partner submits the next few claims to this payer. It will be the partner who is impacted when the payer withholds payment for those claims. Patients may also be affected, as the practice won’t be able to post a payment to a patient’s account if actual funds aren’t available for deposit.

**Scenario 2: Kicking the can down the road.** A request for 30 records is received. Rather than putting her best foot forward and making sure all the documentation that the auditor requested is submitted, the practice administrator determines that the practice will just send in records and hope for the best, knowing that the practice can always appeal. While appealing denied claims is always an option, it is a costly one. Best practice is to review the request and carefully compile the documentation. When you send the documentation, include a cover letter that can provide further explanation and can help set the tone for the audit.

3. **Identify the due date for sending records.** Respond within the time limits provided, or immediately request an extension. Make sure you document written confirmation of new due date.

4. **Look for the common theme.** Does the auditor seem to be zeroing in on a particular level of E&M or Eye visit code? A consistent modifier? A particular testing service? A high-volume surgery? Is it a single date of service versus a series of encounters?

5. **Note the date of service requested.** Make sure that you are gathering documentation for the correct date of service.

6. **Check the records for signatures.** For paper charts, is the physician signature present and identifiable? If signatures are illegible, immediately prepare a signature log. Include the names of all who document in the medical record and identify their title (i.e., MD, DO, OD, technician, scribe, receptionist,

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**BY SUE VICCHRILLI, COT, OCS, ACADEMY DIRECTOR OF CODING AND REIMBURSEMENT.**
If the signature is missing from the medical documentation, it is acceptable for the author of the medical record entry to add a signed attestation that he or she had entered the original information into the record.

If you use electronic health records (EHRs), provide documentation that the physician signature is “secure” and nobody else has or uses the physician password. Most audits also request EHR signature protocol. Without an identifiable, secure physician signature, the auditors do not have to complete the actual audit—they can just deny payment.

7. Provide a list of abbreviations used. Don’t assume that the auditor will understand the abbreviations used in your records.

8. Check whether LCD(s) apply. If the payer has a Local Coverage Determination (LCD) on a test or surgery performed, quote chapter and verse from that LCD. Be sure to use the LCD that was in place at the time the test or surgery took place.

9. Make sure tests are fully documented. If testing services are part of the audit, make sure there is a written order that identifies by name what test and which eye(s). Furthermore, the medical necessity for the test should be obvious in the medical record; the physician should provide the interpretation and report as soon as possible; and if the delegated test falls under direct supervision, make sure the payer is aware that one of the practice’s physicians was on site during the test.

10. Self-audit. If the auditor is looking at E&M or Eye visit codes, audit internally before submitting the documentation, so you can gauge your worst-case scenario. Next, you can estimate how much money the auditor might seek to recoup and plan accordingly.

11. Make sure that a physician reviews the documentation. Physicians should have the opportunity to review all records before that documentation is sent to the auditor.

With paper charts, if the handwriting is not readily legible, physicians should take the time to dictate (not embellish) the notes. Include the actual chart note plus the dictation. After all, only that which can be read can be audited.

With EHR, check whether all fields are populated. For example, if documentation shows only those body systems that have a problem and not those that are normal, you won’t receive credit for reviewing 10 or more systems. Work with the vendor to make sure all fields show when the record is printed.

12. Remember that the Academy is here for you. Email coding@aao.org.

Codequest 2018

Strengthen your audit armor. Stay up to date with shifting regulations by attending Codequest 2018, a half-day event that will be tailored to the region where you practice.

New for Codequest’s 2018 program. Audit-proof your documentation with payer-specific checklists for the top surgical procedures for each subspecialty. Learn about new CPT, HCPCS, and ICD-10 codes as well as new CCI edits. Get tips on coding for telemedicine, blepharoplasty, and much more.

