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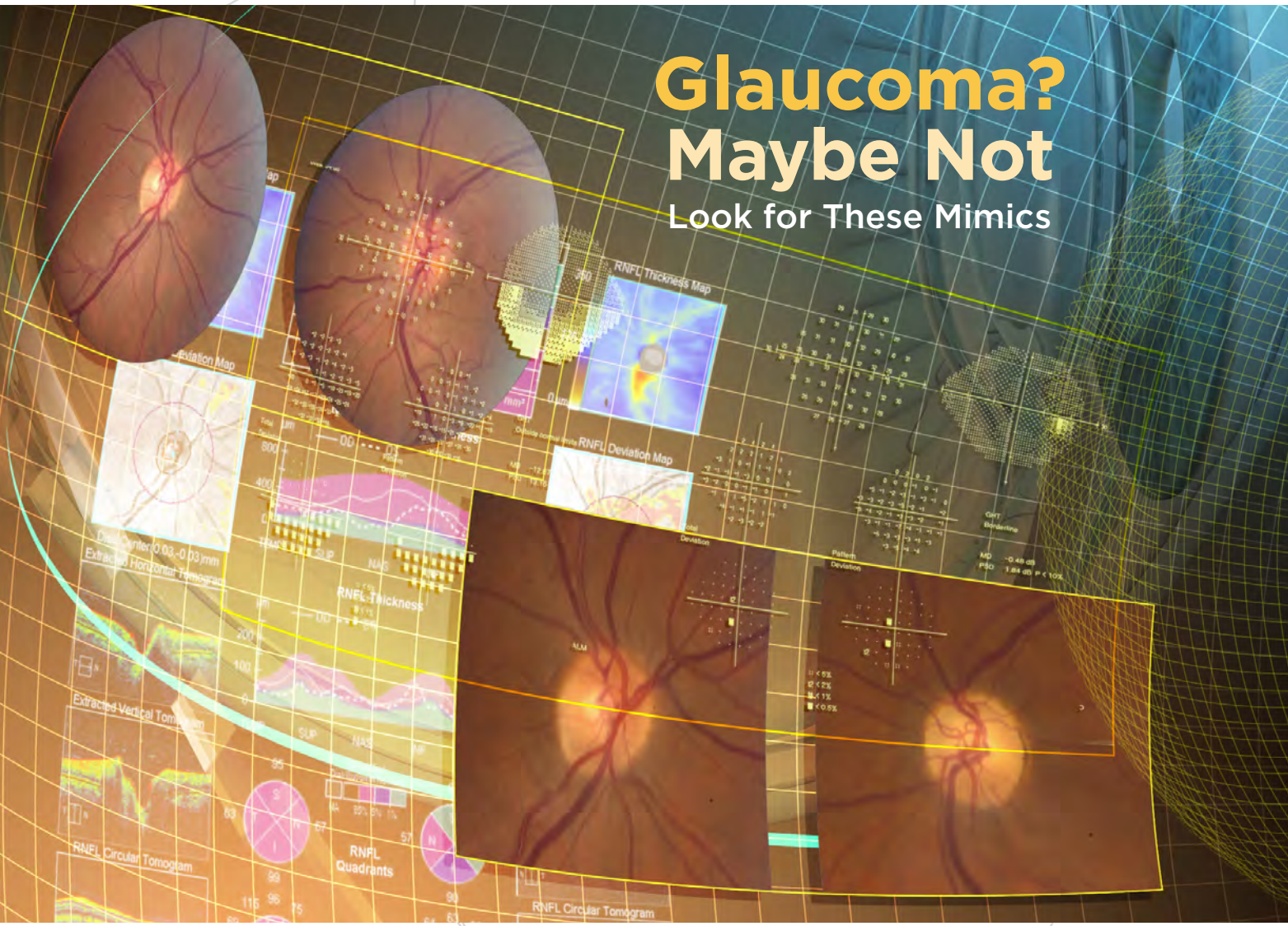
NOVEMBER 2018



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CASE STUDY
The Surprising Reasons for a Practice's Poor Profitability

RHOPRESSA® (netarsudil ophthalmic solution) 0.02%
Rx Only

BRIEF SUMMARY
Consult the Full Prescribing Information for complete product information.

INDICATIONS AND USAGE
RHOPRESSA® (netarsudil ophthalmic solution) 0.02% is indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

DOSAGE AND ADMINISTRATION
The recommended dosage is one drop in the affected eye(s) once daily in the evening.

If one dose is missed, treatment should continue with the next dose in the evening. Twice a day dosing is not well tolerated and is not recommended. If RHOPRESSA is to be used concomitantly with other topical ophthalmic drug products to lower IOP, administer each drug product at least 5 minutes apart.

WARNINGS AND PRECAUTIONS
Bacterial Keratitis
There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been previously contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Use with Contact Lenses
RHOPRESSA contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to instillation of RHOPRESSA and may be reinserted 15 minutes following its administration.

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

The most common ocular adverse reaction observed in controlled clinical studies with RHOPRESSA dosed once daily was conjunctival hyperemia which was reported in 53% of patients. Other common (approximately 20%) ocular adverse reactions reported were: corneal verticillata, instillation site pain, and conjunctival hemorrhage. Instillation site erythema, corneal staining, blurred vision, increased lacrimation, erythema of eyelid, and reduced visual acuity were reported in 5-10% of patients.

Corneal Verticillata
Corneal verticillata occurred in approximately 20% of the patients in controlled clinical studies. The corneal verticillata seen in RHOPRESSA-treated patients were first noted at 4 weeks of daily dosing. This reaction did not result in any apparent visual functional changes in patients. Most corneal verticillata resolved upon discontinuation of treatment.

USE IN SPECIFIC POPULATIONS
Pregnancy
There are no available data on RHOPRESSA use in pregnant women to inform any drug associated risk; however, systemic exposure to netarsudil from ocular administration is low. Intravenous administration of netarsudil to pregnant rats and rabbits during organogenesis did not produce adverse embryofetal effects at clinically relevant systemic exposures.

Animal Data
Netarsudil administered daily by intravenous injection to rats during organogenesis caused abortions and embryofetal lethality at doses ≥0.3 mg/kg/day (126-fold the plasma exposure at the recommended human ophthalmic dose [RHOD], based on C_{max}). The no-observed-adverse-effect-level (NOAEL) for embryofetal development toxicity was 0.1 mg/kg/day (40-fold the plasma exposure at the RHOD, based on C_{max}).

Netarsudil administered daily by intravenous injection to rabbits during organogenesis caused embryofetal lethality and decreased fetal weight at 5 mg/kg/day (1480-fold the plasma exposure at the RHOD, based on C_{max}). Malformations were observed at ≥3 mg/kg/day (1330-fold the plasma exposure at the RHOD, based on C_{max}), including thoracogastroschisis, umbilical hernia and absent intermediate lung lobe. The NOAEL for embryofetal development toxicity was 0.5 mg/kg/day (214-fold the plasma exposure at the RHOD, based on C_{max}).

Lactation
There are no data on the presence of RHOPRESSA in human milk, the effects on the breastfed infant, or the effects on milk production. However, systemic exposure to netarsudil following topical ocular administration is low, and it is not known whether measurable levels of netarsudil would be present in maternal milk following topical ocular administration. The developmental and health benefits of breastfeeding should be considered along with the mother's clinical need for RHOPRESSA and any potential adverse effects on the breastfed child from RHOPRESSA.

Pediatric Use
Safety and effectiveness in pediatric patients below the age of 18 years have not been established.

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

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, Impairment of Fertility
Long-term studies in animals have not been performed to evaluate the carcinogenic potential of netarsudil. Netarsudil was not mutagenic in the Ames test, in the mouse lymphoma test, or in the *in vivo* rat micronucleus test. Studies to evaluate the effects of netarsudil on male or female fertility in animals have not been performed.

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For more information, go to www.RHOPRESSA.com or call 1-855-AerieRx (1-855-237-4379).

U.S. Patent Nos.: 8,450,344; 8,394,826; 9,096,569; 9,415,043

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› Provides IOP reduction of up to 5 mmHg[1]

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The most common ocular AE observed in controlled studies with Rhopressa® was conjunctival hyperemia (reported in 53% of patients)[1]

AE, adverse event; IOP, intraocular pressure; ROCK, rho-associated protein kinase.

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INDICATION

RHOPRESSA® (netarsudil ophthalmic solution) 0.02% is a Rho kinase inhibitor indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Dosage and Administration: The recommended dosage is one drop in the affected eye(s) once daily in the evening.

IMPORTANT SAFETY INFORMATION

Dosage and Administration: Twice a day dosing is not well tolerated and is not recommended. If RHOPRESSA® is to be used concomitantly with other topical ophthalmic drug products to lower IOP, administer each drug product at least 5 minutes apart.

Warnings and Precautions:

Bacterial Keratitis - There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers had been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface.

Adverse Reactions: The most common ocular adverse reaction observed in controlled clinical studies with RHOPRESSA® dosed once daily was conjunctival hyperemia, reported in 53% of patients. Other common (approximately 20%) adverse reactions were: corneal verticillata, instillation site pain, and conjunctival hemorrhage Instillation site erythema, corneal staining, blurred vision, increased lacrimation, erythema of eyelid, and reduced visual acuity were reported in 5-10% of patients. The corneal verticillata seen in RHOPRESSA®-treated patients were first noted at 4 weeks of daily dosing. This reaction did not result in any apparent visual functional changes. Most corneal verticillata resolved upon discontinuation of treatment.

Please see the adjacent page for Brief Summary of Safety Information. For full Prescribing Information, please visit Rhopressa.com.

REFERENCES: 1. Rhopressa [prescribing information]. Irvine, CA: Aerie Pharmaceuticals, Inc; 2017. **2.** Serle JB, Katz LJ, McLaurin E, et al; and ROCKET-1 and ROCKET-2 Study Groups. Two phase 3 clinical trials comparing the safety and efficacy of netarsudil to timolol in patients with elevated intraocular pressure. *Am J Ophthalmol*. 2017;S0002-9394(17)30513-5. **3.** US Department of Health and Human Services, Food and Drug Administration Dermatologic and Ophthalmic Drugs Advisory Committee briefing document: NDA 208254. Published October 13, 2017. **4.** Bansal R, Tsai J. Compliance/adherence to glaucoma medications—a challenge. *J Curr Glaucoma Pract*. 2007;1(2):22-25.

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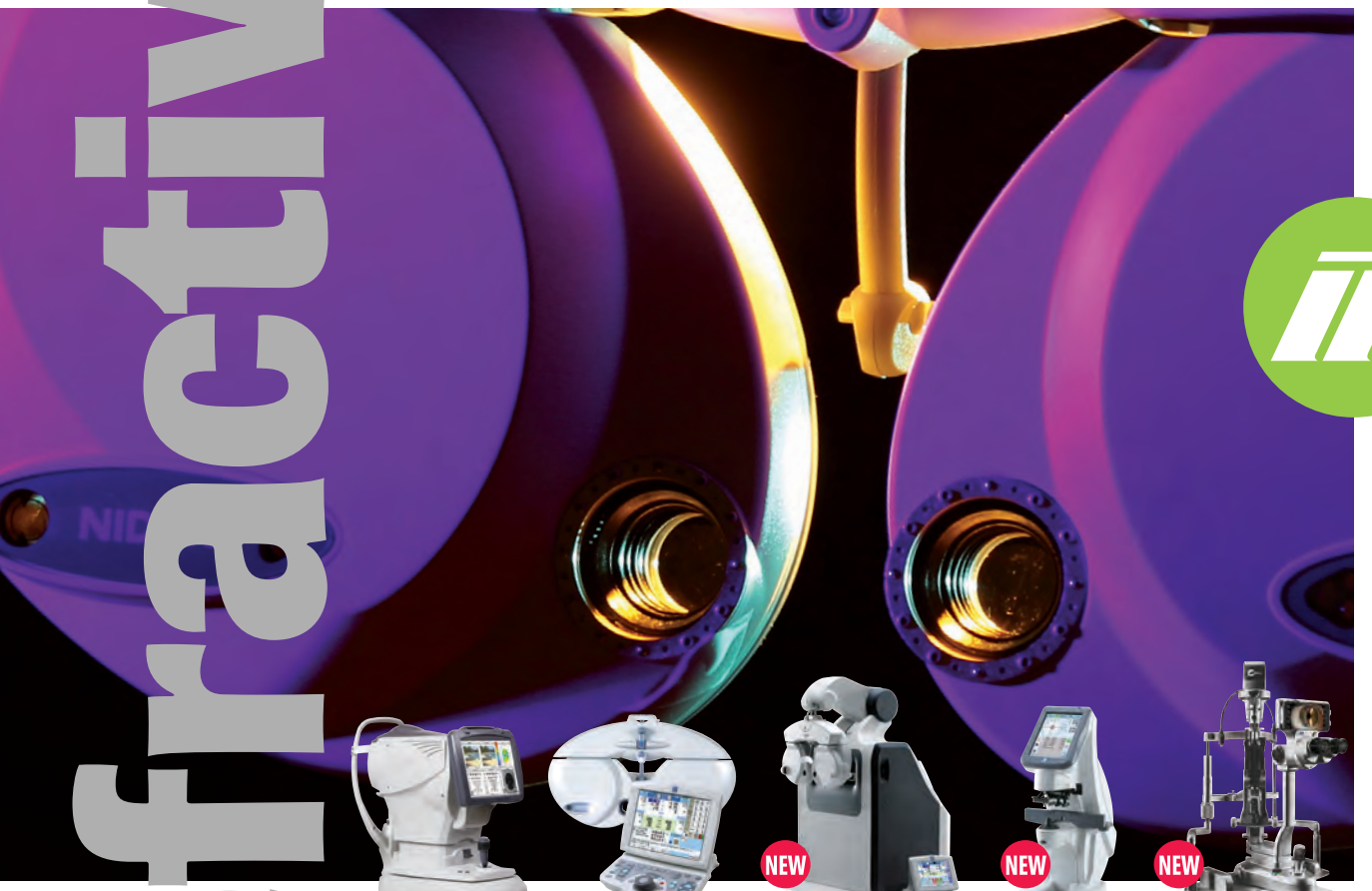
Refractive



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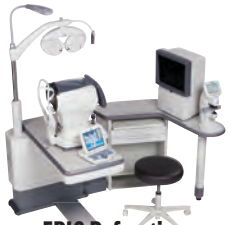

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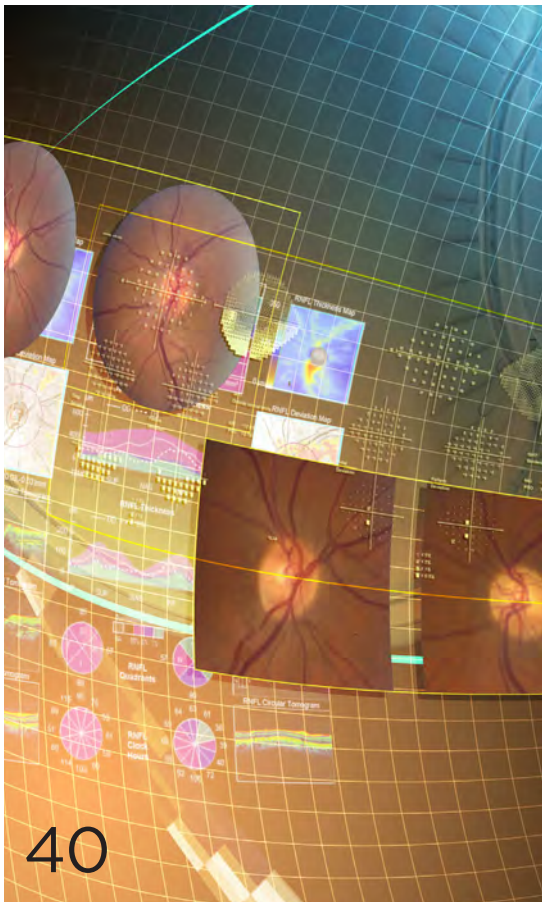

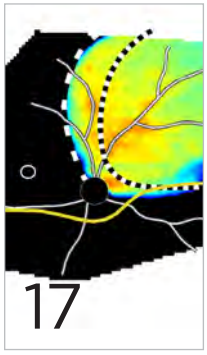

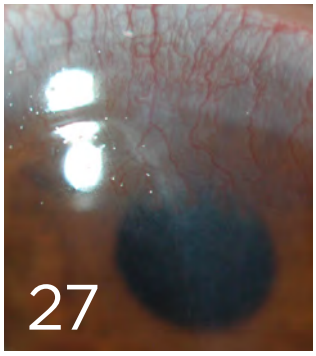

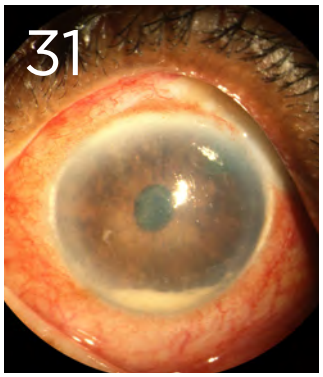

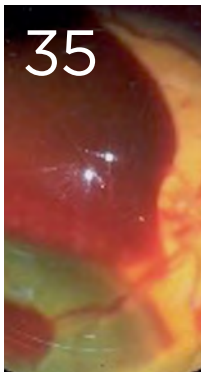

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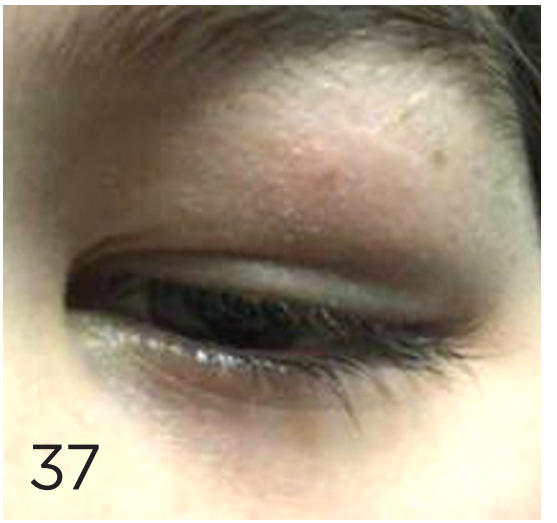

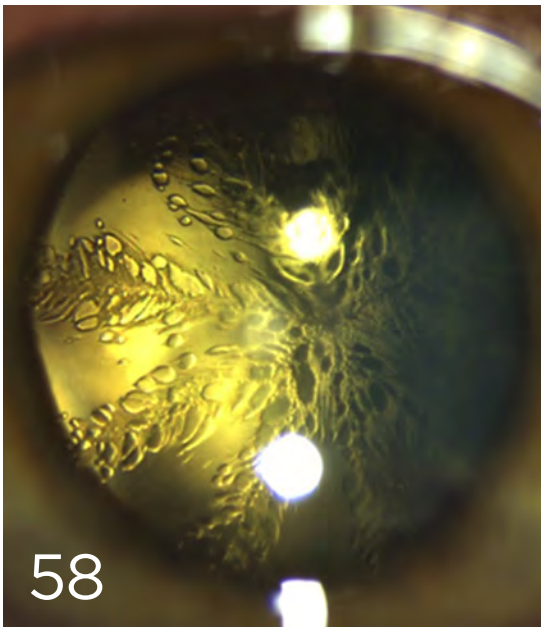

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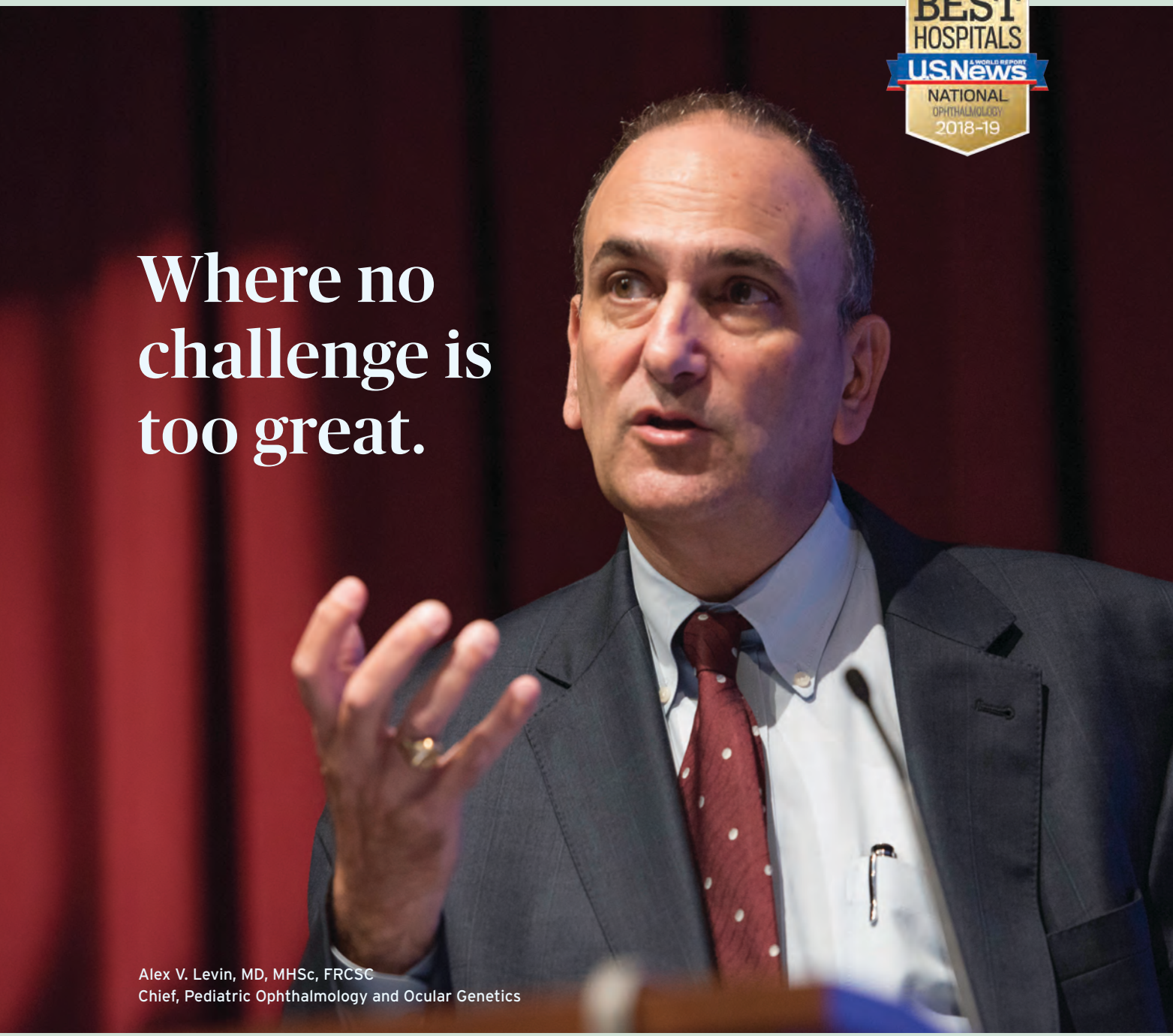

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Opinion

RUTH D. WILLIAMS, MD

Collaboration in Academic Research

When Bob Dylan was awarded the 2016 Nobel Prize in Literature, his fans were astonished and delighted. His Nobel acceptance speech (recorded after the ceremony that he didn't attend) is mostly an ode to his influences, from Buddy Holly and Appalachian ballads to *Don Quixote,* the *Odyssey,* and *All Quiet on the Western Front,* among others. While Dylan appears to be a singular genius, and the Nobel Prize in Literature is given to 1 person, the Nobel Prize in Physiology or Medicine can be given to 3 people (and almost always leaves out a significant contributor). Scientific research is, by nature, collaborative.

