AMERICAN ACADEMY
OF OPHTHALMOLOGY®

EyeNet®

JUNE 2018

Aesthetics
How to Get Started

Smartphones in Practice
Low-Cost Funduscopy

MD ROUNDTABLE
Normal Tension Glaucoma: The Ins & Outs of Diagnosis

60-PAGE SUPPLEMENT
MIPS 2018: A Primer and Reference

Protecting Sight. Empowering Lives.®

Experience IntelleChartPRO

CHART SMARTER

NEW
Assisted Compliance

NEW
Assisted Coding

IMPROVED
Knowledge Base

IntelleChartPRO

#1 No. of Registered Practices

IRIS® Registry EHR Collaborator

AMERICAN ACADEMY OF OPHTHALMOLOGY®

Nextech

(800) 868-3694

Nextech.com/Ophthalmology

DIOPSYS® ffERG

FULL FIELD ELECTRORETINOGRAPHY
MULTI-LUMINANCE FLICKER

Quantify retinal function. Manage retinal disease.

Diopsys® ffERG / Flicker vision tests provide objective, functional information about global retinal health using intuitive, color-coded reports to help you:

- Evaluate retinal disease severity[1,2]
- Predict retinal ischemia[2-4]
- Quantify retinal function loss and recovery[1,2,5]
- Monitor retinal function for more appropriate and timely treatment[1,2,5]

ffERG is clinically effective in helping to manage retinal disorders like **diabetic retinopathy, central retinal vein occlusion, retinal concerns obscured by media opacities, and uveitis.**[1-5]

Objective, functional results for you. Enhanced care for your patients.

To learn more, visit Diopsys.com/Eye

1. Yasuda S, Kachi S, Ueno S, Piao CH, Terasaki H. Flicker electroretinograms before and after intravitreal ranibizumab injection in eyes with central retinal vein occlusion. Acta Ophthalmol. 2015;93:e465-8. 2. Moschos MM, Gouliopoulos NS, Kalogeropoulos C. Electrophysiological examination in uveitis: a review of the literature. Clin Ophthalmol. 2014;8:199-214. 3. Larsson J, Andréasson S. Photopic 30 Hz flicker ERG as a predictor for Rubeosis in central retinal vein occlusion. Br J Ophthalmol. 2001;85:683-5. 4. Ratanapakorn T, Patarakittam T, Sinawat S, Sanguansak T, Bhoomibunchoo C, Kaewpanna S, Yospaiboon Y. Effect of cataract on electroretinographic response. J Med Assoc Thai. 2010 Oct;93(10):1196-9. 5. Holm K, Schroeder M, Lövestam Adrian M. Peripheral retinal function assessed with 30-Hz flicker seems to improve after treatment with Lucentis in patients with diabetic macular oedema. Doc Ophthalmol. 2015;131:43-51.

Diopsys Vision Testing Systems carry the CE mark; are FDA 510(k) cleared; and IEC 60601 Certified.

DIOPSYS®
Seeing tomorrow, today.™

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

Ophthalmology Job Center

Staff Your Practice Through the #1 Job Site in Ophthalmology

Access the most qualified and talented pool of physicians and ophthalmic staff professionals—or find a new position that's right for you—on the Academy's Ophthalmology Job Center.

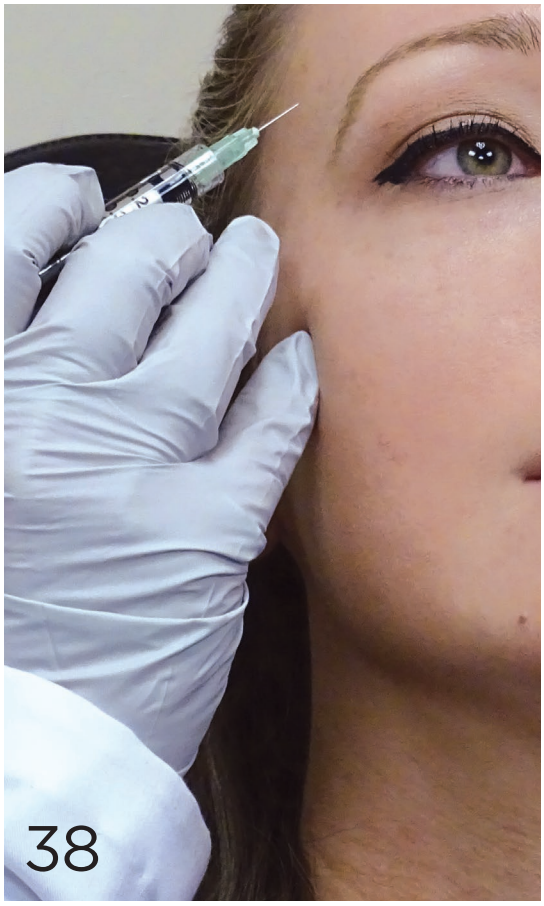
Find the Right Candidate Today.

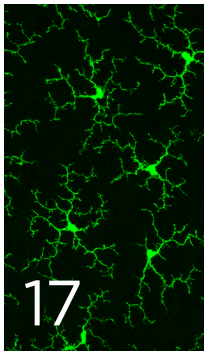
aao.org/jobcenter

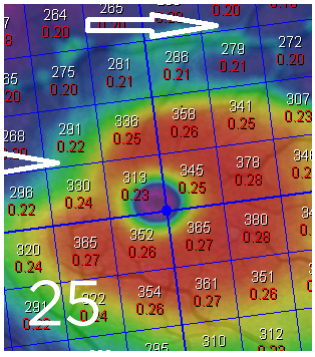
Protecting Sight. Empowering Lives.®

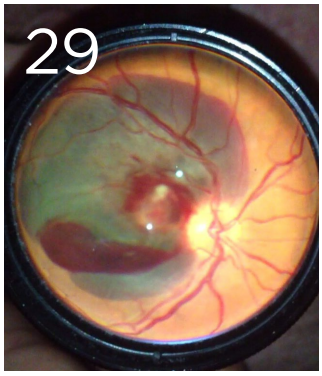
CONTENTS

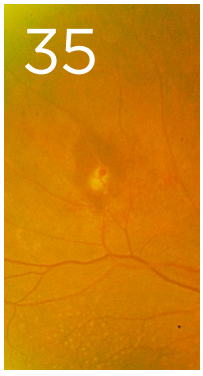
JUNE 2018
VOLUME 22 • NUMBER 6





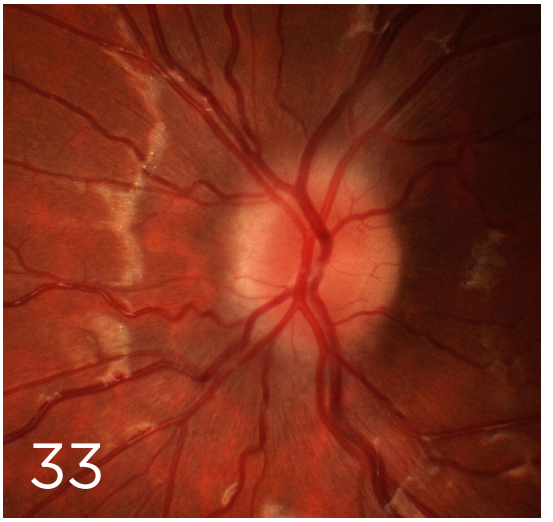


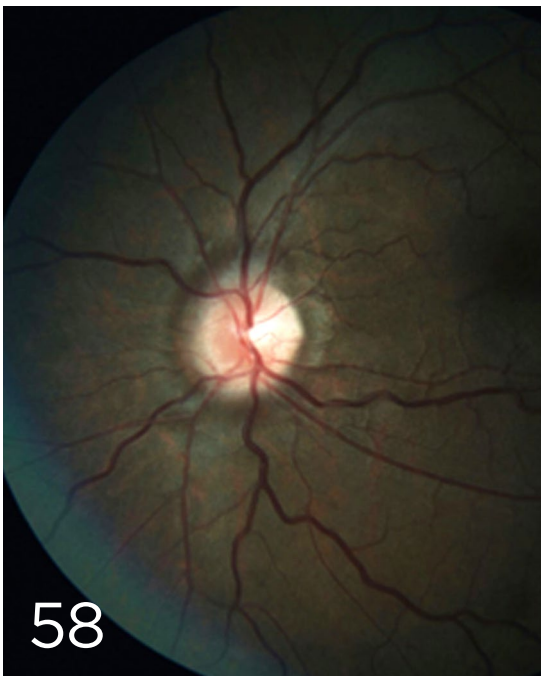




AMERICAN ACADEMY OF OPHTHALMOLOGY®
Protecting Sight. Empowering Lives.

***EyeNet*® Magazine** (ISSN 1097-2986) is published monthly by the American Academy of Ophthalmology, 655 Beach St., San Francisco, CA 94109-1336, as a membership service. Subscription is included in U.S. members' annual dues. International Member, IMIT, $135 per year. Nonmember in U.S., $150 per year. Nonmember outside U.S., $210 per year. Periodicals Postage Paid at San Francisco, CA, and at additional mailing offices. POSTMASTER: Send address changes to *EyeNet*, P.O. Box 7424, San Francisco, CA 94120-7424.





I AM MODERNIZING OPHTHALMOLOGY

WITH A SMARTER EHR

It's so advanced, it actually learns from you. Modernizing Medicine®'s all-in-one platform was designed by practicing ophthalmologists to streamline treatment and improve outcomes. From the moment you first log in, it begins learning how you practice, diagnose and treat patients, customizing itself to give your practice greater efficiency.

So you can see more patients, while seeing more of your patients. It's time to demand more from your EHR.

VIEW OUR 2-MINUTE DEMO

MODMEDOPHTH.COM

TOGETHER, WE ARE MODERNIZING MEDICINE.

For desktop and mobile devices

MODERNIZING MEDICINE

EDITORIAL BOARD

ACADEMY BOARD

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

EyeNet® MAGAZINE

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

Ruth D. Williams, MD
Chief Medical Editor

Dale E. Fajardo, EdD, MBA
Publisher

Patty Ames
Executive Editor

Carey S. Ballard
Art Director / Production Manager

Chris McDonagh, Jean Shaw
Senior Editors

Catherine Morris
Associate Editor / Content Manager

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

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

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

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

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

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

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

Benefit From Expert Clinical Insights

Membership in ISRS provides access to insights from experts in cornea and lens-based refractive surgery from around the world.

Journal of Refractive Surgery

Practice effectively and enhance patient care with original research, review and evaluation from the highest-ranked journal in refractive surgery. A $288 value.

Multimedia Library and Ophthalmic News & Education (ONE®) Network

Learn the latest techniques and developments from the world's top refractive and cataract surgeons. Access more than 1,000 on-demand clinical videos. More than ASCRS and ESCRS combined.

Refractive Surgery Outlook

Get the latest on SMILE/femtosecond lasers, IOL calculations, complications management and more in this monthly e-newsletter.

Review your benefits or join now at
www.isrs.org

AMERICAN ACADEMY
OF OPHTHALMOLOGY®
Protecting Sight. Empowering Lives.

Join William L. Rich III, MD, FACS in Supporting Academy Programs

Become a Partners for Sight Donor

Make a bigger impact than you ever thought possible by giving to the Foundation at the Partners for Sight level ($1,000 - $2,499). You can help Academy programs to educate more ophthalmologists and do even more good for patients worldwide.

"We as Academy members need to support the educational programs that benefit us throughout our careers. I see the Academy as my university for life. For me, giving back is a win-win."

WILLIAM L. RICH III, MD, FACS
PARTNERS FOR SIGHT CHAMPION

Learn how $1,000 can make a difference at **aao.org/foundation**

Foundation

Letters

An Initial MIGS Procedure

I appreciate *EyeNet*'s article "MIGS: Expanding Options for Glaucoma Treatment" (Feature, February) and how aptly it addresses the evolution of MIGS procedures in glaucoma. However, an important MIGS procedure (in fact, the first MIGS procedure), excimer laser trabeculostomy (ELT), was unfortunately not included in this otherwise comprehensive article. Readers would certainly have benefited from this information. Excimer laser-based MIGS glaucoma surgery has been in clinical use for more than 2 decades in Europe.

History. In the late 1980s, Michael S. Berlin, MD, invented a new technique for bypassing outflow obstruction of the trabecular meshwork/inner wall of Schlemm's canal. This "trabeculostomy" procedure uses an excimer laser to nonthermally ablate channels connecting the anterior chamber to Schlemm's canal for the treatment of glaucoma. Known as ELT, this method minimizes scarring of the adjacent tissue, which thereby enables longevity of IOP lowering. Although similar to the canal-based MIGS procedures discussed in the article (which theoretically treat the pathology at the known site of outflow obstruction), ELT requires no implantation of foreign bodies and does not evoke a significant healing response, resulting in a longer duration of IOP lowering postoperatively.

ELT, used clinically in Europe, has a verified, long-lasting efficacy for reducing IOP. Data for more than 8 years of postop follow-up has been evaluated, confirming the sustained IOP-lowering effect of ELT.[1]

For the sake of completeness, it is appropriate to mention ELT and credit Dr. Berlin, the first person to conceptualize and successfully clinically apply lasers capable of nonthermal photoablation in glaucoma surgery. Excimer lasers do and will enable much improved glaucoma surgical options.

Maayan Agam
Research Assistant/Study Coordinator
Glaucoma Institute of Beverly Hills
Office of Michael S. Berlin, MD, Los Angeles

1 Berlin M et al. Excimer laser trabeculostomy, MIGS procedure using no implants while lowering intraocular pressure over 8 years, alone and with phaco. In: Proceedings of the ASCRS Annual Meeting; May 5-9, 2017; Los Angeles. ASCRS submission number: 30587.

Opinion

RUTH D. WILLIAMS, MD

Dilation and Informed Consent

It's too often overcast in the Midwest—especially in the late fall and early spring. When I tell patients that they will be dilated, it's common here in Illinois for them to respond, "At least it's a cloudy day." Experienced patients know that dilation can cause light sensitivity, difficulty driving, and, occasionally, decreased vision.

Ophthalmologists dilate the pupils of most new patients and many of their existing patients every day. It's so routine that perhaps we don't think about it enough.

Informed consent isn't needed for certain routine tests and procedures with negligible risks, such as blood tests or x-rays. It's assumed that the patient understands that these common procedures have few risks, and consent is implied. Ophthalmologists often assume that these considerations apply to dilation, as well. But what are our obligations to our patients? What are our medicolegal risks?

Anne Menke, RN, PhD, OMIC Patient Safety Manager, explained that the legal doctrine of informed consent is based on what a "reasonable layperson" would like to know before a procedure, not on what the ophthalmologist assumes is common knowledge. "Because dilating drops can cause several hours of photophobia, blurred vision, glare, and decreased contrast threshold, a reasonable person might feel that informed consent is needed."[1] Anne also pointed out that dilation could potentially incite an attack of angle-closure glaucoma, an allergic reaction, dizziness, tachycardia, or arrhythmia; it also can contribute to falls. For these reasons, she suggested, "consider asking patients to sign a consent the first time they are dilated."

When asked about the responsibility of the ophthalmologist as it relates to dilation, Ron Pelton, MD, chair of the Academy's Ethics Committee, quoted the Code of Ethics: "It is the responsibility of an ophthalmologist to act in the best interest of the patient." But precisely how this plays out in a particular ophthalmologist's practice is open to interpretation. (See also "Ask the Ethicist" on page 52.)

While no clear recommendation exists, OMIC provides a few suggestions. When possible, advise patients about dilation when the appointment is made so that they can arrange for a ride or allow extra time after dilation for their eyes to adjust before driving themselves home. Remind patients each time about the impact of dilating drops on their vision, and briefly note the discussion in the medical record. Be prepared to offer assistance to patients with mobility problems while they are in the office. Consider offering sunglasses as patients leave the office so that glare is less of a problem.

My glaucoma partner, David Gieser, MD, goes a step further. He is adamant that every dilated patient should have his or her vision rechecked before driving home. David shared several examples of glaucoma patients who drove to an appointment with vision that was legal for driving but that dropped below the legal requirements after dilation. He pointed out that a technician can check the vision of both eyes very quickly. And he added that every few months, he asks a patient to call a family member for a ride or to wait in the office until the drops begin to wear off and vision returns to baseline. "It's an ethical issue for me," David said. "My duty is do everything in my power to protect the patient, and I cannot allow a patient to drive home after the dilation has caused the vision to drop below the legal requirement."

Ruth D. Williams, MD *Chief Medical Editor,* EyeNet

We all embrace patient safety. Cultivating a culture of patient safety includes reviewing everyday procedures, and this includes a review of how we inform patients about the risks of dilation. It's worth reminding ourselves that what seems like common knowledge to us may not be to our patients—even our experienced patients.

1 Menke AM. www.omic.com/warn-patients-about-side-effects-of-dilating-drops. Accessed April 12, 2018.

EXTRA **MORE ONLINE.** For links to resources mentioned above, find this article at aao.org/eyenet.

Current Perspective

DAVID W. PARKE II, MD

Hitting at Least a Triple

The profession of ophthalmology has just experienced a monumental milestone—but one that escaped most of us. Something that started out as a risky endeavor, more likely to fail than succeed but with transformative potential, the IRIS Registry (Intelligent Research in Sight) silently recorded its 200 millionth patient encounter last month! It is now the largest single-specialty clinical database in the world.

Why is it a big deal? Consider this. Six years ago, the Academy's Board of Trustees approved planning for the IRIS Registry and launched it 4 1/2 years ago with the hope that it would provide ophthalmologists with more control over their future. How? First and foremost, it would, for the first time, give us contemporaneous, benchmarked, actionable information on our clinical activities—the processes and outcomes of our patient care. Second, it would yield new scientific insights that would advance the profession.

Since 2013, the Academy invested (through the Foundation) over $14 million in the IRIS Registry, hired data analysts, tapped the phenomenal skills of very talented member-volunteers, and entered into some innovative partnerships. The results:

- Over 14,000 ophthalmologists are using the IRIS Registry to report to CMS under the Merit-Based Incentive Payment System (MIPS)—now saving nearly $200 million each year in cost avoidance, penalty avoidance, and bonus qualification. It averages about $15,000 per year per member. Not bad considering that the IRIS Registry remains free of charge!
- For reporting year 2016 of the Physician Quality Reporting System (now part of MIPS), the submission error rate for ophthalmologists submitting electronically through their EHR to the IRIS Registry was 0%. (The national error rate for all physicians was over 20%.)
- About 15% of the U.S. population now has records in the IRIS Registry—over 200 million encounters.
- Ophthalmologists who monitor their IRIS Registry data actually improve measured clinical care outcomes, according to a published study.
- The ABO accepts custom practice improvement projects through use of the IRIS Registry dashboard for Improvement in Medical Practice of Maintaining Certification.
- IRIS Registry data has been used to support ophthalmology's health policy priorities.
- The FDA is receptive to sponsors using IRIS Registry data to inform decisions on new device approvals and to monitor post-approval device safety.
- The Centers for Disease Control and Prevention is working with IRIS Registry staff and other data sources to create a national vision and eye health surveillance system.
- A number of scientific papers have been published using IRIS Registry analytics to refine our knowledge of disease natural history, rare diseases, real-world (as opposed to clinical trials) treatment patterns and results, and complications of treatment.
- We have decreased the annual cost to the Academy to under $2 million.

David W. Parke II, MD
Academy CEO

And all this was accomplished while preserving your and your patients' privacy.

While maybe it's not yet a home run, this is at least a solid triple! How often do we get something that costs each of us nothing, is low hassle, saves money, improves quality, and promises to add immeasurably to the science that drives our profession? Why isn't it a home run? Because we haven't yet added more quality measures and analytic tools, haven't tapped its potential for robust individual practice benchmarking and analytics in all subspecialties, haven't used it as a practice management tool, and have yet to add powerful imaging data, genomics, and effective patient-reported outcomes. That will come.

None of this would have happened without you—the IRIS Registry user. By participating, you are supporting clinical investigation, getting innovations to market more quickly, monitoring drug and device safety, and improving patient care. You are strengthening your profession. Congratulations, and thank you on behalf of your patients.

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

AAO 2018

ART + SCIENCE

In conjunction with the
Pan-American Association of Ophthalmology

Join Us...

Art of relaxation — EyePlay Experience in Hall A is your wellness destination. Recharge yourself and your mobile devices. Spend some time with the therapy dogs, get a chair massage or challenge a colleague to a game of pingpong.

Science of innovation — The AAO 2018 exhibition is the largest ophthalmic marketplace with over 550 companies showcasing cutting-edge products sure to revolutionize the industry.

Also, gain knowledge from the experts as they examine aerospace ophthalmology, concussion and the eyes, smartphone apps for low vision, and more.

Jackson Memorial Lecture:
Philip J. Rosenfeld, MD, PhD

Dr. Rosenfeld, principal investigator and study chairman for numerous AMD clinical trials, pioneered the use of intravitreal Avastin for the treatment of neovascular AMD and macular edema.

2018 Laureate awardee:
Steven T. Charles, MD

Dr. Charles is a distinguished surgeon known for developing many of the vitreoretinal techniques and devices used by surgeons all over the world.

Watch this short video at **aao.org/2018** to see what's in store for you at AAO 2018.

Registration Opens

June 13 – Academy, AAOE and PAAO Members

June 27 – Nonmembers

Register by August 15 and save

Protecting Sight. Empowering Lives.®

Where All of Ophthalmology Meets®

AAO 2018
October 27 – 30

Subspecialty Day
October 26 – 27

AAOE Program
October 26 – 30

in Chicago

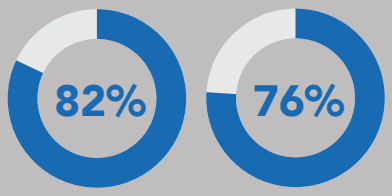
At the end of your day, let loose in the Windy City. Deemed the No. 1 Best Big City in the U.S. in 2017 by Conde Nast Traveler readers, Chicago is a haven for foodies, art lovers and science aficionados.

Enjoy the art and science of molecular gastronomy, a niche part of Chicago's dining scene — which includes over 20 Michelin-starred restaurants.