When is Codequest coming to your state? Codequest will have visited 15 states by the end of April and several more by the end of the year. Here are the first 16 Codequests:

- Columbia, S.C. (Friday, Jan. 12)
- Nashville, Tenn. (Saturday, Jan. 13)
- Southern California (Friday, Jan. 19)
- Little Rock, Ark. (Thursday, Jan. 25)
- Northern California (Friday, Jan. 26)
- Lubbock, Texas (Friday, Feb. 2)
- San Marcos, Texas (Saturday, Feb. 3)
- Greensboro, N.C. (Saturday, Feb. 3)
- St. Paul, Minn. (Saturday, Feb. 17)
- Salt Lake City, Utah (Saturday, March 3)
- Manhattan, N.Y. (Thursday, March 15)
- Long Island, N.Y. (Friday, March 16)
- Detroit, Mich. (Saturday, March 17)
- Rochester, N.Y. (Thursday, March 22)
- Albany, N.Y. (Friday, March 23)
- Dallas, Texas (Saturday, March 24)

For the full schedule, plus information on educational credits (including CME for physicians), visit aao.org/codequest.
Help Low Vision Patients Avoid Depression: Get Them Started on Social Media

We all derive support from family and friends. But after patients develop visual impairment, that network of support can start to unravel. This is because new impediments—such as the inability to recognize an acquaintance’s face or the inability to drive—can prevent patients from maintaining social ties.

One potential remedy: online social networks. “I believe that this opportunity for social interaction can bring hope to our patients,” said Rahul N. Khurana, MD, a retina specialist in Mountain View, California.

Feeling Isolated and Miserable

Recognize the risk of depression. “As ophthalmologists, we often give all of our attention to disease management and overlook the importance of managing the impairment caused by the disease. But it is essential to recognize that individuals with low vision are up to 3 times more likely to develop depression than are those without a visual impairment,” said low vision specialist John D. Shepherd, MD. “Furthermore, the degree of depression directly correlates with the level of disability. This essentially means that the more difficult it is for our patients to participate in their favorite activities, such as socializing, the greater the likelihood of depression,” said Dr. Shepherd, at the Weigel Williamson Center for Visual Rehabilitation in Omaha, Nebraska.

Look for cues and ask questions. Because patients are prone to report the physical symptoms that they are experiencing rather than identifying tasks that they are unable to accomplish, it may be necessary to delve a little deeper to determine the level of impact that vision loss may be having on an individual’s activity participation.

Vision loss is on the rise. A study published in *JAMA Ophthalmology* found that the number of new cases of low vision and blindness is projected to double during the next 30 years. According to the authors, however, this estimate may be low due to the limited sample size of particular populations (e.g., certain racial/ethnic groups). In any event, the number of your patients at risk for depression is set to rise.

Urge Patients to Go Online

Keeping patients engaged is thought to reduce feelings of isolation and depression that frequently accompany vision loss. And for many people, social media platforms—Facebook, Instagram, and Twitter, for example—are a good option for maintaining social ties. “These and other platforms have made tremendous strides to make the internet, and specifically social media, more accessible to individuals with low vision and vision loss,” said Dr. Khurana, who has observed patients socially withdraw and become depressed once they lose vision. “It is important for us to inform them about the various options that can help them connect or remain connected with others,” he said.

Support networks are important. Although there is currently no empirical evidence to suggest that starting to use social media will help prevent or reduce depression, it is likely that this
social interaction could minimize the sense of loneliness that often accompanies visual impairment.

**Patients can exchange tips with their peers.** Patients can connect with others who are experiencing the challenges of low vision and blindness; ideas and suggestions can be exchanged.

**The Tools**

Usage patterns are similar. More than 100 million people use the zoom feature in a desktop browser, and 1 in 5 increase the text size on their mobile device for a more readable online experience, according to Jeff Wieland, director of accessibility at Facebook. His department is responsible for educating Facebook’s product teams about accessibility so that they can build products for people with disabilities. “We have found that people with vision loss and blindness use social media in the same ways as everyone else,” said Mr. Wieland. “The only difference is the mechanism employed for interacting with Facebook. For instance, someone who is blind will use a screen reader to access Facebook and, therefore, navigation patterns change. This individual is likely to navigate by page headings or landmarks and, in some cases, from user-interface element to user-interface element to gain context,” he explained.