David Calkins, at Vanderbilt Eye Institute in Nashville, Tennessee, credits the Human Genome Project as one of the best examples of collaborative research. The project required support from the NIH and private industry, along with the partnership of scientists from nearly a dozen countries with expertise in genetics, molecular biology, information technology, biochemistry, and biostatistics. At the University of Toronto, Neeru Gupta believes such collaboration is necessary because of the rapid growth of specialized knowledge. Her own research into the lymphatic vessels as a new target for eye disease draws on the expertise of physiologists, pathologists, physicists, and engineers. And Gary Novack, a pharmacologist at the University of California, Davis, asserted that basic science research and drug development require working together. "You cannot be successful unless you realize that you do *not* know everything."

Yet academic researchers can be somewhat isolated. This isn't a new issue: In 1963, *Science* published a letter by Bernard K. Forscher, in which he compared academic research to a brickworks.[1] Warning of academic isolationism, he suggested that the brickmaking could become an end unto itself.

What are some of the barriers to collaborative research in ophthalmology? First, most academic scientists must build an individual extramural funding portfolio. NEI funding for research is a competitive process, and scientists contend for the same too-small pool of money. As Carla Siegfried, at Washington University in St. Louis, said, "If one views the funding source as a 'zero-sum game,' then the competition may suppress potential valuable collaborations."

Second, since major breakthroughs usually require a multidisciplinary approach, ophthalmic researchers must recognize and woo individuals who may not currently be working on vision research. Neeru finds this task exciting and rewarding, but it requires creativity, great communication skills, time, and investment in relationships.

Third, as David pointed out, promotion in academic institutions is based on individual metrics, which are easier to assess than collaborative efforts. Neeru agreed, although she noted a positive shift "toward recognizing collaborative efforts, both in publications and at the institutional level, including promotions."

Ruth D. Williams, MD
Chief Medical Editor, EyeNet

How to overcome these barriers? Many academic researchers encourage teamwork. At Vanderbilt, David aspires to create a culture of collaboration by emphasizing the values of teamwork, accountability, and data sharing. And philanthropic and organizational efforts can promote innovative collaborative projects. For example, the Glaucoma Research Foundation (GRF) initiated Catalyst for a Cure. In this program, a team of 4 researchers is selected by a scientific advisory board and funded to work together on a specific challenge. GRF's current team is gearing up to coordinate innovative research on neuroprotection. And let's not forget the IRIS Registry (see page 13), which is the world's largest specialty clinical database and can be employed to answer specific questions quickly.

In looking ahead, Carla imagines that "Ophthalmology can be a leader—as we have been in other aspects of medicine—to elevate the profession and provide guidelines for this new perspective of collaboration in research development, adding value to our scarce research dollars."

1 Forscher BK. *Science.* 1963;142(3590):339.

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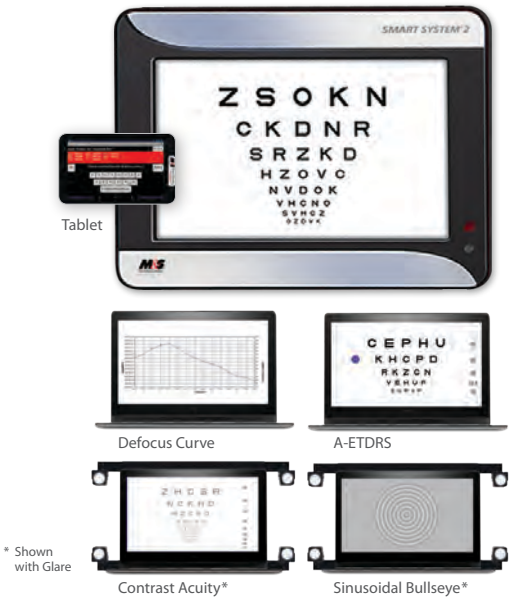

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Current Perspective

DAVID W. PARKE II, MD

All About Trust

On September 20, *The New York Times* and ProPublica broke a story about Memorial Sloan Kettering Cancer Center (MSKCC) and its health care data start-up Paige.AI. They detailed how the start-up company had exclusive access to MSKCC tissue resources and that 3 board members and 3 key executives were investors or had equity stakes. This all came on the heels of an investigation into drug industry ties of its chief medical officer (who then resigned). Questions were also raised about using individual identifiable information about patients and physicians without their knowledge. MSKCC in response noted the expense and risk of an enterprise with the potential to change the future of cancer diagnosis. Overall, the report stimulated questions about transparency, optics, and conflicts of interest.

The American Academy of Ophthalmology adheres to a robust set of policies that govern our approach to financial (and nonfinancial) conflicts of interest. These can be found on aao.org and include our internal policies, policies of the Accreditation Council for Continuing Medical Education, and those from the Council of Medical Specialty Societies' Code for Interactions With Companies (which I helped write). Their collective objective is not to eliminate all potential conflicts, but to create a path for disclosure and management, recusal when appropriate, and elimination where necessary. It is meant to give members, and the public, trust in the transparency and integrity of the Academy.

The IRIS Registry

In the aftermath of the MSKCC debacle, I received questions about the relationship between the Academy IRIS (Intelligent Research in Sight) clinical registry data and Verana Health, the for-profit company to which the Academy has licensed commercialization of IRIS Registry data. Here are the facts.

As you are probably aware, health-related data has significant potential commercial value. One company in the oncology space, Flatiron Health, sold last year for over $2 billion. Several companies have been founded by Academy members to monetize various subsets of clinical data.

Each Academy member whose electronic health record (EHR) system is integrated with the IRIS Registry has signed an agreement that permits data to be used—but only if it is stripped of patient and physician identifiers when used for commercial purposes. Further, it can be used for analysis only if it is aggregated with other data to further preclude discovery of personal identification. Additionally, the data can be used only for projects that are scientifically valid and consistent with the Academy's mission.

It became obvious that there was commercial appetite for the data. Accordingly, the Academy decided in 2016 to market some IRIS-derived data to pharmaceutical and device companies under carefully controlled circumstances. I won't go into great detail as to the review and control processes, but suffice it to say that they were drafted by task forces of Academy members, subjected to legal review, and then approved by the Board of Trustees. A Research and Analytics Committee composed of Academy members provided ongoing oversight.

David W. Parke II, MD
Academy CEO

However, marketing data was not the "core business" of the Academy, and the Board concluded that the Academy either had to find a commercialization partner or develop a commercialization arm. At the same time, the need to commercialize the data became critical. Early in the development of the IRIS Registry, we decided to offer it at no cost as a member benefit—which was unusual in the registry space. However, the IRIS Registry's operating costs, due to its size and complexity, grew to exceed $5 million per year. This meant that to sustain the IRIS Registry, the Academy either had to charge its members or find a revenue stream to offset part of that cost.

Choosing a Partner

We therefore looked for a partner organization that (at a minimum) fulfilled the following characteristics:

1. Expertise in the health data space
2. Strong technology team

3. Access to substantive investment capital
4. Knowledge of ophthalmology
5. Expertise with for-profit/nonprofit partnerships
6. Reputation for operational integrity

The Academy found this partner in DigiSight Technologies, a Silicon Valley–based company cofounded by ophthalmologist Mark Blumenkranz. After nearly 6 months of negotiations and constant review by the Board of Trustees, general counsel, outside legal counsel, and extramural advisors, the Board approved licensing commercialization of the IRIS Registry to DigiSight Technologies in early November 2017.

Here are some of the basic terms of that agreement. The Academy continues to own the IRIS Registry. It licenses commercialization to DigiSight. The Academy nominates a member to the DigiSight board. DigiSight is bound to the same restrictions regarding de-identified and aggregated data as is the Academy. The Academy has considerable influence (and at times absolute authority) over many elements of the commercial transactions. In return, the IRIS Registry's operating costs were reduced by 80%, and there is downstream revenue potential. Overall, the final document runs 70 pages. There were weeks when I spent over 20 hours in document review and negotiation.

Benefits. What do the Academy and its members get out of this? First and foremost, it helps to ensure the sustainability of the IRIS Registry—the largest specialty society clinical data registry in all of medicine. The IRIS Registry is transforming our profession, and it also provides a Merit-Based Incentive Payment System quality reporting system that will save our members an estimated $186 million in avoided penalties next year, when the MIPS payment penalties—based on last year's performance—start to take effect. It has led to numerous peer-reviewed scientific papers with novel clinical findings that promise to enhance the quality and delivery of care for our patients. And it is an increasingly important vehicle for clinical benchmarking and quality improvement. The IRIS Registry has received accolades from policymakers, public health experts, data analysts, and other medical organizations as "best of breed."

Second, the Academy will likely now be financially able to continue offering the IRIS Registry at no charge to members. And if it is very successful commercially, IRIS Registry revenue may provide an alternative to dues dollars.

Third, and critically, DigiSight (now renamed Verana Health) makes the data analytic tools and platforms that it develops and uses for commercial purposes available at no charge to the Academy for our own analytic purposes.

Fourth, the Academy retains full authority over noncommercial data projects conducted by members, Academy-affiliated organizations, or the Academy itself. Commercial activities do not interfere with these projects.

Finally, all of ophthalmology retains a high-quality tool that can provide novel insights into real-world evidence—what actually happens in the practice of ophthalmology. It can be a basis for comparing clinical trials to real-world practice, performing postmarket surveillance of drugs and devices, studying rare diseases, comparing outcomes from treatment alternatives, illuminating disease natural history in large populations, and examining the impact of comorbidities and confounding variables on disease progression.

Initial steps. In the year since the relationship was signed with DigiSight what has happened? First, as mentioned earlier, the company was renamed Verana Health. This was intended to signal that the company is now a health care data company—not an ophthalmology company. Second, the company has totally restructured itself around the IRIS Registry—its core asset. Third, it has received a large infusion of capital from some of America's legendary venture capitalists and companies. Fourth, it has recruited outstanding leadership and beefed up its technology and data science teams. It has had commercial success in its mission to accelerate health care innovation through data insights.

Most important for Academy members, nothing has happened to cast a shadow on the Academy's reputation for independence and integrity. Rather, we are getting kudos in the medical society space for the way we executed this relationship. Others are trying to emulate us.

Conflict of Interest

As for potential financial conflicts, these are carefully scrutinized. I sit as the Academy's Board-designated representative on the boards of FIGmd (our registry software vendor) and Verana Health. I receive no compensation, stock, or stock options for my work representing the Academy. And no member of the Academy Board or staff has any financial relationship with Verana or FIGmd—not even a complimentary T-shirt.

The IRIS Registry: A Growing Asset

The IRIS Registry had its fifth birthday and is still growing. Over 18,000 ophthalmologists and their employed optometrists use it. It contains more than 200 million patient encounter records. Over 50 EHR companies are mapped to it. It still has problems, however. EHR updates play havoc with data mapping. Every year CMS approves new quality measures, which must be coded into the IRIS Registry's software. The data must be continuously and carefully curated to ensure quality to avoid the "garbage in/garbage out" dilemma. With time, we hope to ingest more data from images, from genetic testing, and from patients themselves.

Throughout this process, the Academy hopes the IRIS Registry will bring more and more value to its members as a tool to benchmark and judge clinical outcomes and processes of care. We anticipate that ophthalmologists will choose to employ the IRIS Registry to report their quality outcomes to CMS, commercial payers, and health systems as means of avoiding payment penalties, garnering bonuses, and demonstrating their value. It will continue to support our advocacy and policy objectives. And we anticipate that it will become a robust source of generating new scientific information that will change the way we care for patients.

At all times, the Board of Trustees and senior staff pledge to oversee the IRIS Registry and Verana Health to protect the reputation of the Academy for integrity, independence, and trustworthiness. It may be our most important asset.

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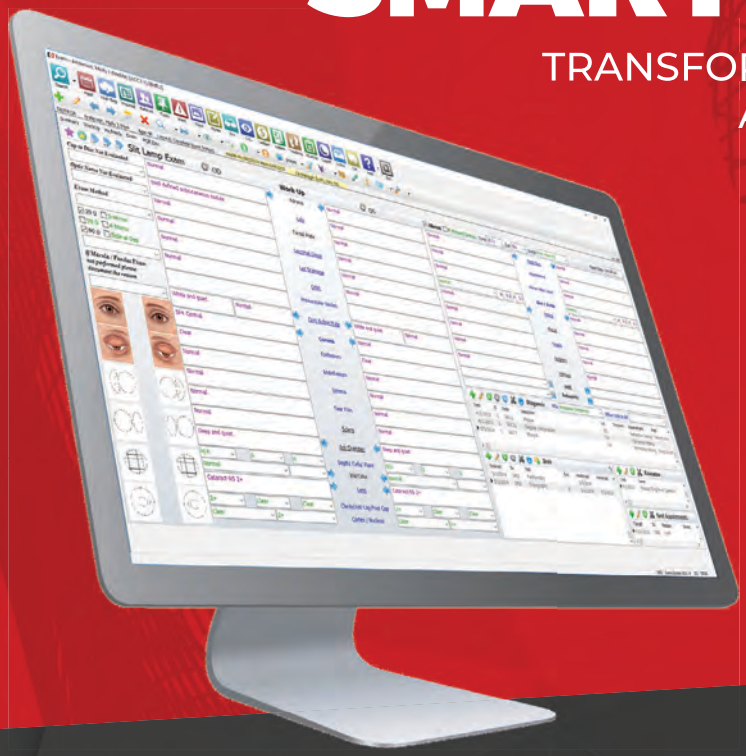

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News in Review

COMMENTARY AND PERSPECTIVE

GENETICS

Potential Gene Therapy for RP

SCIENTISTS HAVE DEVELOPED A GENE therapy for the most common form of autosomal-dominant retinitis pigmentosa (RP) caused by mutations in the rhodopsin (*RHO*) gene—and successfully demonstrated that it can prevent retinal degeneration in a canine model, an approach that someday could be harnessed to halt the disease in humans.

The researchers designed an adeno-associated viral vector to knock down the expression of existing *RHO* (both normal and mutant genes) and replace them with a normal copy of human *RHO*.[1] Retinal imaging and electroretinography showed that this approach kept the rod photoreceptors healthy and prevented retinal degeneration for at least 8 months of follow-up.

A dual-purpose approach. This strategy differs in key ways from the gene augmentation approach that led to a commercially available gene therapy (Luxturna) for Leber congenital amaurosis (LCA). Because LCA is autosomal recessive, that viral vector was engineered solely to transduce the retinal pigment epithelium with a single copy of the *RPE65* gene to produce the missing protein.

In autosomal-dominant RP, rod photoreceptor cells express rhodopsin proteins from both normal and mutant *RHO*. "The mutant protein produced in the rods either interferes negatively with the wild-type protein that comes from the normal allele, or it has on its own a toxic gain of function, meaning that this protein may be toxic to the cell and kill it over time," said William A. Beltran, DVM, PhD, at the University of Pennsylvania in Philadelphia.

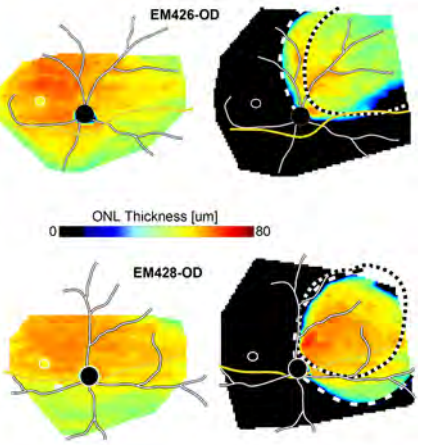
The scientists concluded that their treatment would have to not only prevent the mutant gene already there from producing abnormal, toxic rhodopsin but also provide sufficient normal rhodopsin protein for the rods to survive and function normally. But in order to do this, the therapy also would need to work against the more than 150 gene mutations known to cause autosomal-dominant RP. "The challenge was to develop a treatment that can address any mutation," Dr. Beltran said.

Their solution was a dual-purpose viral vector: One part was targeted at "knocking down" all endogenous rhodopsin mRNAs, both mutant and normal, through a technique known as RNA interference. The second part consisted of normal human *RHO* that was modified to avoid degradation by the knockdown component.

"The rods would not be able to function, or survive over the long term, if you didn't bring back a normal wild-type copy of *RHO*. The vector also delivers a gene that has been modified at some very specific sites so that it still produces the same amino acid sequence as the rhodopsin protein, but it is not knocked down at the RNA level," said coauthor Alfred S. Lewin, PhD, at the University of Florida in Gainesville.

What's next. The researchers will study whether the viral vector can successfully treat areas where the retina is already degenerating. "We're going to be looking at whether we can intervene at stages that are clinically relevant—and target areas where there are still rod photoreceptor cells left that can be rescued," Dr. Beltran said. "If we're able to show that, that will expand the potential candidates for gene therapy."

—Linda Roach



NOVEL STRATEGY. *Topographical maps of outer nuclear layer thickness show how the combined* RHO *knockdown and replacement therapy protected against severe retinal degeneration in a naturally occurring canine model of autosomal-dominant RP (right panels).*

1 Cideciyan AV et al. *Proc Natl Acad Sci U S A.* 2018;115(36):E8547-E8556.

Relevant financial disclosures—Dr. Beltran: Foundation Fighting Blindness: S; NIH/NEI: S; Research to Prevent Blindness: S; The Shaler Richardson Professorship Endowmment: S; University of Pennsylvania: P. Dr. Lewin: NEI: S; University of Florida: P.

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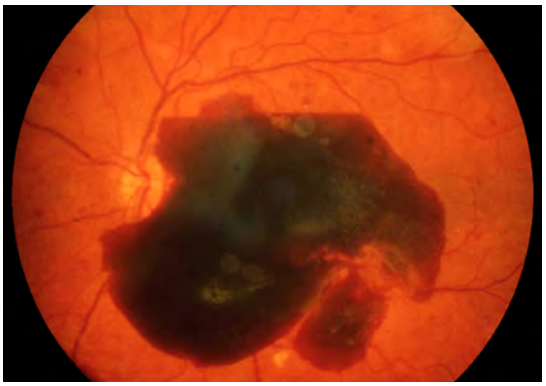
DRUG SIDE EFFECTS

Bleeding Risk and NOACs

A REVIEW OF OUTCOMES IN MORE than 100,000 patients suggests that one of the novel oral anticoagulant medications (NOACs) on the market might be less likely than warfarin to cause ocular hemorrhages.