Satisfy your curiosity at any of Chicago's renowned museums, including the Museum of Science and Industry, the largest science center in the West; the Art Institute of Chicago, home of the iconic lion statues; and the American Writers Museum — one of the 10 best attractions in Illinois.

Plus, with more than 200 theater companies to choose from, you have plenty of options for live entertainment. Celebrating over 50 years, The Second City sketch and improv comedy club has launched some of Hollywood's biggest stars — Tina Fey, Chris Farley, Bill Murray, Steve Carell and Stephen Colbert.

aao.org/2018 **#aao2018**



OMIC **Industry**

Reported claims without a payment

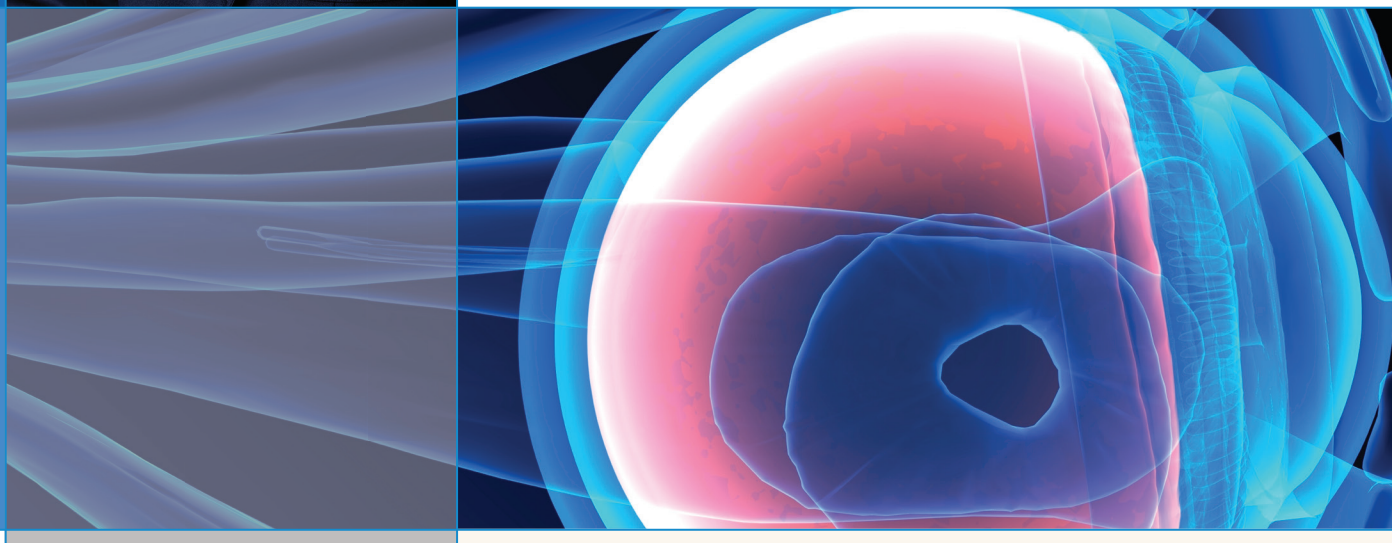
OMIC settles 25% fewer of the claims and lawsuits reported to us than our peer companies.

OMIC consistently outperforms multispecialty malpractice insurance companies in almost all claim defense results, benchmarks, and ratios used to evaluate performance in our industry.

OMIC makes a payment to the plaintiff is 25% fewer of the total claims reported vs. the traditional industry. When we do make a settlement, our average indemnity payment is 27% lower than the industry.

Our better claims experience is reflected in OMIC's superior operating performance, higher dividends, and lower rates.

Daniel Briceland, MD
Chair, Claims Committee



800.562.6642

www.omic.com/request-a-quote

OPHTHALMIC MUTUAL INSURANCE COMPANY
A Risk Retention Group

News in Review

COMMENTARY AND PERSPECTIVE

NEUROSCIENCE

Microglia Can Repopulate Retinas After Depletion

RESEARCHERS AT THE NATIONAL EYE Institute (NEI) have discovered that the eye has the potential to regenerate the intraretinal immune cells that it needs to keep retinal synapses functioning properly.[1]

The finding represents the first time that neuroscientists have been able to observe the regeneration of these immune cells, called microglia, directly in a living animal and demonstrate that the repopulated cells can do their normal job within a neural system, said the study's lead investigator, Wai T. Wong, MD, PhD, at the NEI.

It also suggests that targeted control of these cells might one day allow ophthalmologists to tamp down destructive inflammation in diseased retinas without the use of corticosteroids, Dr. Wong said.

Rethinking neurodegeneration. "In the business of trying to save neurons from dying, people have been trying to directly sustain the neurons," Dr. Wong said. More recently, however, researchers have recognized that "many diseases in which neurons degenerate actually involve a maladaptive, maladjusted immune system within the brain or retina."

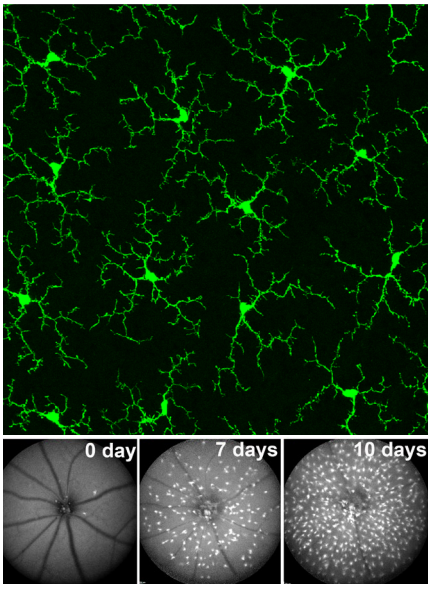
As a result, "finding ways in which the immune cells behave and can change, as well as discovering the agents that can manipulate them, is a new way of thinking about cures to neurodegeneration," he explained.

Road to repopulation. In this animal study, Dr. Wong and his colleagues were following up on their own and other scientists' work showing that microglia in the brain and the retina are essential to synaptic functioning of the neurons. "This is something that is quite recent in the field. We had studied this question a few years ago and found that, in the prolonged absence of microglia, the fidelity of the transmission of the signal between retinal neurons begins to break down. It's like having a bad electrical connection. You still get some transmission, but the amount is decreased," he said.

The researchers used the investigational drug PLX5622 (Plexxikon), an inhibitor of the colony-stimulating factor 1 receptor, to almost entirely deplete the microglia in the inner and outer plexiform layers of mouse retinas. When they withdrew the drug 1 week later, the few surviving cells began multiplying and, over subsequent weeks, redistributed themselves across the plexiform layers into the same functional, mosaic arrays that existed before the drug treatment, they reported.

"We were actually able to witness the repopulation process by looking into the eyes of living animals and document it in a video," Dr. Wong said.[2]

Looking ahead. Dr. Wong said that reversibility of microglial depletion suggests that targeted delivery of PLX5622 or another drug with similar action might someday be used to temporarily suppress microglia from sending inflammatory signals that would eventually lead to photoreceptor malfunction or death.



RECOVERY. *Top: Healthy microglia in an adult mouse retina. Bottom: Mouse eyes after being treated with a drug that nearly eliminates microglia. On Day 0, almost all microglia are gone, except for a few near the optic nerve head. By Day 7, the microglia have migrated across the retina, and by Day 10, they have increased in number.*

However, more research is needed to understand how to time and deliver the treatment in each disease scenario, he cautioned. Because the molecule is not soluble, intravitreal injection would require a special formulation or delivery device, Dr. Wong said. Human research on the drug is limited but ongoing; www.ClinicalTrials.gov lists only 2 PLX5622 clinical studies, both safety trials in patients with rheumatoid arthritis, and the outcomes have not been published.

For now, much research remains to be done, Dr. Wong said. "We were aiming at a proof of concept. So this

Neuron-Glia Interactions in Retinal Diseases Section, NEI

is a step toward understanding what the retina's immune system is capable of and how to control and manipulate that for therapeutic purposes," he said.

—Linda Roach

1 Zhang Y et al. *Sci Adv.* 2018;4(3):eaap8492.
2 See http://advances.sciencemag.org/cgi/content/full/4/3/eaap8492/DC1. (Note: Three movies are toward the bottom of the web page.)
Relevant financial disclosures—Dr. Wong: None.

RETINA

Evidence Review: Lasers for PDR

SINCE THE EARLY TREATMENT OF Diabetic Retinopathy Study (ETDRS), argon laser photocoagulation has been the gold standard for treating proliferative diabetic retinopathy (PDR). And, in recent years, there have been attempts to modify the technique and introduce new laser technologies. But do these strategies provide safe and effective alternatives? A team from the United Kingdom reviewed the literature and found a significant gap in the evidence.[1]

Intervention review. To assess the effects of different lasers and different laser protocols, the U.K. researchers identified and evaluated 11 randomized controlled trials proposing alternative laser modalities for the treatment of PDR. These trials compared a variety of modifications to the ETDRS standard of care, including different laser types, a variety of pulse intensities and durations, and altered scatter distributions for laser burns.

"After assessing and grading the overall certainty of the results, we found that these trials provide limited evidence with respect to the efficacy and safety of alternative laser systems or strategies," said Tanya Moutray, MB BCh, BAO, FRCOphth. In particular, the review found, the trials were small in size, poorly conducted, and poorly reported. They also contained a high risk of bias and failed to clearly define study outcomes.

Potential for confusion. The ETDRS standard of care calls for a single-spot treatment—specifically, an initial treatment of midperipheral scatter laser consisting of 1,200 to 1,600 burns, 200- to 500-µm spot size, and an argon pulse duration of 100-200 ms with power titrated to produce moderate-intensity burns.

However, guidelines set by the Royal College of Ophthalmologists (RCO) contradict this standard, stating that "technological advances in new laser technology using multispot and micropulse abilities have widened clinical

NEURO-OPHTHALMOLOGY

Measuring Intracranial Pressure: Is Ultrasound Acceptable?

A STUDY BY RESEARCHERS AT JILIN UNIVERSITY IN Changchun, China, furthers the case for orbital/optic nerve ultrasound's potential as an alternative to lumbar puncture for measuring changes in intracranial pressure (ICP).[1] Previously, the researchers confirmed that ultrasonographic measurements of optic nerve (ON) sheath diameter could be used to identify patients with elevated ICP.[2]

Dynamic assessments. For this study, the researchers measured both ON sheath diameter and ICP in 60 patients who had been admitted for lumbar puncture. Of those, 37 were found to have elevated ICP, most caused by cerebral infection. One month later, following treatment, the 25 patients not lost to follow-up underwent an additional round of measurements.

In both situations—upon admission and after treatment—the ON sheath diameter and lumbar puncture measurements were strongly correlated. What's more, there was no difference in mean ON sheath diameter between patients with higher or lower levels of elevated ICP.

The researchers speculated that the elasticity of the ON sheath may explain why sheath diameter examinations can be used to dynamically assess variations in ICP. They also noted that the technique is easy to learn, has high interobserver reliability, and may be generalizable and applicable in a variety of potential clinical settings.

Clinical implications. "This study adds further evidence [supporting] the sensitivity and specificity of ultrasonography for the purpose of determining in a noninvasive manner whether or not there is elevated ICP," said Andrew G. Lee, MD, at the Blanton Eye Institute at Houston Methodist Hospital.

In fact, Dr. Lee said in an accompanying editor's note, he has used orbital ultrasound as either an adjunct or surrogate to actual direct measurement of ICP in a number of common clinical circumstances.[3] Among them: differentiating difficult cases of pseudopapilledema from papilledema, and following patients who either refuse or cannot undergo lumbar puncture.

Nevertheless, Dr. Lee noted that the technique "is still in development." And he agreed with the researchers that larger studies are needed, in part to determine whether the results are generalizable at ICP levels outside the study's parameters. The maximum ICP value in the study was 400 mm H_2O, so the accuracy of the technique at higher levels is not clear.

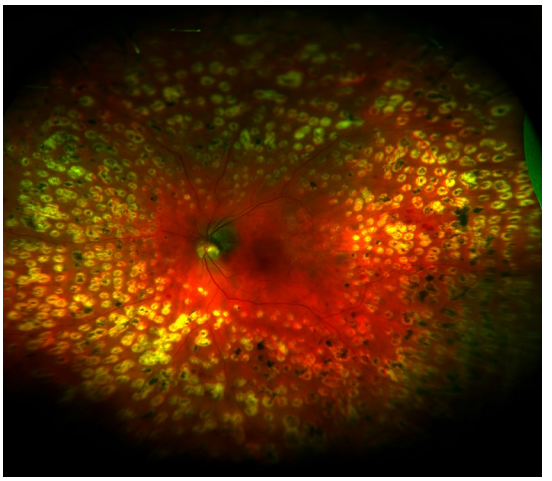
Despite ultrasonography's potential as a noninvasive alternative to lumbar puncture, Dr. Lee said, "Direct measurements of ICP remain the gold standard."

—Miriam Karmel

1 Wang L et al. *JAMA Ophthalmol.* 2018;136(3):250-256.
2 Wang L et al. *PLoS One.* 2015;10(2):e0117939.
3 Lee AG. *JAMA Ophthalmol.* 2018;136(3):256.
Relevant financial disclosures—Dr. Lee: None.

knowledge and treatment options."[2] Dr. Moutray voiced concern regarding the RCO guidelines, noting that "our review was unable to find evidence to definitively support these alternative modalities."

Advancing the discussion. Even so, physicians and clinicians should not ignore newer photocoagulation strategies because of the quality of these trials, said Dr. Moutray. Instead, she said, she hopes that her team's work will set a framework for future research.



PHOTOCOAGULATION. *After panretinal laser treatment.*

"New clinical trials focusing on PDR management and modern laser therapies can build on the research by using our findings and recommendations. This will help avoid research waste and encourage researchers to conduct studies that are large enough to provide definitive answers and evaluate the long-term outcomes most relevant to patients," she said. —*Mike Mott*

1 Moutray T et al. *Cochrane Database Syst Rev.* 2018;3:CD012314. doi:10.1002/14651858.CD012314.pub2.

2 https://www.rcophth.ac.uk/wp-content/uploads/2014/12/2013-SCI-301-FINAL-DR-GUIDELINES-DEC-2012-updated-July-2013.pdf. Accessed April 17, 2018.

Relevant financial disclosures—Dr. Moutray: None.

WORLD HEALTH

Visual Symptoms in Diplomats Posted to Cuba

HOW AMERICAN DIPLOMATS IN Havana, Cuba, came to suffer a constellation of symptoms characteristic of neurotrauma remains as mysterious today as it was when first reported in 2016 and 2017. But the first comprehensive clinical study of a cohort of "Havana syndrome" patients has concluded that their oculomotor and other neurological symptoms look a lot like those of a well-established diagnosis: persistent concussion.

A team of experts assembled by the University of Pennsylvania's Center for Brain Injury and Repair reached this conclusion after extensive examinations of 21 diplomats (mean age, 43 years) referred by the U.S. State Department for evaluation, treatment, and rehabilitation.[1]

"Much to our surprise—and even though a lot of people on the team were a little skeptical that someone without history of a head impact could display symptoms similar to concussion—one by one, each member of our multidisciplinary panel felt that these symptoms really did look like persistent concussion," said Douglas H. Smith, MD, who directs the center, which is located in Philadelphia.

What caused it? Eighteen of the 21 diplomats told the physicians that they heard a localized, intensely loud sound, with pure and sustained tonality, just as their symptoms began. Most of the patients also reported that the sound was accompanied by pressurelike or vibratory sensory stimuli.

Visual symptoms. Examinations at the Philadelphia center began an average of 203 days (range, 3-331 days) after exposure.

In addition to having cognitive difficulties, the patients exhibited an array of oculomotor and visual problems similar to those seen in persistent concussion, Dr. Smith said. These symptoms included convergence insufficiency (n = 11, 52%); abnormal smooth pursuits (n = 11, 52%); saccadic dysfunction (n = 10, 47%); and impairment of the vestibulo-ocular reflex (n = 15, 71%). In addition, the patients complained of light sensitivity (n = 13, 62%); difficulty reading (n = 12, 57%); and eye strain (n = 11, 52%), particularly with reading, and associated with headaches, disequilibrium, and nausea.

Need for rehab. The majority of the patients required intervention by multiple rehabilitation experts, including those specializing in oculomotor evaluations, for their symptoms to subside. "In contrast to patients with classic concussions, most Havana syndrome patients exhibited significant impairment that persisted for months [and they experienced] no significant improvement until rehabilitation was initiated," the researchers wrote.

What's next? The origin of the sound and the apparently coincident mechanism through which the patients' brains were injured remain unknown, Dr. Smith said. Neuroimaging was performed on all 21 patients, 18 of whom had conventional findings well within the normal limits. Findings for the other 3 were nonspecific. Thus, he said, the researchers hope to use advanced neuroimaging techniques to look for structural and functional alterations in the brain that might account for the various symptoms of Havana syndrome.

Networks of axons in the visual system are especially sensitive to any injury that disrupts their serial communication, he pointed out. "So, for instance, eye tracking requires a really complex system of the brain to work together just correctly, at 100 meters per second. At each node the information has to be processed and sent on, and finally at the end the muscles can move the eyes back and forth to track motion." —*Linda Roach*

1 Swanson RL II et al. *JAMA*. 2018;319(11):1125-1133.

Relevant financial disclosures—Dr. Smith: None.

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

2018 S.E. Eye Annual Regional Meeting

July 26-28, 2018

Sandestin Golf & Beach Resort | Destin, Florida

Co-Sponsored by the: Alabama, Louisiana, Mississippi, and Tennessee Academies of Ophthalmology

SouthEast Eye Regional Meeting
Alabama | Louisiana | Mississippi | Tennessee

More information will be posted when available at: www.regonline.com/SEEye2018
or contact Mike Merrill at: jmikemerrill@gmail.com

2018 REGIONAL
OPHTHALMOLOGY
CONFERENCE

SPONSORED BY:
- *Arkansas Ophthalmological Society*
- *Kansas Society of Eye Physicians & Surgeons*
- *Missouri Society of Eye Physicians & Surgeons*
- *Oklahoma Academy of Ophthalmology*

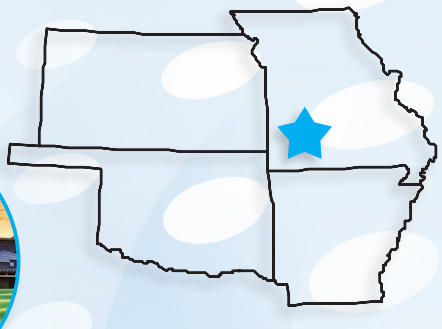
SEPTEMBER 27 – SEPTEMBER 29 2018

TABLE ROCK
REGIONAL ROUNDUP

JOIN US AT

BIG CEDAR®
America's Premier Wilderness Resort

IN RIDGEDALE, MISSOURI
LOCATED OUTSIDE OF BRANSON



PROGRAM HIGHLIGHTS:

- Over 8 hours of CME
- OMIC hour for malpractice premium discount
- Coding update
- Resident Competition
- Family Cookout!

FOR ADDITIONAL INFORMATION:
Online at www.TableRockRoundup.org
or contact us at questions@tablerockroundup.org.

Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

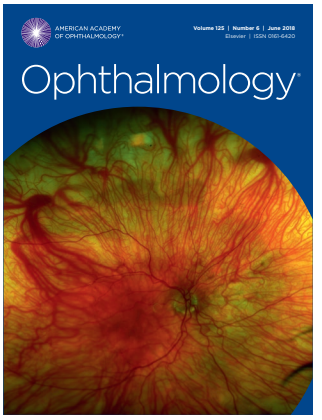
Nocturnal BP Patterns That May Signal Glaucoma in Hispanics

June 2018

Melgarejo et al. observed nocturnal blood pressure (BP) readings from Hispanic patients to identify characteristics that may increase the risk of glaucomatous damage. They found that episodes of extreme reduction in blood pressure ("BP dipping") are more worrisome than generally low BP itself during the night.

This observational study included 93 participants of the Maracaibo Aging Study who had normal intraocular pressure (IOP) and were at least 40 years old (mean, 62 years). They were required to have undergone optical coherence tomography scanning, visual field (VF) tests, and 24-hour and office BP monitoring. Approximately 14% of the study population had diabetes. Based on results of office and ambulatory BP monitoring, the prevalence of hypertension was 65% and 56%, respectively; and 47% of those with office-identified hypertension were taking antihypertensive medications.

The authors used univariate and multivariate logistic regression analyses to observe relationships between glaucomatous damage and BP parameters, with particular emphasis on nocturnal BP levels. The main outcome measure was glaucomatous optic neuropathy (GON), denoted by the presence of optic nerve damage and VF defects.



Of the 185 eyes evaluated, 49 had signs of GON. It was determined, via gonioscopy, that all GON cases in this study were open angle. Patients with GON had significantly lower nighttime and 24-hour diastolic BP than did those without this neuropathy ($p = .009$ and .014, respectively). However, the multivariate models with generalized estimating equations suggested that the glaucomatous damage was unrelated to average systolic or diastolic BP measured at daytime, at nighttime, or over 24 hours. Overall, extreme nocturnal drops (>20% compared with daytime BP) in systolic or diastolic BP were significant risk factors for glaucomatous damage (odds ratios: systolic, 19.78; diastolic, 5.55).

This research supports the use of ambulatory 24-hour BP monitoring to help identify individuals with extreme BP dips who require further ophthalmologic assessment. Additional studies of nocturnal BP decreases in people at risk of glaucoma are warranted to clarify the utility of "extreme dipper" status as a risk factor. Therapies that modify glaucoma risk are urgently needed, as are new approaches to avoid extreme dipping, which may include changing the time that antihypertensive drugs are administered.

Real-World Burden and Progression of Geographic Atrophy

June 2018

Chakravarthy et al. conducted research to better understand the progression of geographic atrophy (GA) to choroidal neovascularization (CNV) and the effect of GA on visual acuity (VA) in real-world settings. They found that the atrophy is linked to substantial visual impairment that often renders those with GA ineligible to drive.

For this multicenter retrospective study, an anonymized dataset was constructed from the electronic health records (EHRs) from October 2000 to February 2016 at 10 clinical sites in the United Kingdom. An algorithm was used to identify cases with a GA diagnosis. From these records, the researchers isolated a study population of 1,901 patients (≥50 years of age) with bilateral GA and no history of CNV. A random sample of records from each center was used to validate the definitions of disease and progression.

