REVIEW® of Ophthalmology

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Retirement: Preparing for Your Next Act

Creating a Smooth Path to Retirement P. 22

jmi

For the treatment of elevated IOP

UNLOCK TREATMENT POSSIBILITIES

SIMBRINZA™ Suspension provided additional 1-3 mm Hg IOP lowering compared to the individual components[1]

- IOP measured at 8 AM, 10 AM, 3 PM, and 5 PM was reduced by **21-35%** at Month 3[2-4]
- Efficacy proven in two pivotal Phase 3 randomized, multicenter, double-masked, parallel-group, 3-month, 3-arm, contribution-of-elements studies[2,3]
- The most frequently reported adverse reactions (3-7%) in a six month clinical trial were eye irritation, eye allergy, conjunctivitis, blurred vision, dysgeusia (bad taste), conjunctivitis allergic, eye pruritus, and dry mouth[5]
- Only available beta-blocker-free fixed combination[2,3]

INDICATIONS AND USAGE

SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is a fixed combination indicated in the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

Dosage and Administration

The recommended dose is one drop of SIMBRINZA™ Suspension in the affected eye(s) three times daily. Shake well before use. SIMBRINZA™ Suspension may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

IMPORTANT SAFETY INFORMATION

Contraindications

SIMBRINZA™ Suspension is contraindicated in patients who are hypersensitive to any component of this product and neonates and infants under the age of 2 years.

Warnings and Precautions

Sulfonamide Hypersensitivity Reactions—Brinzolamide is a sulfonamide, and although administered topically, is absorbed systemically. Sulfonamide attributable adverse reactions may occur. Fatalities have occurred due to severe reactions to sulfonamides. Sensitization may recur when a sulfonamide is readministered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation.

Corneal Endothelium—There is an increased potential for developing corneal edema in patients with low endothelial cell counts.

Severe Hepatic or Renal Impairment (CrCl <30 mL/min)—SIMBRINZA™ Suspension has not been specifically studied in these patients and is not recommended.

Adverse Reactions

In two clinical trials of 3 months' duration with SIMBRINZA™ Suspension, the most frequent reactions associated with its use occurring in approximately 3-5% of patients in descending order of incidence included: blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, and eye allergy. Adverse reaction rates with SIMBRINZA™ Suspension were comparable to those of the individual components. Treatment discontinuation, mainly due to adverse reactions, was reported in 11% of SIMBRINZA™ Suspension patients.

Drug Interactions—Consider the following when prescribing SIMBRINZA™ Suspension:

Concomitant administration with oral carbonic anhydrase inhibitors is not recommended due to the potential additive effect. Use with high-dose salicylate may result in acid-base and electrolyte alterations. Use with CNS depressants may result in an additive or potentiating effect. Use with antihypertensives/cardiac glycosides may result in additive or potentiating effect on lowering blood pressure. Use with tricyclic antidepressants may blunt the hypotensive effect of systemic clonidine and it is unknown if use with this class of drugs interferes with IOP lowering. Use with monoamine oxidase inhibitors may result in increased hypotension.

For additional information about SIMBRINZA™ Suspension, please see Brief Summary of full Prescribing Information on adjacent page.

Learn more at myalcon.com/simbrinza

SIMBRINZA™
(brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2%

ONE BOTTLE. MANY POSSIBILITIES.

References: 1. SIMBRINZA™ Suspension Package Insert. **2.** Katz G, DuBiner H, Samples J, et al. Three-month randomized trial of fixed-combination brinzolamide, 1%, and brimonidine, 0.2% [published online ahead of print April 11, 2013]. *JAMA Ophthalmol.* doi:10.1001/jamaophthalmol.2013.188. **3.** Nguyen QH, McMenemy MG, Realini T, et al. Phase 3 randomized 3-month trial with an ongoing 3-month safety extension of fixed-combination brinzolamide 1%/brimonidine 0.2%. *J Ocul Pharmacol Ther.* 2013;29(3):
290-297. **4.** Data on file, 2013. **5.** Whitson JT, Realini T, Nguyen QH, McMenemy MG, Goode SM. Six-month results from a Phase III randomized trial of fixed-combination brinzolamide 1% + brimonidine 0.2% versus brinzolamide or brimonidine monotherapy in glaucoma or ocular hypertension. *Clin Ophthalmol.* 2013;7:1053-1060.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE

SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2% is a fixed combination of a carbonic anhydrase inhibitor and an alpha 2 adrenergic receptor agonist indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

DOSAGE AND ADMINISTRATION

The recommended dose is one drop of SIMBRINZA™ Suspension in the affected eye(s) three times daily. Shake well before use. SIMBRINZA™ Suspension may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes apart.