Facebook utilizes shortcut keys that enable individuals who only use their keyboards for online navigation to “Friend,” “Like,” “Comment,” and “Share,” just as sighted users can. This is particularly relevant to those with low vision because research indicates that patients with a strong desire for social interaction use online social groups to make one-to-one connections with other users by friending.  

**Font size and screen readers.** All computer operating systems have capability features that enable the end-user to increase the font size or change the text and background colors for improved readability. When this is not sufficient, screen readers enable even those who have extremely low vision or are completely blind to access the internet and social media. This technology converts text to speech and reads aloud what is displayed on the screen.

**What about images?** Now that every smartphone includes a camera, photographs often play a starring role in social media posts. And the text that accompanies these image-based posts might not make much sense without the context that the image provides.

**Automated Alt Text technology can help unlock the meaning of image-based Facebook posts.** “Automated Alt Text uses Facebook’s proprietary object recognition service that currently detects approximately 120 distinct objects and concepts within the hundreds of millions of photographs that are uploaded and shared on Facebook daily,” said Mr. Wieland. “The service runs instantaneously at the time of an upload and is supported in 20 languages.” The result is a brief but descriptive narrative of what is depicted in the photograph. Now, when the screen reader encounters a photograph on Facebook, rather than simply stating “image,” Automatic Alt Text enables screen readers to read aloud a description of the photo (e.g., “Image may contain: Two people, smiling, beach”).

**Refer Patients When Necessary**

Patients who struggle with using the computer, navigating the internet, and other day-to-day activities due to their visual impairments should be referred to a low vision specialist. “The goal of the low vision specialist is first to identify all of the functional difficulties that an individual is having and then to minimize the disability through the use of optical devices, accessibility options, skill training, environmental adaptations, and counseling,” said Dr. Shepherd. For those in areas without a low vision specialist, state and local services for the blind and visually impaired are a good starting point for helpful information.

**Additional Resources**


**Facebook** offers some basic resources to get started:

- The Facebook Accessibility Help Center: www.facebook.com/help/
- The Facebook Accessibility Page for news and updates: www.facebook.com/accessibility

**More than 100 iOS apps** designed for blind and low vision users can be found at www.applevis.com/apps/ios-apps-for-blind-and-vision-impaired.

**The Academy initiative in vision rehabilitation** will help you to refer low vision patients or provide them with vision rehabilitation. To learn more, visit aao.org/low-vision-and-vision-rehab.

**Related reading.** Visit aao.org/eyenet and click “Archive” for the following articles: Low Vision Drivers: The Ophthalmologist’s Role and Responsibility (Clinical Update, October 2017); Boost Website Accessibility for Those With No Vision and Low Vision (Practice Perfect, October 2017); A Guide to Vision Aid Apps for Apple and Android Smartphones (Practice Perfect, April 2016); Make Your Office Safer for Patients With Low Vision (Practice Perfect, November 2014).
From PQRS to MIPS, the IRIS Registry Is a Winning Tool for Quality Reporting

The IRIS Registry (aao.org/iris-registry) helped ophthalmology succeed at Physician Quality Reporting System (PQRS) and is now the specialty’s tool of choice for the Merit-Based Incentive Payment System (MIPS). Indeed, CMS chief Seema Verma, MPH, has said that although quality reporting is too burdensome, “one bright spot” is the IRIS Registry.

The IRIS Registry has 2 reporting options. Use a web portal to manually report up to 3 MIPS performance categories; if you integrate your electronic health record (EHR) system with the IRIS Registry, an automated process extracts data for quality reporting.

PQRS—Widespread Success, Plus Some Lessons Learned
In fall of 2017, practices learned whether they had successfully reported PQRS for the 2016 performance year.