Outcomes of interest were progression to blindness (VA <20 Early Treatment Diabetic Retinopathy Study letters or Snellen 20/400 in the better eye), driving ineligibility (VA ≤70 letters or Snellen 20/40 in the better eye), progression to CNV, loss of ≥10 letters, and mean change in VA over time. Another goal was to identify risk factors associated with progression.

At the time of their first record of a GA diagnosis, 7.1% of patients had VA in the better eye that was at or below the threshold for legal blindness; 71.1% had VA that was too low for driving privileges. Over time, 16% patients became legally blind (median time to outcome, 6.2 years), and 67% became ineligible to drive (median time to outcome, 1.6 years). Among the participants with VA measurements at both baseline and 24 months, the mean decline in VA was 6.1 letters in the worse eye and 12.4 letters in the better eye. The rate of progression to CNV in either eye was 7.4% per patient-year. Older age and poorer VA at diagnosis were risk factors for a decline in VA to below the UK standard for driving.

Assessing Whiplash-Related Convergence Insufficiency

June 2018

Whiplash related to motor vehicle accidents may cause complaints of visual disturbance and ocular discomfort, including convergence insufficiency (CI). **Stiebel-Kalish et al.** compared CI findings between patients who experienced whiplash during an accident and age-matched controls. They found that although patients with whiplash had more visual symptoms, they did not have a higher incidence of CI by objective measures.

For this prospective study, adults with whiplash-associated disorder (WAD) following a motor vehicle accident (n = 57; mean age, 37 years) were recruited from an orthopedic emergency department between July 2014 and March 2017. Control participants (n = 39; mean age, 39 years) were hospital personnel and relatives of the patients with WAD. All participants completed the Convergence Insufficiency Symptom Survey (CISS), which is a validated questionnaire, and underwent a detailed visual exam. Assessments included near and distance best-corrected visual acuity and near and distance cover tests, as well as Randot stereopsis and Maddox distance and Maddox-Thorington near heterophoria tests. The CISS score and binocular measure findings of CI were documented and analyzed with the Student *t* test, chi-squared test, and multiple logistic regression; and adjustments were made for age and gender.

The analyses showed that 26 (45.6%) of the 57 patients with WAD had a pathologic CISS score of at least 16, compared with only 6 (15.4%) of the 39 controls ($p = .002$). The absolute CISS score was higher for the WAD group (15.3 ± 10.0 vs. 7.7 ± 7.7; $p < .001$). However, objective findings consistent with CI were similar for the WAD and control groups (7.0% and 7.7%, respectively).

—Summaries by Lynda Seminara

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Baseline Predictors and Vision in Comparison of AMD Treatments Trials Study

June 2018

In a secondary analysis of data from the Comparison of AMD Treatments Trials (CATT) study, **Ying et al.** set out to determine baseline predictors of 5-year visual acuity (VA) outcomes in patients who were treated with either bevacizumab or ranibizumab for wet age-related macular degeneration (AMD).

For this study, the researchers evaluated 647 patients who had participated in CATT and completed a 5-year follow-up visit. At the 5-year mark, the mean VA in the study eye was approximately 20/63, and the mean loss from baseline was 3.3 Early Treatment Diabetic Retinopathy Study letters. Of these patients, 114 (17.6%) had gained ≥3 letters, and 129 (19.9%) had a VA of 20/200 or worse.

In keeping with their earlier analyses of the CATT patient population, the researchers found that the presence at baseline of worse VA, larger choroidal neovascularization (CNV) lesion area, and any retinal pigment epithelium (RPE) elevation remained independently associated with worse VA at the 5-year mark. The researchers also evaluated 5-year VA outcomes according to genotype; in another confirmation of earlier findings, no association emerged between VA outcomes at 5 years and any of the 21 SNPs (single nucleotide polymorphisms) evaluated. Finally, they found that male sex, cigarette smoking, absence of subretinal fluid, and treatment with ranibizumab during the first 2 years of CATT were independently associated with worse visual outcomes at 5 years.

The association with current smoking had not emerged in the earlier analyses; in this study, current smokers were 2.6 times more likely than nonsmokers to have a VA of 20/200 or worse at 5 years.

—Summary by Jean Shaw

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Large Intereye Asymmetry in Vessel Density May Signal Glaucomatous Damage

June 2018

Hou et al. measured intereye retinal vessel density of glaucomatous and healthy eyes to assess whether asymmetry may indicate early glaucomatous damage, which often is asymptomatic. They found that intereye asymmetry of vessel density is much greater in glaucoma suspects than in people with healthy eyes.

This cross-sectional study included 55 individuals with healthy eyes, 32 glaucoma suspects, and 66 patients with mild or moderate glaucoma. Age, sex, and racial distributions were comparable for the 3 cohorts. Retinal vessel density was measured using optical coherence tomography angiography (OCTA) of the macula and optic nerve head. Thickness of the peripapillary retinal nerve fiber layer and the macular ganglion cell complex was measured with spectral-domain OCT. Intereye asymmetry was calculated as the difference in vessel density and thickness between each subject's eyes. Univariate and multivariate analyses were performed to compare findings.

Results showed substantial differences between the study groups. Univariate and multivariate analyses demonstrated that intereye asymmetry in both peripapillary and macular vessel density was significantly greater for glaucoma

suspects than for individuals with healthy eyes, but intereye asymmetry in thickness was similar for these groups. For all thickness-related parameters, there were significant differences between glaucoma suspects and glaucoma patients, both with and without adjustment for confounders; median values for glaucoma patients were roughly double those for suspects.

Examining intereye asymmetry of retinal vessel density may be a helpful adjunct to glaucoma screening programs; a better understanding of events that precede the onset of glaucoma would facilitate early diagnosis. Longitudinal studies are needed to further characterize the relationship between intereye variation in vessel density and the development and progression of glaucoma.

Does Cataract Surgery Improve Vision in Patients With Neovascular AMD?

June 2018

The question of whether cataract surgery improves vision in patients with certain types of age-related macular degeneration (AMD) continues to be the subject of some debate. **Daien et al.** looked at visual acuity (VA) data for patients with neovascular AMD who did and did not receive cataract surgery. They found that, although cataract surgery appeared to modestly increase the activity of choroidal neovascular (CNV) lesions, visual outcomes were good.

For this retrospective case-control study, the researchers gathered information from the Fight Retinal Blindness! observational database. Records for eyes that underwent cataract surgery and were monitored since the start of neovascular AMD treatment (n = 124) were compared with records for unoperated phakic eyes that also were being treated for neovascular AMD (control group; n = 372). Cases were matched for age, baseline VA, and duration of treatment and follow-up.

By 12 months postoperatively, cataract surgery resulted in a mean gain of 10.6 letters, and the mean VA was better for operated eyes (65.8 vs. 61.3 letters; p = .018). The mean number of anti-VEGF intravitreal injections and the proportion of visits in which CNV lesions were active did not change substantially after cataract surgery. However, both numbers declined in the control group, suggesting that the surgery increased lesion activity. Patients whose surgery occurred in the first 6 months of receiving intravitreal injections were more likely to lose rather than gain vision. Factors that had no discernible influence on VA outcomes included age, type of CNV lesion, and intravitreal injection at least 2 weeks before surgery.

These findings suggest that, when possible, cataract surgery should be avoided in the first 6 months of treatment for neovascular AMD. The authors emphasized that observation is a sensible design for studying the efficacy of cataract surgery because it does not pose the ethical concern of assigning patients who require surgery to a nonsurgical control group.

—Summaries by Lynda Seminara

JAMA Ophthalmology

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

Small Uveal Melanoma: Yield Rates and Other Traits of FNAB

May 2018

Assessing the adequacy of biopsy samples intraoperatively may help to ensure appropriate cell yield, which can be challenging for small lesions. In a retrospective study, **Kim et al.** documented yield rates for transscleral and transvitreal fine-needle aspiration biopsies (FNAB) of small uveal melanomas (apical height <3.6 mm); they found that intraoperative evaluation was associated with high yield and a favorable safety profile.

This observational study of consecutive cases included 44 patients (mean age, 63.3 years) with uveal melanoma of the ciliary body or choroid. In all cases, FNAB and intraoperative histopathologic analysis were performed before administration of iodine-125 (^{125}I) brachytherapy. Tumor locations and dimensions were determined from B-scan ultrasonography and histopathologic analysis. Transscleral biopsy was performed for tumors anterior to the equator, and transvitreal biopsy was used for posterior lesions. The adequacy of each biopsy specimen was checked intraoperatively. Specimens underwent hematoxylin-eosin staining, double immunostaining with human melanoma black 45 and *Ki67*, and gene expression profiling.

The median tumor height was 2.7 mm (interquartile range, 2.3-2.9 mm). Of the 44 biopsy samples, 40 (90.9%) contained ample cells for gene expression analysis. Yield rates were 100% (11 of 11) for transscleral specimens and 87.9% (29 of 33) for transvitreal specimens.

Localized vitreous hemorrhages occurred in 24 eyes, and most resolved within 3 months. A moderate association was observed between localized vitreous hemorrhage and the transvitreal biopsy method (phi value, −0.526; p < .001).

As the role of genetic testing for uveal melanoma continues to expand, greater emphasis is being placed on obtaining specimens of adequate size. The authors' findings suggest that intraoperative assessment helps ensure that samples contain a sufficient number of cells for analysis. Their research also affirms the safety and efficacy of FNAB as a diagnostic tool for uveal melanoma. Large prospective multicenter trials of various biopsy techniques are needed to determine the ones best suited for achieving high yield rates. The authors are participating in such an effort and plan to report their findings. *(Also see related commentary by Carol L. Shields, MD, Arman Mashayekhi, MD, and Jerry A. Shields, MD, in the same issue.)*

Preferred Practice Pattern Guidelines and the Process of Attaining Reliable Evidence

May 2018

Golozar et al. described their experience in identifying reliable evidence supporting the topics addressed in the 2016 update of the Academy's 2011 *Preferred Practice Pattern (PPP)* guidelines for treating cataract in adults. They

found that the partnership between the Academy and Cochrane Eyes and Vision US Satellite (CEV@US) facilitated the process of locating robust data relevant to the update.

Initially, searches of systematic reviews on the management of cataract, published in English or Chinese, were conducted. Reliable systematic reviews were required to include the following: eligibility criteria, a comprehensive search/review of the literature, assessment of methodologic quality of studies included, use of appropriate meta-analysis methods, and conclusions derived from the studies reviewed. Each relevant review was mapped to at least 1 of the 24 management categories listed in the table of contents of the 2011 Academy *PPP* guidelines. Data were extracted from each review to determine its reliability, and the reviews deemed reliable were cross-checked against the guidelines. The authors studied whether any reliable reviews published before February 2010 (the cutoff search date for the 2011 guidelines) had been cited in the 2011 version. (CEV@US did not supply systematic reviews for the 2011 guidelines.)

The search returned 99 systematic reviews on cataract management, 46 of which were classified as reliable. The most common reason for exclusion was no mention of a comprehensive literature search. All 46 reliable reviews have been cited in the Academy's 2016 *PPP* guidelines. In the 2011 guidelines, which were published before the Academy/CEV@US partnership began, only 8 of 15 reliable systemic reviews were referenced.

The authors believe that the partnership was successful for producing robust evidence to enrich the practice guidelines and, in turn, improve the care of adults with cataract.

Vitamin A Supplements and Retinitis Pigmentosa in Children

May 2018

Supplementation with vitamin A may slow the loss of retinal function in adults with retinitis pigmentosa (RP), but little is known about its effect in children with the disease. **Berson et al.** compared the disease course of RP between children using oral vitamin A palmitate and a control group. Although definitive conclusions could not be drawn from their small retrospective study, the findings suggest that vitamin A therapy may slow the loss of cone function in children with common forms of RP.

For this nonrandomized retrospective study, the researchers evaluated 80 children with RP, 55 of whom received ≤15,000 IU of vitamin A palmitate per day. The remaining 25 children served as a control group. Both cohorts were followed for several years by the Electroretinography Service of the Massachusetts Eye and Ear Infirmary (dates for patient evaluations ranged from 1976 to 2016, and data were analyzed in 2016). Sex distribution and mean age appeared similar for the study cohorts. The primary outcome was the mean exponential rate of change of full-field cone electroretinogram (ERG) amplitude to 30-Hz flashes, estimated by repeated-measures longitudinal regression, with and without adjustment for potential confounders.

According to the unadjusted model, the estimated mean rate of change was −0.0713 $\log_e$ unit/year for the vitamin cohort and −0.1419 $\log_e$ unit/year for the control cohort (difference, 0.0706 $\log_e$ unit/year; p = .01). The adjusted model showed that the mean rate of decline was slower for the vitamin cohort (difference, 0.0771 $\log_e$ unit/year; p = .009). Ocular safety and the mean exponential change rates in visual acuity and visual field area appeared similar for the study groups.

The authors acknowledged that their study has several limitations, but the findings appear to support consideration of age-appropriate vitamin A therapy in children with common forms of RP and normal liver function. They suggest that vitamin A supplementation may be particularly beneficial for children with long cone ERG implicit time, who have a high risk for aggressive disease. *(Also see related commentary by Caroline C.W. Klaver, MD, PhD, and Alberta A.H.J. Thiadens, MD, PhD, in the same issue.)*

—Summaries by Lynda Seminara

OTHER JOURNALS

Selected by Deepak P. Edward, MD

IV or Oral Corticosteroids for Acute Optic Neuritis

JAMA Neurology

Published online March 5, 2018

Morrow et al. compared visual recovery after treatment of acute optic neuritis (ON) with either a high-dose intravenous (IV) corticosteroid or a bioequivalent oral corticosteroid. They found no significant difference in outcomes.

This randomized trial was conducted over several years at a tertiary care center in Canada and included a 6-month follow-up period. Assessors were masked with respect to treatment assignment. Eligible patients were adults aged 18 to 64 years who presented within 14 days of onset of unilateral demyelinating ON, had no prior history of ON in the affected eye, and had no evidence of recovery by the time of randomization. Other criteria were best-corrected visual acuity (BCVA) of 20/40 or worse and a documented need for corticosteroid treatment.

Of the 89 candidates screened, 55 were enrolled and received IV methylprednisolone sodium succinate (1,000 mg) or oral prednisone (1,250 mg) daily for 3 days. Visual evoked potentials were measured, and the primary outcome was recovery of the VEP P100 latency at 6 months. Secondary outcomes were P100 latency at month 1 and BCVA at months 1 and 6.

Forty-five patients completed the analyses (23 in the IV group, 22 in the oral group). By 6 months, P100 latency had improved to 62.9 ms (from 181.9 ms) in the IV group and 66.7 ms (from 200.5 ms) in the oral group (p = .07). There were no significant differences in P100 latency recovery at 1 month or BCVA recovery at 1 or 6 months, including low-contrast BCVA. In addition, there was no significant difference in adverse events between the groups.

—Summaries by Lynda Seminara

EXTRA **MORE ONLINE.** For a study on bullous keratopathy, see this article online at aao.org/eyenet.

Smartphone Funduscopy: A High-Tech, Low-Cost Imaging Alternative

Consider the many settings in which fundus photography may be needed: the emergency department, nursing homes, the clinic, remote settings, and more. Yet the current gold standard—the tabletop fundus camera—is bulky and expensive, depends on a trained technician, and requires that a patient be seated upright, a challenge for those who are immobile or hospitalized.

The evolution of the high-resolution smartphone camera offers the potential to revolutionize traditional fundus photography. By replacing a binocular indirect ophthalmoscope with a smartphone, many ophthalmologists are innovating a new field of funduscopy. Not only is the technique inexpensive and relatively easy to learn, but the expansion of mobile networks into all sectors of everyday life also is creating unique opportunities for telemedicine, resident training, and clinical care around the world.

What Is Smartphone Funduscopy?

"The main concept is to use the smartphone screen to perform the exam rather than a binocular indirect ophthalmoscope," said Michael Ullman, MD, at Georgetown University/Washington Hospital Center in Washington, D.C. "You still need a 20- or 28-diopter lens in the other hand, but your smartphone serves as the ophthalmoscope, the coaxial light source, and the recording device."

And it's relatively simple to capture useful fundus images:

1. Enable the device's video mode.
2. Set the flash to "on" for uninterrupted illumination.
3. With the lens held in the other hand, start recording.
4. Use the smartphone's "pinch" zoom feature to focus as needed.
5. Once the exam is complete, stop the recording.
6. To obtain a still image from the sequence, replay the video and capture a screenshot at the desired time.

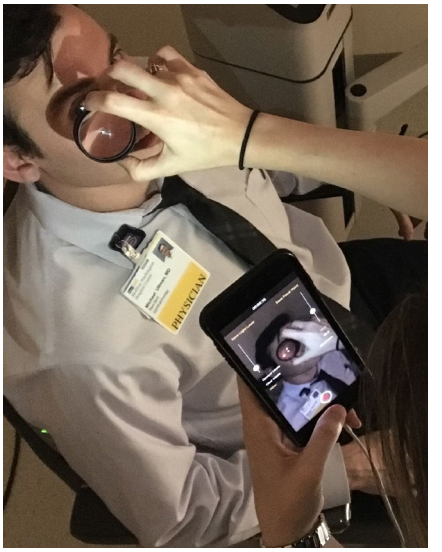
Practice, practice, practice. Don't expect get the best photos from your first attempt, said Carolyn K. Pan, MD, at Stanford Medicine in Palo Alto, California. "Don't get discouraged. Like most procedures, it's all about muscle memory. With practice, you'll figure out the best distance from the retina and how to position the patient relative to your hands."

Applications Across the Board

Who currently uses this technology and who should consider adopting it?

Residency. Smartphone funduscopy is quickly becoming common practice in residency programs as a learning tool. "It plays an essential role in training," said Luis J. Haddock, MD, at the Bascom Palmer Eye Institute in Miami. "If a patient's fundus finding is atypical or particularly interesting, for example, a smartphone provides an ideal educational opportunity for residents to share the case with other trainees and colleagues." (See "Keep It Secure," p. 31.)

Residents are also using the technology as a teleconsultation tool, said Andrew M. Hendrick, MD, at Emory Eye Center in Atlanta. "A resident on call might see retinal whitening, for example, and might be unable to discern if it's due to necrotizing retinitis or chorioretinitis. Having the ability to share the image and communicate with a specialist via a smartphone is why this new technology is a major boon for training," he said.



SMARTPHONE IN USE. *A colleague performs smartphone funduscopy on Dr. Ullman.*

Michael Ullman, MD

BY MIKE MOTT, CONTRIBUTING WRITER, INTERVIEWING **LUIS J. HADDOCK, MD, ANDREW M. HENDRICK, MD, CAROLYN K. PAN, MD,** AND **MICHAEL ULLMAN, MD.**

Because young ophthalmologists have grown up around smartphones, they are taking to this technique rather quickly, said Dr. Hendrick. Recent studies have shown that medical students and residents inexperienced with traditional indirect ophthalmoscopy can learn smartphone funduscopy after just brief training.[1,2]

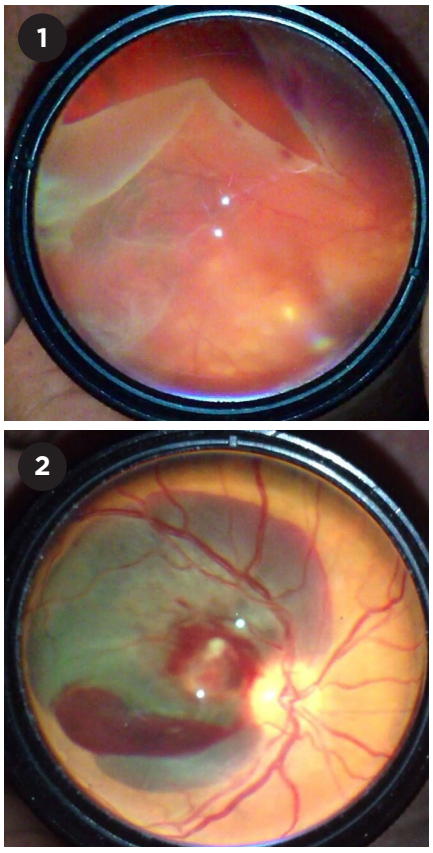
Telemedicine. The ease of use, portability, and availability of smartphones also presents a unique opportunity for telemedicine. "Today's expansive mobile networks make this technique ideal for community settings and isolated rural areas with poor resources," said Dr. Haddock.

Although the smartphone does not typically produce images that are as sharp as traditional cameras, he said, researchers have found that they are of sufficient quality for glaucoma and diabetic retinopathy screening.[3,4] "Many medical mission and humanitarian organizations—at home and abroad—are already using smartphone funduscopy in the field as a way to screen for eye disease by sending out images for remote consultation to determine which patients need to be referred for the proper care."

In the clinic. While it's uncommon for ophthalmic clinics or private practices with traditional desktop cameras to employ smartphone funduscopy, that might change in the near future, said Dr. Haddock. For ophthalmologists considering adding smartphone funduscopy to their repertoire, he recommends identifying needs and determining if it fits into current workflows.

"This technology isn't for everyone," he said, "but there are many different reasons why an ophthalmologist might want to embrace it." Some might want to enhance their ability to document and track clinical findings quickly and easily. Others might want to fill a gap in their practice to avoid using their staff photographer for imaging lower priority cases. Others might simply love the latest gadgets and want to embrace early adoption of new technologies.

"Regardless of the different motivations," said Dr. Pan, "as interest in smartphone funduscopy continues to grow, ophthalmologists will become increasingly excited about it—and this will foster more development and further expansion into practice settings."



FUNDUS IMAGES. *(1) Giant retinal tear and (2) retinal macroaneurysm images taken via smartphone funduscopy.*

Benefits—But With Caveats

The advantages of smartphone funduscopy are numerous. Smartphones are portable and inexpensive, come equipped with a safe light source,[5] and provide ready access to secure networks for data transmission—plus, they are everywhere. "This type of imaging is compelling simply because of the instrument's ubiquity," said Dr. Hendrick. "If you're examining a young child or an immobile patient who's unable to be positioned for conventional funduscopy, it's nice to know you have a high-quality camera in your back pocket."

But, it isn't without limitations.