DOSAGE FORMS AND STRENGTHS

Suspension containing 10 mg/mL brinzolamide and 2 mg/mL brimonidine tartrate.

CONTRAINDICATIONS

Hypersensitivity - SIMBRINZA™ Suspension is contraindicated in patients who are hypersensitive to any component of this product.

Neonates and Infants (under the age of 2 years) - SIMBRINZA™ Suspension is contraindicated in neonates and infants (under the age of 2 years*) see Use in Specific Populations*

WARNINGS AND PRECAUTIONS

Sulfonamide Hypersensitivity Reactions - SIMBRINZA™ Suspension contains brinzolamide, a sulfonamide, and although administered topically is absorbed systemically. Therefore, the same types of adverse reactions that are attributable to sulfonamides may occur with topical administration of SIMBRINZA™ Suspension. Fatalities have occurred due to severe reactions to sulfonamides including Stevens-Johnson syndrome, toxic epidermal necrolysis, fulminant hepatic necrosis, agranulocytosis, aplastic anemia, and other blood dyscrasias. Sensitization may recur when a sulfonamide is re-administered irrespective of the route of administration. If signs of serious reactions or hypersensitivity occur, discontinue the use of this preparation *[see Patient Counseling Information]*

Corneal Endothelium - Carbonic anhydrase activity has been observed in both the cytoplasm and around the plasma membranes of the corneal endothelium. There is an increased potential for developing corneal edema in patients with low endothelial cell counts. Caution should be used when prescribing SIMBRINZA™ Suspension to this group of patients.

Severe Renal Impairment - SIMBRINZA™ Suspension has not been specifically studied in patients with severe renal impairment (CrCl < 30 mL/min). Since brinzolamide and its metabolite are excreted predominantly by the kidney, SIMBRINZA™ Suspension is not recommended in such patients.

Acute Angle-Closure Glaucoma - The management of patients with acute angle-closure glaucoma requires therapeutic interventions in addition to ocular hypotensive agents. SIMBRINZA™ Suspension has not been studied in patients with acute angle-closure glaucoma.

Contact Lens Wear - The preservative in SIMBRINZA™, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of SIMBRINZA™ Suspension but may be reinserted 15 minutes after instillation *[see Patient Counseling Information]*.

Severe Cardiovascular Disease - Brimonidine tartrate, a component of SIMBRINZA™ Suspension, has a less than 5% mean decrease in blood pressure 2 hours after dosing in clinical studies; caution should be exercised in treating patients with severe cardiovascular disease.

Severe Hepatic Impairment - Because brimonidine tartrate, a component of SIMBRINZA™ Suspension, has not been studied in patients with hepatic impairment, caution should be exercised in such patients.

Potentiation of Vascular Insufficiency - Brimonidine tartrate, a component of SIMBRINZA™ Suspension, may potentiate syndromes associated with vascular insufficiency. SIMBRINZA™ Suspension should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangitis obliterans.

Contamination of Topical Ophthalmic Products After Use - There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products. These containers have been inadvertently contaminated by patients who, in most cases, had a concurrent corneal disease or a disruption of the ocular epithelial surface *[see Patient Counseling Information]*.

ADVERSE REACTIONS

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

SIMBRINZA™ Suspension - In two clinical trials of 3 months duration 435 patients were treated with SIMBRINZA™ Suspension, and 915 were treated with the two individual components. The most frequently reported adverse reactions in patients treated with SIMBRINZA™ Suspension occurring in approximately 3 to 5% of patients in descending order of incidence were blurred vision, eye irritation, dysgeusia (bad taste), dry mouth, and eye allergy. Rates of adverse reactions reported with the individual components were comparable. Treatment discontinuation, mainly due to adverse reactions, was reported in 11% of SIMBRINZA™ Suspension patients.