Outcomes better with edoxaban. A network meta-analysis of findings from 12 randomized controlled clinical trials found a statistically significant reduced risk of ocular bleeding in anticoagulated patients who took edoxaban when compared to warfarin (odds ratio: 0.59, confidence interval 0.34-0.98).[1] Traditional meta-analyses, using pooled pairwise and subgroup comparisons, also supported this conclusion (both $p = 0.02$).

The authors hypothesized that the molecular inhibition characteristics of edoxaban and warfarin might explain the difference in bleeding outcomes. "In the case of edoxaban . . . it can be speculated that the direct inhibition of Factor Xa confers enhanced control over the coagulation cascade; in contrast, warfarin targets factors II, VII, IX, X and regulatory factors protein C, S, and Z, offering poorer pharmacodynamic precision," they wrote.



BLEEDING. *This image shows a preretinal subhyaloid hemorrhage.*

Equivalent outcomes with other NOACs. No statistically significant reductions in risk were found with 3 other available NOACs (rivaroxaban, dabigatran, and apixaban). "There was a nonsignificant trend toward apixaban having more intraocular bleeding adverse events compared with warfarin, whereas dabigatran and rivaroxaban appeared to have similar intraocular bleeding complications profiles relative to warfarin," the researchers wrote.

Study limitations. However, the possible ophthalmic lessons from this review study are limited because of deficiencies in the underlying data, commented M. Gilbert Grand, MD, of The Retina Institute in St. Louis.

No sham control. One difficulty is that there is no sham control, Dr.

INFECTIOUS DISEASE

Neuroborreliosis: Add Lyme Disease to Your Differential

OCULAR MANIFESTATIONS OF LYME DISEASE MAY be more prevalent than commonly thought, a small prospective Swedish study suggests.

The study, conducted in western Sweden, found that the majority of patients diagnosed with neuroborreliosis (typically found in stage 2 of Lyme disease) had ophthalmic signs and symptoms.[1] The most frequent findings were blurred vision, diplopia, photophobia, redness, sixth nerve involvement, and palpebral diastasis resulting from facial palsy. Moreover, there was a positive correlation between signs and symptoms and cerebrospinal fluid (CSF) antibody titres.

Study rationale. The research team was motivated in part by evidence that "ticks are increasing in number and becoming more widespread in the northern parts of Europe," said coauthor Marita A. Grönlund, MD, PhD, at Sahlgrenska University Hospital in Gothenburg, Sweden.

And although previous studies have documented the ocular manifestations of Lyme disease, they have been case reports and case studies, she noted. "Therefore, we and our coworkers at the [hospital's] department of infectious diseases thought that it was of great importance to further evaluate and follow up ophthalmic symptoms and findings in individuals diagnosed with neuroborreliosis verified by CSF analysis."

Study specifics. Over a 6-year period, 24 patients who had either been diagnosed with Lyme disease or were strong suspects were referred to the hospital's department of ophthalmology. All were tested for *Borrelia burgdorferi* antibodies no later than 2 days after admission and underwent lumbar puncture no later than 3 days after admission.

Results. Neuroborreliosis was confirmed in 16 patients, while 2 patients were classified as possible cases. Diagnosis was negative in 4 patients and unknown in the remaining 2. Of the 18 patients classified as definite or possible, 14 (78%) had ophthalmic signs and symptoms. All patients improved except for 1 with fulminant papilledema; this patient still had optic disc atrophy and affected visual fields at last follow-up.

A surprise. In contrast with previous studies, the researchers found no evidence of either conjunctivitis or uveitis, Dr. Grönlund said. The reason for this remains unknown.

Take-home message. "For ophthalmologists, there might be reason to think twice about neuroborreliosis not only in subjects with facial palsy but also in those with [new-onset] diplopia and/or sixth nerve affection," Dr. Grönlund concluded. *—Jean Shaw*

1 Škiljić D et al. *Acta Ophthalmol.* Published online Aug. 26, 2018.

Relevant financial disclosures—Dr. Grönlund: None.

M. Gilbert Grand, MD

Grand cautioned. The researchers did not "calculate how many people get ocular bleeding because of preexisting ocular disease, without taking warfarin and the NOACs."

No definition of hemorrhage. In addition, they did not define intraocular hemorrhage, Dr. Grand said. For instance, subconjunctival hemorrhages were included in a list of potential intraocular bleeds. "So we don't know what type of events they were really analyzing."

Need for clarification. The study does support the conclusion that spontaneous ocular hemorrhages occur rarely in patients undergoing anticoagulation therapy, Dr. Grand said. However, it "does not add any data describing the risk of hemorrhage in anticoagulated patients who undergo intraocular surgery," he said. "So this dataset, while valuable in itself, does not provide insights for ophthalmologists who must make decisions as to whether to continue or discontinue anticoagulation at the time of ophthalmic surgery."

Fortunately, there are published data from earlier research on the safety of vitreoretinal surgery in patients taking warfarin[2] or the NOACs,[3] Dr. Grand noted.

Need for further research. This study also raises an issue worthy of further examination, Dr. Grand pointed out. "There are certain ophthalmic diseases, such as exudative age-related macular degeneration or proliferative retinopathies, in which patients bleed spontaneously whether or not they're taking anticoagulants," he said. "What this study does not determine, and what we need to know, is whether anticoagulation therapy in those patients increases their risk of hemorrhages."

—Linda Roach

1 Phan K et al. *Br J Ophthalmol.* Published online June 20, 2018.

2 Dayani PN, Grand MG. *Arch Ophthalmol.* 2006; 124(11):1558-1565.

3 Grand MG, Walia HS. *Retina.* 2016;36(2):299-304.

Relevant financial disclosures—Dr. Grand: None.

RETINA

PRP Preferred for Some Patients?

IN THE IDEAL WORLD OF CON-trolled scientific studies, the strategy of treating proliferative diabetic retinopathy (PDR) with intravitreal injections has proved effective and possibly superior to panretinal photocoagulation (PRP). Now researchers report that in the "real" world, where patients are often lost to follow-up, PRP may be the better option.[1]

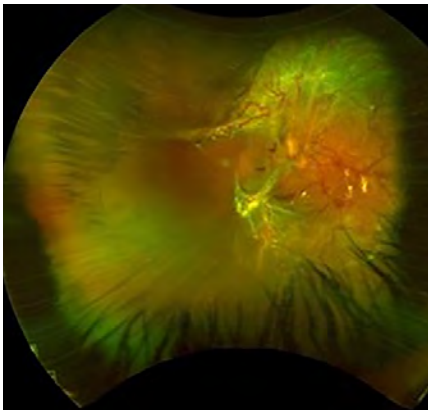
"Part of the impetus for this study was that we know PRP has long-lasting effects on stabilizing PDR, but we have little data on whether anti-VEGF therapy has any long-lasting effects once it is stopped," said Jason Hsu, MD, at Wills Eye Hospital in Baltimore.

Now, data exist. "Our study suggests that if there is a period of loss to follow-up, patients with PDR who receive PRP may have better outcomes compared to those who received only anti-VEGF therapy," said coauthor Anthony Obeid, MD, MPH, also at Wills Eye Hospital.

Retrospective cohort. The findings are based on medical records of 59 patients with PDR (76 eyes) who returned at various time points for follow-up treatment. All of the 59 patients had been lost to follow-up for 6 or more months immediately after receiving either intravitreal injections (20 patients; 30 eyes) or PRP (39 patients; 46 eyes).

Findings include the following:

- Visual acuity (VA) scores worsened in anti-VEGF eyes, from 20/54 at the visit before patients were lost to follow-up to 20/187 at the return visit and 20/166 at the final visit.
- In PRP eyes, VA significantly worsened from 20/53 at the visit before patients were lost to follow-up to 20/83 at the return visit. However, VA improved by the final visit to 20/58.
- There was a significantly greater incidence of neovascularization of the iris in the anti-VEGF group compared to the PRP arm at the final visit (4 vs. 0).
- A significantly greater number of eyes in the anti-VEGF group had tractional retinal detachment (RD) after patients returned to care. At the return visit, 5 in the anti-VEGF group experienced tractional RD, versus none in the PRP group. At the final visit, 10 anti-VEGF patients had tractional RD, versus 1 PRP patient. However, the incidence of tractional RD was lower in eyes that received a greater number of anti-VEGF injections prior to being lost to follow-up. "This may suggest that receiving a certain minimum number of injections may have lasting effects on PDR regression," Dr. Obeid said.



RD RISK. *This eye with PDR developed an RD after being lost to follow-up.*

Stick with PRP. The findings are particularly relevant as practice patterns are shifting toward anti-VEGF monotherapy for eyes with PDR, the authors said. They assume even greater relevance given the "strikingly high" rates of patients lost to follow-up,[2] said Dr. Hsu.

"Some clinicians believe that PRP may not be necessary or can be delayed while the patient is actively receiving anti-VEGF treatments," Dr. Hsu added. "However, our study suggests that physicians may want to proceed with PRP at an earlier time point given the potential for poorer outcomes with erratic follow-up." (For more on this topic, see pg. 23.)

—Miriam Karmel

1 Obeid A et al. *Ophthalmology.* Published online Aug. 2, 2018.

2 Obeid A et al. *Ophthalmology.* 2018;129(9): 1386-1392.

Relevant financial disclosures—Drs. Hsu and Obeid: None.

Anthony Obeid, MD, MPH

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

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Journal Highlights

NEW FINDINGS FROM THE PEER-REVIEWED LITERATURE

Ophthalmology

Selected by Stephen D. McLeod, MD

Predicting RNFL Thinning in Glaucoma

November 2018

Moghimi et al. investigated potential links between thinning of the retinal nerve fiber layer (RNFL) and baseline vessel density of the macula and optic nerve head (ONH). They hypothesized that the degree of vessel density may predict RNFL thinning of eyes with mild or moderate glaucoma. Their findings suggest that lower macular and ONH vessel density are associated with faster RNFL decline, as measured by spectral-domain optical coherence tomography (SD-OCT).

For this prospective observational study, 83 patients with mild or moderate primary open-angle glaucoma (132 eyes) received follow-up for at least 2 years (average, 27.3 ± 3.36 months). Measurements of macular whole-image vessel density (m-wiVD) and ONH whole-image vessel density (onh-wiVD) were acquired at baseline, using OCT angiography. Measurements of RNFL thickness, minimum rim width, and ganglion cell plus inner plexiform layer thickness were obtained semiannually using SD-OCT. Random-effects models were used to ascertain relationships between vessel density parameters at baseline and the rates of RNFL loss, after adjusting for confounding factors. Outcomes of interest were the effects of m-wiVD and onh-wiVD on rates of RNFL loss.

The average RNFL thickness at baseline was 79.5 ± 14.8 µm, which declined by a mean slope of –1.07 µm per year. In the univariate model, which included just a predictive factor and time plus their interaction, each 1% lower m-wiVD and onh-wiVD was associated with a 0.11-µm per year and 0.06-µm per year faster rate of RNFL decline, respectively. A similar relationship between low m-wiVD/onh-wiVD and faster rates of RNFL loss was observed with other multivariate models. Nevertheless, in this study, the link between vessel density measurements and rate of RNFL loss was weak. In univariate and multivariate analyses, average central corneal thickness predicted faster RNFL decline.

Eyes with advanced glaucoma were not included in the study because their RNFL is unlikely to undergo rapid change. This research offers new insight for glaucoma management and supports the role of OCT parameters in predicting the risk and rate of glaucoma progression. Macular and ONH vessel density may be specific parameters to include in this assessment.

Baseline Influencers of Vision and Edema in Proliferative DR: Ranibizumab Versus PRP

November 2018

In a post hoc analysis of data from randomized multicenter trials, **Bressler et al.** aimed to identify baseline factors associated with change in visual acuity (VA) or development of vision-impairing central-involved diabetic macular edema (DME) occurring after treatment of proliferative diabetic retinopathy (PDR) with ranibizumab or panretinal photocoagulation (PRP).

The study included 328 eyes that received 2 years of follow-up and 302 eyes that did not have vision-impairing central-involved DME at baseline in Protocol S of the Diabetic Retinopathy Clinical Research Network (DRCR.net). The latter eyes were not required to complete the 2-year visit because the analysis incorporated all available and censored data for participants without vision-impairing central-involved DME.

Treatments were intravitreous ranibizumab (0.5 mg/0.05 mL) or PRP. Primary outcome measures were change in VA (area under the curve) and development of vision-impairing (20/32 or worse) central-involved DME during the 2-year period.

After multivariable analysis with adjustment for baseline VA and central subfield thickness, no factors were identified as being relevant to either primary outcome. In the PRP group, worsening VA was more common with higher levels of hemoglobin A_{1c}, greater severity of diabetic retinopathy

(DR), and higher mean arterial pressure. Vision-impairing central-involved DME was more likely to occur in the presence of high hemoglobin A_{1c}, more severe DR, and cystoid defects within 500 µm of the macula center.

Overall, VA improved and vision-impairing central DME was rare with ranibizumab in Protocol S. The analysis suggests that these favorable outcomes occur regardless of baseline factors. However, when PRP is the main treatment for PDR, patients with poor glycemic control or severe DR may be more susceptible to vision-impairing central-involved DME and VA loss than are those with better glycemic control or milder DR, even if the DME is treated with ranibizumab.

—Summaries by Lynda Seminara

Ophthalmology Retina

Selected by Andrew P. Schachat, MD

Vascular Safety Profile of Ranibizumab

November 2018

Intravitreal anti–vascular endothelial growth factor (VEGF) drugs carry an increased risk of systemic events, including those of a cardiovascular and cerebrovascular nature. **Zarbin et al.** set out to evaluate the vascular safety profile of ranibizumab 0.5 mg relative to sham treatment, with or without verteporfin, in patients with neovascular age-related macular degeneration (AMD). In addition, they compared ranibizumab 0.3 mg to sham and 0.3 mg to 0.5 mg of ranibizumab. They found low rates of vascular events in these patients overall and no clinically meaningful differences between patients treated with ranibizumab and those treated with sham or verteporfin.

For this study, researchers evaluated data from 7 randomized trials (phases 2-4). The pooled dataset comprised 4,080 patients with wet AMD. Of these, 1,764 patients were treated with ranibizumab 0.3 mg, and 1,854 were treated with ranibizumab 0.5 mg. Relevant safety endpoints included arterial thromboembolic events (ATEs), myocardial infarction (MI), stroke, transient ischemic attacks (TIAs), and vascular deaths. Pairwise comparisons for ranibizumab 0.5 mg (the globally approved dosage for wet AMD) and sham or verteporfin were performed using Cox proportional hazard regression and rates per 100 patient-years.

Hazard ratios (95% confidence intervals) included 1, indicating no significant treatment differences, for all endpoints, between ranibizumab 0.5 mg and sham or verteporfin. Although this supports the established risk-benefit profile of ranibizumab in patients with neovascular AMD, the authors noted that extrapolating these findings to the real-world population is limited by the enrollment criteria of the selected studies—and that more data are needed on the systemic safety of anti-VEGF drugs in clinical practice.

—Summary by Jean Shaw

American Journal of Ophthalmology

Selected by Richard K. Parrish II, MD

Cataract Surgery Alters Corneal Biomechanics and IOP

November 2018

Using the updated Corvis ST tonometer, **Hirasawa et al.** studied the effects of cataract surgery on corneal biomechanics and intraocular pressure (IOP). They noted a decrease in the stiffness parameter at applanation 1 (SP A1) and increases in deformation amplitude maximum (DA max) and integrated radius, suggesting that the cornea is less stiff following cataract surgery.

This prospective, interventional case series included 39 patients (39 eyes) with cataract. Measurements with the Corvis ST tonometer were obtained before surgery and at 1 week, 1 month, and 3 months postoperatively; parameters included DA max, DA ratio max (1 mm and 2 mm), integrated radius, SP A1, Ambrosio relational thickness to the horizontal profile (ARTh), Corvis biomechanical index, central corneal thickness, noncorrected IOP, and biomechanically corrected IOP. In addition, they measured IOP with Goldmann applanation tonometry and a noncontact tonometer. The linear mixed model was used to compare measurements for each time point, with and without adjustment for biomechanically corrected IOP and central corneal thickness.

All IOP measurements decreased over time. Increased central corneal thickness was noted at 1 week and 3 months. Although the Corvis biomechanical index was elevated at 1 week, it returned to preoperative status by 1 month. A decrease in ARTh was observed at 1 week and 1 month; this parameter returned to its preoperative level by 3 months. DA max and integrated radius had increased by month 3, and SP A1 had decreased by this time.

The authors advise caution when applying these results to clinical practice. They noted that 1 week following surgery may be too soon to use the Corvis biomechanical index to identify keratoconus.

Is It Time to Reclassify Large Macular Holes?

November 2018

In the Manchester Large Macular Hole Study, **Ch'ng et al.** looked at anatomic and functional outcomes after vitrectomy for large full-thickness macular holes (FTMH). They found that standard treatment for FTMH is adequate for most holes under 650 µm in diameter.

This retrospective interventional study included 258 eyes with idiopathic large FTMH (diameter >400 µm) treated during a 5-year period. All eyes underwent pars plana vitrectomy (PPV), internal limiting membrane (ILM) peel, gas tamponade, and face-down posturing. The face-down position was maintained for 1-5 days. Anatomic and functional success rates were measured, as was the relationship between the size of the macular holes and their closure.

Anatomic closure was achieved in 90% of eyes. Rates of closure were ≥91% for patients with holes <650 µm. This coincides with the currently accepted success standard of ~90%. Among patients with larger FTMH (650 µm to 1,416 µm), the success rate was only 76%. Maximum sensitivity and specificity were obtained at a cutoff diameter of ≤630 µm (76.7% sensitivity, 69.2%

specificity), yielding a Youden index of 0.46. By 3 months postoperatively, 57% of eyes had improved ≥0.3 LogMAR units from preoperative status.

—Summaries by Lynda Seminara

JAMA Ophthalmology

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

Five-Year Outcomes of Randomized Trial Comparing Laser with Ranibizumab for PDR

October 2018

Gross et al. compared the efficacy and safety of intravitreous ranibizumab and panretinal photocoagulation (PRP) for proliferative diabetic retinopathy (PDR) through 5 years in a randomized clinical trial. They found that visual acuity (VA) was very good for most patients in both study arms, consistent with 2-year outcomes. Rates of vision-impairing diabetic macular edema (DME) were lower in the ranibizumab group.

This study included patients who had enrolled in the Diabetic Retinopathy Clinical Research Network (DRCR.net) Protocol S trial by December 2012. Eyes had been assigned randomly to receive intravitreous ranibizumab (n = 191) or PRP (n = 203). The frequency of ranibizumab treatment was based on a protocol-specified algorithm. The 5-year analysis began in January 2018. The main outcome was the mean change in VA; secondary outcomes included peripheral visual field loss, development of vision-impairing DME, and adverse events.

The 5-year visit was completed for 240 eyes (184 patients), 117 of which received ranibizumab. The mean number of treatments over 5 years was 19.2 in the ranibizumab group (with an average of 3 injections each year in years 2, 3, 4, and 5) and a mean of 5.4 treatments over 5 years in the PRP group. Mean changes in VA letter score were 3.1 and 3.0, respectively, for the ranibizumab and PRP groups. The mean change in cumulative visual field total point score was −330 dB for ranibizumab recipients and −527 dB for patients with PRP. Vision-impairing DME occurred in 27 and 53 eyes, respectively, for a cumulative probability of 22% in the ranibizumab group and 38% in the PRP group (hazard ratio = 0.4; 95% confidence interval [CI]: 0.3-0.7; p < 001).

Despite a mean VA of 20/25 in both groups at 5 years, vitreous hemorrhage occurred in 48% of eyes treated with ranibizumab and in 46% of eyes treated with PRP. Vitrectomy was performed in 11% and 19% of eyes, respectively. Both groups had low rates of iris neovascularization and neovascular glaucoma, although retinal detachment occurred in 6% of the ranibizumab group and 15% of the PRP group. Rates of systemic adverse events were comparable.

The authors note that these findings support either anti–vascular endothelial growth factor therapy or PRP as viable treatments for patients with PDR through at least 5 years and emphasize the importance of considering patient-specific factors when selecting a treatment, including the patient's anticipated likelihood of compliance and overall health status as well as cost issues.

Racial Differences in Long-Term Trabeculectomy Outcomes

October 2018

Evidence indicates that failure after trabeculectomy without antimetabolites is more common among patients of African descent. Although adjunctive use of mitomycin C (MMC) improves the likelihood of success, data are lacking for patients of African descent who have undergone trabeculectomy combined with MMC. To identify prognostic indicators of failure, **Nguyen et al.** compared outcomes of initial trabeculectomy plus MMC between patients of African and European descent and found that those of African descent were more likely to experience failure after trabeculectomy and bleb leak.