Field of view. "Compared with traditional tabletop devices, smartphone cameras don't have the ability to access the full retina, and so your peripheral view is significantly smaller," said Dr. Hendrick. Good dilation is also a necessity. But even then, the camera flash can induce a high frequency of optical artifacts—especially if the media is too dense.

Image quality. "Unfortunately, you are also sacrificing a lot in terms of image quality when using smartphone funduscopy," said Dr. Ullman. "Because of the technology involved, the resolution is nowhere near that of a professional desktop camera." Glare and improper exposure are the major culprits, but capturing a screenshot of the video sequence can further degrade image quality.

Learning curve. Similar to the conventional method of indirect ophthalmoscopy, the smartphone technique involves many moving parts—physician, camera, lens, patient—so the learning curve can be steep, said Dr. Hendrick. "One of the most important questions to ask when considering whether to adopt smartphone funduscopy is 'Who will perform the imaging?' There's a fairly sophisticated skill set that needs to be cultivated, so unless you have someone already adept at indirect ophthalmoscopy or someone who takes quickly to smartphones in general, it can be challenging to obtain high-quality images that are useful for a comprehensive ophthalmologist or retina specialist."

Smartphone Funduscopy 2.0

To overcome some of these limitations, innovators are developing new approaches and pushing the limits of the smartphone.

Apps. Many developers are introducing apps unique to funduscopy for streamlining the exam process. "The native smartphone settings simply aren't designed for this type of work," said Dr. Ullman, creator of the Ullman Indirect app. "But a new wave of downloadable software is allowing for independent manipulation of the camera."

With the Ullman Indirect app, for example, users can control the camera's functionality as follows:

- Manually focus the camera and save focal points for various condensing lenses
- Manually control the exposure of

Luis J. Haddock, MD

the camera to reduce glare
- Control the light level of the flashlight similar to a rheostat
- Rotate images and video to document findings in the correct orientation
- Export high-quality still images without the need to screenshot a video

3D-printed adapters. Ophthalmologists are also taking advantage of the 3D-printing revolution to expand the power of their mobile devices. Using free, open-source designs, you can print hardware adapters that attach the condensing lens to the smartphone at a prescribed—but adjustable—distance from the camera.[6]

"With this method, you are reducing the number of moving parts necessary to conduct the exam," said Dr. Pan. "These adapters take a lot of the guesswork out of estimating distances and make it much easier to achieve reproducible, high-quality images; they also free up your second hand."

All-in-one devices. Regardless of whether you use the apps or adapters mentioned above in conjunction with your smartphone, they are not FDA approved for funduscopy. As a result, the smartphone exam is designated for educational purposes only and is not billable as a service. However, several imaging companies, like Remidio, D-Eye, and Volk, are changing that.

Digital ophthalmoscopes are standalone, handheld devices that connect your smartphone to a specifically designed professional funduscope. Although this technology is still in its infancy, a growing number of these "point-and-shoot" fundus cameras include:
- Built-in data encryption for collecting patient data
- HIPAA-compliant storage and export capabilities
- Infrared lighting for nonmydriatic viewing
- A view of the peripheral retinal approaching 80 degrees
- Proprietary apps for independent camera control, autofocus, and autocapture
- FDA approval for billing purposes

"These devices are still using smartphone technology and so they do suffer from some of the limitations mentioned earlier," said Dr. Pan. "But the benefit is that these all-in-one cameras do everything for you, sensing exactly what you are trying to image and making the necessary adjustments. Whether it be light, focus, exposure, or image stabilization, there's really not much to troubleshoot. You're basically on autopilot."

Although these cameras are significantly more expensive than a smartphone, they are also cheaper than a table fundus camera. And according to a recent report, these point-and-shoot devices offer a high sensitivity and specificity for detecting retinal disease compared with traditional systems.[7]

Keep It Secure

When a mobile device is used to receive, send, access, or store a patient's protected health information, it must strictly adhere to HIPAA guidelines. For smartphone funduscopy, compliance typically involves limiting access to the device and securely storing and sharing your images.

Access. At a minimum, you should password-protect your smartphone, avoid automatic logins for apps, and use an additional access key such as a fingerprint. You'll also want to set the smartphone to log out or lock automatically if left idle. And if the device is ever lost or stolen, make sure you have the capability to "wipe" the smartphone remotely.

Storing and sharing. "Most native email or text applications don't meet HIPAA requirements," said Dr. Hendrick. "So you can't simply take a patient photo, keep it on your phone, and send it to your colleagues thinking it's secure."

When storing any patient photographs, you'll need a secure cloud-based server to restrict access from unauthorized individuals. When sharing, use an email account and text service with message encryption as well as an additional login to ensure that no one can intercept the transmission.

"In the end, consult with your IT department to make sure you are following all the necessary rules and regulations," said Dr. Ullman. "And don't forget to obtain the proper patient consent documentation."

What's Next

It remains to be seen whether smartphones will take the place of traditional desktop machines or the ultra-widefield capabilities of scanning laser ophthalmoscopy.

However, given the ongoing evolution in mobile operating systems and devices, this type of funduscopy will likely grow to be an important adjunct to traditional binocular indirect ophthalmoscopy, said Dr. Ullman.

Smartphones might also carve out entirely new niches in imaging. Augmented reality in combination with mobile technology could lead to an entirely new funduscopy experience, he said, in which examiners are prompted with heads-up displays about subtle pathology that can be automatically identified and graded in real time. "Smartphone funduscopy really is more than a passing fad or niche. It has an exciting future."

1 Adam MK et al. *Invest Ophthalmol Vis Sci.* 2014; 55:1608.
2 Haddock LJ et al. *J Ophthalmol.* 2013;2013: 518479. doi:101155/2013/518479.
3 Giardini ME et al. *Conf Proc IEEE Eng Med Biol Soc.* 2014:2177-2180.
4 Russo A et al. *Am J Ophthalmol.* 2015;159(2): 360-364.
5 Kim DY et al. *Ophthalmology.* 2012;119(10): 2200-2201.
6 Myung D et al. *J Mob Technol Med.* 2014;3(1):9-15.
7 Rajalakshmi R. et al. *PloS One.* 2015;10(9): e0138285. doi:10.1371/journal.pone.0138285.

Dr. Haddock is an assistant professor of clinical ophthalmology at the Bascom Palmer Eye Institute in Miami. *Relevant financial disclosures: None.*
Dr. Hendrick is an assistant professor of ophthalmology at Emory Eye Center in Atlanta. *Relevant financial disclosures: None.*
Dr. Pan is a clinical assistant professor of ophthalmology at Stanford Medicine in Palo Alto, Calif. *Relevant financial disclosures: None.*
Dr. Ullman is a second-year ophthalmology resident at Georgetown University/Washington Hospital Center in Washington, D.C. *Relevant financial disclosures: Prevention of Blindness Society of Metropolitan Washington: S; Ullman Indirect: O.*

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

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

Google Isn't Good Enough. PubMed Isn't Practical.

Turn to the reference that is vetted by 100 ophthalmologists every year.

The **BCSC**® is your definitive source in an ever-expanding universe of clinical information.

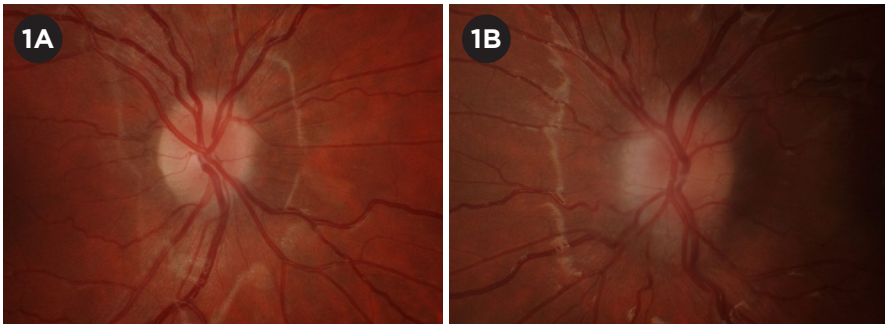
Update your complete Basic and Clinical Science Course™ set. Visit aao.org/bcsc

Protecting Sight. Empowering Lives.®

Doctor, There's a Screaming Sound in My Ears

Laura Mitchell,* an 11-year-old girl, had been experiencing worsening headaches over the past several weeks. Two months before coming to our office, she had seen an optometrist, who told her family that Laura's optic nerves looked normal and referred her to a neurologist.

It took a few weeks for her to get in to see the neurologist and undergo magnetic resonance imaging (MRI). The family was told that the MRI appeared normal, and Laura was sent to us for further evaluation.



BEFORE TREATMENT. *Patient's right (1A) and left (1B) fundus. Note the optic nerve edema and indistinct margins, especially at the nasal side of the left eye.*

We Get a Look

The patient's story. Laura told us that the headaches were occurring more frequently. At first, they occurred only once every few days, but recently they had been striking daily and lasting for a few hours.

She described the pain as radiating from the back of her head to her right eye. The headaches were so severe that she had to lie down for relief, and they had caused her to miss a few days of school. She said that she heard a "screaming" sound in her ears several times per week, and it sometimes lasted for hours. She did not complain of blurry vision or other ocular symptoms.

She was not taking any medications and had no history of trauma. There was a family history of retinitis pigmentosa in her 2 brothers. Laura was notably overweight, and her body mass index was approximately 30, although there was no specific recent weight gain.

Exam findings. On examination, Laura's visual acuity was 20/20 at distance and near without correction. She had normal results on color plates and stereo acuity testing, as well as on the slit-lamp exam.

However, a dilated exam showed abnormalities of both optic nerves (Fig. 1). The optic nerve borders were elevated, and no central cup was visible. The vessels, especially at the nasal border in the left eye, were obscured. The retina and vitreous exam was otherwise normal.

Visual field testing was normal in Laura's right eye, and the left eye had a slightly enlarged blind spot.

Diagnosis

In a young patient with bilateral optic nerve edema and headache with a normal MRI, the next step would be lumbar puncture to evaluate the cerebrospinal fluid (CSF) opening pressure and content.

Based on Laura's weight, idiopathic intracranial hypertension (IIH) was the most likely diagnosis. (This condition is also known as pseudotumor cerebri or benign intracranial hypertension.) However, IIH is a diagnosis of exclusion, and it is important to carefully evaluate the CSF to rule out other possible causes such as inflammation, infection, or tumor. For "Conditions to Consider in a Patient With Suspected IIH" see this article at aao.org/eyenet.

The opening pressure was found to be elevated at 34 mm Hg, and the CSF was normal. Thus, we established IIH as the definitive diagnosis.

Treatment and Disease Course

The neurologist started Laura on oral acetazolamide (Diamox) at 500 mg twice daily. She did not tolerate this dosage well at first because of stomach upset. Subsequently, a lower starting dose was prescribed and was gradually increased; on this regimen, she ob-

BY **STEVE L. GERBER, MD,** AND **CRISTINA LYNN, OSC.** EDITED BY STEVEN J. GEDDE, MD.

tained relief from her headaches and had less severe gastrointestinal upset.

It was repeatedly emphasized to her parents that weight loss would improve Laura's condition significantly and might possibly allow her to stop taking medication. It was not until 6 months later that the family finally saw a dietitian and made a concerted effort to help her lose weight.

At her most recent exam, 9 months after diagnosis, Laura had lost 10 pounds. She was still taking Diamox, and her optic nerve edema had improved significantly (Fig. 2).

AFTER TREATMENT. *Patient's right (2A) and left (2B) fundus. Nine months after diagnosis and subsequent treatment with acetazolamide and weight loss, the optic nerve edema had improved, and the margins were more distinct.*

Discussion

Idiopathic intracranial hypertension refers to elevated intracranial pressure without an obvious cause such as tumor. The term also encompasses secondary causes such as medications (tetracycline, minocycline, lithium, vitamin A, isotretinoin, and growth hormone) and venous sinus thrombosis.

Although this disorder is sometimes called benign intracranial hypertension, we and many other authors prefer the designation *idiopathic,* as the disease is not benign in its effects on the patient.

Mechanisms. The mechanisms of IIH are still being explored, and multiple hypotheses have been presented. These include decreased resorption and/or excess production of CSF, elevated venous pressure, or decreased leptin levels.

The association with obesity may be due to elevated central venous pressure caused by increased intrathoracic and intra-abdominal pressure or possibly elevated estrogen production in obese patients.[1]

Types. Pediatric IIH occurs in 2 distinct types. In children younger than 9 years, IIH occurs equally in boys and girls and is not associated with excess weight. In contrast, in older children, there is a female preponderance and an association with excess body weight. Brara and colleagues found that childhood obesity is strongly associated with an increased risk of pediatric IIH.[2]

Gonadal hormones in the pubertal age group are likely to contribute to IIH. It is also suggested that increased estrogen exposure from use of oral contraceptives is correlated with IIH in females of pubertal age. The disease may also be more severe in this group compared with prepubescent girls.[3]

Symptoms

The most common symptom of IIH is frequent headache, reported by 90% of patients. Pulsating tinnitus occurs in 58% of patients and is often described as a "whooshing" sound. In Laura's case, she compared it to a screaming sound. Neck pain, transient visual decrease, and diplopia are also frequently reported. Permanent visual field defects may occur as a result of optic nerve damage from papilledema.[4]

Treatment

Medical. First-line therapy involves weight loss and oral acetazolamide, a carbonic anhydrase inhibitor. In children, the recommended starting dose is 25 mg/kg per day, with a maximum dose of 100 mg/kg.[5] Diuretics such as furosemide can be used alone or in conjunction with acetazolamide.

Topiramate, a weak carbonic anhydrase inhibitor, is sometimes used as an alternative to acetazolamide. Because its side effects include appetite suppression, it may aid in weight loss.[6]

Surgical. If a patient does not respond adequately to weight loss and medical therapy, surgical treatment may be considered for cases that are intractable or pose a threat to vision.

The main surgical procedures for IIH are optic nerve sheath fenestration (ONSF) and CSF shunting. ONSF is preferred for patients with visual symptoms, whereas shunting is used mainly for those with headaches.

Follow-up. All patients with IIH should have ongoing follow-up for visual field measurements and evaluation of papilledema. Length of treatment may vary according to the patient's condition, and follow-up appointments are recommended for at least 6 months after optic nerve appearance and visual acuity stabilize.[2]

Take-Home Points

As the obesity epidemic spreads among children, pediatric IIH is likely to increase as well. Counseling families about the value of weight loss is vital to reducing the incidence of permanent visual loss and may also decrease long-term dependence on medications. Involving a dietitian early in the course of treatment may be helpful in achieving these goals.

* Patient name is fictitious.

Dr. Gerber is a practicing ophthalmologist, and **Ms. Lynn** is a certified ophthalmic scribe. Both are at Advanced Ophthalmology of Michiana in South Bend, Indiana. *Financial disclosures: None.*

1 Goldman L, Schafer AI, eds. *Goldman-Cecil Medicine,* Vol. 2. 25th ed. Philadelphia: Elsevier Saunders; 2016:2362.
2 Brara SM et al. *J Pediatr.* 2012;161(4):602-607.
3 Sheldon CA et al. *Ophthalmology.* 2016;123(11):2424-2431.
4 Degnan AJ, Levy LM. *AJNR Am J Neuroradiol.* 2011;32(11):1986-1993.
5 Albakr A et al. *Sudan J Paediat.* 2016;16(2):67-76.
6 Thurtell MJ, Wall M. *Curr Treat Options Neurol.* 2013;15(1):1-12.

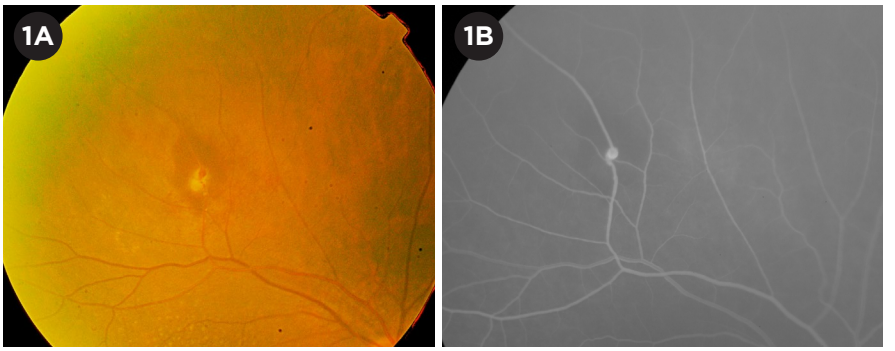
EXTRA **MORE ONLINE.** For a list of conditions associated with IIH, find this article at aao.org/eyenet.

Steve L. Gerber, MD

Diagnosis and Management of Retinal Arterial Macroaneurysm

Retinal arterial macroaneurysm (RAM) is an acquired focal aneurysmal dilation of an arteriole, usually within the first 3 orders of the retinal arterial system (Fig. 1). RAM is uncommon (approximately 1 in 4,500 people)[1] and has a predilection for elderly, hypertensive women. RAM typically occurs along the temporal branches, often at points of bifurcation or arteriovenous crossing.

The thickening of the arteriolar vessel wall is similar to arteriosclerotic changes elsewhere, resulting in focal areas of ischemia, remodeling of the greater intimal collagen, and, finally, dilation of the vessel diameter.[2] Breaks within the arteriolar wall result in a fusiform dilation of the wall, increasing the risk of exudation and rupture.



EVIDENCE OF RAM. *(1A) Fundus photograph of eye with a retinal arteriole macroaneurysm, evidenced by exudation and subretinal blood in the area of an arteriolar bifurcation. (1B) FFA in the early phase highlights the focal hyperfluorescent dilation of the arteriole.*

Signs and Symptoms

The onset of RAM is often insidious, but patients occasionally present with acute, severe visual loss. Lavin and colleagues classified RAM into 3 clinical forms: quiescent, hemorrhagic, and exudative.[3]

Quiescent RAM. This is an incidental finding on routine examination; it seldom results in visual symptoms.

Hemorrhagic RAM. The hemorrhagic form tends to present acutely, with rapid visual deterioration. On clinical examination, a saccular or fusiform dilation along the first- or second-order arteriole might be seen. It often presents with a characteristic multilayered hemorrhage involving the the vitreous, as well as the preretinal, intraretinal, and subretinal spaces.

Exudative RAM. Compared to hemorrhagic RAM, the exudative form has a more gradual, indolent course. It is characterized by the presence of lipid deposition in a circinate pattern surrounding the lesion, as well as intraretinal edema and accumulation of subretinal fluid. If the accumulation of hard exudates and retinal edema occurs at the fovea, permanent loss of central vision may result.

Clinical Evaluation

A complete assessment of RAM requires a combination of clinical examination and imaging studies, such as B-scan ultrasonography, fundus fluorescein angiography (FFA), indocyanine green angiography (ICGA), and optical coherence tomography (OCT).

B scan. If extensive vitreous hemorrhage obscures the view of the fundus, ultrasound B scan can be used to exclude conditions such as retinal tears, detachments, and breakthrough hemorrhage from polypoidal choroidal vasculopathies.

FFA. This is the ancillary study of choice to diagnose and delineate the suspected lesion. The typical RAM fills up uniformly in the early phase, revealing a fusiform dilation of the arteriole with late leakage. The presence of a thrombus may result in filling defects. Areas of blocked fluorescence due to the overlying blood may also be present. With the aid of dynamic FFA, pulsatility of the macroaneurysm may be observed in 10% of cases.

ICGA. If significant hemorrhage

BY **WEI YAN NG, MD, MMED (OPHTH), RANJANA MATHUR, FRCS (ED),** AND **DANIEL SHU WEI TING, MD, PHD.** EDITED BY INGRID U. SCOTT, MD, MPH, AND SHARON FEKRAT, MD.

renders FFA inconclusive, ICGA may be a useful alternative because it has an absorption and emission peak in the near-infrared range, allowing deeper penetration through the areas of hemorrhage (Fig. 2). However, both FFA and ICGA are considered invasive and relatively time-consuming.

OCT. Spectral-domain OCT (SD-OCT) enables visualization of the lesion as well as associated complications. The macroaneurysm will appear as a round or oval hyperreflective lesion in the inner retinal layers. In addition, SD-OCT may demarcate the extent of lipid deposition and accumulation of intraretinal and/or subretinal fluid. However, SD-OCT is significantly affected by the presence of media opacities such as vitreous hemorrhage. In such circumstances, ICGA may be more informative.

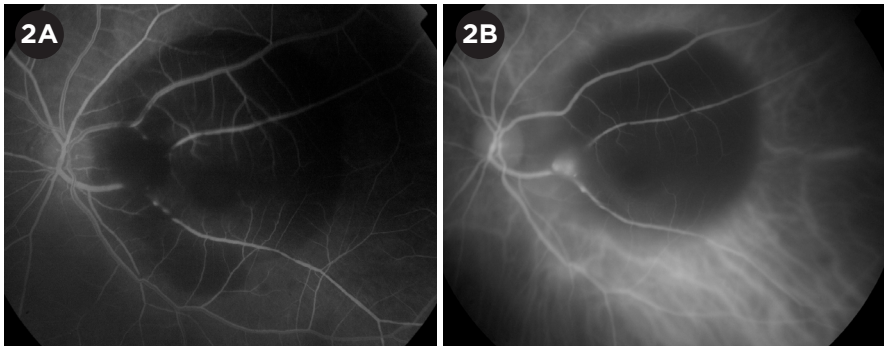
Diagnostic challenges. Despite several imaging options at our disposal, diagnosing RAM may prove challenging when extensive hemorrhage is present. If a clear focal lesion cannot be identified, the patient may be misdiagnosed with other conditions such as polypoidal choroidal vasculopathy or exudative age-related macular degeneration.

In such cases, examining the fellow eye closely may help guide the physician. Important diagnostic clues for RAM include absence of drusen and the presence of significant hypertensive retinopathy in the fellow eye in the setting of an asymmetric vascular lesion with lipid or blood concentrated around the bifurcation of an arteriole in the affected eye.

Treatment

Hypertensive patients with RAM should be referred to their primary care physician to optimize blood pressure control. Management of the ocular manifestations of RAM depends on the visual acuity in the affected eye, as well as the location of the lesion and associated consequences.