Other adverse reactions that have been reported with the individual components during clinical trials are listed below.

Brinzolamide 1% - In clinical studies of brinzolamide ophthalmic suspension 1%, the most frequently reported adverse reactions reported in 5 to 10% of patients were blurred vision and bitter, sour or unusual taste. Adverse reactions occurring in 1 to 5% of patients were blepharitis, dermatitis, dry eye, foreign body sensation, headache, hyperemia, ocular discharge, ocular discomfort, ocular keratitis, ocular pain, ocular pruritus and rhinitis.

The following adverse reactions were reported at an incidence below 1%: allergic reactions, alopecia, chest pain, conjunctivitis, diarrhea, diplopia, dizziness, dry mouth, dyspnea, dyspepsia, eye fatigue, hypertonia, keratoconjunctivitis, keratopathy, kidney pain, lid margin crusting or sticky sensation, nausea, pharyngitis, tearing and urticaria.

Brimonidine Tartrate 0.2% - In clinical studies of brimonidine tartrate 0.2%, adverse reactions occurring in approximately 10 to 30% of the subjects, in descending order of incidence, included oral dryness, ocular hyperemia, burning and stinging, headache, blurring, foreign body sensation, fatigue/drowsiness, conjunctival follicles, ocular allergic reactions, and ocular pruritus.

Reactions occurring in approximately 3 to 9% of the subjects, in descending order included corneal staining/erosion, photophobia, eyelid erythema, ocular ache/pain, ocular dryness, tearing, upper respiratory symptoms, eyelid edema, conjunctival edema, dizziness, blepharitis, ocular irritation, gastrointestinal symptoms, asthenia, conjunctival blanching, abnormal vision and muscular pain.

The following adverse reactions were reported in less than 3% of the patients: lid crusting, conjunctival hemorrhage, abnormal taste, insomnia, conjunctival discharge, depression, hypertension, anxiety, palpitations/arrhythmias, nasal dryness and syncope.

Postmarketing Experience - The following reactions have been identified during postmarketing use of brimonidine tartrate ophthalmic solutions in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to brimonidine tartrate ophthalmic solutions, or a combination of these factors, include: bradycardia, hypersensitivity, iritis, keratoconjunctivitis sicca, miosis, nausea, skin reactions (including erythema, eyelid pruritus, rash, and vasodilation), and tachycardia.

Apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in infants receiving brimonidine tartrate ophthalmic solutions *[see Contraindications]*.

DRUG INTERACTIONS

Oral Carbonic Anhydrase Inhibitors - There is a potential for an additive effect on the known systemic effects of carbonic anhydrase inhibition in patients receiving an oral carbonic anhydrase inhibitor and brinzolamide ophthalmic suspension 1%, a component of SIMBRINZA™ Suspension. The concomitant administration of SIMBRINZA™ Suspension and oral carbonic anhydrase inhibitors is not recommended.

High-Dose Salicylate Therapy - Carbonic anhydrase inhibitors may produce acid-base and electrolyte alterations. These alterations were not reported in the clinical trials with brinzolamide ophthalmic suspension 1%. However, in patients treated with oral carbonic anhydrase inhibitors, rare instances of acid-base alterations have occurred with high-dose salicylate therapy. Therefore, the potential for such drug interactions should be considered in patients receiving SIMBRINZA™ Suspension.

CNS Depressants - Although specific drug interaction studies have not been conducted with SIMBRINZA™, the possibility of an additive or potentiating effect with CNS depressants (alcohol, opiates, barbiturates, sedatives, or anesthetics) should be considered.

Antihypertensives/Cardiac Glycosides - Because brimonidine tartrate, a component of SIMBRINZA™ Suspension, may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with SIMBRINZA™ Suspension is advised.

Tricyclic Antidepressants - Tricyclic antidepressants have been reported to blunt the hypotensive effect of systemic clonidine. It is not known whether the concurrent use of these agents with SIMBRINZA™ Suspension in humans can lead to resulting interference with the IOP lowering effect. Caution is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines.