In their study, 135 eyes from patients of African descent (n = 105) were matched to 135 eyes from patients of European descent (n = 117). Matching criteria included age (within 5 years), surgeon, lens status, and follow-up time (within 1 year).

Three levels of qualified success were defined as follows:

- For criteria A, final intraocular pressure (IOP) of ≤18 mm Hg with either ≥20% reduction in IOP or reduction of at least 2 medications.
- For criteria B, a final IOP of ≤15 mm Hg and either ≥25% reduction in IOP or reduction of at least 2 medications.
- For criteria C, a final IOP of ≤12 mm Hg or less and either ≥30% reduction in IOP or reduction of at least 2 medications.

Complete success was similarly defined with the additional requirement of no need for glaucoma medication(s).

At 5 years, the qualified success rates for patients of African descent and those of European descent were as follows: For criteria A, 61% versus 67% (difference, 7.3%, 95% confidence interval [CI], 4.4-10.4); for criteria B, 43% versus 60% (difference, 17.6%, 95% CI, 15.2-20.0); and for criteria C, 25% versus 40% (difference, 15.8%, 95% CI, 11.1-20.5). On multivariable Cox regression analyses, being of African descent was associated with higher failure rate for criteria B and C for qualified success and with all criteria for complete success. The incidence of bleb leaks was higher in those of African descent (29 vs. 11 eyes); these patients also required additional glaucoma surgeries more often than did those of European descent (47 vs. 26 eyes).

These results suggest new strategies to control wound healing after trabeculectomy are needed, and the role of nonfiltering glaucoma surgery should be explored in this subpopulation. *(Also see related commentary by Paul Palmberg, MD, PhD, in the same issue.)*

Fellow-Eye Treatment of Open-Angle Glaucoma: CIGTS Results

October 2018

Once it's clear that a patient requires unilateral treatment for open-angle glaucoma (OAG), it may help to know which traits portend disease progression and need for eventual treatment in the fellow eye (FE). In a post hoc analysis of data from the Collaborative Initial Glaucoma Treatment Study (CIGTS), **Niziol et al.** estimated the time between initial treatment of

the study eye (SE) and the need for treatment of the FE. They found that by 7 years after OAG treatment of the SE, roughly two-thirds of patients had undergone treatment of the FE.

In CIGTS, 607 participants with newly diagnosed OAG in at least 1 eye were assigned randomly to receive topical medication or trabeculectomy. FEs were treated when eligible or at the physician's discretion. Data were collected for up to 11 years. Survival analysis was used to estimate the probability of FE treatment over time and to test potential baseline and time-dependent predictors of treatment need. Using linear regression, disease trajectory was calculated as the eye-specific slopes of mean deviation (MD) and intraocular pressure (IOP) over time. In addition, correlations between SE and FE trajectories also were calculated. Main outcomes were time to FE treatment and the slopes over time (MD and IOP) for SEs and FEs.

Among the FEs, 291 (47.9%) were treated at baseline along with SEs, 123 (20.3%) were treated eventually, and 193 (31.8%) did not receive treatment. The probability of FE treatment for OAG was 0.57 by year 1 and 0.68 by year 7 after SE randomization. Correlations in IOP slopes were 0.57, 0.24, and 0, respectively. The similarity of slopes observed for SEs and treated FEs implies that SE change is a harbinger of FE change and, therefore, warrants close surveillance. Two variables that predict FE intervention are modifiable: hypertension and IOP. Proper attention to these factors may reduce the need for FE treatment. *(Also see related commentary in the same issue by Rohit Varma, MD, MPH, and Xuejuan Jiang, PhD.)*

—Summaries by Lynda Seminara

OTHER JOURNALS

Selected by Deepak P. Edward, MD

Conjunctivitis Secondary to Dupilumab Treatment of Atopic Dermatitis

JAMA Dermatology
Published online Aug. 29, 2018

Treister et al. set out to pinpoint risk factors for conjunctivitis among patients with dupilumab-treated atopic dermatitis (AD). They found the strongest predictors to be severe AD at baseline and the presence of a concomitant atopic disorder.

From a cohort of 142 patients who received dupilumab for AD, conjunctivitis occurred in 12 (8.5%). Dupilumab exposure consisted of a 600-mg loading dose, followed by weekly injection of 300 mg. AD severity, as measured by investigator global assessment, was documented at the start of treatment and at the onset of conjunctivitis.

At baseline, 9 (75%) of the 12 patients had severe AD. The mean age at conjunctivitis onset was 30 years. The conjunctivitis occurred at a mean of 15.8 weeks of treatment (range, 8-41 weeks) and was considered severe or moderate-to-severe in 4 patients. Dupilumab was stopped in 3 patients, all of whom had severe conjunctivitis. These 3 patients had severe AD at baseline plus at least 1 other atopic condition. The 2 patients who discontinued the drug permanently also had a history of hay fever. In both of these patients, the conjunctivitis improved after treatment and dupilumab discontinuation, but it did not resolve fully.

Larger, multicenter studies are needed to confirm risk factors and determine effective treatment for conjunctivitis. At-risk patients may benefit from early ophthalmology referral and prophylactic care.

Ophthalmic NSAIDs for Corneal Dystrophy Caused by *SLC4A11* Mutation

Investigative Ophthalmology & Visual Science
2018;59(10):4258-4267

Some mutations of the *SLC4A11* gene cause misfolding of the SLC4A11 protein, which may lead to Fuchs endothelial corneal dystrophy (FECD) or congenital hereditary endothelial dystrophy (CHED). **Alka and Casey** tested 5 ophthalmic nonsteroidal anti-inflammatory drugs (NSAIDs) for their ability to correct SLC4A11 folding defects. They found that 4 of the 5 NSAIDs provided significant rescue of *SLC4A11* mutants to the cell surface. In addition, 2 of the drugs restored osmotically driven water flux of *SLC4A11* mutants. The 5 drugs studied were bromfenac, diclofenac, flurbiprofen, ketorolac tromethamine, and nepafenac.

HEK293 cells expressing CHED- and FECD-causing *SLC4A11* mutants were grown in 96-well dishes, with or without an NSAID. Except for ketorolac, the tested drug concentrations were twice the EC50. The amount of ketorolac was much lower (0.25 μM) because concentrations >5 μM are toxic to HEK293 cells.

Using bioluminescence resonance energy transfer (BRET) and confocal microscopy, the authors tested each NSAID's ability to correct mutant *SLC4A11* cell-surface trafficking. Upon treatment, they also tested the ability of mutant *SLC4A11*-expressing cells to mediate water flux, which may mimic water flux across the corneal endothelial cell basolateral membrane.

BRET assays showed significant rescue of *SLC4A11* mutants to the cell surface by 4 of the 5 NSAIDs. Diclofenac and nepafenac were the most effective for moving endoplasmic reticulum –retained missense mutant *SLC4A11* to the cell surface. In 20 of 30 intracellular-retained *SLC4A11* mutants, diclofenac significantly restored cell-surface abundance. In some cases, diclofenac restored mutant *SLC4A11* water flux activity to the level of wild-type *SLC4A11*. Ketorolac had no effect on cell-surface abundance. Of the 3 mutants examined for cell-surface abundance (L843P, G709E, and E143K), L843P had the greatest improvement in trafficking.

This research suggests that topical ophthalmic NSAIDs possess sufficient permeability to reach the corneal endothelium. The authors encourage testing of diclofenac eyedrops to treat corneal dystrophy in patients with certain *SLC4A11* missense mutations. Wide use of NSAIDs for FECD or CHED would require robust data from well-designed clinical trials in which appropriate dosing regimens are established.

—Summaries by Lynda Seminara

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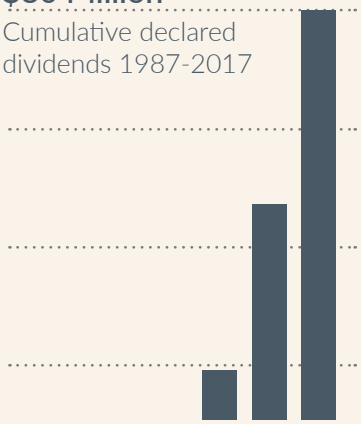

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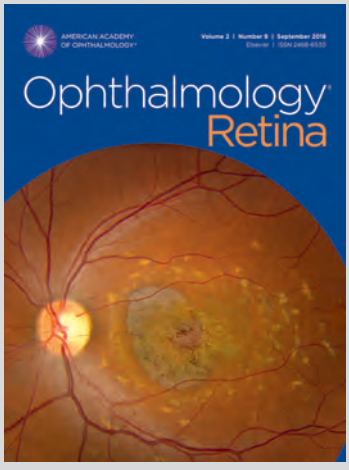

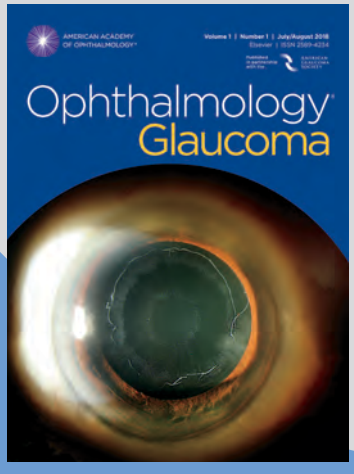

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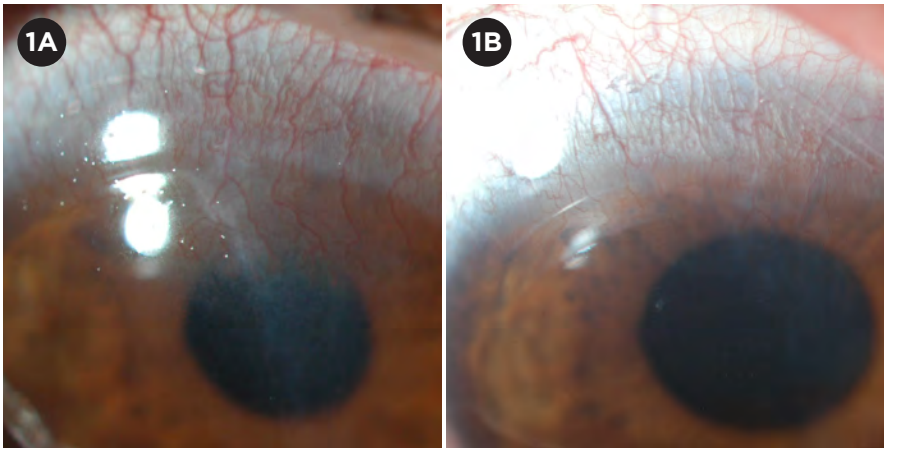
Update on Scleral Lenses

While awareness of the potential benefits of scleral lenses—large-diameter rigid gas-permeable lenses—has steadily increased over the past decade, it still lags among ophthalmologists.

Although fitting contact lenses is typically managed by optometrists, it is important for ophthalmologists to understand the potential role for scleral lenses, particularly in corneal ectasia and ocular surface disease, noted Sanjay V. Patel, MD, at the Mayo Clinic in Rochester, Minnesota.



IMPROVEMENT. *This 10-year-old was diagnosed with Stevens-Johnson syndrome at age 5. (1A) Six months after being switched from extended-wear soft contacts to PROSE treatment. (1B) At the 24-month mark after being switched to PROSE, the eye is quiet and regression of pannus is evident.*

Scleral Lenses 101

Designed to vault over the entire corneal surface and rest on the sclera, scleral lenses can morph an irregular cornea into a smooth optical surface to correct vision problems caused by keratoconus and other forms of corneal ectasia. Furthermore, the space between the cornea and the back of the scleral lens acts as a fluid reservoir, continuously bathing the cornea. This can provide relief for people with severe ocular surface disease and may help the ocular surface to heal.

Indications. The primary indications for scleral lenses are corneal irregularity, ocular surface disease, and severe refractive error.

At the Kellogg Eye Center in Ann Arbor, Michigan, Shahzad I. Mian, MD, has been using scleral lenses for 16 years. "Scleral lenses have transformed the management of both corneal ectasia and ocular surface disease," he said. "They've helped reduce the need for surgical intervention and significantly improved the quality of life for so many patients, especially those with severe ocular surface disease [e.g., Stevens-Johnson syndrome, graft-versus-host disease, neurotrophic keratitis, exposure keratitis, and neuropathic pain] who have symptoms [that are] refractory to other therapies."

When Dr. Mian first started prescribing scleral lenses, it was only for dry eye disease. That is still a common indication, but he is more likely to use them nowadays for corneal ectasia—both the ectasia seen with keratoconus and that which occurs following refractive surgery—and refractive error from irregular corneal shapes, including that occuring after corneal transplantation or linked to scarring.

Advantages. The main benefit of scleral lenses is that they can be designed to accommodate any degree of corneal steepness or irregularity, said Deborah S. Jacobs, MD, at Massachusetts Eye and Ear and Harvard Medical School in Boston. They provide better centration and stability than corneal lenses, and they are more comfortable because the conjunctival tissue on which scleral lenses rest is less sensitive than corneal tissue.

Furthermore, in patients who have experienced damage to corneal tissue, scleral lenses do not touch the cornea but rather bathe it continuously in preservative-free saline so that scar

BY GABRIELLE WEINER, CONTRIBUTING WRITER, INTERVIEWING **DEBORAH S. JACOBS, MD, SHAHZAD I. MIAN, MD,** AND **SANJAY V. PATEL, MD.**

Deborah S. Jacobs, MD

formation is not exacerbated.[1]

Drawbacks. Availability of scleral lenses has improved over the last decade, but other obstacles remain, namely cost and convenience.

Time. The optometrist who is fitting the lens requires special training, and the fitting process is time consuming, requiring several visits.

Cost. The fitting process is reflected in the cost, which ranges broadly from $500 per lens plus a fitting fee to an all-inclusive fee of several thousand per eye, depending on the type of lens and the fitting process (see below). This is not covered by many health insurance plans, though some vision care plans may cover it all or in part, Dr. Jacobs noted.

Convenience. "Other limiting factors are debris collection in the reservoir, fogging, and fouling of the front surface of the lens," Dr. Jacobs said. In addition, Dr. Patel pointed out, "Patients may need to pop them out in the middle of the day to give them a scrub, then pop them back in. It can be inconvenient for some patients."

Which Lens Is Best?

At Kellogg Eye Center, Dr. Mian and his colleagues have fitted many hundreds of patients with sclerals. Initially, they used only PROSE (Prosthetic Replacement of the Ocular Surface Ecosystem) and sent patients to Boston, where PROSE was developed by BostonSight in the early 1990s. About 10 years ago, Kellogg became one of the early satellite clinics for PROSE treatment.

Since then, "there has been an explosion of different types of scleral lenses, and our contact lens specialists fit both PROSE and commercially available lenses," Dr. Mian said. "Often PROSE is still the preferred lens for the most severe patients, particularly the severe dry eye patients. That said, many patients can be fit successfully with the other types of sclerals," he added.

PROSE. "PROSE is really a treatment approach more than a piece of plastic. Yes, it produces a large-diameter gas-permeable lens that the patient wears on a daily basis, but the endpoint of the whole design, fit, and customization [process] is prosthetic function, and that involves an assessment, then customization, then monitoring," explained Dr. Jacobs, formerly with BostonSight.

Fitting and customization. "The capability of the fitter in customizing the design and shape of the lens is different for PROSE than it is for the commercial lenses, for which there are just a few parameters the fitter can adjust and then communicate to the lab that makes the lens," Dr. Jacobs said. In contrast, in PROSE, fitters use a computer-assisted design system that enables them to manipulate directly each prosthetic device to the patient's precise and unique eye shape.

"The academic centers that became PROSE satellites brought on an optometrist who typically had specialized in cornea and contact lens in a 'residency' year following optometry school. In that year, optometrists learn to fit specialty lenses and get comfortable with a broader spectrum of corneal disease," said Dr. Jacobs.

Delivery and cost. PROSE is delivered through a medical model, with a single fee per eye set by the institution with all services related to treatment wrapped in, Dr. Jacobs said.

The approximate cost for PROSE, which is sometimes referred to as the Rolls Royce of scleral lenses, is on the order of $5,000-$7,000 per eye for the entire process.

Commercially available scleral lenses. At Mayo, Dr. Patel and his colleagues popularized fitting lenses from a diagnostic set. "It is cheaper for the patients, and most eyes—not all—can be fit that way," he said.

Fitting and customization. As with PROSE, the goals of fitting are that the lens is completely supported by the sclera, achieves complete clearance over the cornea and limbus, and achieves an even bearing zone on the sclera to avoid compression of blood vessels. The fitter uses the diagnostic set of trial lenses to determine the correct sagittal depth and then does overrefraction to obtain lens power. The back surface peripheral curve system can be modified to provide the best fit.

Although commercially available sclerals can't offer complete customization, like that offered with PROSE, they meet the needs of most patients at a lower but variable cost.

Delivery and cost. Scleral lenses are sold through a optometric model: The lab sells them to the optometrist who fits the lenses. In turn, the optometrist sells them to the patient. Thus, it is up to the optometrist to determine what to charge for the lens and what the fitting fees are.

In the United States, the estimated average overall cost per eye (the lens plus the fitting) runs from $1,000-$5,000, depending on the complexity of the condition and the technology required.

Another option: Scleral variations. Modified, smaller rigid gas-permeable lenses are separated by size into mini-scleral, semiscleral (also called intralimbal), or corneoscleral types. Respectively, their edges rest slightly outside the limbus, slightly inside it, or partly on the cornea and partly on the sclera.

These smaller lenses are not true scleral lenses and may only be used for corneal irregularity, not for ocular surface disease. Definitions and terminology are still evolving, but Dr. Jacobs defines true scleral lenses as having a diameter greater than 18 mm. In contrast, the diameters of the lenses mentioned above range from 13-17 mm.

Updated Treatment Algorithms

New paradigm for keratoconus. It used to be that treatment of keratoconus consisted of glasses or soft lenses for mild stages, rigid gas-permeable corneal contact lenses for moderate stages, and corneal transplantation for severe cases. The indication for surgery was contact lens failure.

But the advent of specialty lenses, including custom soft lenses, better hybrid lenses, and now scleral lenses and PROSE treatment, has extended the limit of what can be accomplished with contact lenses. "A case [of keratoconus] is not a 'contact lens failure' without a trial of specialty lens," Dr. Jacobs emphasized.

"Many patients who would have come to surgery a decade or 2 ago can retain good vision for life with specialty lenses and particularly scleral lenses,"

said Dr. Jacobs. "The surgeons who have access to scleral lenses for their patients report anecdotally that their rate of corneal transplant for ectasia and astigmatism has gone way down." Indeed, Drs. Patel and Mian confirmed a significant reduction in surgery rates in their practices. And in a Belgian study published earlier this year, 40 of the 51 eyes with severe keratoconus that would have undergone transplant surgery were successfully treated with long-term scleral lens wear, reducing the indication for keratoplasty by more than half.[1]

Management of ocular surface disease. Scleral lenses are usually used later in the disease course. One exception, according to Dr. Mian, is patients with severe ocular surface disease associated with graft-versus-host disease. "Those patients often progress quickly to the very severe stage and typically don't respond to other therapies, so we will move to scleral lenses faster."

In all cases, over-the-counter lubricants are started immediately, then topical medication (e.g., cyclosporine or a topical steroid) and punctal occlusion are considered. The next option may be serum tears. Dr. Mian then turns to PROSE treatment before considering amniotic membrane contact lenses like Prokera (Bio-Tissue). Tarsorrhaphy and conjunctival flap come after that.

Clinical Pearls

Especially in patients who have ocular surface disease, Dr. Patel urged ophthalmologists to think about a scleral lens as an alternative to tarsorrhaphy or jumping to amniotic membrane or keratoplasty. "Think of scleral lenses and seek them out," he said.

Don't count out the young—or the old. Dr. Mian reported that some of his youngest patients have greatly benefitted from scleral lenses. These children had severe dry eye or neurotrophic disease (from herpetic infection) and were unable to heal the surface of their eye on their own. "Despite multiple other treatments that hadn't worked, scleral lenses made a big difference in improving the health of their eyes and maintaining vision in their eyes," said Dr. Mian. "My youngest patient was 2 years old."

With regard to the other end of the age spectrum, he added, "It's also feasible to fit patients into their 80s or 90s, as long as they can take care of the lenses."

Work with the optometrist. When scleral lenses are used for ocular surface disease, the comprehensive ophthalmologist or cornea specialist will need to collaborate on an ongoing basis with the optometrist, because the underlying disease that will need to be monitored for neovascularization or potential infection continues to exist, Dr. Patel said.

"Supplemental treatments are still needed, especially when the patient takes the lenses out. They'll still use lubricants; they'll often still use topical steroids; they might still use serum tears," he said. For corneal ectasia, the optometrist can often handle the case alone, but the lines of communication should be kept open if a complication arises, Dr. Patel noted.