Observation. Observation is generally recommended for eyes with good visual acuity, with the RAM located inferiorly or nasally, and minimal exudation or hemorrhage; in most of these cases, spontaneous involution and resolution will occur. Often, RAM with associated retinal or breakthrough vitreous hemorrhage will thrombose and subsequently regress without further intervention.



FFA VS. ICGA. *In the presence of excessive blood with significant blocked hyperfluorescence, ICGA may be superior to FFA. RAM is completely obscured by blood on FFA (2A) but can be seen clearly on ICGA (2B).*

Argon laser photocoagulation. If the patient develops significant hemorrhage or exudation threatening the macula, especially when the RAM is located superotemporally, early retinal argon photocoagulation is recommended.

RAMs complicated by subfoveal hemorrhage tend to have a worse visual prognosis due to the disorganization of the retinal inner layers and associated neurosensory detachment.[4] Subsequent fibrosis and atrophy may result in permanent central vision loss.

Direct application. Direct argon laser to the entire macroaneurysm should be applied cautiously, with relatively low power, long burn duration, and large spot size to avoid rupture of the RAM. Potential complications of laser photocoagulation of the RAM include breakthrough hemorrhage, development of choroidal neovascularization, vascular occlusion at the site of treatment, and early increase in exudates following laser application. It has been reported that only 16% to 27% of RAMs are successfully thrombosed after treatment with laser photocoagulation.[5]

Indirect application. Indirect retinal laser photocoagulation is thought to reduce oxygen consumption and thus blood flow to the RAM as well as decreasing exudation from surrounding capillaries. This technique avoids direct thermal energy to the lesion, which could result in arteriolar occlusion and rupture. However, it has not been established which of these methods is superior, and some physicians prefer a combination of both direct and indirect laser.[6]

Threshold versus subthreshold. Battaglia Parodi and colleagues compared subthreshold laser versus threshold laser treatment. They found comparable visual and anatomic outcomes between the groups, with reduced epiretinal membrane formation in the subthreshold group.[7] It is hypothesized that retinal hyperthermia below the cell-death threshold results in selective damage to retinal pigment epithelial cells, with improved balance of angiogenic factors and cytokine release.

Anti–vascular endothelial growth factor (anti-VEGF). Intravitreal anti-VEGF may provide an alternative treatment option.[8] In a case series of 37 patients with complicated RAM, Pichi et al. reported that 3 monthly injections of intravitreal bevacizumab were associated with rapid improvement in best-corrected visual acuity and reduction of central retinal thickness. Inhibition of VEGF may close the permeable arteriole and normalize its function.[8]

YAG laser hyaloidotomy. If a large, nonresolving premacular hemorrhage is present, YAG laser hyaloidotomy may be performed to promote dispersion of the blood into the vitreous, where it may be more readily absorbed. This approach remains controversial due to the possible complications of macular hole, retinal detachment, or vitreous hemorrhage requiring vitrectomy.[9]

Intravitreal gas. Prolonged submacular hemorrhage may be toxic to the underlying photoreceptor and retinal pigment epithelial cells. Displacement of the hemorrhage may be achieved by injection of expansile intravitreal gas, with or without the aid of adjunctive tissue plasminogen activator.[10]

Pars plana vitrectomy. In cases involving a breakthrough vitreous hemorrhage that does not clear, pars plana vitrectomy can be considered. Coexisting submacular hemorrhage may be displaced at the same time.[11]

Conclusion

RAMs generally involute spontaneously and have a favorable visual prognosis. However, severe complications such as extensive hemorrhage and exudation involving the fovea can lead to severe, permanent central visual loss. Therefore, it is important for the treatment regimen to be tailored for each patient according to the lesion's characteristics.

1 Xu L et al. *Br J Ophthalmol.* 2007;91(6):840-841.
2 Fichte C et al. *Am J Ophthalmol.* 1978;85(4):509-518.
3 Lavin MJ et al. *Br J Ophthalmol.* 1987;71(11):817-825.
4 Cahuzac A et al. *Eur J Ophthalmol.* 2016;26(1):36-43.
5 Meyer JC et al. *Graefes Arch Clin Exp Ophthalmol.* 2015;253(4):537-541.
6 Koinzer S et al. *Br J Ophthalmol.* 2015;99(10):1345-1353.
7 Battaglia Parodi M et al. *Invest Ophthalmol Vis Sci.* 2012;53(4):1783-1786.
8 Pichi F et al. *Am J Ophthalmol.* 2013;155(2):287-294 e281.
9 Ulbig MW et al. *Arch Ophthalmol.* 1998;116(11):1465-1469.
10 Johnson MW. *Curr Opin Ophthalmol.* 2000;11(3):201-206.
11 Wu TT et al. *Acta Ophthalmol.* 2011;89(2):194-197.

Dr. Ng is an ophthalmology resident at the Singapore National Eye Centre. **Dr. Mathur** is the senior consultant at the Singapore National Eye Centre and assistant professor at the Duke-National University Singapore (Duke-NUS). **Dr. Ting** is the associate consultant at the Singapore National Eye Centre and assistant professor at Duke-NUS Medical School. *Financial disclosures: None.*

A PRIMER ON Expanding Into Aesthetics

Ophthalmologists are uniquely positioned to perform certain aesthetic procedures. These treatment and practice management considerations can help you get started.

By Lori Baker-Schena, MBA, EdD, Contributing Writer

ARE YOU PONDERING THE POSSIbility of adding aesthetics to your practice? Short of bringing in an oculoplastic-trained surgeon and providing the capital support that this type of aesthetic practice requires—decidedly the best route according to some experts—you might wonder if you can do it yourself. The proliferation of neurotoxins, fillers, and laser technology may make this an intriguing prospect for some ophthalmologists.

While the benefits, including new revenue streams and cash-paying patients, might sound enticing, the reality is that adding aesthetics may require that you change your practice management patterns, alter staffing, and potentially renovate waiting and patient treatment rooms, said oculoplastic surgeon Jill A. Foster, MD, medical director of Plastic Surgery Ohio in Columbus.

And on the clinical side, you will need to learn an array of new skills and technologies. Dr. Foster suggested that comprehensive ophthalmologists interested in expanding into aesthetics ease into the field starting with the basic neurotoxins and then slowly adding fillers and lasers.

"Ophthalmologists must be aware that there is a learning curve, both in acquiring new skills and in terms of managing patient expectations," Dr. Foster said. "The cosmetic patient is more demanding and is paying up front for an expected result. Physicians must be clear about what they can and cannot do in order to meet patient expectations and satisfy patient desires."

She added that expanding into aesthetics is a multifactorial decision involving science, artistry, practice management, and financial considerations.

Neurotoxins

Neurotoxins are a common and essential component of aesthetic rejuvenation, Dr. Foster noted.

History. The U.S. Food and Drug Administration (FDA) approval for onabotulinumtoxinA (Botox) in 1989 for treatment of strabismus and blepharospasm was followed in 2002 by FDA approval to treat glabellar lines, which expanded aesthetics beyond the realm of oculoplastic surgeons. And Gayle L. Shimokaji, MD, of 2020 Ophthalmic Consultants in Greenbrae, California, was there from the beginning. She worked closely with a pioneer of Botox, Alan Scott, MD, in the late 1980s at California Pacific Medical Center in San Francisco, where they were injecting botulinum toxin to treat blepharospasm and strabismus.

"When I started to inject patients for blepharospasm and they returned for follow-up looking amazing, I knew we were onto something," Dr. Shimokaji said. "It became FDA approved for frown lines in 2002 and, just in October 2017, the FDA approved Botox for forehead lines."

Evan H. Black, MD, FACS

Dr. Shimokaji noted that 30 years later, the demand for Botox continues to be strong, even among her older patients. "I have added a wide array of fillers, dermal stimulators, skin-rejuvenating products, and lasers, so that my office is a practice where you can have your cataracts removed and look terrific."

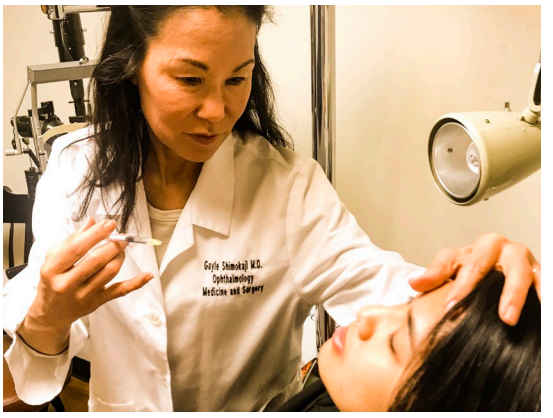
Three neurotoxins. After approving Botox, the FDA approved abobotulinumtoxinA (Dysport) in 2009 for treatment of glabellar lines and incobotulinumtoxinA (Xeomin) in 2010 for blepharospasm and facial wrinkles. While the drugs share the same mechanism of action, dosing varies.

In a comparative assessment of the literature that included a systematic review with meta-analyses, researchers found a benefit of the 3 neurotoxins over placebo for facial rhytides, with inconclusive findings of superiority. Only high-dose onabotulinumtoxinA (compared with a standard dose) offered additional benefit at 30 days.[1]

Shift in usage. The Global Aesthetics Consensus Group identified a paradigm shift in neurotoxin treatment toward neuromodulation rather than paralysis of target muscles.[2] Dr. Foster said this is accomplished by customizing the volumes and dose for different locations on the face, varying the locations by how the individual moves those target muscles, and taking into account the patient's sex and muscle mass. The depth of injections can also impact the results of the treatment in the forehead and lower eyelids.

In addition, the use of botulinum toxin has expanded from the upper face to treating the lower face, neck, and midface. "We take a panfacial approach, making anatomy-based decisions involving the forehead, glabella, nasalis, orbicularis oculi, and depressor anguli oris," Dr. Foster said. "Treatment planning is highly individualized—the patient is a partner in how we proceed."

Scars. Additional uses for neurotoxins include the treatment of hypertrophic scars (except keloid scars), which improves the scar's appearance by relaxing muscle tension, inhibiting fibroblast proliferation in the wound, decreasing production of inflammatory cytokine transforming growth factor, and increasing expression of vascular endothelial growth factor (VEGF). "Faster vascularization and more rapid re-epithelialization of the wound result in a smaller scar," Dr. Foster said.



BOTOX. *Dr. Shimokaji is about to give one of her patients a Botox treatment.*

Combination treatments. "Synergistic treatments potentially used with neuromodulators include dermal fillers, resulting in an increased effect on flattening wrinkles as well as a greater duration of effect; laser/light-based energy, enhancing efficacy for fine lines, wrinkles, and erythema; and skin care products that promote collagen synthesis," she added.

How to use. Brett S. Kotlus, MD, a Manhattan-based oculoplastics specialist who is board certified in ophthalmology and cosmetic surgery, advised, "For comprehensive ophthalmologists interested in expanding into aesthetics, mastering neurotoxin injections for on-label indications is the first step. Start with basic treatment such as glabella, crow's feet, and forehead lines."

Once ophthalmologists are comfortable with these indications, said Dr. Foster, they can use neurotoxin injections off-label to address neck bands (platysma), smokers' lines (orbicularis oris), gummy smile (levator labii), nasal tip (depressor septi nasi), and chin dimples (mentalis).

To gain skills with neurotoxins and other modalities, Dr. Kotlus suggested attending hands-on courses and cosmetic medical meetings, purchasing video series, and doing a preceptorship—or, "even better, a cosmetic fellowship with an expert."

WRINKLES. *This patient received Dysport for crow's feet, plus a skin care regimen.*

Brett S. Kotlus, MD; Gayle L. Shimokaji, MD

Dermal Fillers

While the effects of neurotoxins last from 3 to 6 months, the effects of dermal fillers range from 6 months to 3 years, and they are usually used for volume enhancement.

Types of fillers. Dermal fillers can be categorized into temporary, semipermanent, and permanent. FDA-approved uses for dermal fillers include treatment of moderate to severe nasolabial folds, cheek and lip augmentation, and increasing the volume of the back of the hand.

Reversible fillers. "Ophthalmologists starting out with injectable dermal fillers should use products that are reversible, such as gel fillers," Dr. Kotlus said.

Hyaluronic acid fillers are the most popular type of gel filler, Dr. Kotlus said, and they help restore the appearance of volume and elasticity. The most widely used reversible fillers are the Juvederm family of products, Restylane family of products, and Belotero Balance, he added. In addition, he noted that off-label uses include filling in hollowness in the temples, brow, jawline, or tear troughs.

Semipermanent fillers. Semipermanent fillers are also referred to as biostimulatory fillers, stimulating the body to form its own collagen around the injected filler substance to increase volume. The most commonly used semipermanent filler in the United States is Sculptra, Dr. Kotlus said.

Permanent filler. The FDA has only approved one permanent injectable filler, Bellafill, indicated for correction of the nasolabial folds.

How to use them. Dr. Kotlus noted that while an abundance of fillers is available, using them successfully requires following an approach that encompasses both strategies and tactics.

"If you don't have a strategy, how can you solve a problem?" he asked. "In aesthetics, the strategy refers to the patient's concerns and the broad idea of what you are trying to accomplish to solve that concern. Tactics are the specific tools to serve that strategy. If you just have a tactic without a strategy, there is no direction for your tools."

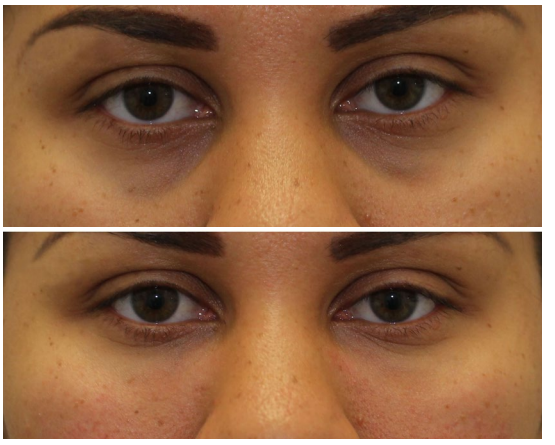
Dr. Kotlus gave some examples.

Strategy: Reduce nasolabial shadows. Tactics: Injectable fillers, subdermal placement.

Strategy: Restore volume loss to cheeks. Tactics: Large particle injectable filler in mid/upper cheek.

Strategy: Minimize malar mounds and nasaolabial creases. Tactics: Submalar nasolabial filler plus barbed PDO (polydioxanone) threads.

"Using this 'strategy and tactics' approach gives you a framework for how to approach the patient," said Dr. Kotlus. "If you don't have a system in place, you are reinventing the wheel with every patient."



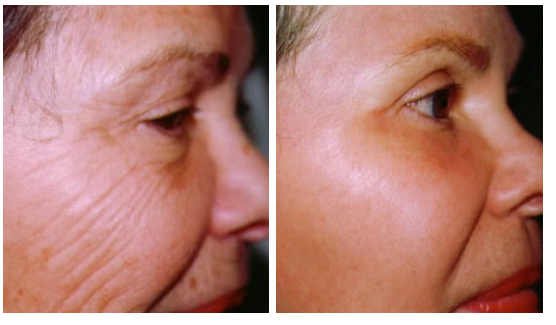
TEAR TROUGHS. *Off-label Restylane and Restylane Lyft were used for this patient's tear troughs.*

Lasers and Other Technology

Once comprehensive ophthalmologists introduce neurotoxins and fillers into their practice, they may want to consider the next step: lasers. It is a move that should not be taken lightly, according to John J. Martin Jr., MD, in private practice in Coral Gables, Florida. "When considering lasers, ophthalmologists really must make a commitment," he stressed. "You have to use the machine on a regular basis, not just once a week, and maximize the results to keep patients happy."

Dr. Martin also noted that there is a significant learning curve. "Some companies will give doctors a hard sell, saying utilizing lasers is a piece of cake and a great, easy way to make money," he said. "Nothing could be further from the truth." The complexity of the lasers and the process of choosing the right laser, selecting the appropriate patients, and avoiding complications must be considered when introducing lasers into a practice.

CO_2 laser. Dr. Martin noted that CO_2 was the first laser used for resurfacing, and it is still considered the gold standard for fully ablative resurfacing to rejuvenate the skin. On the downside, the recovery time for ablative resurfacing is relatively long (2 weeks), and there are several possible



CO2. *Patient who underwent CO2 laser treatment in Dr. Martin's practice before (left) and 5 months after the procedure (right).*

Brett S. Kotlus, MD; John J. Martin Jr., MD

complications, including scarring, hypopigmentation/hyperpigmentation, infection, and prolonged erythema.

Because of the possible changes in pigmentation postoperatively, it can only be used on fairer skin tones, Dr. Martin pointed out.

Erbium laser. The other fully ablative resurfacing laser is the erbium. While the erbium laser does not produce as much tightening as the CO_2 laser, it has the benefit of a shorter recovery time, about 1 week.

Fractionated ablative resurfacing. "One of the

Advice From a Full-Service Cosmetics Practice

Patients who seek a true one-stop shop in terms of cosmetic surgery need look no further than Hass Plastic Surgery in Palm Beach, Florida.

Andrea N. Hass, MD, is an oculoplastic surgeon who, 22 years ago, set up practice with her husband, Brian Hass, MD, a board-certified plastic surgeon, to offer the full spectrum of cosmetic surgery treatment options for patients. They have since added another plastic surgeon, and they divvy up the work: Dr. Andrea Hass focuses on the eyes, her husband focuses on the head and neck, and the third surgeon performs breast and body surgeries.

While the 3 surgeons share staff and overhead, they meet with patients individually, each devising a plan of treatment that they subsequently share with each other. "As an ophthalmologist, I have great insight into the nuances of the periocular anatomy, which gives me an edge over plastic surgeons in this area," Dr. Andrea Hass said.

Must have vision and skill. While aesthetics is a growing area of ophthalmology, Dr. Andrea Hass cautioned that introducing cosmetic treatments into a comprehensive practice has its challenges.

First, it is vital that the ophthalmologist has an aesthetic eye and can visualize in 3 dimensions.

"Aesthetic treatments involve multiple steps," she said. "You have to identify where the volume losses are, predict what you can achieve with the fillers, have the mental image of the endpoint, and then communicate this to the patient. It takes experience, training, and the constant pursuit of perfection."

Must deliver excellent customer service. Second, she said, "the way a general ophthalmology practice is set up is dramatically different from our office. We devote a great deal of time consulting with each patient—a factor that can clog up a general ophthalmology practice."

Indeed, she said that her practice runs like a "well-oiled" machine, and she credits her practice manager, Veronica Wagner, for running the office —from scheduling to billing to patient education—with an intense focus on customer service. "Our practice is large, and customer service is ingrained in the entire staff," Ms. Wagner said. "Every single day we do everything we can to make our customers happy."

Key questions. Before introducing aesthetics into your practice, Ms. Wagner said that you need to answer the following questions:

- How is the office set up in terms of staffing?
- What are the general upfront costs in terms of purchasing equipment/supplies related to aesthetic procedures?
- How will you schedule the doctors?
- What are the business/monetary benefits/challenges of running an aesthetics office (cash patients vs. insurance patients)?

"Introducing aesthetics requires a lot of thought," Ms. Wagner added. "If you are going to be making the transition, you must be prepared."

AESTHETIC ROOM. *Multipurpose room for cosmetic evaluations and treatment. The room should have a skin care display, informational brochures to provide to patients, exam chair that reclines for treatment or surgery, oxygen and suction, laser shade on window, refrigerator for storage, and blank wall for photography. All are elements to consider in planning an aesthetic room.*

Jill A. Foster, MD

biggest advances in the last few years has been the introduction of fractionated ablative resurfacing for both CO_2 and erbium," Dr. Martin said. "With fractionated resurfacing, microscopic zones of the skin are ablated instead of removal of the whole epidermis."

He explained that leaving normal skin around the treated skin allows for faster healing, with less redness, and decreased risk of pigmentation changes postoperatively. This laser can be used on the face, and, at lower powers, it can even be used cautiously on the neck, chest, and hands. "There will not be as much skin tightening as can be seen with the fully ablative CO_2 and erbium, but the fractionated lasers have become the lasers of choice for most resurfacing procedures due to the better safety profile," he said.

Intense pulsed light. For physicians who are just beginning to treat the skin, intense pulsed light (IPL) can give excellent results, said Dr. Martin. It's not a laser but a high-output flash lamp that has been used to treat vascular and pigmented lesions as well as epidermal and dermal atrophy associated with photoaging and other imperfections.[3] "There is minimal downtime for the patient and significantly less risk of complications than with the ablative lasers," Dr. Martin said.

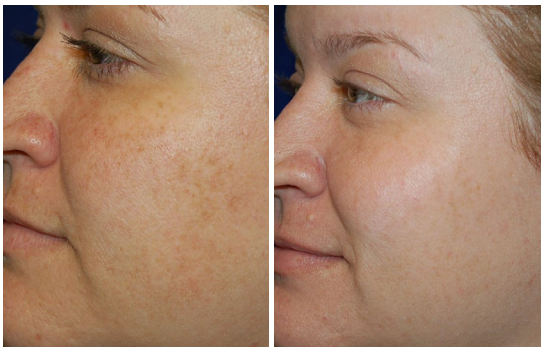
"This device has been a workhorse for us," he added. "It helps decrease dark circles under the eye, redness, pigment spots, and the appearance of scars, while helping rejuvenate the skin with fewer complications. It is important to stay beyond the orbital rim, and the surgeon and patient will need eye protection—goggles and shields—when this device is in use."

Two recent options. Newer options include microfocused ultrasound, which is a transcutaneous heat delivery modality that reaches the deeper subdermal connective tissue and is used to tighten the neck. And microneedling with radiofrequency, a handheld device that sends radiofrequency energy to subdermal tissue to stimulate the body's natural collagen and healing processes, is useful in treating acne scars and wrinkles.

About his practice, Dr. Martin said, "We are doing more laser treatments than we used to because a lot of people don't want surgery. These devices are an investment, so you need to choose wisely. I would suggest talking to colleagues and spending time with their technology to see what is the best alternative for you."

Practice Management and Marketing

For comprehensive ophthalmologists who are interested in introducing aesthetics into their practice, Dr. Shimokaji's advice is to shadow a fellow ophthalmologist who has successfully done so. Specifically, she advised focusing on learning how the office functions in terms of managing patient expectations, patient flow, up-front costs, and marketing.