What was at stake. What happens to those who failed to successfully report PQRS measures for the 2016 reporting period? In 2018, their Medicare Part B service payments will be adjusted downward. This penalty will be 2% plus an additional value-based modifier penalty of 1% or 2% for smaller (no more than 10 eligible clinicians) and larger practices, respectively. Based on an average Medicare Fee Schedule of $270,036 for all PQRS-eligible ophthalmologists, this would translate into a penalty adjustment of $8,101 to $10,801 per ophthalmologist in 2018.

Most ophthalmologists reported PQRS via IRIS Registry–EHR integration. For the 2016 performance year, the IRIS Registry sent CMS 11,612 files for eligible clinicians and group practices. Of these, 9,177 files were from practices that had integrated their EHR system with the IRIS Registry.

Closing in on 100% success for IRIS Registry–EHR integrated practices. Through Dec. 1, 2017, the IRIS Registry had not been notified of any participating practice’s fully completed EHR submission receiving the penalty adjustment due to unsuccessful reporting of quality measures. However, there were a handful of cases with incorrect combinations of the 2 identifiers: the National Provider Identifier (NPI), which is used to identify individual clinicians, and the Tax Identification Number (TIN), which is used to identify the practice. These were corrected upon appeal to CMS.

Most manual reporters were successful. Practices could manually report PQRS measures through the IRIS Registry web portal and were responsible for their own data entry. While it seems that most of these manual reporters were successful, several practices did receive penalty notification letters for the following reasons:

• incorrect TIN, NPI, or TIN/NPI combination
• not reporting for a physician in the practice (in some cases the physician had joined the practice partway through the year; there also were cases in which the physician worked in the practice part time or only occasionally)
• not reporting and instead relying on an Accountable Care Organization that failed PQRS

MIPS: Beat the Jan. 15 Deadline
First, see if you’re exempt from MIPS (https://qpp.cms.gov/participation-lookup). Next, if you signed up to use the IRIS Registry for 2017 MIPS reporting, make sure you meet the Jan. 15 deadline for (1) providing the TIN/NPI combinations, (2) submitting Data Release Consent Forms, (3) attesting to improvement activities and advancing care information measures, and, if reporting quality measures manually via the web portal, (4) entering quality measure data. (For consent form instructions, see aao.org/consent-form.)

If your practice is one in which eligible clinicians are reporting MIPS as individuals, ensure that the correct TIN/NPI combination(s) is entered for each one. Also be sure that every eligible clinician expected to remain in the practice in 2019 is included and signs a Data Release Consent Form. If your practice is group reporting, ensure that all the applicable TINs used in Medicare billing are correct in their Data Release Consent Forms.


BY FLORA LUM, MD, VICE PRESIDENT OF THE ACADEMY QUALITY AND DATA SCIENCE DIVISION.
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WHAT’S HAPPENING

State Societies Honored
On Nov. 13 during AAO 2017, the Academy’s Secretariat for State Affairs recognized 2 societies with its 2017 Star Award. The Star Award program provides special recognition to state ophthalmology societies for outstanding efforts on programs or projects they have implemented in the previous year. The winning societies are as follows.

- **North Carolina Society of Eye Physicians and Surgeons (NCSEPS)**—for its Ocular Melanoma Cluster Response project, which focused on investigating and increasing patient awareness about an increased rate of diagnosis of ocular melanoma among younger people in the Huntersville, North Carolina area. With other health care organizations, NCSEPS encouraged citizens to get eye examinations to screen for ocular melanoma and other eye diseases.

- **Virginia Society of Eye Physicians and Surgeons (VSEPS)**—for its Protecting Patients’ Access to Emerging Technologies effort, which worked to pass legislation that protects physicians’ right to evaluate and adopt new technologies that may improve patient care.

To date, the Secretariat for State Affairs has recognized 64 state ophthalmology society programs and projects with the Star Award. State ophthalmology societies may apply for this award by responding to the Secretariat for State Affairs’ annual organizational survey of state societies.