Observe your patients with their lenses on. Dr. Jacobs encouraged all ophthalmologists to have a look at their patients with their scleral lenses on so that they can gain an appreciation for fit and physiologic function. "In contemporary practice, where there is so much emphasis on volume, the standard is that the staff measures vision in lenses, then takes them out to proceed with the rest of the eye exam prior to the physician seeing the patient," Dr. Jacobs said. "But even if not trained in fitting, the ophthalmologist can gain a better understanding of scleral lenses when examining the eyes with them on and then off."

Lowering the Clinical Threshold

Because severe refractive error is an indication for scleral lenses, what's stopping clinicians from using them for more typical refractive errors?

No added value. Soft lenses remain the primary way to correct refractive error because most patients can tolerate them, they're easy to use, and there's less maintenance. "Convenience is the No. 1 factor," said Dr. Mian, "and scleral lenses are inconvenient. Using them solely for refractive error doesn't add more value to the average patient and is far more expensive."

Concerns over long-term use. In order to consider using scleral lenses for vision correction, not for disease, ophthalmologists need to know more about potential long-term side effects. Although the lenses sit on the sclera, they come very close to the limbus. "If scleral lenses damage the limbus, it can cause big problems long term. We have no clinical evidence of that happening, but we worry about it," said Dr. Mian.

Possible exception: Athletes with astigmatism. One exception to physician reluctance to prescribe might be the use of minisclerals for serious athletes with astigmatism.

Take a professional baseball player, for example. "Soft lenses don't correct sharply enough, glasses are a problem if you're diving after a line drive, and corneal lenses move around and can get dirt and grit under them," Dr. Jacobs said. "For serious baseball players with ordinary astigmatism, a miniscleral would be easy to fit and would correct them well." To address concerns regarding long-term use, the athlete could wear the miniscleral lenses just for games and practices.

But can an athlete—or anyone else—wear minisclerals for 12-14 hours a day over many years? "The miniscleral world is working on answering that question," Dr. Jacobs said.

1 Koppen C et al. *Am J Ophthalmol.* 2018;185:43-47.

Dr. Jacobs is associate professor of ophthalmology at Harvard Medical School. She is also faculty on the Cornea Service and director of the Ocular Surface Imaging Center at Massachusetts' Eye and Ear in Boston. *Relevant financial disclosures: BostonSight: E (through February 2018).*

Dr. Mian is professor of ophthalmology and visual sciences, the Terry J. Bergstrom Collegiate Professor for Resident Education in Ophthalmology and Visual Sciences, and associate chair for education at the University of Michigan's Kellogg Eye Center in Ann Arbor, Mich. *Relevant financial disclosures: None.*

Dr. Patel is professor and chair of ophthalmology at the Mayo Clinic in Rochester, Minn. *Relevant financial disclosures: None.*

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A Ticking Time Bomb: How to Fix a Leaking Bleb

A leaking filtration bleb is a common complication of trabeculectomy that can occur days, months, or years after the initial surgery. It's also a vision-threatening danger that shouldn't be ignored.

The bottom line: There should be no delay when addressing any type of bleb leak, said Neeru Gupta, MD, PhD, MBA, at the University of Toronto. "If the leak does not seal, the patient will have fluid leaving the eye, which can drop the pressure and lead to a whole host of complications." Moreover, she pointed out, "the leaking eye has no barrier to the outside world and, suddenly, it's open season for pathogens."

Thus, "It's really important to see each leaking bleb as a ticking time bomb," Dr. Gupta said. "Yes, the bleb surgery can be technically challenging, but the general ophthalmologist has a critically important role to play. Although a glaucoma specialist may be involved in fixing the [actual] leak, it's imperative that every ophthalmologist knows how to read the signs of what can be a very sight-threatening condition."

A Faulty Filter

The conjunctival tissue of a bleb can become thinned and cystic due to the constant flow of aqueous, and the thinnest and most avascular areas are most susceptible to developing a leak.

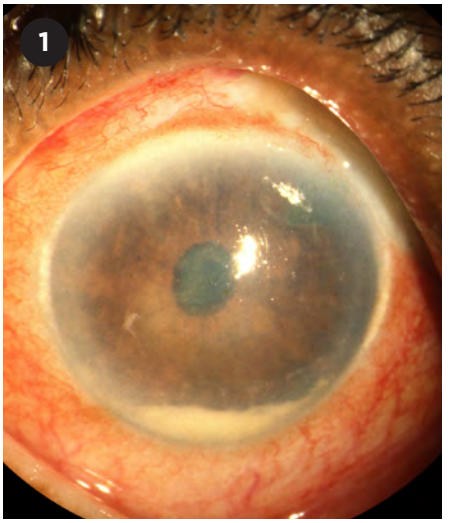
This leakage can result from the surgical technique and/or the nature of the conjunctival tissue itself. "Early-onset bleb leakage occurs in the immediate period following surgery," said Sunita Radhakrishnan, MD, at the Glaucoma Center of San Francisco. "There might be a leak at the incision site due to incomplete conjunctival closure or wound dehiscence, for example. Or the surgeon might have created an inadvertent opening in the conjunctival tissue." The area where the bleb is most elevated can also develop a leak due to drying or microtrauma from repeated blinking.

Late-onset bleb leakage, on the other hand, is typically the result of thin bleb tissue. "The biggest reason a patient would develop this type of avascular tissue is the use of antifibrotics," Dr. Radhakrishnan said. "Mitomycin C and 5-fluorouracil are commonly used as adjunctive treatment in filtering surgery to help prevent fibrosis and scarring. Although this can increase the survival of a filtering bleb, it can also result in more fragile tissue that is prone to leakage in the future."

Danger, Danger

Regardless of when the leakage occurs, "A leaking bleb is not a minor issue," said Alan L. Robin, MD, at the University of Michigan in Ann Arbor and John Hopkins University in Baltimore. "Early detection and management can help prevent serious complications."

Potential complications. "If left untreated, the leak can lead to hypotony, which can result in a shallow or flat chamber, peripheral anterior synechiae, hypotony maculopathy, choroidal effusion, corneal striae, or even bleeding and surgical failure," Dr. Robin said.



ENDOPHTHALMITIS. *Three years after undergoing trabeculectomy, this patient presented with pain, redness, and loss of vision in the left eye.*

Risk of infection. "Bleb-related infection is a very dangerous and volatile situation if not managed promptly," Dr. Gupta emphasized. "An open barrier in the ocular surface exposes the eye to any number of pathogens and microorganisms, so there's a serious risk of intraocular infection. This can range from blebitis, an infection in or around the bleb without vitreous involvement, to endophthalmitis [Fig. 1]."

Signs of trouble. The surgeon can usually monitor for early-onset bleb leaks during surgery or in the immedi-

BY MIKE MOTT, CONTRIBUTING WRITER, INTERVIEWING **NEERU GUPTA, MD, PHD, MBA, SUNITA RADHAKRISHNAN, MD,** AND **ALAN L. ROBIN, MD.**

ate postoperative period.

After this point—and during normal follow-up—common signs of bleb leakage include a newly tearing eye, a noticeable change in vision, redness, or a drop in intraocular pressure (IOP) from baseline. "If you suspect a patient might have a leak, perform a Seidel test at the slit lamp to confirm," said Dr. Gupta. "After painting the conjunctiva with a fluorescein strip under cobalt blue light, you'll see the leak in the form of a greenish fluid escaping from behind the brown stain."

Referral. "The bleb should be examined at every visit," Dr. Robin said. "If a leak is present, given the potential serious sequelae, it should be addressed immediately."

Stopping the Flow

Bleb leaks can resolve spontaneously, but if they don't, what's the fix? Treatment depends largely on your patient's needs and how they present.

Medical treatment. "Conservative management is my first-line approach," said Dr. Radhakrishnan, "especially if the leak is small with no infection, the visual acuity and pressure are stable, and the patient has no past history of bleb-related infection. Initially, I'll use aqueous suppressants alongside prophylactic antibiotics to protect against infection. As long as the eye is stable and the bleb leak is decreasing, this approach can be followed until complete resolution in many cases."

Other conservative approaches include:

- Direct pressure patching
- Bandage contact lens
- Collagen shields
- Autologous blood injections
- Compression sutures
- Cyanoacrylate glue

Surgical treatment. "There's no hard-and-fast rule as to when you need to fix a bleb leak surgically," Dr. Robin said. "But if the leak is not responding to initial management—or is brisk enough to cause corneal decompensation—or if the patient has experienced repeated episodes of bleb-related infection, definitive treatment always requires surgical repair."

Although there is no gold standard for bleb leak repair, the common goal in the various surgical techniques is to cover the filtration site with healthy conjunctiva. The unhealthy bleb tissue is usually denuded or excised.

"Conjunctival advancement is 1 technique of bleb repair that entails covering the leaking bleb with a new flap of healthy conjunctival tissue that is advanced from the region posterior to the bleb," said Dr. Radhakrishnan. "I typically remove the tissue that is leaking or ischemic. If there is not enough healthy conjunctiva for this approach, then a free conjunctival autograft from either the same eye or the fellow eye can be used."

To test the bond after tacking down the advancement, Dr. Robin will inject balanced salt solution into the anterior chamber to check for any leakage and then confirm the result with a fluorescein test.

Learning curve. "Repairing a bleb leak surgically is not a particularly easy fix," said Dr. Gupta. "Suturing through an avascular bleb that is already thin and friable—even with a fine suture like 10-0 nylon—can be challenging. The tissue may be as delicate as wet tissue paper, and punching holes in it can be like operating on Saran Wrap: One hole creates another even larger one."

Because of these difficulties, ophthalmologists are continually searching for innovative ways to achieve the same results. "The patient might have unhealthy conjunctiva lacking useable tissue," said Dr. Gupta. "For example, there might be too much scarring to perform a successful bleb revision. To fill these gaps, ophthalmologists have experimented with different patch graft materials other than conjunctiva, such as corneal tissue, amniotic membranes, mucosa from inside the cheek, and even fascia. It's a struggle to manage aggressive bleb leakages, so we're always looking for better ways."

Postoperative Complications

Although positive outcomes are typically high for bleb repair, the clinician should expect that a few patients will develop complications, Dr. Radhakrishnan said.

The primary concern, she noted, is disturbing the preexisting aqueous flow. "Once you've repaired a leak, the conjunctiva is now thicker, so the pressure-lowering efficacy of the original trabeculectomy can decrease. You might see an early postoperative pressure spike from closing the bleb leak, or a slow rise in pressure over time as the bleb function slowly decreases. In our study, for example, 9% of patients required additional glaucoma surgery anywhere from 2 months to 7 years following bleb revision."

Aside from glaucoma control, there are a few other—and less common—complications to be mindful of, said Dr. Gupta. These include hypertropia, ptosis, and dysesthesia. "When we're performing advancement surgery, we are tugging on tissue from behind the upper lid close to the muscle and pulling it forward. This can result in muscle misalignment and drooping of the eyelid. And because the advanced conjunctiva might not sit flat at the limbus, the patient may experience eye discomfort when blinking."

Risk of another leak. Of course, the patient might also develop another leak, she added. "There might also be something about the quality of the patient's conjunctiva that predisposes it to leakage, and, voila, after plugging 1 hole, you've got another, and you have to treat all over again."

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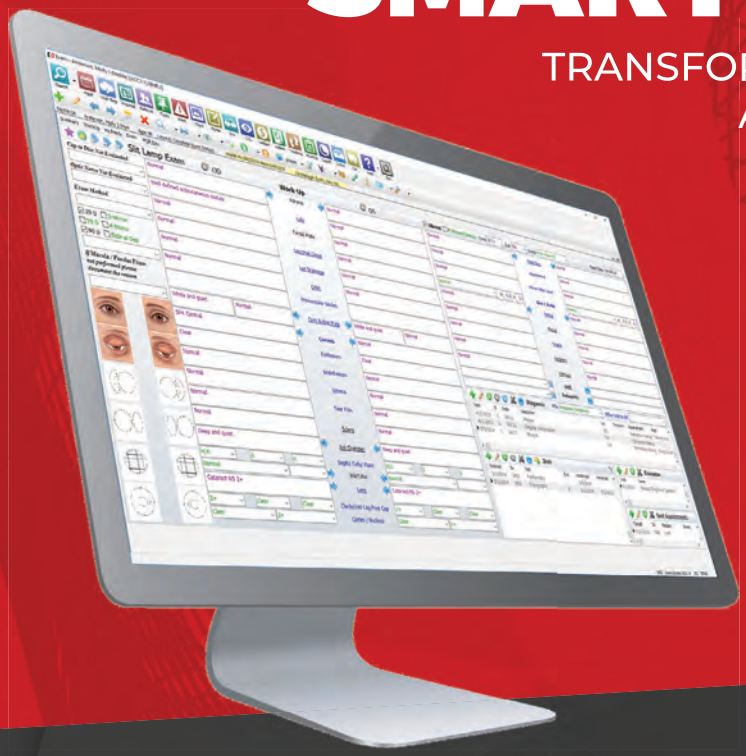

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Diana R. Shiba, Academy fellow since 2010, shares an uplifting moment with her patient. The Academy's IRIS Registry aggregates patient data to facilitate new scientific discoveries.

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Terson Syndrome: Don't Let It Go Unrecognized

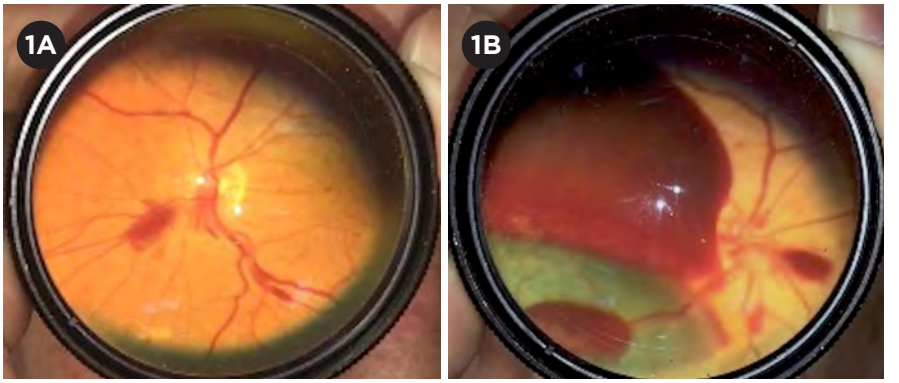
Terson syndrome (TS) is the presence of any intraocular hemorrhage, including vitreous, subhyaloid, intraretinal, or subretinal bleeding, in patients with intracranial hemorrhage or traumatic brain injury. The term originally referred only to vitreous hemorrhage in the setting of a subarachnoid hemorrhage (SAH), but the definition has since been expanded.

Incidence. In part due to this change in diagnostic criteria, estimates of the incidence of TS vary. In a systematic review of SAH patients, McCarron et al. reported a 13% incidence of TS among patients evaluated prospectively.[1] Czorlich et al. reported an incidence of 19% in patients with SAH, 9% in those with intracerebral hemorrhages, and 3% in patients with traumatic brain injury.[2]

The incidence of TS is significantly higher in patients with greater impairment in consciousness (as indicated by a low Glasgow Coma Scale) or more severe subarachnoid hemorrhage (based on either a high Hunt and Hess grade or a high Fisher grade).[2] TS is more likely to occur in patients who have had prolonged episodes of unconsciousness or elevated intracranial pressure[3]; and some, but not all, studies have observed a stronger association with anteriorly located aneurysms.[4] Although TS usually develops within hours of the neurological event, it can occur days or weeks later.[2]

Delayed diagnoses. Despite the relatively high incidence of TS in patients with SAH, the syndrome remains underdiagnosed. One reason may be that the patients who are most likely to have TS are also more likely to be neurologically impaired and, therefore, limited in their ability to verbalize their ocular complaints.[2] In addition, given the neurological acuity and severity of these patients' conditions, an ocular examination may not be performed until other, more emergent, interventions have been undertaken.

Thus, referral of patients with TS to ophthalmology is often delayed. In a review of TS patients who later underwent vitrectomy, Gnanaraj et al. reported an average of 5.2 months between the time that a TS patient first complained of ocular symptoms and when an ophthalmology consultation occurred.[5] This delay in diagnosis can lead to permanent visual impairment and impede neurorehabilitation efforts.



FUNDUS FINDINGS. *Fundi of a 48-year-old woman who had an anterior communicating cerebral artery aneurysm, diffuse subarachnoid hemorrhage, and left inferior frontal cerebral hematoma. (1A) Right eye, showing intraretinal hemorrhages nasal and superior to the disc. (1B) Left eye, showing a large area of preretinal hemorrhage overlying the macula, subretinal hemorrhage along the superior arcade, and intraretinal hemorrhage nasal to the disc. (Images, taken with a 20 D lens and iPhone 7 camera with flash, are inverted vertically and horizontally.)*

Pathophysiology

The pathophysiology of TS is debatable, and multiple mechanisms have been proposed. The leading theory suggests that an increase in intracranial pressure causes a rapid efflux of cerebrospinal fluid or hemorrhage via the optic nerve sheath into the orbit. This, in turn, compresses the central retinal vein, obstructing venous outflow and subsequently rupturing the smaller retinal venules.[6]

Another theory proposes that an

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Bing Chiu, MD

acute elevation in intracranial pressure can increase orbital venous pressure, leading to backflow of blood through the retinal veins.[7] A third theory suggests that the intraocular hemorrhages may be the result of direct extension of blood from the subarachnoid space itself via the optic nerve sheath.[8]

Although the exact etiology remains unknown, an association with intracranial pressure has been supported by Czorlich et al., who found that patients with TS were more likely to have had periods of elevated intracranial pressure greater than 25 mm Hg.[3]

Symptoms

The symptoms reported by TS patients can vary widely, depending on the degree and location of the hemorrhage as well as the individual's neurological status. Many patients, especially those who are most neurologically compromised, may not be able to perceive or communicate ocular complaints. In such cases, prompt diagnosis depends on the primary physician's first being aware of the possibility of Terson syndrome and then arranging for evaluation by an ophthalmologist. Patients who are able to describe their symptoms typically report an acute decrease in vision in 1 or both eyes in the setting of a recent severe headache or head trauma.

Diagnosis

Given the notable incidence of TS in patients with intracranial hemorrhage, SAH, or traumatic brain injury—especially in patients with a loss of consciousness or low initial Glasgow Coma Scale—screening for TS is important once the patient is medically stable.[2,3]

Fundus examination. Funduscopy is the gold standard for detecting and diagnosing TS. Hemorrhages involving multiple intraocular layers may be seen; they can manifest as a "double ring" sign, in which blood is present below the internal limiting membrane and posterior hyaloid.[9] Patients may also have a loss of the red reflex.

TS has been linked with development of macular holes, epiretinal membranes, retinal folds, proliferative vitreoretinopathy, retinal detachment, and optic nerve sheath hemorrhage as early as 1 week after onset.[9]

Imaging. It can be challenging to identify this pathology by funduscopy if the view is obscured by vitreous hemorrhage; in such cases, other modalities, such as B-scan ultrasonography, should be considered to aid in the diagnosis. In a study of patients with SAH, B-scan ultrasonography was 100% sensitive and specific for identifying vitreous or preretinal hemorrhages and 44% sensitive for identifying intraretinal hemorrhages. Head CT scans, in contrast, were 60% sensitive for detecting preretinal hemorrhages and 32% sensitive for any intraocular hemorrhage.[4] Thus, these modalities may be viable screening options.

Management and Outcomes

Ophthalmologic. The ophthalmic prognosis for TS patients is quite good. Many intraocular hemorrhages resolve spontaneously over several months. For those that do not, vitrectomy has been successful in improving visual outcomes.[5,10]

In a series of 25 TS eyes undergoing vitrectomy, 88% of eyes achieved 20/30 vision or better.[5] A study of 44 vitrectomized TS eyes found that patients who underwent early vitrectomy (within 90 days of vitreous hemorrhage) achieved better visual outcomes than those who were operated on after 3 months.[11] Thus, many experts advocate for early vitrectomy, especially in cases of bilateral vitreous hemorrhages, dense unilateral hemorrhage, or hemorrhages in young children.[5,7,9,10]

The other types of retinal pathology associated with TS, including retinal detachment and macular holes, can also have profound effects on vision if not promptly recognized and treated.[9]

Neurological and systemic. In terms of neurological and survival outcomes, the prognosis for these patients is notably poor. In a systematic review of outcomes in SAH, patients with TS had a risk of mortality almost 5 times higher than that of patients with SAH alone (50% vs. 11%, respectively, among patients studied prospectively).[1] Furthermore, TS patients who do survive have significantly lower Glasgow scales at 3 months than SAH patients without TS.[2] Thus, it is important for TS be recognized early, not only for its prognostic significance and impact on patients' neurorehabilitation efforts, but also because its complications may lead to permanent vision loss if left untreated.