IPL. *Dr. Martin's patient before (left) and 4 months after intense pulsed light treatment (right).*

Patient expectations. Dr. Kotlus pointed out that expectations are different for patients seeking cosmetic treatment. "First, they are spending money out of their pocket rather than using insurance, so they expect a high level of care. Second, aesthetics is considered a luxury service, and attention should be given to patient's needs. I think it is nice to have an office that is suitable for the cosmetic patient, including a well-appointed, comfortable waiting area."

Dr. Martin added that patients often desire a smaller, more intimate waiting area and possibly a backdoor entrance for added privacy. "It is a different environment for these patients," he said. "They are paying cash and don't want to be herded through the office."

"Ophthalmologists have the hand control and technical abilities to perform aesthetic procedures. The challenges are the ability to properly evaluate patients' concerns and to understand which tools would be most appropriate to address those concerns."

—Dr. Kotlus

Patient flow. Dr. Shimokaji explained that patients should be given the opportunity to express what they want in terms of aesthetic procedures. "You need to ask the patient, 'What is bothering you?' Even though the patient may have wrinkles on her forehead, if she replies that her smile lines have always bothered her, then you need to focus on her smile lines."

Treating aesthetics patients is about "less volume, more intensity," Dr. Foster said. Ophthalmologists spend more time talking about options and potential treatment plans. "Instead of a 15-minute

John J. Martin Jr., MD

visit, you may need an hour for a new patient," she said. "The first visit often covers more than one aesthetic concern with multiple alternatives of treatment that should be discussed. In addition, some new patients want to be treated that same day, so your schedule and staffing must be flexible enough to accommodate these needs."

Dr. Kotlus also mentioned the importance of giving patients your full attention and "not rushing to get to the next room. They need to know that you are listening to them and understand them." He recommended hiring a physician extender, either a medical assistant or aesthetician, to help patients maintain their results and discuss lifestyle issues such as the importance of smoking cessation and sun avoidance.

Up-front costs. Introducing aesthetics requires the purchase of unique equipment and supplies. Dr. Foster listed several, including camera/photographic technology, topical skin care products, chemical peels, microdermabrasion products, neurotoxins, soft tissue fillers, IPL/lasers, and non-facial cosmetic technology.

"We added product lines as we could afford them and upgraded once the devices were paid off," Dr. Foster noted. Financing may be needed if the ophthalmologist opts to acquire lasers and other expensive equipment. "One can find companies that offer daily rental of lasers; this may be a practical solution for the ophthalmologist who wishes to incorporate aesthetics on a part-time basis but not transform his or her practice," she said.

Dr. Shimokaji uses a wide variety of lasers and other devices including CO_2, erbium, IPL, and Ultherapy ultrasound in her practice. She has managed the costs by partnering with plastic surgeons at a local surgery center. She also has leased some lasers, installing them in different rooms in her practice. "I have hired a laser tech, which allows me to become very efficient in my treatment," she said.

Marketing. Dr. Foster said that marketing efforts begin with current patients. "Potential patients seeking this treatment are already in your office," Dr. Foster noted. Dr. Shimokaji, who has a busy comprehensive ophthalmology practice, said she has a box on her intake questionnaire asking if the patient is interested in any cosmetic changes. If the patient checks the box, she will introduce and explore options with those patients.

Dr. Kotlus noted that social media and cosmetic websites are excellent marketing tools to reach patients. "When you have an active practice and a base of patients who trust you, then internal marketing such as patient referrals is the most cost-efficient approach. Yet a good percentage of patients find me online. I am seeing a lot more patients coming from Instagram. Twenty years ago, I would have had to walk door to door telling doctors of my services."

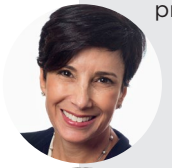
An Evolving Field

Looking ahead, Dr. Kotlus noted that the field of aesthetics is constantly evolving, and "cosmetic procedures have become more accepted among all walks of life, from the working class to professionals, and from younger individuals to older patients." He anticipated that the field will continue to grow as new technologies are introduced.

1 Bonapart JP et al. *Plast Reconstr Surg.* 2016;137(4):1125-1140.
2 Sundaram H et al. *Plast Reconstr Surg.* 2016;137(3):518e-529e.
3 Goldberg DJ. *J Clin Aesthet Dermatol.* 2012;5(6):45-53.

MEET THE EXPERTS

Jill A. Foster, MD Medical director of Plastic Surgery Ohio, a division of Ophthalmic Surgeons and Consultants of Ohio; head of Aesthetic Services at The Eye Center; and associate clinical professor of ophthalmology at The Ohio State University. All positions are in Columbus, Ohio. *Financial disclosure: Mallinckrodt: C.*



Andrea N. Hass, MD Oculoplastic surgeon and cofounder of Hass Plastic Surgery in Palm Beach, Fla. *Financial disclosure: None.*

Brett S. Kotlus, MD Oculoplastic surgeon who is also certified by the American Boards of Ophthalmology and Cosmetic Surgery. In private practice in New York City. *Financial disclosure: None.*

John J. Martin Jr., MD Oculoplastic surgeon in private practice in Coral Gables, Fla. *Financial disclosure: Merz: L.*

Gayle L. Shimokaji, MD Oculoplastic surgeon with 2020 Ophthalmic Consultants in Greenbrae, Calif. *Financial disclosure: None.*

Veronica Wagner Practice manager at Hass Plastic Surgery in Palm Beach, Fla. *Financial disclosure: None.*

Injectable Drugs, Part 1—How to Get Reimbursed for a Multidose Vial

When you code for injectable drugs, use a J-code to indicate the drug you used, and also report how many "units" of the drug you are billing for.

What are the J-codes? These are 5-character alphanumeric codes—J3301, for example, is the J-code for Kenalog (triamcinolone acetonide). J-codes are a subset of the Healthcare Common Procedure Coding System (HCPCS) codes.

What is a J-code's unit? Each J-code's descriptor includes a dosage amount, known as the HCPCS code dosage, which is the billable unit for that code. The descriptor for J3301 is *Injection, triamcinolone acetonide, not otherwise specified, 10 mg.* This indicates that the billable unit for that J-code is 10 mg.

Multidose or single-use vial? If a drug's packaging indicates that the vial is multidose, billing is based on the amount of drug administered to the patient; if single-use (see next month's "Savvy Coder"), billing is based on the amount of drug in the vial.

Start With the ASP Listings

Download the Average Sale Price (ASP) Drug Pricing file, an Excel spreadsheet that the Centers for Medicare & Medicaid Services (CMS) updates quarterly (see "Resources").

For each J-code, the file lists:

- a short descriptor, which often abbreviates the code's formal descriptor,
- HCPCS code dosage (or billable unit), and
- a payment limit (the allowable).

To continue the Kenalog example, J3301's listing includes "Triamcinolone acet inj nos" as the short descriptor, "10 mg" as the HPCS code dosage, and "1.887" as the payment limit.

Coding for Multidose Vials

If you are using a multidose vial, you will be paid for *only* the amount administered to the patient and *not* for any discarded amounts of the drug. Here's how to determine what J-code to use and how many units to bill for.

Step 1: Review the current CMS ASP Pricing file for each drug that you are using. Use the file to identify a drug's J-code and its HCPCS code dosage. When determining the appropriate J-code, take into account the specific payer's requirements. To continue the example above, we have learned that Kenalog's J-code is J3301 and its HCPCS code dosage (or billable unit) is 10 mg.

What if there is no J-code? You can use Not Otherwise Classified (NOC) codes if—and only if—there is no valid HCPCS code that describes the drug.

Step 2a: If you injected less than the HCPCS code dosage, bill for 1 unit. If you inject 4 mg of triamcinolone acetonide, this is less than the 10-mg HCPCS code dosage. In this case, you would submit 1 unit.

Step 2b: If you injected the HCPCS code dosage or more, bill a whole number of units (no fractional units). If the dosage that you inject is the same as the HCPCS code dosage, you would submit 1 unit; if twice as big, submit 2 units; etc. For example, if the HCPCS code dosage is 50 mg and 200 mg is administered, bill for 4 units.

Step 3: Fill out CMS form 1500. Indicate (a) the exact name of the drug, (b) the dosage given to the patient, and (c) the National Drug Code (NDC) billing identifier (it typically has 10 digits in a 5-4-1 format). Check the payer's guidelines to see if all this goes in box 19 or box 24 (in the shaded area) of CMS form 1500. Next, complete box 24 as you normally would (including the J-code and number of units billed).

Only bill if you are paying for the drug. If there is no expense to you for the drug (as with samples, for example), don't bill the payer or the patient for it.

Resources

Take advantage of these resources:

- ASP Drug Pricing spreadsheet: www.cms.gov/Medicare/Medicare-Fee-for-Service-Part-B-Drugs/McrPartBDrugAvgSalesPrice/2018ASPFiles.html
- Cheat sheet for commonly used drugs: aao.org/Assets/c850e98f-fc7e-4ac2-85da-f79d59ace5fc/636590827677530000/table-of-common-drugs-apr-2018-pdf?inline=1
- NCD numbers: www.accessdata.fda.gov/scripts/cder/ndc/index.cfm
- Buy a HCPCS book: aao.org/store.

BY **SUE VICCHRILLI, COT, OCS, OCSR,** ACADEMY DIRECTOR OF CODING AND REIMBURSEMENT, AND **JOY WOODKE, COE, OCS, OCSR,** ACADEMY CONSULTANT.

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

Access Innovative Tools to Enhance Quality Eye Care

Renew your Academy membership to take advantage of these unparalleled ophthalmic resources.

IRIS® Registry (Intelligent Research in Sight) — Benchmark your practice against 16,000+ other ophthalmologists using medicine's largest clinical database. In 2017, qualifying participants who reported MIPS successfully in 2016 will save an average of $18,600 through penalties avoided.

Ophthalmology® comes to you monthly, packed with the latest research and clinical updates (a $542 value).

EyeNet® ***Magazine*** delivers 12 issues of the latest industry news, plus clinical roundups and in-depth supplements such as the recent "MIPS Manual 2017" (a $150+ value).

Activate your benefits and renew your valuable membership today.
aao.org/benefits

Diana R. Shiba, Academy fellow since 2010, shares an uplifting moment with her patient. The Academy's IRIS Registry aggregates patient data to facilitate new scientific discoveries.

Protecting Sight. Empowering Lives.®

Four Strategies for Effectively Using Your Patient Portal

Communicating with your patients about their care is a fundamental part of your practice. In today's electronic world, online interaction should be an integral part of your overall communication strategy.

Patient portals are the *only* way to make such interaction possible in a secure and documentable manner that adheres to federal requirements. And they confer benefits on your practice, including increasing efficiency, boosting revenue, improving documentation, and facilitating your participation in the Merit-Based Incentive Payment System (MIPS). Beyond that, your patients will appreciate the additional services and convenience that portals provide them.

Here are 4 straightforward strategies for communicating effectively and efficiently with your patients.

Strategy 1: Use a Portal

"Never use personal email or texting for anything related to your practice," warned Joy Woodke, COE, OCS, OCSR. "Patient portals were created so communications from and to the practice would be secure, trackable, and HIPAA compliant when the software is certified." Ms. Woodke is chair of the AAOE Electronic Health Record (EHR) Committee and administrator at Oregon Eye Consultants in Eugene.

Understand the basics. Patient portals are typically an add-on software component that integrates with your practice management and EHR systems so that personal health information (PHI) is externally accessible to patients in a secure format while remaining protected by internal checks and balances. PHI is not transmitted directly to your patients; rather, they are invited by your practice to join your portal. Here they can, at a minimum, log in securely to access information regarding their medical status and history, diagnoses, and medication lists.

The portal enables them to view, download, and print their medical record, as well as to transmit copies of it to other physicians. The latter capability was formerly a federal requirement for participation in the EHR meaningful use program and is now part of MIPS.

Explore the options. Portals offer a variety of additional communication features that can be customized and implemented based on your practice's preferences. Sending out appointment reminders, accepting prescription refill requests, allowing patients to pay bills, and facilitating patient inquiries are just a few of the features you can include.

Before enabling these functionalities and rolling them out to patients, practices should first determine the degree of interactivity they want the patient to have with the portal. Each practice can then develop an implementation strategy that gradually incorporates one feature at a time, establishing solid protocols and providing appropriate staff training.

Jeffery Daigrepont, EFMP, CMPE, senior vice president at the Coker Group in Atlanta, outlined 3 broad categories of engagement that progressively build upon each other.

One-way communication. Patients

MIPS and Patient Portals

Use your portal to help achieve some of the MIPS advancing care information (ACI) measures and improvement activities.

ACI. If you are reporting the 2018 ACI transition measure set, for example, a patient portal can help you with the following measures:

- Provide Patient Access
- View, Download, or Transmit (VDT)
- Patient-Specific Education
- Secure Messaging

Improvement activities. Of the 24 improvement activities that you can report via the IRIS Registry, a patient portal is critical for one of them—IA_BE_4: Engagement of patients through implementation of improvements in patient portal—and could play a role in several others.

To learn more about MIPS, visit aao.org/medicare and also see June's *EyeNet* supplement, *MIPS 2018: A Primer and Reference.*

BY LESLIE BURLING-PHILLIPS, INTERVIEWING **JEFFERY DAIGREPONT, EFMP, CMPE,** AND **JOY WOODKE, COE, OCS, OCSR.**

can log in to the portal and look at, print, and download information and receive notices from the practice via secure email or text. However, reciprocal interaction from patient to practice is not permitted.

Two-way (limited) communication. Additional functionalities enable patients to contact the practice for routine queries such as scheduling an appointment or requesting prescription refills.

Two-way (comprehensive) communication. Patients can initiate, as well as receive, a wide range of communications. For example, they can confirm appointments, update their demographic information, and send and receive secure messages. Mr. Daigrepont said, "My physician allows his patients to contact him directly through his practice's portal, and he personally responds, which is incredibly convenient."

Prioritize patient privacy. Be sure to emphasize your commitment to protecting their privacy when you ask patients to sign up for your portal. "Before you correspond with your patients online, they should first give the consent to receive email or texts from your practice," said Mr. Daigrepont. He added that you can help increase your patients' level of security by providing guidance on protecting personal data and instructions for creating—and safeguarding—strong passwords.

Keep PHI secure. PHI such as a patient's demographics, medical history, laboratory and other test results, and diagnoses should never, under any circumstances, be transmitted in an insecure way. Because most personal email is not HIPAA compliant, all electronic communications related to a patient's PHI should be disseminated solely through a certified patient portal.

Mr. Daigrepont said, "The safest and most proper way to electronically communicate PHI is to invite patients to come in to your environment with their personal log-in credentials to access this information. Although anyone's credentials can be compromised, if the practice is not transmitting this information, it has little liability."

Strategy 2: Monitor Your Portal

Plan ahead. One of the greatest errors a practice can make is setting up a portal without first determining how it will be used to interact with patients and who on your staff should be involved with its day-to-day use, cautioned Mr. Daigrepont. He recommended designating a person or team responsible for responding to incoming communications through your portal, just as you would for triaging phone calls or handling face-to-face encounters.

Ms. Woodke agreed and added, "Our overall goal is to ensure that our patients feel like we are just as efficient electronically as we are when they call on the phone." She said that this goal can be achieved through training staff to follow practice protocols and approved scripts for communicating with patients. For example, if a technician receives a call regarding a patient's condition, the protocol is not to offer medical advice but rather to consult with a physician and then relay any message from the physician to the patient. "These policies apply to all practice communications, and portals should be treated no differently," she noted.

Strategy 3: Market Your Portal

No matter how functional and well honed your portal is, implementation will not be effective without a marketing campaign that involves patient education and portal promotion.

Initially, some ophthalmologists were concerned that their elderly patients would not embrace portals, the assumption being that these patients would be inexperienced or uncomfortable with electronics or not be able to use them because of low vision. These concerns have proved false—many senior ophthalmic patients are adept at using of smartphones, tablets, and other digital devices. "Indeed," said Ms. Woodke, "our first online appointment request was from an 80-year-old patient with macular degeneration." She added that at least half of her practice's patients use the portal.

See the big picture. Practices should think beyond using portals simply as a tool for communicating with patients. They can also be a mechanism for providing a higher level of ongoing support and education that can generate greater patient involvement with their health, possibly leading to better outcomes.

When utilized to its fullest, a patient portal can promote your practice as well, said Mr. Daigrepont. "One of the greatest benefits of collecting patients' email addresses and cell phone numbers is that they rarely change, making this a much more affordable way of reaching out to your patients than through traditional postal mail, which is quickly becoming an obsolete practice."

Build your brand. Design your portal to resemble your website, and incorporate your practice name and logo. And make sure that your website includes an easy-to-find link that launches the portal.

Mr. Daigrepont offered the following suggestions: "Maximize your marketing opportunity and integrate portal promotion with your online presence so your brand is consistent and complements all other forms of communication. Keep information up to date, add new features regularly, and make it easy for your patients to navigate so they will want to return."

Strategy 4: Learn From Your Portal

All correspondence that comes in to or goes out of your practice via the portal is documented within the system, so relevant reports can easily be generated. For example, if an appointment reminder is sent through the portal, the portal tracks the appointment's status, including when the reminder was sent and when the appointment was confirmed by the patient. You can then create a report that indicates how many appointments were confirmed through the portal. Ms. Woodke said, "Based on these reports, you can determine how much your efficiency has improved when compared to confirming patients by phone." She recommended using these data to identify areas needing improvement and to set goals for your staff.

Mr. Daigrepont is senior vice president at the Coker Group, a nationwide consultancy group based in Atlanta. *Financial disclosures: None.*
Ms. Woodke is the administrator of Oregon Eye Consultants in Eugene, an Academy consultant, and chair of the AAOE EHR Committee. *Financial disclosures: None.*

Experience IntelleChartPRO

CHART SMARTER

NEW
Assisted Compliance

NEW
Assisted Coding

IMPROVED
Knowledge Base

IntelleChartPRO

#1 No. of Registered Practices

IRIS® Registry EHR Collaborator

AMERICAN ACADEMY OF OPHTHALMOLOGY®

Nextech

(800) 868-3694

Nextech.com/Ophthalmology

AMERICAN ACADEMY
OF OPHTHALMOLOGY®
Protecting Sight. Empowering Lives.

2018 Orbital Gala

Join Your Cool Academy Cats for an Outta-Sight Night

Get hip to the AAO 2018 scene and let your psychedelic prints fly at the Academy Foundation's 1960s-themed Orbital Gala-a-go-go. At this 15th annual fundraiser, you'll support our quest to protect sight and empower lives while showing off your favorite love beads and scarfing down far-out food and cocktails. Take your groovy moves to the dance floor and catch some live jams; or if that's not your bag, throw some bread at the silent auction. Proceeds support Academy programs. Dig it?

Chicago Cultural Center

Sunday, Oct. 28
6 to 10 p.m.

To purchase tickets, visit aao.org/foundation

Foundation

Academy Notebook

NEWS • TIPS • RESOURCES

LEADERSHIP DEVELOPMENT PROGRAM. *Academy 2018 Visionary Award recipient Rep. Erik Paulsen (R-Minn.) with his constituent from Minnetonka Jill Melicher Larson, MD, who is in the Academy's Leadership Development Program (LDP) XX, class of 2018. LDP participants were special guests at the Mid-Year Forum.*

WHAT'S HAPPENING

Mid-Year Forum 2018

In late April, more than 500 Academy members gathered in Washington, D.C., to discuss some of ophthalmology's most critical issues with regulators, legislators, and Academy leaders.

EyeNet summarizes 3 key Mid-Year Forum 2018 sessions below.

Private Equity and Other Equity Transfers: What's My Practice Worth? Recent publicity has highlighted the purchase of ophthalmology practices by private equity firms. Understanding how practices are valued is important for any ophthalmologist with ownership in a practice as well as associates considering purchasing an equity position within the practice. This session explored what issues should be considered, whether selling a practice to a hospital, private equity firm, or an ophthalmology or a multispecialty group; merging with other doctors; or buying in or out of a practice. It was moderated by **Robert E. Wiggins, Jr., MD, MHA,** Senior Secretary for Ophthalmic Practice, and **Ruth D. Williams, MD,** *EyeNet*'s Chief Medical Editor.

Drinking From a Firehose: How Not to Drown in the Era of Information Overload. Information overload challenges practitioners at all levels of training and throughout our entire careers. Maintaining and acquiring new clinical skills and knowledge, advocating for the best care for our patients, navigating reimbursement and changes in practice management, and many other facets of being a physician confront all of us daily. At this session, attendees learned best practices, tips, and tricks on how to keep their heads above water. It was moderated by **Louis B. Cantor, MD,** Senior Secretary for Clinical Education.

The Future of Artificial Intelligence in Ophthalmology. The next transformation in ophthalmology is the application of artificial intelligence in diagnosing and treating disease in clinical practice. It is beginning to be used in retinal disease for detecting diabetic retinopathy and diabetic macular edema from fundus photographs, and it has potential to provide more efficient and objective analysis of images and prediction of disease progression. This session explored what artificial intelligence means for practicing ophthalmologists, its promise and limitations, and what the future holds. It was moderated by **Rahul Khurana, MD,** Editor in Chief, The ONE Network.

To view the full Mid-Year Forum Report, visit aao.org/myf.

TAKE NOTICE

Opt In to the Academy's *Conversations* Newsletter

Conversations, a weekly Academy email newsletter, highlights topics that Academy members are discussing on social media and on aao.org. Find out what your colleagues are saying about the latest key issues affecting ophthalmology. Join the conversation.

To sign up for the newsletter, visit aao.org/conversations.

AMERICAN ACADEMY OF OPHTHALMOLOGY®

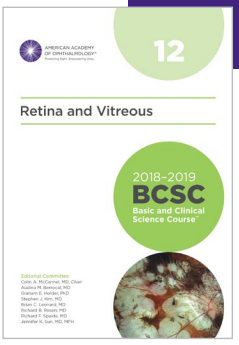
2018-2019 BCSC: Important Updates

The 2018-2019 edition of the *Basic and Clinical Science Course* (*BCSC*) is available for advance order and will ship by mid-June (eBooks also are available starting mid-June).