Monoamine Oxidase Inhibitors - Monoamine oxidase (MAO) inhibitors may theoretically interfere with the metabolism of brimonidine tartrate and potentially result in an increased systemic side-effect such as hypotension. Caution is advised in patients taking MAO inhibitors which can affect the metabolism and uptake of circulating amines.

USE IN SPECIFIC POPULATIONS

Pregnancy - *Pregnancy Category C:* Developmental toxicity studies with brinzolamide in rabbits at oral doses of 1, 3, and 6 mg/kg/day (20, 60, and 120 times the recommended human ophthalmic dose) produced maternal toxicity at 6 mg/kg/day and a significant increase in the number of fetal variations, such as accessory skull bones, which was only slightly higher than the historic value at 1 and 6 mg/kg. In rats, statistically decreased body weights of fetuses from dams receiving oral doses of 18 mg/kg/day (180 times the recommended human ophthalmic dose) during gestation were proportional to the reduced maternal weight gain, with no statistically significant effects on organ or tissue development. Increases in unossified sternebrae, reduced ossification of the skull, and unossified hyoid that occurred at 6 and 18 mg/kg were not statistically significant. No treatment-related malformations were seen. Following oral administration of ^{14}C-brinzolamide to pregnant rats, radioactivity was found to cross the placenta and was present in the fetal tissues and blood.

Developmental toxicity studies performed in rats with oral doses of 0.66 mg brimonidine base/kg revealed no evidence of harm to the fetus. Dosing at this level resulted in a plasma drug concentration approximately 100 times higher than that seen in humans at the recommended human ophthalmic dose. In animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent.

There are no adequate and well-controlled studies in pregnant women. SIMBRINZA™ Suspension should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers - In a study of brinzolamide in lactating rats, decreases in body weight gain in offspring at an oral dose of 15 mg/kg/day (150 times the recommended human ophthalmic dose) were observed during lactation. No other effects were observed. However, following oral administration of ^{14}C-brinzolamide to lactating rats, radioactivity was found in milk at concentrations below those in the blood and plasma. In animal studies, brimonidine was excreted in breast milk.

It is not known whether brinzolamide and brimonidine tartrate are excreted in human milk following topical ocular administration. Because many drugs are excreted in human milk and because of the potential for serious adverse reactions in nursing infants from SIMBRINZA™ (brinzolamide/brimonidine tartrate ophthalmic suspension) 1%/0.2%, a decision should be made whether to discontinue nursing or to discontinue the drug, taking into account the importance of the drug to the mother.

Pediatric Use - The individual component, brinzolamide, has been studied in pediatric glaucoma patients 4 weeks to 5 years of age. The individual component, brimonidine tartrate, has been studied in pediatric patients 2 to 7 years old. Somnolence (50-83%) and decreased alertness was seen in patients 2 to 6 years old. SIMBRINZA™ Suspension is contraindicated in children under the age of 2 years *[see Contraindications]*.

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

OVERDOSAGE

Although no human data are available, electrolyte imbalance, development of an acidotic state, and possible nervous system effects may occur following an oral overdose of brinzolamide. Serum electrolyte levels (particularly potassium) and blood pH levels should be monitored.

Very limited information exists on accidental ingestion of brimonidine in adults; the only adverse event reported to date has been hypotension. Symptoms of brimonidine overdose have been reported in neonates, infants, and children receiving brimonidine as part of medical treatment of congenital glaucoma or by accidental oral ingestion. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained.

PATIENT COUNSELING INFORMATION

Sulfonamide Reactions - Advise patients that if serious or unusual ocular or systemic reactions or signs of hypersensitivity occur, they should discontinue the use of the product and consult their physician.

Temporary Blurred Vision - Vision may be temporarily blurred following dosing with SIMBRINZA™ Suspension. Care should be exercised in operating machinery or driving a motor vehicle.

Effect on Ability to Drive and Use Machinery - As with other drugs in this class, SIMBRINZA™ Suspension may cause fatigue and/or drowsiness in some patients. Caution patients who engage in hazardous activities of the potential for a decrease in mental alertness.

Avoiding Contamination of the Product - Instruct patients that ocular solutions, if handled improperly or if the tip of the dispensing container contacts the eye or surrounding structures, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions *[see Warnings and Precautions]*. Always replace the cap after using. If solution changes color or becomes cloudy, do not use. Do not use the product after the expiration date marked on the bottle.