Key Points

- When medically stable, patients with intracerebral and subarachnoid hemorrhages should receive a prompt funduscopic exam to evaluate for TS.
- B-scan ultrasonography or CT head scan can be used as to screen for TS.
- Early vitrectomy should be considered in patients with severe vision loss or bilateral hemorrhages and in young children at risk for amblyopia.
- The presence of TS is associated with a worse neurological prognosis and higher risk of mortality.

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EXTRA **MORE ONLINE.** See this article at aao.org/eyenet for brain imaging of the patient in Fig. 1.

A Bothersome Bump

One morning, Mark Mario* woke up with a tender, swollen left eyelid. The 8-year-old had a history of sinus infections but otherwise had been in good health, with no history of trauma or recent illness. After several days of worsening swelling and pain, Mark's mother sought help.

At the pediatrician's office. When Mark presented at the pediatrician's office, he was afebrile and, overall, seemed well—except for his left eyelid, which was swollen, droopy, and painful. The pediatrician found the left eyelid tender to touch and was concerned that he might have early preseptal cellulitis, so she prescribed a 2-week course of Augmentin (amoxicillin with clavulanate). When Mark's condition did not improve after 1 week, she referred him to us.

What We Saw

On examination, Mark's best-corrected visual acuity was 20/20 in the right eye and 20/25 in the left. There was no afferent pupillary defect in either eye, and his color vision was full. His intraocular pressure was 16 mm Hg in the right eye and 13 mm Hg in the left.

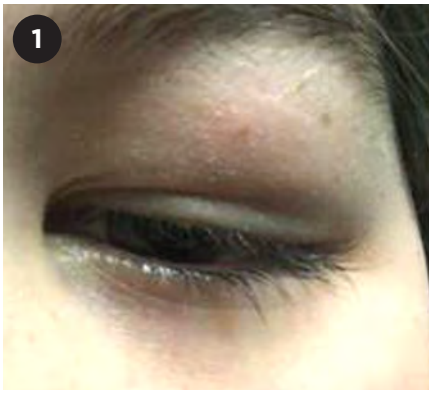
Most remarkable was the fullness of his left eyelid (Fig. 1). On palpation, he had a firm, nonmobile, approximately 2-cm mass of the left anterior orbit. It was contiguous with the left superior orbital rim and was tender to light touch. The mass limited his eyelid elevation, and he demonstrated ptosis with an associated superior visual field defect to confrontation.

Eyelid eversion was difficult due to pain and mass effect; however, the palpebral conjunctiva appeared normal. Mark had mild hypoglobus but no axial proptosis. He had symmetric sensation in the V1-V3 distribution on both sides. His slit-lamp exam was normal in both eyes, and he had a normal fundus exam without evidence of retrobulbar mass effect.

Our Differential Diagnosis

It was apparent to us that this lesion was not a preseptal or orbital cellulitis, as even an abscess would not cause such a very firm lesion in the anterior orbit, and Mark seemed too well overall to have an aggressive orbital infection.

A rapidly appearing orbital lesion in a child always gives the ophthalmologist a sense of fear, with rhabdomyosarcoma, metastatic neuroblastoma, osteosarcoma, and leukemia jumping quickly to mind. However, we didn't see the proptosis typical of rhabdomyosarcoma, nor the typical ecchymoses of orbital neuroblastoma. Lymphangioma seemed possible given the rapid onset, but there was no antecedent upper respiratory infection. An eosinophilic granuloma seemed possible especially given the bony pain, although it is less common in children than the previously mentioned orbital neoplasms.



WHEN WE FIRST SAW MARK. *His left eyelid was swollen, and we noted trace ptosis and hypoglobus.*

We Send Mark to the ED

With a high level of concern, we immediately sent our patient to the emergency department for radiologic studies and a systemic investigation for a potential malignancy.

A computed tomography (CT) scan showed an enhancing soft-tissue mass centered in the left frontal bone and left orbital roof with erosion into the frontal bone (Figs. 2A and 2B). Same-day magnetic resonance imaging (MRI) demonstrated a mass effect on the dura and left frontal lobe (Fig. 2C). A thorough systemic lab workup was unremarkable except for an elevated eosinophil count.

Otolaryngology performed an image-guided biopsy of the lesion through a left medial supraorbital incision; a soft-tissue mass that appeared granulomatous was noted intraoperatively.

Frozen tissue analysis revealed multiple eosinophilic granules and dendritic cells positive for the CD1a and S100

BY **SAILAJA BONDALAPATI, MD, SARA GRACE, MD,** AND **KENNETH COHEN, MD.** EDITED BY STEVEN J. GEDDE, MD.

markers and the *BRAF* V600E mutation (Fig. 3), confirming that Mark had Langerhans cell histiocytosis (LCH), formerly known as histiocytosis x.

Discussion

LCH is a rare medical condition of unclear etiology that commonly presents with a triad of exophthalmos, diabetes insipidus, and solitary bone lesions (eosinophilic granuloma). Other variants reported in the literature are Hand-Schüller-Christian disease and, if infants present with severely disseminated disease, Letterer-Siwe disease.

In 1893, Alfred Hand initially misdiagnosed a young child with polyuria, exophthalmos, and skull lesions as tuberculosis.[1] Later—in collaboration with Artur Schüller and Henry Christian—Hand coined the term histiocytosis for this medical condition, which has characteristics of multiple skeletal lesions, pituitary infiltration, and exophthalmos.

Incidence. In the United States, the incidence is rare (5-6 cases per million per year); most patients are between 5 and 15 years old. The incidence in males is 2 to 3 times greater than in females.[2]

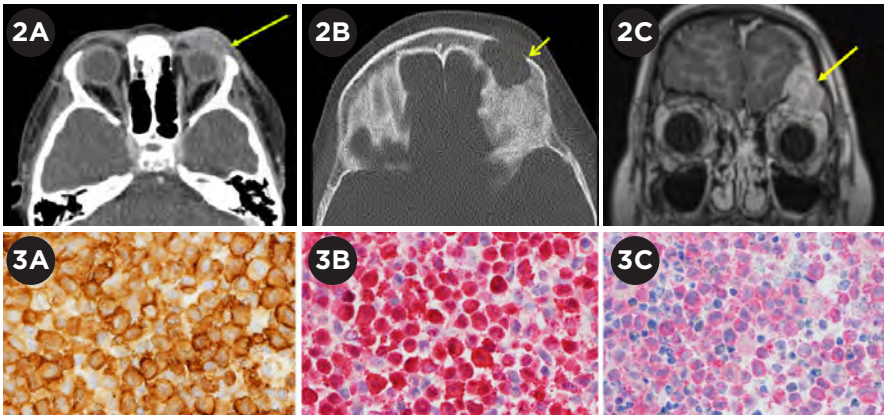
Presentation. Patients usually see a pediatrician or an orthopedist for bone pain before the diagnosis is made. Disease presentation is variable, with bone being the most commonly affected organ in up to 80% of cases.[2] Skin is the next most frequent site of involvement, followed by pituitary, liver, spleen, lungs, and lymph nodes.

Neuroendocrinopathies related to hormonal deficiencies (such as polyuria from diabetes insipidus, growth failure, and gonadotropin disturbances) are also reported due to both anterior and posterior pituitary involvement.[3]

Evaluation and diagnosis. A thorough physical exam is essential. This should include inspection of skin and mucous membranes. Laboratory studies should include a complete blood count and basic chemistry, urinalysis, inflammatory markers, thyroid, and coagulation studies. Radiological studies delineate bone and tissue involvement, and histopathological analysis is required for confirmative diagnosis.

Treatment. Multiple treatment modalities are reported in the literature, including observation, surgical resection, localized high-dose steroids, radiation, and chemotherapy, which are tailored depending on the organ involvement and medical conditions of the patient.[4] The multitude of treatments reflects the spectrum of disease presentations—although the treatment of choice for isolated lesions is usually excision or local radiation therapy to limit systemic morbidity.

Prognosis. The prognosis is excellent, with 1 study reporting a 10-year survival rate of 100%, with low rates of recurrence for monostotic disease and 71% recurrence for multiorgan disease.[5]



IMAGING AND SOFT TISSUE ANALYSIS. *CT scan shows (2A,B) soft tissue mass. MRI (2C) demonstrates erosion of the orbital roof. There was positive staining for (3A) CD1a, (3B) S100, and (3C)* BRAF *mutation.*

Mark's Treatment

Following the orbital biopsy, a full-body positron emission tomography (PET) scan was performed to search for other sites of involvement. This was negative, and our neurosurgery colleagues recommended surgical excision and reconstruction to decompress his orbit and reconstruct the orbital bar and roof.

Two weeks following Mark's initial presentation to the ophthalmology clinic, he underwent left eyebrow craniotomy with resection of the tumor. The surgery was successful at eliminating the mass effect, and his pain, ptosis, and extraocular motility restriction have resolved (Fig. 4, available online at aao.org/eyenet).

Mark continues to demonstrate a postsurgical hypoesthesia in the left V1 distribution as well as a left frontalis palsy. Every 4 months, he is checked by the oncology service to assess for local recurrence, with skull plain films, and he undergoes urinalysis to rule out diabetes insipidus.

Conclusion

LCH is a rare neoplasm in children but should be considered in patients who present with orbital lesions, especially if they are experiencing bone pain.

Bony erosion on imaging is a hallmark of the disease, although it may be seen in other orbital lesions, both malignant and benign.

Surgical biopsy is needed for definitive diagnosis; once confirmed, a finding of eosinophilic granuloma should prompt complete systemic evaluation for other sites of disease.

* Patient name is fictitious.

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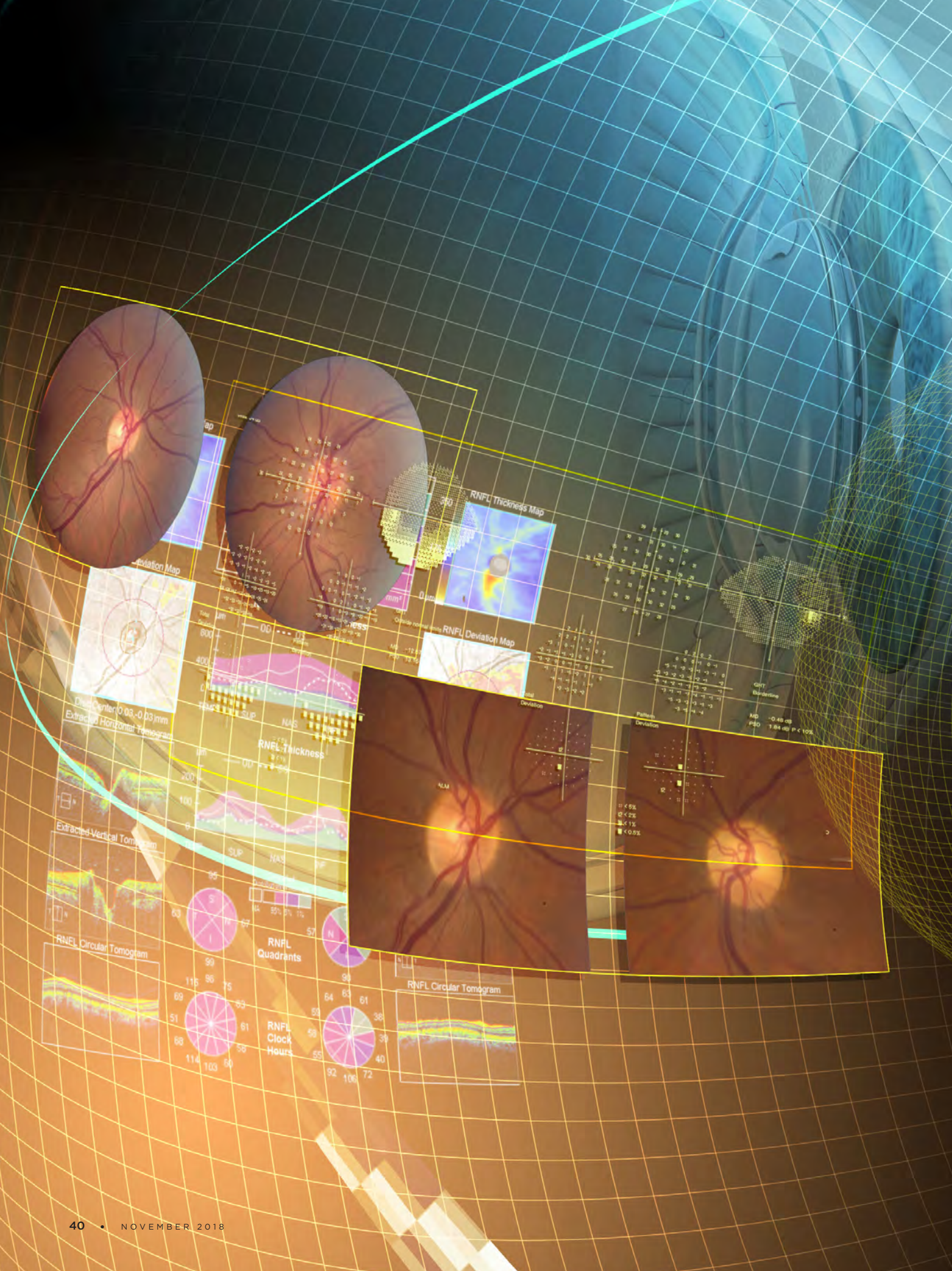
Sailaja Bondalapati, MD


RNFL Thickness Map
RNFL Deviation Map
RNFL Thickness
RNFL Quadrants
RNFL Clock Hours
RNFL Circular Tomogram

When It's Not Glaucoma

A variety of conditions can produce visual field defects, OCT findings, optic nerve abnormalities, and nerve fiber layer loss that mimic glaucoma

By Annie Stuart, Contributing Writer

HOW OFTEN ARE PATIENTS MISDIAGNOSED WITH GLAUCOMA? "It happens more frequently than you might think," said Steven D. Vold, MD, at Vold Vision in Fayetteville, Arkansas.

Kimberly Cockerham, MD, FACS, who practices in Stockton, California, agreed. "This is not something I see once in a blue moon. It is fairly common to see a patient who is on glaucoma drops and may not need them."

Whether it's glaucoma, an intracranial problem (such as pituitary adenoma, meningioma, or carotid or ophthalmic artery aneurysm), or an orbital problem (such as thyroid eye disease or an orbital tumor), certain cases can be a complex challenge for even the most experienced observer. But finding your way through the challenge is essential, as a misdiagnosis may lead to unnecessary testing and treatment. Even worse, it may seriously threaten the patient's health or vision. Four experts offer guidance for sorting out the differences.

The History

Patient histories can offer clues to suggest there's something other than glaucoma at play. Make sure these clues don't go unnoticed, said Dr. Cockerham. Among her most baffling cases was a recent referral—a patient who was diagnosed as a "glaucoma suspect" decades ago and had been on eyedrops ever since.

Listen for clues. "He was a good historian," she said, "but nobody had listened to him." The patient described being hospitalized after a severe motor vehicle accident that resulted in a brain abscess. He recalled losing his visual field immediately after the accident and could provide specific details about which areas of his visual field were lost. He had had a completely stable visual field abnormality and optical coherence tomography (OCT) test results for years.

Consider age. Consider the patient's age when taking the history and think about potential causes other than glaucoma, said Dr. Cockerham. "In a young patient, the cause is more likely hereditary, post-traumatic, inflammatory, or infectious. In middle age, compressive conditions and vascular events can occur. In older patients, giant cell arteritis can cause posterior ischemia that results in cupping and pallor."

Nonglaucomatous problems that look like glaucoma can be asymptomatic. However, 1 common clue is sudden vision loss, which is typical of ischemic optic neuropathies, but not of glaucoma, said Dr. Vold. In contrast, compressive optic neuropathy tends to progress more gradually, confounding the diagnosis.

Watch symptoms, signs. Other symptoms and signs can help you begin to piece together the puzzle. The key is asking the right questions about vision, as well as asking probing questions about neurologic symptoms, said Prem S. Subramanian, MD, PhD, at the University of Colorado Health/Sue Anschutz-Rodgers Eye Center in Aurora, Colorado. "For example, loss of libido is a cardinal sign of some pituitary tumors in men, but patients often won't volunteer this information."

Ocular symptoms. Ask patients whether they have experienced any of the following symptoms:

- Sudden or quickly progressing vision loss
- Vision that's different in only 1 eye
- Lack of color vision in 1 eye (red desaturation)
- Vision loss with eye movement
- Vision loss that came on with a severe headache
- Double vision
- Temporary graying or blacking out
- Orbital ache or pain

Neurologic symptoms. Ask whether patients have experienced any of the following neurologic symptoms or problems:

- Previous brain trauma or brain problem
- Numbness, weakness, or tingling
- Headaches, especially those that awaken them in the morning
- A loss of libido

Signs. Although optic disc pallor is a hallmark of a nonglaucomatous condition, said Dr. Subramanian, look for other signs like these as well:

- Proptosis, droopy eyelid, or facial asymmetry
- Loss of central visual acuity without a loss of peripheral vision
- Central scotoma or visual field that respects the vertical meridian
- Optic nerve pallor
- Optic nerves that are symmetric in appearance to each other, but 1 visual field is very different

GLAUCOMA PLUS

A Case of "Ticks and Fleas on the Same Dog"

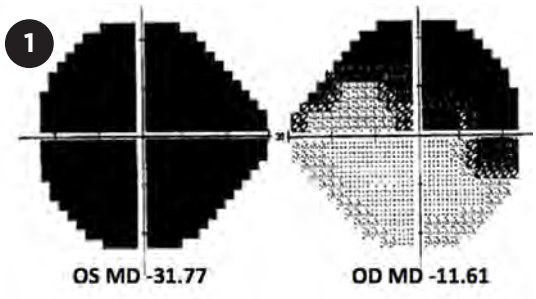
A 70-year-old woman was referred to Dr. Levi's clinic with chronic visual loss. Her medical history included hypertension, obstructive sleep apnea, well-controlled diabetes, and breast cancer that was treated in 1999 and was in remission.

Her ocular history included laser and cryotherapy in each eye in the 1990s for retinal holes due to lattice degeneration. She had cataract extraction in her right eye in 2005 and in her left eye in 2011.

The patient began to notice a cloud in the vision of her left eye in 2010. This progressed over several months. She was told by a glaucoma specialist that she had normal-tension glaucoma that was worse in the left eye than the right, and he started her on latanoprost.

She was then lost to ophthalmological follow-up but her primary care physician apparently continued to refill the drops. Over the next 2-3 years, she gradually lost vision in the left eye. In 2014 she began to notice visual changes in the right eye and returned to the retina specialist who had seen her in the 1990s. In July 2014, her IOP was 24 mm Hg in each eye. She was placed on brinzolamide/brimonidine drops and was referred for neuro-ophthalmological evaluation.

On initial neuro-ophthalmological evaluation in August 2014, acuity was 20/30 in the right eye and bare light perception in the left. Hardy Rand and Rittler (HRR) color plates was 3/6 in the right eye. Visual field testing showed a dense superior arcuate defect in the right eye and the mean deviation



was –11.61, and no responses in the left (Fig. 1). There was a left relative afferent pupillary defect. There was no clinical evidence of Horner syndrome. Extraocular movements were full. Trigeminal nerve function, including corneal sensation, was symmetric and normal. IOP was 14 mm Hg in each eye. There was 0.8 cupping of the right disc with pallor of the remaining neuroretinal rim. The left disc was completely cupped. Because of the pallor of the neuroretinal rim in both eyes, an MRI scan was done; it showed a large sellar mass with suprasellar extension and

- Unilateral or very asymmetric damage
  - Afferent pupillary defect (APD)
  - Color desaturation
- Conjunctival injection or chemosis

Ophthalmic Exam: Keep an Open Mind

Above all, be suspicious, said Dr. Cockerham. "Once a person gets a label of glaucoma, it often doesn't get challenged, even when the patient ends up with a different doctor. The most suspicious diagnosis is unilateral normal-pressure glaucoma with an afferent pupillary defect. This is never the correct diagnosis."

If a patient says they have glaucoma, make sure you agree, said Dr. Subramanian. "If something 'smells funny' or doesn't quite fit, don't be afraid to question another ophthalmologist's diagnosis."

A comprehensive ophthalmic exam. To confirm or rule out a diagnosis of glaucoma, Leah Levi, MD, at Scripps Health in San Diego, conducts a comprehensive ophthalmic exam.

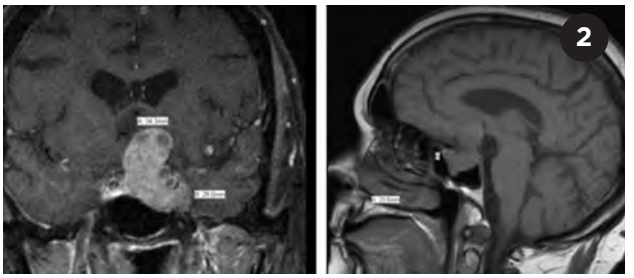
"This includes checking acuity, color vision, pupils, and visual fields, and looking for eye movement problems," she said.