The *BCSC* is a comprehensive reference used by ophthalmologists and residents worldwide. The new edition includes major revisions to the following sections:

- Clinical Optics
- Pediatric Ophthalmology and Strabismus
- Retina and Vitreous

Choose from the print or eBook format. Purchase an individual section, or save when you purchase a complete set of all 13 sections.



For pricing and more information, visit aao.org/bcsc.

New! *BCSC* Self-Assessment Program

The Academy has launched a new tool for residents and practicing ophthalmologists: the *Basic and Clinical Science Course (BCSC) Self-Assessment Program.*

The *BCSC* is the Academy's definitive compilation of scientific research and clinical experience and is continually updated by a faculty of more than 90 experts. This new self-assessment program includes 1,000+ questions to help identify knowledge gaps, and each answer provides a thorough discussion, excerpts from the *BCSC*, and complete references. This activity has been approved for *AMA PRA Category 1 Credit.*

For more information and to purchase, visit aao.org/bcsc.

Be a Foundation Champion

The Academy Foundation supports important programs that benefit our members and patients. From the vast wealth of clinical knowledge on the ONE Network to IRIS Registry data from nearly 200 million patient visits, the Academy continues to grow and evolve these resources and more, thanks to generous donor contributions.

Consider becoming a Partner for Sight today. With just $1,000, you can host and stream 20 surgical education videos on the ONE Network or refer 13 medically underserved seniors for sight-saving care through EyeCare America.

To learn more, visit aao.org/foundation.

D.C. REPORT

Salary Change for VA's Ophthalmic Technicians

As a result of the Academy's decade-long advocacy, the U.S. Department of Veterans Affairs (VA) will raise ophthalmic technicians' salary to a higher pay classification. Technicians will also receive pay adjustments based on the market in which they are employed.

The Academy lobbied for this change because it is critical for the VA to recruit and retain qualified, experienced ophthalmic technicians in order to increase physician productivity and serve more VA patients—studies show that ophthalmologists' productivity improves by 30% when supported by an ophthalmic technician. Productivity and efficiency are especially important today because demand for eye care is growing; recently there has been an average 3.4% increase in patient visits every year. To address this need, the Academy helped advance the salary increase legislation in Congress. It's notable that this change will further reinforce the viability of ophthalmic technician as a career path within the VA.

Ask the Ethicist: Warning Patients About Effects of Dilating Drops

The Ethics Committee response, below, is based on the Ophthalmic Mutual Insurance Company (OMIC) article "Warning Patients About Side Effects of Dilating Drops," by Anne Menke, RN, PhD, OMIC Risk Management.[1]

Q: *A patient of mine was killed in a car accident. The other driver's eyes had been dilated. What are the ophthalmologist's responsibilities regarding informing patients about the effects and risks of pupil dilation?*

A: Informed consent is based on what a "reasonable layperson" would want to know prior to undergoing a procedure, such as pupil dilation. Ophthalmologists can make patients aware of potential side effects, such as blurry vision for the following 4 to 8 hours. Dilating drops may induce photophobia, lack of accommodation, glare, and decreased contrast threshold and high-contrast visual acuity. These visual changes can be a problem, particularly for those patients whose vision and mobility may already be compromised. Dilating drops can—although this is rare—provoke allergic reactions, angle-closure attacks, and systemic reactions such as increased blood pressure, arrhythmias, tachycardia, and dizziness—a reasonable person might want to be informed of these possible side effects.

Q: *Is it necessary to have the patient sign a consent form if a procedure will include dilation?*

A: No, but you should consider fully documenting your discussion with the patient, and you may want to consider asking first-time patients whose eyes will be dilated to sign a form acknowledging that they have been apprised of the risks. OMIC has a sample dilation consent form available at www.omic.com.

Q: *What is my office's responsibility before the appointment to apprise the patient of these risks?*

A: It is helpful to advise new patients as they are making their appointment

that their eyes will be dilated so that they can prepare. Patients can be told that they will need to wear sunglasses and avoid driving and operating machinery until their pupil dilation wears off.

Q: *What needs to happen during the exam?*

A: Involve the patient in the decision-making process, and discuss potential side effects with the patient. Consider making notes about the discussion, the offer of sunglasses (or the reminder to wear them), and any warning, especially the possible impact on driving.

Q: *Should I refuse to dilate if a patient insists on driving?*

A: If a patient insists on driving after dilation, consider the patient's visual acuity and driving ability, the driving conditions, and how urgently you need to diagnose and/or treat the presenting condition. As you know, the patient may be at more risk from a delayed diagnosis.

Q: *What is my office's responsibility to patients who are experienced with dilation?*

A: It may be helpful to place a sign in your practice's waiting room reminding patients whose eyes are dilated not to drive, to wear sunglasses, and to let the staff know whether they need assistance walking while their eyes are dilated. Disposable sunglasses can be given to the patient in the exam room. Some practices place a bowl of sunglasses at the check out desk with a sign.

To submit a question to the Ethics Committee, email ethics@aao.org.

1 www.omic.com/warn-patients-about-side-effects-of-dilating-drops/.

Recruit on the No. 1 Job Site for Ophthalmology

A talented and qualified staff is a practice's greatest asset. Find the right match through the Academy's Ophthalmology Job Center—the No. 1 recruiting site for ophthalmology. It has 10 times more listings for ophthalmologists than its closest competitor and more than 10,000 visitors per month.

To advertise open positions or post your CV, visit aao.org/jobcenter.

For the latest information and innovation from Alcon, visit us at **alcon.com**

ALCON AT AAO 2018

Come see Alcon at **booth #2708** in Chicago, October 27-30.

Alcon is reimagining eye care. We are the forefront of innovation, pursuing new technologies and techniques to help surgeons address unmet patient needs. Our mission is clear: discover new ways to enhance sight and improve people's lives.

As the global leader in eye care, we offer the most complete line of ophthalmic devices for cataracts, glaucoma, retina, and refractive surgery. However, our commitment to the eye care professional community goes beyond our innovative products. We provide service like no other, and support eye care professionals around the world with educational and training opportunities.

CHECK BACK EACH MONTH FOR MORE INFORMATION ON WHAT ALCON HAS PLANNED DURING THE 2018 AAO ANNUAL MEETING IN CHICAGO!

CONNECT WITH US! **@AlconEyeCare** **@Alcon**

Alcon A Novartis Division

Destination AAO 2018

GET READY FOR CHICAGO • PART 2 OF 6

AVOID LINES. *Save precious time onsite by registering for AAO 2018 this month.*

BEAT THE CLOCK

This Month: Register, and Search the Program

AAO 2018 will be held at McCormick Place in Chicago Oct. 27-30 and is preceded by Subspecialty Day Oct. 26-27. Academy, AAOE, and Pan-American Association of Ophthalmology members can register online beginning June 13; nonmember registration opens June 27. Once you've registered, access the online Program Search to find course information and abstracts—you can search by day, topic, special interest, or presenter, and you can begin to build your schedule for AAO 2018 in your AAO 2018 calendar.

For more registration information, including fees, visit aao.org/registration.

EVENTS

Schedule Time for *EyeNet* Corporate Lunches

Be sure to leave room in your schedule for *EyeNet*'s free corporate educational lunches on Saturday, Oct. 27, Sunday, Oct. 28, and Monday, Oct. 29, located onsite at McCormick Place. Check-in and lunch pickup is at 12:15 p.m., and the program is 12:30-1:30 p.m. These non-CME events are developed independently by industry—they are not affiliated with the official programs of AAO 2018 or Subspecialty Day. By attending these presentations, you may be subject to reporting under the Physician Payment Sunshine Act.

For more information, visit aao.org/eyenet/corporate-events.

Join the Cool Academy Cats

The Academy Foundation invites you to this year's Orbital Gala on Sunday, Oct. 28, at the Chicago Cultural Center, home of the world's largest Tiffany stained-glass dome. This 15th annual fundraiser will be the social event of AAO 2018, complete with dinner, cocktails, and music. The theme is the 1960s, so be sure to let your psychedelic prints fly, show off your favorite love beads, and take your groovy moves to the dance floor. Proceeds will support the Academy's educational, quality of care, and service programs.

To purchase tickets, visit aao.org/foundation.

PROGRAM

Skills Transfer Courses

Do you learn best in a hands-on setting? Perfect your technique in a Skills Transfer lab—60 labs and 35 didactic courses will be offered at AAO 2018. It is strongly recommended (but not required) that you attend the didactic lecture associated with the Skills Transfer lab. Didactic lectures are free if you have an Academy Plus course pass (which you may purchase when registering for AAO 2018). Lab tickets, however, must be purchased separately.

A limited number of Skills Transfer labs will be offered on Saturday:

- Sutureless Scleral Buckling
- Photo/Video Editing for Ophthalmologists
- No Capsule, No Problem: Intrascleral Haptic Fixation of IOLs
- Laser Refractive Surgery
- Laser Retinopexy for Retinal Breaks
- Gonioscopy and Anterior Segment Imaging for Glaucoma Surgery

New Skills Transfer labs for AAO 2018 include the following: Ocular Trauma: Translating Lessons Learned From the Battlefield Into Everyday Practice, and Pupilloplasty Techniques and Innovations in Iris Repair.

For more information, visit aao.org/skills.

AMERICAN ACADEMY OF OPHTHALMOLOGY®

OFFICIAL AAO 2018 HOTELS

Registration for housing opens June 13 for Academy, AAOE, and Pan-American Association of Ophthalmology members; it opens on June 27 for nonmembers. Visit aao.org/hotel for reservations, an interactive map, and information on hotel amenities and availability.

Beware of scams. Fraudulent companies pretending to be associated with the Academy and AAO 2018 may appear in web searches or contact you via email. Only book hotel rooms and registration through the Academy's website and official housing provider, Expovision. If you are ever in doubt, email meetings@aao.org or call 1-415-561-8500 to confirm.

1. AC Hotel Chicago Downtown
   630 N. Rush St.
2. Best Western Grant Park
   1100 S. Michigan Ave.
3. Blackstone, Autograph Collection
   636 S. Michigan Ave.
4. Chicago Marriott Downtown Magnificent Mile
   540 N. Michigan Ave.
5. Conrad Chicago
   101 E. Erie St.
6. Courtyard Chicago Magnificent Mile
   165 E. Ontario St.
7. Doubletree Hotel Chicago Magnificent Mile
   300 E. Ohio St.
8. Embassy Suites Chicago Downtown
   600 N. State St.
9. Embassy Suites Chicago Magnificent Mile
   511 N. Columbus Dr.
10. Fairfield Inn & Suites Chicago Magnificent Mile
    216 E. Ontario St.
11. Fairmont Chicago, Millennium Park
    200 N. Columbus Dr.
12. Four Seasons Hotel Chicago
    120 E. Delaware Pl.
13. Gwen Hotel Chicago
    521 N. Rush St.
14. Hampton Inn and Suites Chicago Downtown
    33 W. Illinois St.
15. Hampton Inn Chicago Mag Mile
    160 E. Huron St.
16. Hampton Inn Majestic Chicago Theatre District
    22 W. Monroe St.
17. Hilton Chicago
    720 S. Michigan Ave.
18. Hilton Garden Inn Chicago Downtown Magnificent Mile
    10 E. Grand Ave.
19. Hilton Suites Chicago Magnificent Mile
    198 E. Delaware Pl.
20. Homewood Suites Chicago Downtown
    40 E. Grand Ave.
21. Homewood Suites Chicago Mag Mile
    152 E. Huron St.
22. Hotel Cass- A Holiday Inn Express
    640 N. Wabash Ave.
23. Hotel EMC2, Autograph Collection
    228 E. Ontario St.
24. Hyatt Centric Chicago Magnificent Mile
    633 N. Saint Clair St.
25. Hyatt Regency Chicago
    151 E. Wacker Dr.
26. Hyatt Regency McCormick Place
    2233 S. Martin Luther King Dr.
27. Inn of Chicago Magnificent Mile
    162 E. Ohio St.
28. InterContinental Chicago Magnificent Mile
    505 N. Michigan Ave.
29. James Chicago
    55 E. Ontario St.
30. JW Marriott Chicago
    151 W. Adams St.
31. Langham Chicago
    330 N. Wabash Ave.
32. Loews Chicago Hotel
    455 N. Park Dr.
33. LondonHouse Chicago
    85 E Wacker Dr.
34. Marriott Marquis Chicago at McCormick Place
    2121 S. Prairie Ave.
35. Omni Chicago Hotel
    676 N. Michigan Ave.
36. Palmer House Hilton
    17 E. Monroe St.
37. Palomar Chicago, A Kimpton Hotel
    505 N. State St.
38. Park Hyatt Chicago
    800 N. Michigan Ave.
39. Peninsula Chicago
    108 E. Superior St.
40. Radisson Blu Aqua Hotel Chicago
    221 N. Columbus Dr.
41. Renaissance Chicago Downtown Hotel
    1 W. Upper Wacker Dr.
42. Residence Inn Chicago Magnificent Mile
    201 E. Walton Pl.
43. Ritz-Carlton Chicago
    160 E. Pearson St.
44. Sheraton Grand Chicago
    301 E. North Water St.
45. Silversmith Hotel Chicago Downtown
    10 S. Wabash Ave.
46. Sofitel Chicago Water Tower
    20 E. Chestnut St.
47. St. Jane Chicago- formerly Hard Rock
    230 N. Michigan Ave.
48. Swissotel Chicago
    323 E. Wacker Dr.
49. Trump International Hotel & Tower Chicago
    401 N. Wabash Ave.
50. Virgin Hotels Chicago
    203 N. Wabash Ave.
51. W Chicago City Center
    172 W. Adams St.
52. W Chicago Lakeshore
    644 N. Lake Shore Dr.
53. Warwick Allerton Hotel Chicago
    701 N. Michigan Ave.
54. Westin Chicago River North
    320 N. Dearborn St.
55. Westin Michigan Avenue Chicago
    909 N. Michigan Ave.

AMERICAN ACADEMY
OF OPHTHALMOLOGY®

EyeNet Corporate **Lunches**

EyeNet*® *Magazine **helps you make the most of your time at AAO 2018 by bringing you free corporate educational program lunches* onsite at McCormick Place.**

Programs

Saturday, Oct. 27

Sunday, Oct. 28

Monday, Oct. 29

Room E353c

McCormick Place

Check-in and Lunch Pickup

12:15-12:30 p.m. Lunches are provided on a first-come basis.

Program

12:30-1:30 p.m.

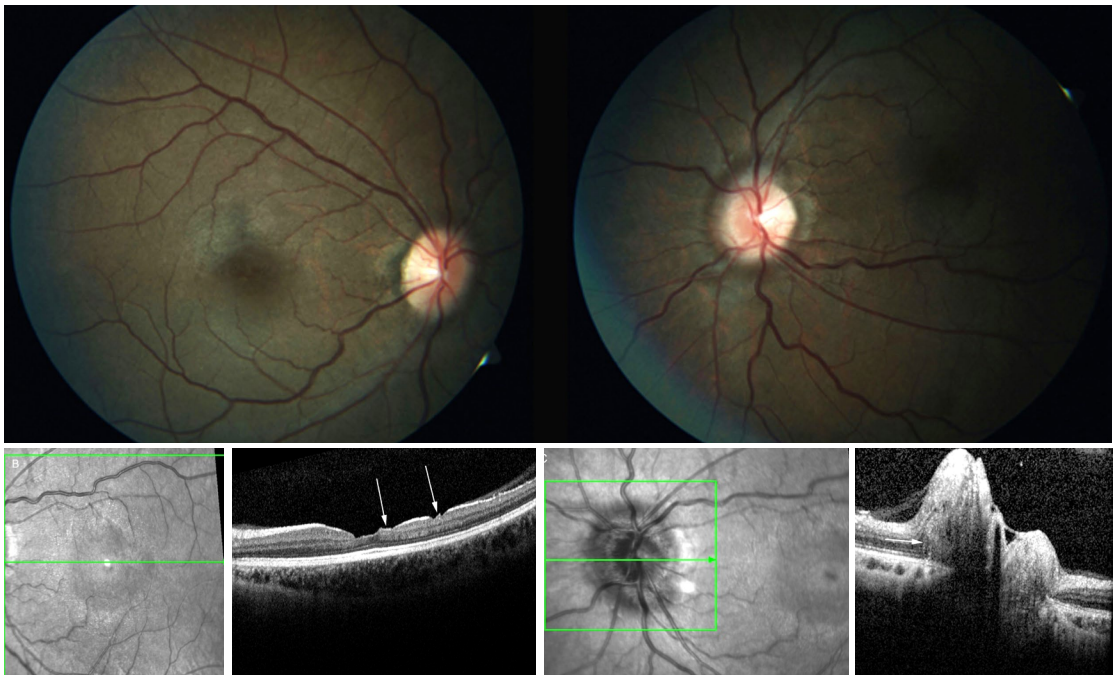
Check aao.org/eyenet/corporate-events for updated program information.

** These programs are non-CME and are developed independently by industry. They are not affiliated with the official program of AAO 2018 or Subspecialty Day. By attending a lunch, you may be subject to reporting under the Physician Payment Sunshine Act.*

Protecting Sight. Empowering Lives.®

MYSTERY IMAGE

BLINK



Michael P. Kelly, FOPS, Duke University, Department of Ophthalmology, Durham, N.C.

WHAT IS THIS MONTH'S MYSTERY CONDITION? *Visit aao.org/eyenet to make your diagnosis in the comments and get the answer to last month's mystery.*

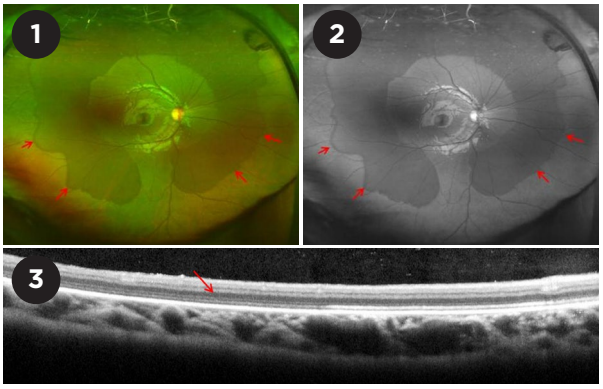
LAST MONTH'S BLINK

Dark-Without-Pressure Fundus Lesions

A 13-year-old boy was diagnosed with anterior uveitis in his left eye. BCVA was 20/20 in his right eye and 20/25 in his left. The fundus examination of the left eye was normal; that of the right eye showed a well-defined lesion darker than the surrounding area and sparing the macula, suggestive of a large, dark-without-pressure fundus lesion (Fig. 1, 2).[1]

There were no vascular abnormalities and no evidence of vitreous separation or traction. On spectral-domain OCT (Fig. 3), an abrupt transition to hyporeflectivity of the ellipsoid and outer segments of the photoreceptors was seen within the dark fundus lesion. Visual fields and full fields via electroretinogram were normal, suggesting that the lesions represent structural changes without associated functional deficits.

Dark-without-pressure lesions are asymptomatic and exhibit relative reflectivity, which occurs at the level of the outer retina.[1] Specific biochemical or structural etiology remains unclear, and no functional defects have been reported in these dark areas without pressure; therefore, they do not require treatment. It has been reported[1] that these lesions are transient and change shape, and they occasionally completely disappear over weeks. It has been hypothesized that they represent altered reflex at the internal limiting membrane or retinal pigment epithelium. The altered reflex has been attributed to the presence of photopigment with different density or spectral range within these lesions compared with the rest of the fundus. These dark-without-pressure focal lesions are associated with photopigment that absorbs short-wavelength light more effectively, which explains the good visibility on red-free photography.



1 Fawzi AA et al. *Retina.* 2014;34(12):2376-2387.

WRITTEN BY **GAURAV GUPTA, MBBS, PRIYA BAJGAI, MBBS,** AND **RAMANDEEP SINGH, MBBS.** PHOTO BY **ARUN KAPIL.** ALL ARE AT ADVANCED EYE CENTRE, CHANDIGARH, INDIA.

LUCENTIS®
RANIBIZUMAB INJECTION

Brief summary–please see the LUCENTIS® package insert for full prescribing information.

1 INDICATIONS AND USAGE
LUCENTIS is indicated for the treatment of patients with:

1.1 Neovascular (Wet) Age-Related Macular Degeneration (AMD)

1.2 Macular Edema Following Retinal Vein Occlusion (RVO)

1.3 Diabetic Macular Edema (DME)

1.4 Diabetic Retinopathy (DR)

1.5 Myopic Choroidal Neovascularization (mCNV)

4 CONTRAINDICATIONS
4.1 Ocular or Periocular Infections
LUCENTIS is contraindicated in patients with ocular or periocular infections.

4.2 Hypersensitivity
LUCENTIS is contraindicated in patients with known hypersensitivity to ranibizumab or any of the excipients in LUCENTIS. Hypersensitivity reactions may manifest as severe intraocular inflammation.

5 WARNINGS AND PRECAUTIONS
5.1 Endophthalmitis and Retinal Detachments
Intravitreal injections, including those with LUCENTIS, have been associated with endophthalmitis and retinal detachments. Proper aseptic injection technique should always be used when administering LUCENTIS. In addition, patients should be monitored following the injection to permit early treatment should an infection occur *[see Dosage and Administration (2.6, 2.7) in the full prescribing information and Patient Counseling Information (17)]*.

5.2 Increases in Intraocular Pressure
Increases in intraocular pressure have been noted both pre-injection and post-injection (at 60 minutes) while being treated with LUCENTIS. Monitor intraocular pressure prior to and following intravitreal injection with LUCENTIS and manage appropriately *[see Dosage and Administration (2.7 in the full prescribing information)]*.

5.3 Thromboembolic Events
Although there was a low rate of arterial thromboembolic events (ATEs) observed in the LUCENTIS clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause).

Neovascular (Wet) Age-Related Macular Degeneration
The ATE rate in the three controlled neovascular AMD studies (AMD-1, AMD-2, AMD-3) during the first year was 1.9% (17 of 874) in the combined group of patients treated with 0.3 mg or 0.5 mg LUCENTIS compared with 1.1% (5 of 441) in patients from the control arms *[see Clinical Studies (14.1 in the full prescribing information)]*. In the second year of Studies AMD-1 and AMD-2, the ATE rate was 2.6% (19 of 721) in the combined group of LUCENTIS-treated patients compared with 2.9% (10 of 344) in patients from the control arms. In Study AMD-4, the ATE rates observed in the 0.5 mg arms during the first and second year were similar to rates observed in Studies AMD-1, AMD-2, and AMD-3.