**State Societies’ Outstanding Executive Directors**
Each year, the Academy Secretariat for State Affairs publicly acknowledges state ophthalmology society executive directors for their outstanding contributions to their state societies and for their partnership and collaboration with the Academy on its national efforts. During AAO 2017 in New Orleans, the Secretariat recognized executive staff of 2 state ophthalmology societies for their work.

- **2017 Outstanding Executive Director: Organizational Development**—Debra Alderman, Executive Director, Washington Academy of Eye Physicians and Surgeons (www.waeps.org).
- **2017 Outstanding Executive Director: Political Action**—Alan Skipper, Executive Director, North Carolina Society of Eye Physicians and Surgeons (www.nceyemed.org).

The Academy Secretary for State Affairs, Kurt F. Heitman, MD, applauded the dedication and professionalism of all executive directors on behalf of state societies and ophthalmologists across the country. “State society executive directors are crucial members of ophthalmology’s team, and we in State Affairs value their expertise and their commitment to preserving quality eye care in their states.”

**TAKE NOTICE**
Nominate a Colleague for the Laureate Award
The Academy is accepting nominations through Jan. 31 for the 2018 Laureate Recognition Award. This award honors an outstanding ophthalmologist whose scientific contribution to the field has shaped modern ophthalmology.

To submit a nomination, visit aao.org/about/awards/laureate#nominations.
Don't Miss the Jan. 15 Deadline for MIPS
If you are using the IRIS Registry to report the Merit-Based Incentive Payment System (MIPS), Jan. 15 is a key date on 2 counts.

Finish manually entering your MIPS information by Jan. 15. This deadline applies if you are using the IRIS Registry web portal to manually report quality measures, advancing care information (ACI) measures, or improvement activities. If you successfully integrated your electronic health record (EHR) system with the IRIS Registry, your MIPS quality data is automatically extracted from your EHRs, but you can only report ACI measures and improvement activities manually.

Submit a signed data-release consent form for each provider by Jan. 15. The IRIS Registry won’t submit a provider’s MIPS data to Centers for Medicare & Medicaid Services (CMS) unless it has received the signed consent form by Jan 15. You must submit a new consent form each year and can do so via the IRIS Registry dashboard. For instructions, visit aao.org/consent-form.

To learn more about the IRIS Registry and MIPS, visit aao.org/iris-registry and aao.org/medicare.

International Blindness Prevention Award
Established in 1992, the International Blindness Prevention Award is presented at the Academy’s annual meeting to honor individuals who have made significant contributions to the prevention of blindness or restoration of sight. The deadline for 2019 nominations is Feb. 20.

To submit a nomination, visit aao.org/about/awards/blindness-prevention.

Seeking Outstanding Ophthalmologists
Would you like to nominate a colleague for next year’s Outstanding Humanitarian Service Award? The Academy must receive your nomination by March 16, 2018. This award recognizes Academy fellows and members for outstanding contributions to humanitarian efforts, such as participation in charitable activities, care of the indigent, and community service. It acknowledges those who have performed above and beyond the normal duties of an ophthalmologist.

To obtain a nomination form, please contact Member Services by phone, 866-561-8558 (toll-free) or 415-561-8581; by fax, 415-561-8575; or by email, member_services@aao.org. You can also complete a nomination form at aao.org/about/awards/humanitarian.

Follow @AAOjournal for the Latest Academy Journal Articles
Stay up-to-date on research from Ophthalmology and Ophthalmology Retina via the @AAOjournal Twitter handle. New content is posted every day, including new articles in press, fascinating “Pictures and Perspectives,” thought-provoking editorials, and new issue alerts.

MEMBERS AT LARGE

ACS Election
Sarwat Salim, MD, has been elected to the Board of Governors of the American College of Surgeons (ACS), the largest organization of surgeons in the world with over 80,000 members. Dr. Salim said, “I am honored to represent ophthalmology and look forward to working with ACS leadership in raising the standards of surgical practice across the board through education, quality, advocacy, and health policy.”