"A patient with orbital problems may not be able to completely move his or her eyes in all directions," added Dr. Cockerham. "Delegating the pupil and motility testing to your technician can be a problem."

Testing intraocular pressure (IOP) is obviously important, said Dr. Vold, and if there are concerns about optic nerve head disease, additional visual fields may be needed. "A thorough vascular evaluation by an internist may be necessary to rule out uncontrolled diabetes or hypertension, and a fluorescein angiogram [may be needed] to spot a previous retinal injury from an old vein occlusion," he said.

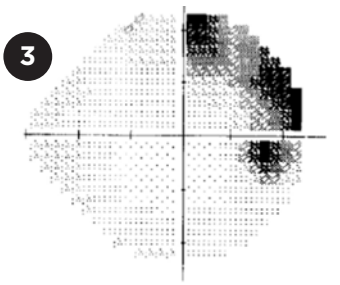
Look—with the light on. "The most confusing patient of all is one with a family history of glaucoma, no history of brain issues, and no symptoms whatsoever," said Dr. Cockerham. If you suspect an abnormality, she said, turn on the light to see the patient's eyes and face more clearly.

"A lot of eye specialists work in dim rooms, going from slit lamp to slit lamp," she said. "We



left cavernous sinus invasion (Fig. 2).

In September 2014 the patient underwent subtotal resection of the mass, which proved to be a pituitary adenoma. The resulting decompression of the anterior visual pathways led to improvement of the color vision to 4.5/6 in the right eye. Visual field testing in the right eye improved; the mean deviation in the right eye improved to –4.43. In addition, a superior vertical step was revealed reflecting the chiasmal compression (Fig. 3). The left eye did not improve. The patient's last examination in June 2018 was stable as was her MRI scan. She has continued to use the drops in her right eye.



TAKE-HOME LESSONS

- **Patients with glaucoma need to be followed by an ophthalmologist.** This patient with glaucoma was lost to ophthalmological follow-up for about 3 years while she progressively lost vision, but her primary care physician continued to prescribe her glaucoma drops.
- **More visual field loss than expected.** This patient had more visual field loss than expected for the degree of cupping as well as faster progression of visual loss than expected for glaucoma, suggesting a nonglaucomatous condition.
- **Pay attention to pallor.** Uncommonly, compression of the anterior visual pathways can produce cupping that is similar to glaucoma, but in these patients the remaining neuroretinal rim will show pallor. The pallor in this case indicated that the patient had a chronic nonglaucomatous optic neuropathy in addition to glaucoma. An MRI scan was therefore indicated.

need to look at these patients in a fully lighted room to see if there is asymmetry of the face or globe position or evidence of bilateral involvement, like thyroid eye disease." Other signs to watch for? "In a patient with a meningioma, for example, the temporal aspect of the face overlying the meningioma may get bigger," she said, "and a carotid-cavernous sinus fistula will cause a characteristic dilation of the vessels on the surface of the eye, and eyelid swelling and proptosis."

Palpate and measure. If you suspect an orbital problem, checking resistance to retropulsion can be helpful in detecting a mass or enlarged muscles behind the eye, said Dr. Cockerham. This is particularly helpful in Asian patients who do not become proptotic like other ethnicities. Dr. Levi also recommends measuring whether 1 eye is more proptotic than the other by using exophthalmometry, if available. Taking a photo from above can also be helpful, said Dr. Cockerham.

Visual fields. Any ischemic optic neuropathy can produce visual field defects similar to those seen in glaucoma, said Dr. Subramanian. Although certain patterns may raise glaucoma red flags, added Dr. Cockerham, visual field defects in a patient with a tumor and another with true glaucoma can be indistinguishable. "There's nothing that's pathognomonic."

In addition, she said, digital perimetry is less clear than manual visual fields are in respecting the vertical meridian and in isolating a cecocentral scotoma. "There's noise in the signal of automated visual fields," said Dr. Cockerham. "The Humphrey visual field SITA testing, for example, fills in the information in between stimulus points, and this can mute neurologic visual field patterns that are more easily seen when a skilled technician has carefully plotted the Goldmann visual field."

Still, automated visual fields can offer clues. For example, central loss is indicative of retina or optic nerve maladies, as opposed to glaucoma, said Dr. Vold. And in normal-tension glaucoma, patients usually don't have visual acuity loss until later in the disease.

Whenever possible, it helps to look at visual fields of both eyes together, said Dr. Subramanian. "If you don't look at them side by side, you may miss a homonymous visual field defect or even a bitemporal hemianopia. Your brain may fail to recognize the pattern if you don't have both visual fields sitting in front of you at the same time."

Fundus exam. "Over time, we've evolved to the point where people equate optic disc cupping to glaucoma," said Dr. Cockerham. "But it is just 1 of many optic nerve processes that can cause cupping." If the neuroretinal rim has pallor, it's definitely a red flag that you are not simply dealing with glaucoma, said Dr. Levi. "With glaucoma, you may have cupping, but the actual surrounding rim is normal in color and looks healthy." Spotting optic disc pallor is key to preventing a misdiagnosis, agreed Dr. Subramanian.

"In addition, with ischemic optic neuropathy, crowded or hypoplastic nerves are more common," said Dr. Vold.

OCT. Because optic nerve fiber changes are not specific to glaucoma, OCT won't be definitive in differentiating it from nonglaucomatous problems, said Dr. Levi, but an OCT scan may be helpful as a baseline for future follow-up.

"Because OCT is structural, however, it can provide a very clean delineation along a particular anatomic boundary," said Dr. Subramanian. "That helps you to say, 'I'm seeing damage here in a more diffuse pattern rather than the typical superior and inferior loss, and that makes me concerned this is something other than glaucoma.'"[1]

With glaucoma, said Dr. Vold, you'll typically see inferior rim retinal nerve fiber layer loss before you see it anywhere else. "This area is usually affected first, then superior next, nasal third, and temporal last," he said.

Even though certain patterns may be generally typical for glaucoma, they are not diagnostic, said Dr. Levi. For instance, if there is a tumor compressing the optic nerve from below, you will also get inferior RNFL thinning—so this finding is not specific to glaucoma and can't be interpreted in isolation of the rest of the clinical picture. "Conversely, certain patterns are very atypical for glaucoma and should raise alarm bells." These patterns include segmental RNFL thinning due to a loss of signal caused by media opacities, or sectoral peripapillary decrease in RNFL due to branch retinal vein occlusion.

In all patients but especially those under age 40, Dr. Subramanian also checks the source images for optic disc

drusen, which can mimic glaucomatous defects.

Specialized imaging. A variety of red flags might warrant specialized imaging. Asymmetry may be one, said Dr. Cockerham, because glaucoma does not tend to be an asymmetric process. The following red flags indicate a nonglaucomatous problem is to blame, rather than glaucoma:

- The patient has unilateral normal-pressure glaucoma with an APD, especially if the APD is more than a subtle one.
- The patient has chronic open-angle glaucoma with an APD, especially if it's more than subtle.
- The optic nerve is more pale than cupped.
- Visual field loss is progressing more rapidly than expected for glaucoma.
- Visual field loss is progressing despite normal IOP or IOP that's under control.
- Severity of cupping doesn't match the visual field defect.
- The OCT of the optic nerve and macula does not correlate with the visual fields.
- The visual fields or macular ganglion cell OCT have a vertical feel to them (homonymous pattern/bitemporal/junctional).
- There are signs or symptoms of other nerve involvement, such as double vision or a droopy eyelid.

Signs and symptoms in synch? Another way to suss out nonglaucoma entities: "When making your assessment, don't rely too heavily on any single particular piece of data and ignore others," said Dr. Subramanian. Symptoms and signs need to align, emphasized Dr. Vold.

For example, it's important to take note when a patient has an elevated IOP and some degree of vision loss—whether central visual acuity or a visual field abnormality—but the appearance of the optic disc doesn't quite match, said Dr. Subramanian.

Or, in a patient with a potential pituitary tumor or other compressive lesion of the optic nerve or retrochiasmal visual pathway, comparing right and left eyes may reveal clues. "Analyzing the macular ganglion cell complex, you may see a pattern of ganglion cell loss that matches the visual field defect and can really demonstrate a homonymous or bitemporal defect," he said. Many glaucoma specialists do not look at this testing and may miss that the problem is retrochiasmal, added Dr. Cockerham.

Refer to a Neuro-Ophthalmologist

If the clinical picture is not consistent with the degree of "glaucoma" you are seeing, it may be time to refer to a neuro-ophthalmologist, said Dr. Levi. What results in most referrals—and is most troubling for many general ophthalmologists and some glaucoma specialists—are patients who are losing visual fields despite what seems to be good control of their IOP. "Much of the time, patients referred to me do have glaucoma, however, and I can ascertain that by careful review of their clinical findings without getting a scan," she said.

If needed, imaging may involve magnetic resonance imaging (MRI) or a magnetic resonance angiogram or computed tomography (CT) angiography. "If you have a high degree of suspicion and don't feel comfortable reviewing these scans," said Dr. Cockerham, "consider referring them to a neuro-ophthalmologist."

Dr. Cockerham cited the case of a patient where this didn't happen. The patient had been seen by 5 previous eye care providers, but over the course of 6 months she lost vision in the involved eye to no light perception. In this patient, the noncontrast CT scan of the brain was done in an emergency department and had been read as normal, but an apical mass was visible on 1 digital slice. An MRI with gadolinium revealed a large orbital apex mass that was found to be steroid-responsive, but there was no return of vision.

1 Gupta PK et al. *Open Neurol J.* 2011;5:1-7.

MEET THE EXPERTS

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

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How the Oct. 1 Changes to ICD-10 Are Impacting Ophthalmologists

On Oct. 1, CMS implemented hundreds of changes to the ICD-10 codes. The updates that are most likely to impact ophthalmology include 26 deleted diagnoses, 6 description changes for the epiphora family, and 120 new ICD-10 codes. This article highlights the key changes.

As payers update their CPT-to-ICD-10 linkage, be sure you also update your practice management software and electronic health record (EHR) systems.

Deleted Codes

Deleted eyelid codes. The codes listed below were deleted and replaced with codes that have greater specificity.

- C43.11 *Malignant melanoma of right eyelid*
- C43.12 *Malignant melanoma of left eyelid*
- The C44- family of codes representing *Other and unspecified malignant neoplasm of skin*
- The D03- family of codes representing *Melanoma in situ*
- The D04- family of codes representing *Carcinoma in situ of skin*

Replacement eyelid codes. The replacement codes don't just indicate whether the diagnosis applies to the left or right eyelid; they also indicate whether it is the upper or lower eyelid.

Example: C43.11 is replaced with C43.111 and C43.112, which represent the upper and lower eyelid, respectively.

Deleted codes for postprocedure infections have more detailed replacements. The T81.4- family of codes representing *Infection following a procedure* have been deleted and replaced with codes that indicate whether it is an initial encounter, a subsequent encounter, or a sequela.

A catch-all code is replaced. The Oct. 1 changes also delete H57.8 *Other specified disorders of eye and adnexa,* but they add H57.89, giving it the same generic catch-all descriptor.

Don't Miss Out on These ICD-10 Resources

Make sure you're up to speed on this year's ICD-10 updates, which went into effect on Oct. 1.

Get the Academy's free ICD-10 materials. Visit aao.org/icd10 and make sure you have the latest versions of the subspecialty-specific guides to ICD-10 codes, as well as the latest versions of the decision trees. The latter will help you identify the correct ICD-10 code for specific conditions, such as blepharitis or lagophthalmos.

Get the updated local coverage determinations (LCDs). Visit aao.org/lcds to find the LCDs that apply to you.

Buy *ICD-10-CM for Ophthalmology: The Complete Reference.* This reference lists all of ophthalmology's new and updated codes. It is available as a book or as an online subscription (aao.org/codingproducts).

Get coding news updates. Go to aao.org/practice-management/news for coding updates, regulatory news, coding top-10s, and "Ask the Expert" responses to common—and not-so-common—coding queries.

Got questions? When ophthalmology practices have a coding conundrum, they can request help via email (coding@aao.org or icd10@aao.org), at their state's Codequest event (aao.org/codequest), and on the AAOE's eTalk listserv (aao.org/practice-management/listserv).

Changes to the Epiphora Codes

Description changes impact the epiphora diagnosis family. In the listings below, underlining and ~~strikethroughs~~ are used to indicate new and deleted text, respectively.

- H04.201 *Unspecified epiphora right side ~~lacrimal gland~~*
- H04.202 *Unspecified epiphora left side ~~lacrimal gland~~*
- H04.203 *Unspecified epiphora, bilateral ~~lacrimal gland~~*
- H04.221 *Epiphora due to insufficient drainage, right side ~~lacrimal gland~~*
- H04.222 *Epiphora due to insufficient drainage, left side ~~lacrimal gland~~*
- H04.223 *Epiphora due to insufficient*

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

drainage, bilateral ~~lacrimal glands~~

Warning. Do not use these 2 codes:

- H04.209 *Unspecified epiphora, unspecified side ~~lacrimal gland~~*
- H04.229 *Epiphora due to insufficient drainage, unspecified side ~~lacrimal gland~~*

While these 2 side-unspecific codes are legitimate ICD-10 codes, they are not payable, and your claim will be denied if you report them.

The ABCs of Eyelid Laterality

A welcome change but a new adjustment occurs with the lagophthalmos (H02-) family of codes. Previously, you needed 1 code for the upper eyelid and a second for the lower eyelid to indicate that lagophthalmos had been diagnosed in both.

Now, when used in the sixth position of those codes, A, B, and C represent both the upper and lower eyelids of the right eye, the left eye, and both eyes, respectively.

Example:

- H02.21A *Cicatricial lagophthalmos right eye, upper and lower eyelids*
- H02.21B *Cicatricial lagophthalmos left eye, upper and lower eyelids*
- H02.21C *Cicatricial lagophthalmos, bilateral, upper and lower eyelids*

Caveat. Some families of codes—such as the meibomian gland dysfunction family (see below) and the blepharitis family (H01-)—don't have a bilateral code.

Example:

- H01.01A *Ulcerative blepharitis right eye, upper and lower eyelids*
- H01.01B *Ulcerative blepharitis left eye, upper and lower eyelids*

Meibomian Gland Dysfunction

The new ICD-10 codes include the following codes for meibomian gland dysfunction (MGD):

- H02.881 *MGD right upper eyelid*
- H02.882 *MGD right lower eyelid*
- H02.884 *MGD left upper eyelid*
- H02.885 *MGD left lower eyelid*
- H02.88A *MGD right eye, upper and lower eyelids*
- H02.88B *MGD left eye, upper and lower eyelids*

Warning. Do not use these 3 codes:

- H02.883 *MGD of right eye, unspecified eyelid*
- H02.886 *MGD of left eye, unspecified eyelid*
- H02.889 *MGD of unspecified eye, unspecified eyelid*

Although H02.883, H02.886, and H02.889 are legitimate ICD-10 codes, their lack of specificity will cause payers to deny your claim.

3 Tips for ICD-10 Coding

When linking CPT codes to ICD-10 codes, remember laterality. When the CPT code requires modifiers –RT or –LT (to indicate the right and left eye, respectively) and the ICD-10 code has laterality, the CPT code that has –RT should be linked to the ICD-10 code for the right eye and the CPT code with –LT linked to the ICD-10 code for the left eye. If you instead report a bilateral ICD-10 code, the claim will probably be denied.

Example: Coding for complex cataract surgery in the right eye. CPT code 66982–RT is linked with H25.11 *Age-related nuclear cataract, right eye,* which indicates the type of cataract. It is also linked with H27.111 *Subluxation of lens, right eye* when the operative report indicates the intraocular lens was supported by using permanent intraocular sutures or a capsular support ring was employed.

Did you inadvertently bill for cataract surgery twice in the same eye? If over the past 12 months you erroneously reported cataract surgery twice in the same eye, you can correct that error over the phone—and avoid a data-driven recovery audit—by calling the Medicare Administrative Contractor for your state. You only get 1 opportunity to make this correction, so make sure you remember to correct the ICD-10 code, too.

Payers typically don't pay for sequelae. Diagnosis codes for injury or trauma use an A, D, or S as the seventh character to indicate initial encounter, subsequent encounter, or sequela, respectively (e.g., S05.01XS *Injury of conjunctiva and corneal abrasion without foreign body, right eye, sequela*). Other than workers' compensation, most federal and commercial payers consider sequela a noncovered diagnosis and would deny the claim.

Case Study: How an Ophthalmic Practice Tackled Its Profitability Problem

Although ophthalmologists collect ample patient data before making a diagnosis, they often lack the resources to collect enough business data before making key decisions about their practice. In the case study below, a physician owner of a practice, Dr. Conch,* thought, "Our employee costs are too high—we need to cut those somehow." If she had acted on that 1 perception, she might have terminated staff, cut employee benefits, or reduced pay rates—responses that could have damaged her practice. Instead, Dr. Conch and her practice manager, Mr. Duenas,* gathered facts before acting. They used free resources from the Academy—the Academetrics Benchmarking Tool and Academetrics Ophthalmic Salary Survey—which provided critical context that helped pinpoint the underlying issues.

Identifying the Problem

Dr. Conch is the managing partner of a practice with 5 full-time comprehensive ophthalmologists and 25 full-time support staff.

Revenue summary. Revenues for the practice in 2017 (not including optical) were $3.5 million, $1 million of which was paid to the employees as wages. Over the course of the year, the doctors had 17,500 patient encounters in their office, including all of the Evaluation & Management and Eye codes that were billed and all postoperative exams.

High staff costs? Concerned that the practice is spending too much revenue on staff members, Dr. Conch approaches her new practice manager, Mr. Duenas, about reducing that cost.

The practice administrator's dilemma. Mr. Duenas is alarmed because he knows that the most obvious solutions could harm the practice. Specifically, cutting staff wages or benefits might cause staff turnover, which tends to increase costs as new employees struggle to learn the operations of the practice. Alternatively, laying off staff could hamper the practice's ability to provide good service to patients, likely resulting in attrition of patients, and, consequently, further reduction in revenues. As a new manager, Mr. Duenas realizes that such a path is not conducive to keeping his job either!

Accessing Helpful Resources

To better understand the practice's financial situation, Mr. Duenas goes to aao.org/benchmarking and registers for both the Academetrics Benchmarking Tool and Ophthalmic Salary Survey (see "Academy/AAOE Benchmarking Resources," above). First, he enters into the 2 surveys his practice's 2017 data, including numbers from the profit-and-loss statement, payroll, and billing reports. After entering all relevant information, he compares his data to the aggregated numbers in the databases. Here, he begins to identify the real challenges for the practice.

Academy/AAOE Benchmarking Resources

The American Academy of Ophthalmic Executives (AAOE), the practice management arm of the Academy, sponsors 2 programs that allow you to track your business data against benchmarks from other ophthalmology practices.

The Academetrics Benchmarking Tool allows you to compare your financial and patient flow data with benchmarks calculated from participating ophthalmology practices.

The Academetrics Ophthalmic Salary Survey, developed in conjunction with the Outpatient Ophthalmic Surgical Society, helps you see how your staff salary rates compare with other practices.

Both resources are free to those practices that participate by adding their information to the confidential database any time throughout the year.

For more information, visit aao.org/benchmarking where you will find details about and instructions for using both the Academetrics Benchmarking Tool and Ophthalmic Salary Survey.

BY **DEREK PREECE, MBA,** AND **DIXON DAVIS, MHSA,** PRINCIPALS AND CONSULTANTS AT BSM CONSULTING.

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

Getting Specific Feedback

Staffing ratios. Mr. Duenas first looks at the staff payroll ratio (employee payroll divided by total collected revenue) and finds that it is 28.5%, which is high—in the 75th percentile for ophthalmology practices that submitted approved data to the survey. The practice's total collections per full-time employee is only $140,000, which is very low—barely above the 25th percentile on the Academetrics Benchmarking Tool. "So maybe Dr. Conch is correct that we spend too much on staff," he thinks.

Investigating further, he sees that his practice's ratio of staff members to doctors is 5.0 (25 staff members divided by 5 doctors). Interestingly, he finds that figure to be low—less than the median figure from the survey and just above the 25th percentile. "So, if we don't have too many staff members but our payroll ratio is high, are we paying employees too much?" he wonders.

Salaries. Turning to the Academetrics Ophthalmic Salary Survey, Mr. Duenas looks at the pay rates for each of his staff members and finds that—although some are paid a little above the median for their positions and others are paid a little below—overall, his employees are compensated within the normal range for their specific jobs.

Thinking through what he has learned so far, Mr. Duenas realizes that the 2 ratios he is most concerned about—the staff payroll ratio (28.5%) and collections per employee ratio ($140,000)—share practice collections as a common factor. Going back through the benchmarking survey reports, he checks how the practice's collections stack up against those of other practices.