Intercurrent Ocular Conditions - Advise patients that if they have ocular surgery or develop an intercurrent ocular condition (e.g., trauma or infection), they should immediately seek their physician's advice concerning the continued use of the present multidose container.

Concomitant Topical Ocular Therapy - If more than one topical ophthalmic drug is being used, the drugs should be administered at least five minutes apart.

Contact Lens Wear - The preservative in SIMBRINZA™, benzalkonium chloride, may be absorbed by soft contact lenses. Contact lenses should be removed during instillation of SIMBRINZA™ Suspension, but may be reinserted 15 minutes after instillation.

U.S. Patent No:
6,316,441

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Academy Plans IRIS Registry to Demonstrate Quality of Care

In November, the American Academy of Ophthalmology launched its Intelligent Research in Sight Registry with an official announcement at its annual meeting in New Orleans.

The Academy describes the registry as a central collection and reporting software tool that amasses and processes patient data from a practice's electronic health records system. The registry's goal is to enable ophthalmologists to statistically analyze their own care, compare it to the care provided by their colleagues and highlight areas for improvement. The registry will also be able to automatically submit the requisite outcomes data to meet requirements for the Physician Quality Reporting System and meaningful use of an EHR system. In the future, the AAO hopes the registry data will enable clinical trials of drugs and interventions, as well.

William L. Rich III, MD, medical director of health policy for the AAO, says the IRIS Registry software is "EHR agnostic," since it can be made to work with any EHR system after a period of installation and testing. After installation, the registry program unobtrusively pulls the requisite data off the EHR system throughout the practice day. "We learned that this cannot interfere with workflow," Dr. Rich says. "And, we learned that if this interferes with workflow, it won't happen. This cannot interfere with workflow—it won't." The registry software is designed and maintained by FIGMD (Hanover Park, Ill.), which also created the PINNACLE Registry for the American College of Cardiology a decade ago.

David May, MD, PhD, a cardiologist from Lewisville, Texas, who oversees his practice's participation in PINNACLE, says ophthalmologists will come to appreciate their registry's benefits. "You can look at the data by office location, provider and even disease process," he says. "You will become very proud of the quality work that you do, because as soon as you begin to get reports back from the registry itself, you begin to make improvements in your processes. And there is a dramatic improvement that takes place, the entire care team will be excited about it." The registry provides a monthly report showing how the practice is measuring up. The report data can also be accessed at any time and manipulated in various ways on the screen, such as comparing a practice's providers' outcomes with each other, to look for ways they can improve.

Since the registry is national, a surgeon can make a query of the entire database to look for trends, get a better understanding of a disease or detect the emerging side effects of drugs. Dr. Rich uses the discovery of intraoperative floppy iris syndrome as an example. "Over a period of years, David Chang discovered he was having more complications, and had a fellow look at the records of the patients he had a complication with, and they found that these patients were 95 percent male," Dr. Rich says. "They then looked at their medication history and made the connection. With the IRIS Registry, you'd just have to push a button and ask: 'How many broken capsules are there, and is there any race, sex or use of meds in which this complication is greater?' You could figure this out in a week rather than in years."

In terms of usage, though a practice that's still using paper charts can enter data through a web portal, Michael F. Chiang, MD, professor of ophthalmology and medical informatics and clinical epidemiology at Oregon Health & Science University, says that can become onerous. "If you don't have an EHR, it takes more time to enter those data fields in," he says. "So, for practical purposes, it's better with an EHR."

Dr. Chiang also says the data will be as secure as possible. "The data are identified data," he says. "They need to be because the registry is certified for PQRS data submission. The data are stored securely in the cloud, to the highest industry standards, and are fully HIPAA compliant. The registry data are stored separately from the protected health information, and everything that gets transmitted back and forth is fully encrypted."

The IRIS Registry is due to go live in April 2014. To see which EHR vendors are currently certified to work with the registry, visit http://www.aao.org/iris-registry/. At this time, 120 ophthalmology practices and around 1,000 physicians are participating, representing approximately 370,000 patient encounters. Dr. Rich estimates the database will have data from more than 18 million patients by 2016. Though the annual fee for participation is still

being determined, Dr. Rich says that during the initial roll-out phase the first 2,000 practices that enroll can use the registry free for two years.