LDP in Sri Lanka
Madhuwanthi Dissanayake, MBBS, MD, a graduate of the Asia Pacific Academy of Ophthalmology’s (APAO) Leadership Development Program (LDP) and now president of the College of Ophthalmologists of Sri Lanka (COSL), presented LDP faculty and Academy past president Michael W. Brennan, MD, with “A Tribute” booklet. It highlights Dr. Dissanayake’s collection of poems in honor of teachers who were instrumental in steering her career, including a poem for the faculty at the APAO LDP. Dr. Dissanayake wrote that the APAO LDP was “a unique experience during a period of 2 years expanding into 3 countries. The journey started in Japan, was followed by the APAO LDP Masterclass in Vietnam, and then wound up in China.” The Academy’s 20th LDP class meets in San Francisco Jan. 12-14. The Academy continues to collaborate with its counterpart LDPs from the supranational societies, including APAO, European Society of Ophthalmology, Pan-American Association of Ophthalmology, and the African Council of Ophthalmology.

OWL Awards
Ophthalmic World Leaders (OWL) is a U.S. not-for-profit organization dedicated to driving ophthalmic innovation and patient care by advancing diversity in leadership. On Nov. 12 during OWL’s signature event at AAO 2017, OWL’s president, Heather Ready, presented Cynthia Matossian, MD, FACS, with the Visionary Award. The OWL Awards are given to those who best exemplify OWL’s core values and vision.
Who’s in the News
Brian Boxer Wachler, MD, was featured on Great Day Washington Morning Show (WUSA9) with hosts Chris Leary, Markette Sheppard, and Meaghan Mooney to discuss his new book, Perceptual Intelligence: The Secret Behind Perception Revealed. Via concrete examples and case studies, the book explains why senses do not always match reality and describes how we can influence the world through perceptions.

For more information, visit www.perceptualintelligence.com.

ACADEMY STORE
Jan. 10 Webinar on New Cataract Surgery Technologies
Join experts Sonia H. Yoo, MD, Eric D. Donnenfeld, MD, Douglas D. Koch, MD, Rachel A. Lieberman, MD, and Bruna V. Ventura, MD, on Jan. 10 for a live, interactive webinar that will expand your repertoire of techniques for achieving improved refractive outcomes. New Technology in Cataract Surgery and Multifocal Implants will deepen your understanding of both manual and femtosecond laser-assisted techniques for limbal-relaxing incisions and multifocal toric intraocular lenses (IOLs). Presenters will also share pearls in patient selection and surgical planning.

Visit aao.org/store to sign up for the webinar or purchase the recording.

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Now Shipping: Ophthalmology’s Leading Coding Tools
The Academy’s complete suite of 2018 coding products are now available for shipping. These updated coding tools developed by coding experts ensure you’re coding correctly so you can maximize your reimbursements and avoid audit triggers. Save 10% when you buy 4 or more.

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D.C. REPORT
Major Quality Program Changes and Stable Payments
The 2018 Medicare fee schedule will provide some relief for ophthalmologists. The policy, unveiled by the Centers for Medicare & Medicaid Services (CMS) in November, adopts much of what it proposed in the summer of 2017, including several major Academy wins. Highlights of the CMS policy include the following:

• All proposed, retroactive changes to the Physician Quality Reporting System (PQRS) have been finalized. This reduced the number of required quality measures physicians must report on. This change stemmed from the Academy spearheading a months-long regulatory relief campaign, and it is a significant win for ophthalmology.
• All proposed, retroactive changes to meaningful use were finalized.
• All changes to the value-based modifier, including a 50% cut in value-based modifier penalties, were finalized.
• There was a zero net change, overall, for ophthalmology during 2017—CMS generally spared us from major reductions.
• All revised work values proposed by the Academy and the AMA/Specialty Society RVS Update Committee were accepted.

Changes to legacy quality programs stick. CMS will adopt changes to legacy quality programs, including PQRS, meaningful use, and the value-based modifier. In doing so, the agency reduces the requirements on which you’ll be scored. It will not, however, reopen PQRS submissions for 2016. The Academy devoted many hours to convincing CMS that these were necessary changes to the existing policy, as they provide significant relief for affected physicians.