In a pooled analysis of 2-year controlled studies (AMD-1, AMD-2, and a study of LUCENTIS used adjunctively with verteporfin photodynamic therapy), the stroke rate (including both ischemic and hemorrhagic stroke) was 2.7% (13 of 484) in patients treated with 0.5 mg LUCENTIS compared to 1.1% (5 of 435) in patients in the control arms (odds ratio 2.2 (95% confidence interval (0.8-7.1))).

Macular Edema Following Retinal Vein Occlusion
The ATE rate in the two controlled RVO studies during the first 6 months was 0.8% in both the LUCENTIS and control arms of the studies (4 of 525 in the combined group of patients treated with 0.3 mg or 0.5 mg LUCENTIS and 2 of 260 in the control arms) *[see Clinical Studies (14.2 in the full prescribing information)]*. The stroke rate was 0.2% (1 of 525) in the combined group of LUCENTIS-treated patients compared to 0.4% (1 of 260) in the control arms.

Diabetic Macular Edema and Diabetic Retinopathy
Safety data are derived from studies D-1 and D-2. All enrolled patients had DME and DR at baseline *[see Clinical Studies (14.3, 14.4 in the full prescribing information)]*.

In a pooled analysis of Studies D-1 and D-2 *[see Clinical Studies (14.3 in the full prescribing information)]*, the ATE rate at 2 years was 7.2% (18 of 250) with 0.5 mg LUCENTIS, 5.6% (14 of 250) with 0.3 mg LUCENTIS, and 5.2% (13 of 250) with control. The stroke rate at 2 years was 3.2% (8 of 250) with 0.5 mg LUCENTIS, 1.2% (3 of 250) with 0.3 mg LUCENTIS, and 1.6% (4 of 250) with control. At 3 years, the ATE rate was 10.4% (26 of 249) with 0.5 mg LUCENTIS and 10.8% (27 of 250) with 0.3 mg LUCENTIS; the stroke rate was 4.8% (12 of 249) with 0.5 mg LUCENTIS and 2.0% (5 of 250) with 0.3 mg LUCENTIS.

5.4 Fatal Events in Patients with DME and DR at baseline
Diabetic Macular Edema and Diabetic Retinopathy
Safety data are derived from studies D-1 and D-2. All enrolled patients had DME and DR at baseline *[see Clinical Studies (14.3, 14.4 in the full prescribing information)]*.

A pooled analysis of Studies D-1 and D-2 *[see Clinical Studies (14.3 in the full prescribing information)]*, showed that fatalities in the first 2 years occurred in 4.4% (11 of 250) of patients treated with 0.5 mg LUCENTIS, in 2.8% (7 of 250) of patients treated with 0.3 mg LUCENTIS, and in 1.2% (3 of 250) of control patients. Over 3 years, fatalities occurred in 6.4% (16 of 249) of patients treated with 0.5 mg LUCENTIS and in 4.4% (11 of 250) of patients treated with 0.3 mg LUCENTIS. Although the rate of fatal events was low and included causes of death typical of patients with advanced diabetic complications, a potential relationship between these events and intravitreal use of VEGF inhibitors cannot be excluded.

6 ADVERSE REACTIONS
The following adverse reactions are discussed in greater detail in other sections of the label:
- Endophthalmitis and Retinal Detachments *[see Warnings and Precautions (5.1)]*
- Increases in Intraocular Pressure *[see Warnings and Precautions (5.2)]*
- Thromboembolic Events *[see Warnings and Precautions (5.3)]*
- Fatal Events in patients with DME and DR at baseline *[see Warnings and Precautions (5.4)]*

6.1 Injection Procedure
Serious adverse reactions related to the injection procedure have occurred in < 0.1% of intravitreal injections, including endophthalmitis *[see Warnings and Precautions (5.1)]*, rhegmatogenous retinal detachment, and iatrogenic traumatic cataract.

6.2 Clinical Studies Experience
Because clinical trials are conducted under widely varying conditions, adverse reaction rates observed in one clinical trial of a drug cannot be directly compared with rates in the clinical trials of the same or another drug and may not reflect the rates observed in practice.

The data below reflect exposure to 0.5 mg LUCENTIS in 440 patients with neovascular AMD in Studies AMD-1, AMD-2, and AMD-3; in 259 patients with macular edema following RVO. The data also reflect exposure to 0.3 mg LUCENTIS in 250 patients with DME and DR at baseline *[see Clinical Studies (14 in the full prescribing information)]*.

Safety data observed in Study AMD-4, D-3, and in 224 patients with mCNV were consistent with these results. On average, the rates and types of adverse reactions in patients were not significantly affected by dosing regimen.

Ocular Reactions
Table 1 shows frequently reported ocular adverse reactions in LUCENTIS-treated patients compared with the control group.

Table 1 Ocular Reactions in the DME and DR, AMD, and RVO Studies

	DME and DR 2-year		AMD 2-year		AMD 1-year		RVO 6-month	
Adverse Reaction	LUCENTIS 0.3 mg n=250	Control n=250	LUCENTIS 0.5 mg n=379	Control n=379	LUCENTIS 0.5 mg n=440	Control n=441	LUCENTIS 0.5 mg n=259	Control n=260
Conjunctival hemorrhage	47%	32%	74%	60%	64%	50%	48%	37%
Eye pain	17%	13%	35%	30%	26%	20%	17%	12%
Vitreous floaters	10%	4%	27%	8%	19%	5%	7%	2%
Intraocular pressure increased	18%	7%	24%	7%	17%	5%	7%	2%
Vitreous detachment	11%	15%	21%	19%	15%	15%	4%	2%
Intraocular inflammation	4%	3%	18%	8%	13%	7%	1%	3%
Cataract	28%	32%	17%	14%	11%	9%	2%	2%
Foreign body sensation in eyes	10%	5%	16%	14%	13%	10%	7%	5%
Eye irritation	8%	5%	15%	15%	13%	12%	7%	6%
Lacrimation increased	5%	4%	14%	12%	8%	8%	2%	3%
Blepharitis	3%	2%	12%	8%	8%	5%	0%	1%
Dry eye	5%	3%	12%	7%	7%	7%	3%	3%
Visual disturbance or vision blurred	8%	4%	18%	15%	13%	10%	5%	3%
Eye pruritus	4%	4%	12%	11%	9%	7%	1%	2%
Ocular hyperemia	9%	9%	11%	8%	7%	4%	5%	3%
Retinal disorder	2%	2%	10%	7%	8%	4%	2%	1%
Maculopathy	5%	7%	9%	9%	6%	6%	11%	7%
Retinal degeneration	1%	0%	8%	6%	5%	3%	1%	0%
Ocular discomfort	2%	1%	7%	4%	5%	2%	2%	2%
Conjunctival hyperemia	1%	2%	7%	6%	5%	4%	0%	0%
Posterior capsule opacification	4%	3%	7%	4%	2%	2%	0%	1%
Injection site hemorrhage	1%	0%	5%	2%	3%	1%	0%	0%

Non-Ocular Reactions
Non-ocular adverse reactions with an incidence of ≥ 5% in patients receiving LUCENTIS for DR, DME, AMD, and/or RVO and which occurred at a ≥ 1% higher frequency in patients treated with LUCENTIS compared to control are shown in Table 2. Though less common, wound healing complications were also observed in some studies.

Table 2 Non-Ocular Reactions in the DME and DR, AMD, and RVO Studies

	DME and DR 2-year		AMD 2-year		AMD 1-year		RVO 6-month	
Adverse Reaction	LUCENTIS 0.3 mg n=250	Control n=250	LUCENTIS 0.5 mg n=379	Control n=379	LUCENTIS 0.5 mg n=440	Control n=441	LUCENTIS 0.5 mg n=259	Control n=260
Nasopharyngitis	12%	6%	16%	13%	8%	9%	5%	4%
Anemia	11%	10%	8%	7%	4%	3%	1%	1%
Nausea	10%	9%	9%	6%	5%	5%	1%	2%
Cough	9%	4%	9%	8%	5%	4%	1%	2%
Constipation	8%	4%	5%	7%	3%	4%	0%	1%
Seasonal allergy	8%	4%	4%	4%	2%	2%	0%	2%
Hypercholesterolemia	7%	5%	5%	5%	3%	2%	1%	1%
Influenza	7%	3%	7%	5%	3%	2%	3%	2%
Renal failure	7%	6%	1%	1%	0%	0%	0%	0%
Upper respiratory tract infection	7%	7%	9%	8%	5%	5%	2%	2%
Gastroesophageal reflux disease	6%	4%	4%	6%	3%	4%	1%	0%
Headache	6%	8%	12%	9%	6%	5%	3%	3%
Edema peripheral	6%	4%	3%	5%	2%	3%	0%	1%
Renal failure chronic	6%	2%	0%	1%	0%	0%	0%	0%
Neuropathy peripheral	5%	3%	1%	1%	1%	0%	0%	0%
Sinusitis	5%	8%	8%	7%	5%	5%	3%	2%
Bronchitis	4%	4%	11%	9%	6%	5%	0%	2%
Atrial fibrillation	3%	3%	5%	4%	2%	2%	1%	0%
Arthralgia	3%	3%	11%	9%	5%	5%	2%	1%
Chronic obstructive pulmonary disease	1%	1%	6%	3%	3%	1%	0%	0%
Wound healing complications	1%	0%	1%	1%	1%	0%	0%	0%

6.3 Immunogenicity
As with all therapeutic proteins, there is the potential for an immune response in patients treated with LUCENTIS. The immunogenicity data reflect the percentage of patients whose test results were considered positive for antibodies to LUCENTIS in immunoassays and are highly dependent on the sensitivity and specificity of the assays.

The pre-treatment incidence of immunoreactivity to LUCENTIS was 0%-5% across treatment groups. After monthly dosing with LUCENTIS for 6 to 24 months, antibodies to LUCENTIS were detected in approximately 1%-9% of patients.

The clinical significance of immunoreactivity to LUCENTIS is unclear at this time. Among neovascular AMD patients with the highest levels of immunoreactivity, some were noted to have iritis or vitritis. Intraocular inflammation was not observed in patients with DME and DR at baseline, or RVO patients with the highest levels of immunoreactivity.

6.4 Postmarketing Experience
The following adverse reaction has been identified during post-approval use of LUCENTIS. Because this reaction was reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate the frequency or establish a causal relationship to drug exposure.
- Ocular: Tear of retinal pigment epithelium among patients with neovascular AMD

7 DRUG INTERACTIONS
Drug interaction studies have not been conducted with LUCENTIS.

LUCENTIS intravitreal injection has been used adjunctively with verteporfin photodynamic therapy (PDT). Twelve (12) of 105 (11%) patients with neovascular AMD developed serious intraocular inflammation; in 10 of the 12 patients, this occurred when LUCENTIS was administered 7 days (± 2 days) after verteporfin PDT.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Risk Summary
There are no adequate and well-controlled studies of LUCENTIS administration in pregnant women.

Administration of ranibizumab to pregnant monkeys throughout the period of organogenesis resulted in a low incidence of skeletal abnormalities at intravitreal doses 13-times the predicted human exposure (based on maximal serum trough levels [C_{max}]) after a single eye treatment at the recommended clinical dose. No skeletal abnormalities were observed at serum trough levels equivalent to the predicted human exposure after a single eye treatment at the recommended clinical dose *[see Animal Data]*.

Animal reproduction studies are not always predictive of human response, and it is not known whether ranibizumab can cause fetal harm when administered to a pregnant woman. Based on the anti-VEGF mechanism of action for ranibizumab *[see Clinical Pharmacology (12.1 in the full prescribing information)]*, treatment with LUCENTIS may pose a risk to human embryofetal development.

LUCENTIS should be given to a pregnant woman only if clearly needed.

Data
Animal Data
An embryo-fetal developmental toxicity study was performed on pregnant cynomolgus monkeys. Pregnant animals received intravitreal injections of ranibizumab every 14 days starting on Day 20 of gestation, until Day 62 at doses of 0, 0.125, and 1 mg/eye. Skeletal abnormalities including incomplete and/or irregular ossification of bones in the skull, vertebral column, and hindlimbs and shortened supernumerary ribs were seen at a low incidence in fetuses from animals treated with 1 mg/eye of ranibizumab. The 1 mg/eye dose resulted in trough serum ranibizumab levels up to 13 times higher than predicted C_{max} levels with single eye treatment in humans. No skeletal abnormalities were seen at the lower dose of 0.125 mg/eye, a dose which resulted in trough exposures equivalent to single eye treatment in humans. No effect on the weight or structure of the placenta, maternal toxicity, or embryotoxicity was observed.

8.2 Lactation
Risk Summary
There are no data available on the presence of ranibizumab in human milk, the effects of ranibizumab on the breastfed infant or the effects of ranibizumab on milk production/excretion.

Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when LUCENTIS is administered to a nursing woman.

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

8.3 Females and Males of Reproductive Potential
Infertility
No studies on the effects of ranibizumab on fertility have been conducted. and it is not known whether ranibizumab can affect reproduction capacity. Based on the anti-VEGF mechanism of action for ranibizumab, treatment with LUCENTIS may pose a risk to reproductive capacity.

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

8.5 Geriatric Use
In the clinical studies, approximately 76% (2449 of 3227) of patients randomized to treatment with LUCENTIS were ≥ 65 years of age and approximately 51% (1644 of 3227) were ≥ 75 years of age *[see Clinical Studies (14 in the full prescribing information)]*. No notable differences in efficacy or safety were seen with increasing age in these studies. Age did not have a significant effect on systemic exposure.

10 OVERDOSAGE
More concentrated doses as high as 2 mg ranibizumab in 0.05 mL have been administered to patients. No additional unexpected adverse reactions were seen.

17 PATIENT COUNSELING INFORMATION
Advise patients that in the days following LUCENTIS administration, patients are at risk of developing endophthalmitis. If the eye becomes red, sensitive to light, painful, or develops a change in vision, advise the patient to seek immediate care from an ophthalmologist *[see Warnings and Precautions (5.1)]*.

LUCENTIS®
[ranibizumab injection]
Manufactured by:
Genentech, Inc.
A Member of the Roche Group
1 DNA Way
South San Francisco, CA
94080-4990

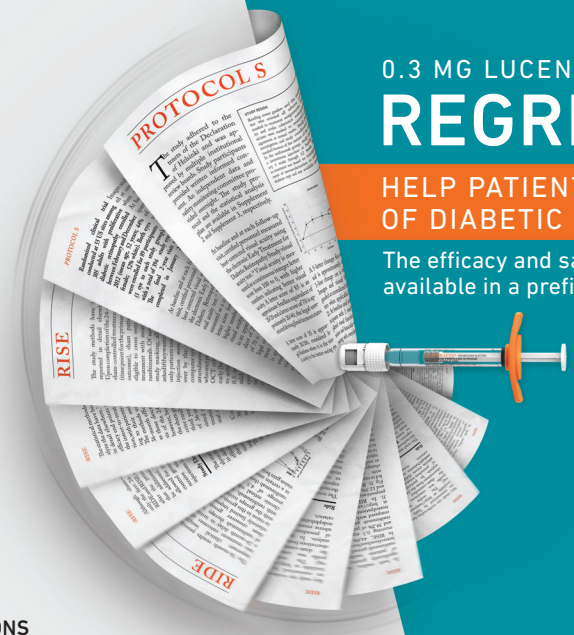
Initial US Approval: June 2006
Revision Date: LUC/021815/0050(4) 2017

0.3 MG LUCENTIS PREFILLED SYRINGE

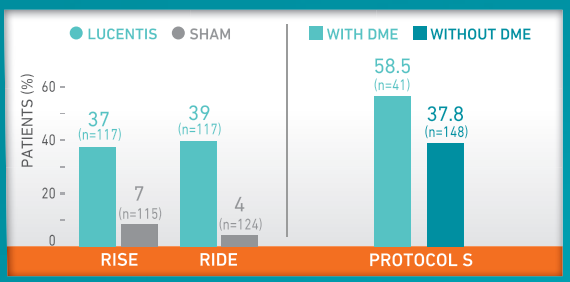
REGRESSION DELIVERED[1]

HELP PATIENTS TURN BACK TO AN EARLIER STAGE OF DIABETIC RETINOPATHY (DR)[1]

The efficacy and safety of LUCENTIS in DR, studied in 3 clinical trials, available in a prefilled syringe.[1]



≥2-STEP IMPROVEMENTS AT 2 YEARS[1]*



≥3-STEP IMPROVEMENTS AT 2 YEARS[1]:

RISE AND RIDE
- LUCENTIS 0.3 mg: 9% (n=117) and 17% (n=117), respectively
- Sham arms: 0% (n=115) and 2% (n=124), respectively

PROTOCOL S
- Patients without DME: 28.4% (n=148)
- Patients with DME: 31.7% (n=41)

Confidence intervals (95%): ≥2-step—RISE: 31% (21%, 40%); RIDE: 35% (26%, 44%). Protocol S (DR with DME): 58.5% (43.5%, 73.6%); (DR without DME): 37.8% (30%, 45.7%). ≥3-step—RISE: 9% (4%, 14%); RIDE: 15% (7%, 22%). Protocol S (DR with DME): 31.7% (17.5%, 46%); (DR without DME): 28.4% (21.1%, 35.6%).[1]

INDICATIONS

LUCENTIS® (ranibizumab injection) is indicated for the treatment of patients with:
- Diabetic retinopathy (DR)
- Diabetic macular edema (DME)

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

- LUCENTIS is contraindicated in patients with ocular or periocular infections or known hypersensitivity to ranibizumab or any of the excipients in LUCENTIS. Hypersensitivity reactions may manifest as severe intraocular inflammation

WARNINGS AND PRECAUTIONS

- Intravitreal injections, including those with LUCENTIS, have been associated with endophthalmitis, retinal detachment, and iatrogenic traumatic cataract. Proper aseptic injection technique should always be utilized when administering LUCENTIS. Patients should be monitored following the injection to permit early treatment, should an infection occur
- Increases in intraocular pressure (IOP) have been noted both pre-injection and post-injection (at 60 minutes) with LUCENTIS. Monitor intraocular pressure prior to and following intravitreal injection with LUCENTIS and manage appropriately
- Although there was a low rate of arterial thromboembolic events (ATEs) observed in the LUCENTIS clinical trials, there is a potential risk of ATEs following intravitreal use of VEGF inhibitors. ATEs are defined as nonfatal stroke, nonfatal myocardial infarction, or vascular death (including deaths of unknown cause)
- In a pooled analysis of Studies DME-1 and DME-2, the ATE rate at 2 years was 7.2% (18 of 250) with 0.5 mg LUCENTIS, 5.6% (14 of 250) with 0.3 mg LUCENTIS, and 5.2% (13 of 250) with control. The stroke rate at 2 years was 3.2% (8 of 250) with 0.5 mg LUCENTIS, 1.2% (3 of 250) with 0.3 mg LUCENTIS, and 1.6% (4 of 250) with control. At 3 years, the ATE rate was 10.4% (26 of 249) with 0.5 mg LUCENTIS and 10.8% (27 of 250) with 0.3 mg LUCENTIS; the stroke rate was 4.8% (12 of 249) with 0.5 mg LUCENTIS and 2.0% (5 of 250) with 0.3 mg LUCENTIS
- Fatal events occurred more frequently in patients with DME and DR at baseline treated monthly with LUCENTIS compared with control. A pooled analysis of Studies D-1 and D-2, showed that fatalities in the first 2 years occurred in 4.4% (11 of 250) of patients treated with 0.5 mg LUCENTIS, in 2.8% (7 of 250) of patients treated with 0.3 mg LUCENTIS, and in 1.2% (3 of 250) of control patients. Over 3 years, fatalities occurred in 6.4% (16 of 249) of patients treated with 0.5 mg LUCENTIS and in 4.4% (11 of 250) of patients treated with 0.3 mg LUCENTIS. Although the rate of fatal events was low and included causes of death typical of patients with advanced diabetic complications, a potential relationship between these events and intravitreal use of VEGF inhibitors cannot be excluded

ADVERSE EVENTS

- Serious adverse events related to the injection procedure that occurred in <0.1% of intravitreal injections included endophthalmitis, rhegmatogenous retinal detachment, and iatrogenic traumatic cataract
- In the LUCENTIS Phase III clinical trials, the most common ocular side effects included conjunctival hemorrhage, eye pain, vitreous floaters, and increased intraocular pressure. The most common non-ocular side effects included nasopharyngitis, anemia, nausea, and cough
- As with all therapeutic proteins, there is the potential for an immune response in patients treated with LUCENTIS. The clinical significance of immunoreactivity to LUCENTIS is unclear at this time

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

*The following clinical trials were conducted for the **DR & DME** indications: ***RISE & RIDE***—Two methodologically identical, randomized, double-masked, sham injection–controlled, Phase III pivotal trials (N=759) that studied the efficacy and safety of LUCENTIS 0.3 mg and 0.5 mg administered monthly to patients with DR and DME at baseline. The primary outcome was the proportion of patients gaining ≥15 letters at 2 years. ***Protocol S***—A randomized, active-controlled study that evaluated LUCENTIS 0.5 mg vs panretinal photocoagulation in DR patients with and without DME. All eyes in the LUCENTIS group (n=191) received a baseline 0.5 mg intravitreal injection followed by 3 monthly injections. Further treatments were guided by prespecified retreatment criteria. FDA approval was based on an analysis of the LUCENTIS arm of Protocol S. The primary outcome was mean change in visual acuity from baseline to 2 years.[2-3]

LUCENTIS 0.3 mg is recommended to be administered by intravitreal injection once a month (approximately 28 days).[1]

DME, diabetic macular edema.

REFERENCES: 1. LUCENTIS [package insert]. South San Francisco, CA: Genentech, Inc; 2018. **2.** Brown DM, et al; RISE and RIDE Research Group. *Ophthalmology*. 2013;120:2013-2022. **3.** Gross JG, et al; Writing Committee for the Diabetic Retinopathy Clinical Research Network. *JAMA*. 2015;314:2137-2146.

Genentech
A Member of the Roche Group

LUCENTIS®
RANIBIZUMAB INJECTION