Problems With Productivity

Upon comparing his practice's collections data against benchmarking data, he discovers a few startling facts.

Revenue seems low. His 5 comprehensive ophthalmologists produce $3.5 million per year in collections, an average of $700,000 per full-time doctor, which is well below the 25th percentile for other practices. Wondering why his numbers are low, he notes that the practice had 17,500 encounters (an average of 3,500 per doctor) for the year, which is also below the 25th percentile.

Per patient collections are subpar. In addition, the doctors' average collections per encounter is $200, which is less than that of a typical comprehensive ophthalmologist. So, his doctors are not seeing as many patients per year as their peers, and they are collecting less cash per patient. The result: a significant shortfall in revenues.

Taking action. His next tasks are clear. First, he needs to help the doctors increase the number of patients they see each year. Then, to see if he can help them raise per-patient collections, he plans to review CPT codes that have been used to bill patient encounters to see if "downcoding" is responsible for below average per-patient collections.

Improving the practice's revenues will decrease the staff payroll ratio and raise collections per full-time employee, plus help the doctors increase earnings.

Looking further. Mr. Duenas realizes that he can examine other ratios to learn more about the practice's situation. For example, he can compare the number of patient encounters per front desk and back office staff to indicate whether he is under- or overstaffed in those areas. In addition, he can check accounts receivable ratios to determine whether the practice is collecting money effectively, and he can check optical shop ratios to evaluate how well that operation is doing.

Compare Your Practice

This case is just 1 example of how the Academetrics Benchmarking Tool and Ophthalmic Salary Survey can tell a story about the inner workings of a practice. These benchmarks provide valuable information for making appropriate, disciplined decisions to both improve your practice and inoculate it against poor choices made in the absence of good, comparative data.

*Doctor and administrator names are fictitious.

Mr. Preece and **Mr. Davis** are principals and consultants with BSM Consulting, headquartered in Incline Village, Nev. *Financial disclosures: None.*

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ASSESSMENT

Cynthia Matossian, MD
Matossian Eye Associates
Hopewell, New Jersey

"Ocular surface disease and dry eye problems are critically important to identify prior to cataract surgery. I use the placido disc map of the OPD III to illustrate tear film instability: rings that are not perfectly round, are wobbly, irregular, or broken, signify an unhealthy surface. I show the warped black and white ring images to my patients to let them know they have a pre-existing disease called dry eye syndrome which is chronic and progressive in nature. I emphasize that dry eye disease needs ongoing treatment whereas cataracts are removed by surgery and will not recur. I distinctly want patients to know that cataract surgery did not give them their dry eye condition. Patients, for the first time, are able to better understand their ocular surface condition by seeing the irregularities of their tear film."

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Academy Notebook

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WHAT'S HAPPENING

Dr. Tuck Named Eye Health Hero Award Recipient

During the Global Welcome lunch at AAO 2018, the American Institute for the Prevention of Blindness presented Kenneth D. Tuck, MD, former Academy President, with the Eye Health Hero Award. Dr. Tuck was recognized for spearheading an international mentoring program when he was President.

Since its start in 2000, the Rotary Club Host Project has provided 122 young ophthalmologists from 57 developing countries the opportunity to experience the innovative educational programs and technology available at the Academy's annual meeting. Developed through the Academy's Host an Ophthalmologist Program and with the help of Rotary Clubs, Dr. Tuck has urged Rotarian ophthalmologists in the United States to host a young international ophthalmologist at their practice the week before the annual meeting. This allows guests time to acclimatize and see U.S. practices before attending the Academy's annual meeting, where they can access all courses, seminars, exhibits, and social events.

After stepping down as head of the Rotary Club last year, Dr. Tuck reflected, "We're building relationships and exposing these young doctors to other cultures and ways of practicing ophthalmology. I am so excited that we are building a global network of young leaders in ophthalmology who reach out and strengthen eye care in their own countries and, indeed, the world."

EYE HEALTH HERO. *Dr. Tuck with his rotary guest from Haiti, Regine Edouard, MD, and his wife, Sarah Tuck.*

To learn more about the program and volunteering, visit aao.org/international/outreach/programs.

2018 Member Engagement Survey Results

The Academy relies on data to develop and enhance programs and services that are responsive and relevant to member needs. Direct feedback from members through surveys and focus groups allows us to both measure awareness and value of Academy member benefits and services and to determine the key drivers of member engagement and value perceptions.

Recently, the Academy enlisted Loyalty Research Center to conduct the 2018 Member Engagement Survey. Results are based on 1,165 responses collected from a representative sample of the Academy's membership.

U.S. practicing ophthalmologist members regard the Academy as an organization that offers year-round value, is forward-thinking, and understands their professional needs.

- 86% believe the Academy helps them to be better ophthalmologists.
- 90% see the Academy as the leading source for reliable ophthalmic information and education.
- 89% consider the Academy as the leading legislative and regulatory advocate for ophthalmologists.

Members say that the most critical issues affecting ophthalmology are reimbursement, optometry scope of practice, and legislation/regulation. These concerns remain unchanged from the 2015 survey findings. Members reinforce the need for the Academy to continue to champion fair physician reimbursement, stop the expansion of optometrists' scope of practice, and advocate for regulatory relief. Most rate the effectiveness of the Academy's advocacy efforts as excellent or very good. Eighty-nine percent feel the Academy provides a collective voice for the profession, and 63% feel the Academy is either very good or excellent at positively affecting federal regulatory and/or legislative issues important to ophthalmology.

International practicing ophthalmologist members see the Academy as a leader in ophthalmic education. The annual meeting, *Ophthalmology* journal, *EyeNet Magazine,* and the Ophthalmic News and Education (ONE) Network all receive best-in-class ratings. Most rank the annual meeting as the best

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ophthalmology conference in the world—with 96% rating the annual meeting as excellent, very good, or good.

TAKE NOTICE

MIPS: Applying for the EHR Hardship Exception?

In the Merit-Based Incentive Payment System (MIPS), the electronic health record (EHR)–based performance category is called promoting interoperability (PI). It is 1 of 4 MIPS performance categories and contributes up to 25 points to your MIPS final score (0-100 points). Typically, if you were to report no PI measures, your PI score would be zero and your maximum MIPS final score would be 75 points.

The significant hardship exception. You can apply to be exempted from the PI performance category if you are facing a significant hardship, such as insufficient internet connectivity or extreme and uncontrollable circumstances.

If the Centers for Medicare & Medicaid Services (CMS) accepts your application for a hardship exception, PI's contribution to your final score will be reweighted to zero, and the quality performance category's contribution will be reweighted upward; thus you could still earn the maximum MIPS final score of 100 points despite not reporting any PI measures.

New for 2018: Special consideration given to small practices. If small practices can demonstrate that obtaining and maintaining certified EHR technology would cause undue hardship, CMS may grant them a PI hardship exception.

Submit your application by Dec. 31, 2018. For guidance on submitting this application, see aao.org/medicare/advancing-care-information-exceptions.

Enter the EyeWiki Contest

U.S. residents and fellows, November is your last opportunity to submit an original EyeWiki article for the chance to win an all-expenses-paid trip in April 2019 to the Academy's Mid-Year Forum in Washington, DC. Submissions, which will be judged based on quality of work, should pertain to 1 of the following categories:

- Cataract/Refractive Surgery/Cornea/Anterior Segment
- Retina/Vitreous/Uveitis/Oncology/Pathology
- Glaucoma/Neuro-Ophthalmology
- Pediatrics/Strabismus/Oculoplastics/Orbit

To enter, use the gray "Enroll in Residents and Fellows Contest" submission button at the top of any EyeWiki article related to your entry. The submission deadline is Dec. 1, 2018. Multiple entries are allowed. See www.eyewiki.org/Residents_and_Fellows for details.

For international doctors interested in contributing to EyeWiki, visit www.eyewiki.org/International_Ophthalmologists for an international contest running through May 2019.

Submit Your Research to *Ophthalmology Glaucoma*

This summer, the Academy and the American Glaucoma Society collaborated in launching *Ophthalmology Glaucoma.*

This new journal provides an opportunity to disseminate your glaucoma research directly to those who find it most relevant. Joining the ranks of the Academy's esteemed *Ophthalmology* and *Ophthalmology Retina, Ophthalmology Glaucoma* provides readers with innovative, peer-reviewed works.

Submit your research at https://www.evise.com/profile/#/OGLA/login. **Subscribe** at www.ophthalmologyglaucoma.org.

Remember the Foundation on Giving Tuesday

After the holiday shopping rush on Black Friday and Cyber Monday, kick off your year-end charitable giving on Giving Tuesday, Nov. 27. Entering its sixth year, this global day of philanthropy encourages donating to initiatives that are important to you.

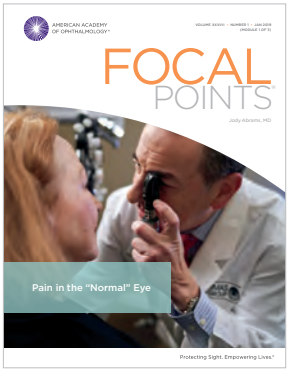
This year, consider supporting Academy programs including the Ophthalmic News and Education (ONE) Network, EyeCare America, global outreach, and the Museum of Vision campaign. Your tax-deductible gift can be made in honor or memory of someone special.

To donate, visit aao.org/foundation/giving-options.

ACADEMY RESOURCES

Evidence-Based Solutions for Your Practice

Starting in 2019, each issue of *Focal Points* will tackle important new research and provide practical tips on how to efficiently integrate new treatments and methods into your practice. Topics for 2019 include "Pain in the 'Normal Eye,'" "Gene and Stem Cell Therapy for Retinal Disorders," "Corneal Endothelial Surgery," and "Optical Coherence Tomography in Glaucoma Progression and Diagnosis."



Subscribe to *Focal Points Digital* to get a new issue every month, plus access to the digital archive. Print subscribers get 12 print issues, plus all the benefits of *Focal Points Digital.* Visit aao.org/focalpoints.

Order 2019 Coding Tools to Maximize Reimbursements

Your coding tools for 2019 are now available. Whether you're a beginner or experienced coder, whether you work at a comprehensive or subspecialty-specific practice, the Academy has the coding references and training guides to ensure you're appropriately reimbursed for the services you provide.

Browse the offerings at aao.org/codingproducts.

New Coding Audit Success Toolkit Available

Stay compliant with payer requirements and proactively navigate the audit process using the Academy's new Coding Audit Success Toolkit (#0120444V). This downloadable PDF includes valuable checklists and helpful guidelines you can use daily.

Order today at aao.org/audit-toolkit.

New Business Handbook for Retina Practices

Strategically Grow Your Retina Practice (#0121003V), the first of 3 handbooks in the new Profitable Retina Practice series, reveals the essentials for growing a retina practice and provides real-life case studies to guide implementation.

Order today at aao.org/business-of-retina.

MEETING MATTERS

AAO 2019 in San Francisco

AAO 2019 will take place Oct. 12-15, preceded by Subspecialty Day, Oct. 11-12, at The Moscone Center in San Francisco. Be inspired at the world's largest and most comprehensive ophthalmic meeting, offering hundreds of courses and sessions on topics ranging from cataract complications to artificial intelligence in ophthalmology.

For more information, visit aao.org/2019.

2019 Abstract Deadlines

Want to create content for AAO 2019 in San Francisco? Submit your ideas for an instruction course or new Skills Transfer lab. Abstracts will be accepted from Dec. 13, 2018, through Jan. 8, 2019.

To submit, visit aao.org/presenter-central.

Claim CME for AAO 2018

AAO 2018 and Subspecialty Day registrants whose attendance was verified onsite in Chicago received an email with a link and instructions for claiming Continuing Medical Education (CME) credits online. Starting Thursday, Dec. 13, attendees can claim credits (if they did not already do so at the meeting) and obtain transcripts that include AAO 2018/Subspecialty Day credits at aao.org/cme-central. The Academy transcript will not list individual course attendance, only overall credits claimed for educational activities.

For more information, visit aao.org/annual-meeting/cme.

View the Virtual Meeting

The Virtual Meeting is a free online component of AAO 2018. View 13 archived sessions from Chicago (approximately 20 hours of educational content) through Jan. 31, 2019. Access the Virtual Meeting with your Academy login and password. The AAO 2018 Virtual Meeting cannot be reported for CME credit.

For more information, visit aao.org/virtual-meeting.

D.C. REPORT

Academy Promotes Veteran Eye Care

SERVING THOSE WHO SERVED OUR COUNTRY. *Dr. Melicher Larson performs an eye exam on a veteran during the American Legion National Convention.*

For veterans, the risk of eye injury is much higher than for the general U.S. population.

Advocacy. Committed to ensuring that veterans and active-duty service members receive the highest quality eye care, the Academy's recent advocacy efforts have focused on a wide range of issues, including the following:

- maintaining a VA directive, which mandates that only ophthalmologists will perform laser surgery in U.S. Department of Veterans Affairs (VA) medical facilities;
- promoting the VA's new Technology-Based Eye Care Services program, which is expanding veterans' access to basic eye care services;
- supporting the joint Department of Defense/VA Vision Center for Excellence, which was created to improve the care of American military personnel and veterans affected by combat eye trauma; and
- advocating for increased funding for research related to combat-related vision trauma.

Volunteering. In addition to its advocacy work with the federal government, the Academy also engages in hands-on acts of service to aid veterans.

As part of this service, each year the Academy collaborates with a state ophthalmology society at the National Convention of the American Legion, the largest U.S. wartime veterans service organization. This year, the Academy joined forces with the Minnesota Academy of Ophthalmology (MAO) to provide glaucoma screenings for veterans during the convention from Aug. 24-30 in Minneapolis.

Over the course of 3 days, Minnesota ophthalmologists screened more than 140 veterans for glaucoma and other eye diseases. MAO volunteers identified several glaucoma suspects and assisted 1 veteran with a vitreous hemorrhage who needed immediate surgery.

"This [was] a special opportunity for the MAO to honor our nation's service members at their 100th national convention and provide them with a valuable public service," said Jill S. Melicher Larson, MD, President of the MAO and participant in the screening event.

Next year, the Academy will continue this public service tradition and reach out to the Indiana Academy of Ophthalmology to solicit volunteers for the American Legion's 101st convention in Indianapolis.

Want to Own Content From AAO 2018?

Enjoy AAO 2018 all year. Meetings on Demand offers 8 Subspecialty Day meetings or the AAOE Program; or save and buy the complete package, which includes AAO 2018 highlights—nearly 200 hours and 1,000 presentations.

To learn more, visit aao.org/on demand.

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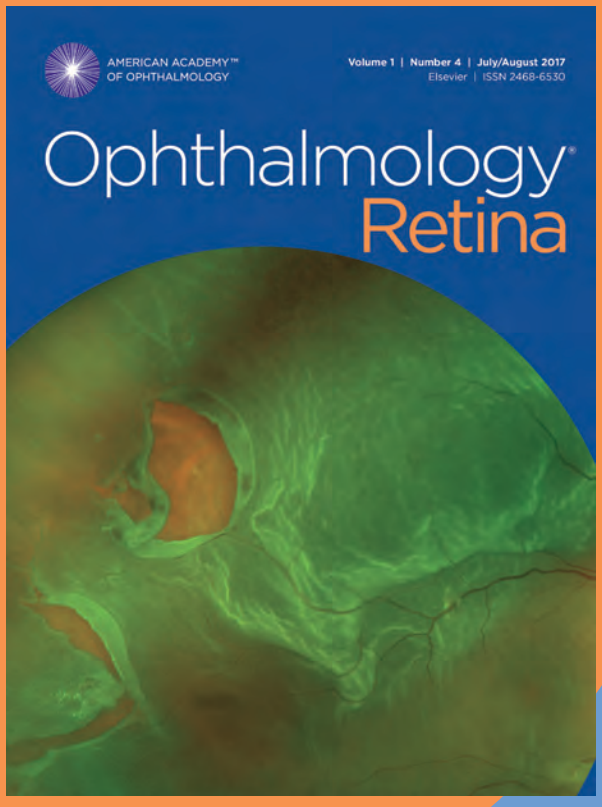

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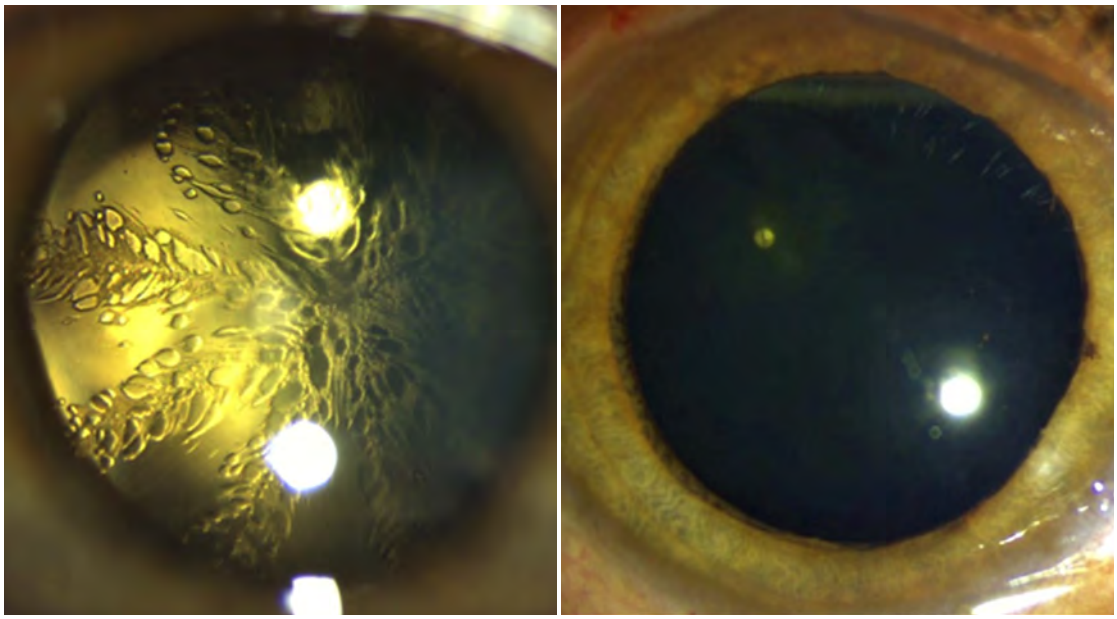
MYSTERY IMAGE

BLINK

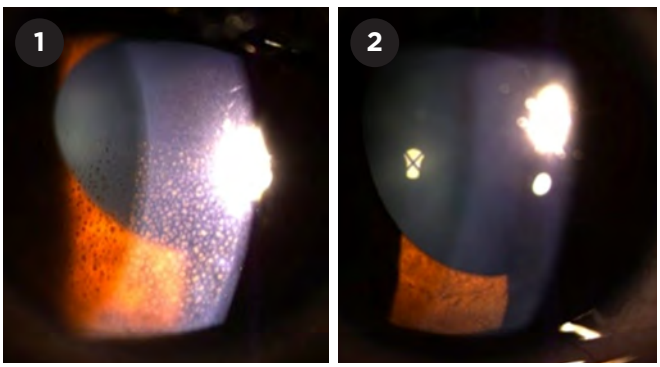


Priya Baigai, MBBS, Advanced Eye Centre, Post Graduate Institute of Medical Education and Research, Chandigarh, India.

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

LAST MONTH'S BLINK

Pigmented Keratic Precipitates in Herpes Simplex Virus Anterior Uveitis



A 27-year-old man presented, complaining of decreased vision in his right eye for 2 weeks. In that eye, best-corrected visual acuity (BCVA) was 20/80 and intraocular pressure (IOP) was 34 mm Hg. The slit-lamp examination showed 2+ cells and flare, along with pigmented keratic precipitates (KPs) in the lower half of the cornea (Fig. 1). In the left eye, BCVA was 20/25, IOP was 12 mm Hg, and the anterior chamber was clear.

Polymerase chain reaction analysis of aqueous humor from the right eye was positive for herpes simplex virus (HSV) DNA. The patient received topical corticosteroids, cycloplegic and antiglaucoma drugs, and oral acyclovir. Three weeks later, the KPs resolved completely and the eye was quiescent (Fig. 2). BCVA at 5 months was 20/20 and IOP was 12 mm Hg.

In addition to high IOP, granulomatous KPs, and sectoral iris atrophy, pigmented KPs are characteristic of HSV-associated anterior uveitis (though a rare association with postoperative endophthalmitis caused by *Propionibacterium acnes* has been reported). Our patient exhibited all of these signs. The authors are following up on this case semiannually for uveitis flare-ups.

WRITTEN BY **ANIRUDDHA K. AGARWAL, MBBS, AMOD K. GUPTA, MBBS, REEMA BANSAL, MD, MBBS.** PHOTOS BY **ARUN KAPIL.** ADVANCED EYE CENTRE, POST GRADUATE INSTITUTE OF MEDICAL EDUCATION AND RESEARCH, CHANDIGARH, INDIA.

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