Slight uptick in physicians’ conversion factor. CMS increased the physician conversion factor to 35.99. This is an increase from 2017’s 35.8887.

CMS limits what the public will see on Physician Compare. The Physician Compare website will not share your value-based modifier results. This is significant because the public lacks the necessary context to understand this program.

No overall reduction in payments. There are some reductions to the low-volume services. These stem from the time for these procedures, which has changed significantly over the years. Overall, though, payments for ophthalmic services will remain stable for 2018.

Jan. 5 Webinar on 2018 Coding Updates
Make sure you’re up to date by attending the 2018 Coding Update on Jan. 5. The 60-minute webinar will spotlight the most significant coding and reimbursement changes impacting ophthalmology. If you can’t attend, you can purchase a recording.


Codequest 2018 Is Coming to a City Near You
Get expert instruction from the recognized leader of ophthalmic coding programs at the Academy’s Codequest 2018 course, a 4-hour course presented...
with the ophthalmic state societies. Stay up-to-date on changing regulations, get strategies for maintaining compliance with federal and commercial payers’ rules, and learn the latest tactics to maximize your reimbursements.

For a list of 2018’s first 16 Codequest events, see page 52.

To learn more and sign up, visit aao.org/codequest.

FOR THE RECORD

Nominations for the Academy Board

By Cynthia A. Bradford, MD

As past president of the Academy, it is my privilege to serve as chairman of the Academy’s Nominating Committee in 2018. This committee represents a variety of interests within the Academy and is charged with identifying appropriate candidates for the open positions on the 2019 Board of Trustees.

We are interested in identifying leaders in our profession with experience in confronting the critical issues facing organized medicine and who reflect the strength and diversity of our members. The Academy’s leaders should be knowledgeable, experienced, and prepared to devote the time and energy required by a large organization in these challenging times. This work is both demanding and rewarding for those interested in helping to assure the Academy’s success and responsiveness to members. With these characteristics in mind, I ask you to assist the committee by suggesting appropriate candidates for the following positions in 2019:

President-elect (to serve as president in 2020). Nominees should have leadership experience within the Academy as well as demonstrated leadership qualities in clinical practice, in their own ophthalmic communities, and in other medical or ophthalmological organizations.

Senior Secretary for Clinical Education (3-year term). This senior secretary coordinates the programs and activities of the Academy’s education division including curriculum development, online education, lifelong learning and assessment, and educational publications.

Trustee-at-large (4-year term). This individual should be an Academy Fellow who demonstrates strong leadership potential and would be able to represent and articulate the needs and concerns of the membership to the Academy board.

International trustee-at-large (3-year term). This individual should be an Academy International Fellow or Member who practices exclusively outside of the United States. He or she should have a strong affinity for the Academy and broad experience and understanding of his or her region. This individual should be able to represent and articulate to the Academy board the perspective of international members.

Public trustee (a renewable 3-year appointment; an advisor to and member of the Board of Trustees). The bylaws allow the board to appoint up to 3 public trustees. We currently are served by Paul B. Ginsburg, PhD. Public trustees provide insight on how ophthalmology can better work with the rest of medicine, the public, government, and industry. The nominating committee will be pleased to receive suggestions for individuals, who may include physicians from other medical specialties or leaders in industry, government, public policy, or advocacy. Thank you for your interest and participation in this process. Membership participation is vital, not only for the Academy but also for our collective goals of being able to provide appropriate, accessible, and affordable eye care to the public. On behalf of the Nominating Committee, I look forward to receiving your suggestions as we seek to identify our profession’s future leaders.

Send your confidential suggestions by Jan. 31 to Cynthia A. Bradford, MD; Nominating Committee Chair, American Academy of Ophthalmology, P.O. Box 7424, San Francisco, CA 94120-7424. Suggestions can also be e-mailed to nominate@aao.org or faxed to 415-561-8526.

For more information, go to aao.org/about/governance/board-nominations.

Election Results

On Nov. 13, voting opened for 5 positions on the 2018 Board of Trustees. The results are as follows:

President-Elect: George A. Williams, MD

Senior Secretary for Advocacy: Daniel J. Briceland, MD

Trustee-at-Large: William S. Clifford, MD

Chair, the Council: Lynn K. Gordon, MD, PhD

Vice Chair, the Council: Sarwat Salim, MD, FACS

For more information about the elections, visit aao.org/about/governance/elections.

ABOUT THE NOMINATING COMMITTEE

The Academy nominating process has been carefully crafted to be inclusive, fair, and efficient. This process encourages a broad base of nominations from the entire Academy membership. The Nominating Committee composition is delineated by the bylaws, and it considers a number of factors when screening potential candidates. These include integrity, ophthalmology leadership ability, special expertise, past committee and leadership experience and performance, and knowledge and interest in the multitude of issues currently facing ophthalmology. In addition to nominations from the current year, the committee reviews prior-year nominations to ensure a wide range of potential candidates for each position. Following months of confidential deliberations, the committee presents final recommendations to the Board of Trustees for approval. This single-candidate method avoids the loss of valuable future leaders, as there are no public “losers” in the election. Often, those considered but not selected for an open position one year become the nominee of choice in a future year.
Help Make a Positive Impact on Ophthalmology’s Future

Mid-Year Forum is one of the Academy’s most significant yearly meetings, bringing the ophthalmology community together to drive change and shape our profession’s future.

- Meet with federal lawmakers during Congressional Advocacy Day.
- Directly advocate for your profession and patients.
- Learn about changes that impact how you practice.
- Develop key strategies for successfully implementing new programs into your patient-care approach.
- Hear from expert panels on the future of our profession.
- Play a key role in driving the highest quality of care for your patients.

Registration Opens in January 2018.
aao.org/myf
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LAST MONTH’S BLINK

Traumatic Aniridia

A 77-year-old woman, 2 weeks after undergoing uncomplicated laser-assisted phacoemulsification of her right eye, presented 2 hours after falling onto the right side of her face. Her vision was hand motion with 2+ corneal folds, total hyphema, and IOP of 40 mm Hg. There was no evidence of corneal or scleral laceration. Upon emergent anterior chamber washout (1A; note residual blood), absence of the iris was observed (1B). No vitreous hemorrhage or retinal detachment was evident. The recently implanted IOL was centered and intact within the capsular bag. The patient was placed on topical glaucoma medications, bed rest, and a short course of oral prednisone. Over 1 month, her corneal edema and hyphema cleared (1C). A year later, with total aniridia and a centered, intact IOL (1D), she denies complaints of glare and has maintained 20/30 uncorrected VA.

There are few reports of isolated aniridia in pseudophakic eyes after nonperforating blunt trauma, without dehiscence/extension of the cataract incision.1-6 Small self-sealing modern cataract incisions appear to be protective against expulsion of intraocular contents, which has led to several theories regarding the mechanism of traumatic aniridia.2,3 Acute rise in IOP from blunt trauma may allow the corneal incision to act as a “release valve,” promoting rapid progression of an iridodialysis to complete avulsion and subsequent expulsion due to the high-velocity injury.3,4 In our case, there was total iris loss, but the remainder of the intraocular contents remained stable and intact. Thus, it is possible that the IOL may have acted to absorb the impact and block disruption of surrounding tissue.5 An additional theory is that the traumatized iris may have remained within the eye, only to undergo rapid phagocytosis by macrophages and trabecular meshwork cells.3


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Rep. Dave Loebsack (D-Iowa), left, met with Academy Advocacy Ambassador Philip I. Niles, MD, MBA, during Mid-Year Forum 2016’s Congressional Advocacy Day. This in-person advocacy allows attendees to directly interface with federal lawmakers on behalf of ophthalmology’s patients, discussing topics such as fair Medicare physician reimbursements, relief from administrative burdens, and preserving access to sight-saving compounded drugs.
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