"This registry is really different," Dr. Rich says. "We've learned from the leaders in registry development—ACC and the Society for Thoracic Surgery—and we've built on their template. We can follow the patients longitudinally and overlay the interventions such as new treatments in macular degeneration, cataract and glaucoma devices. So this is really a game-changer."

Long-term Pill Use Raises Risk of Glaucoma

Women who have taken oral contraceptives for three or more years are twice as likely to suffer from glaucoma, say researchers at University of California, San Francisco, Duke University School of Medicine and Third Affiliated Hospital of Nanchang University in China. The researchers caution gynecologists and ophthalmologists to be aware of the fact that oral contraceptives might play a role in glaucomatous diseases, and inform patients to have their eyes screened for glaucoma if they also have other risk factors.

The study is the first to establish an increased risk of glaucoma in women who have used oral contraceptives for three or more years. The researchers utilized 2005-2008 data from the National Health and Nutrition Examination Survey, administered by the Centers for Disease Control, which included 3,406 female participants aged 40 years or older from across the United States who completed the survey's vision and reproductive health questionnaire and underwent eye exams. It found that females who had used oral contraceptives, no matter which kind, for longer than three years are 2.05 times more likely to also report that

they have the diagnosis of glaucoma.

Although the results of the study do not speak directly to the causative effect of oral contraceptives on the development of glaucoma, it indicates that long-term use of oral contraceptives might be a potential risk factor for glaucoma, and may be considered as part of the risk profile for a patient together with other existing risk factors. These include factors such as African-American ethnicity, family history of glaucoma, history of increased eye pressure or existing visual field defects. Previous studies have shown that estrogen may play a significant role in the pathogenesis of glaucoma.

"This study should be an impetus for future research to prove the cause and effect of oral contraceptives and glaucoma," said Shan Lin, MD, lead researcher and professor of clinical ophthalmology at the University of California, San Francisco. "At this point, women who have taken oral contraceptives for three or more years should be screened for glaucoma and followed closely by an ophthalmologist, especially if they have any other existing risk factors."

NAION: Steroid Plus Standard Care Improves Vision

In a prospective, randomized trial of 60 patients with nonarteritic anterior ischemic optic neuropathy (NAION), investigators have shown that the addition of the corticosteroid fluocortolone (FC) to standard therapy significantly improves both short- and long-term visual acuity, especially when given soon after the onset of symptoms. Their results were published in *Restorative Neurology and Neuroscience*.

NAION can affect both eyes in up to 19 percent of cases within five years and occurs in about 2.3 per 100,000 adults over the age of 50. Incidence increases steadily with age. Patients have few well-tested or effective treatment options beyond the standard administration of pentoxifylline (PFX), which is thought to improve visual acuity by improving the microcirculation in oxygen-deprived optic nerve tissue. No current treatment reverses or limits the course of the disease. The goal of this study was to see whether adding a steroid to PTX could improve vision, perhaps by reducing edema or inflammation.

Researchers from the Institute of Experimental Ophthalmology, University of Münster, Germany, studied 55 patients diagnosed with NAION who had developed sudden loss of visual acuity less than three days before the initial consultation. These patients were treated with PFX as well as adjunctive therapy with FC during the first two to three months (which was gradually tapered). The control group received only PFX.

Investigators found that PFX alone had no significant beneficial effects on either visual acuity (as measured as best-corrected visual acuity) or visual field after three days and six months of treatment. Adding FC significantly boosted outcomes: Those receiving FC were more likely to experience improvement and less likely to have worsened visual acuity. Progress was even more pronounced after six months of therapy. More than two-thirds of NAION patients treated with the combination therapy had better long-term vision compared to only 14 percent of those only treated with PFX.

"NAION is caused by ischemia of the optic nerve head. This restriction of blood supply, depending upon its degree, results in primary irreversible loss of retinal ganglion cells and secondary delayed RGC loss related to subsequent optic-disc edema," says Verena Prokosch, PhD, Institute of Experimental Ophthalmology.

"Corticosteroids do not appear to reduce primary cell death, explaining the lack of benefit of FC therapy in patients with a BCVA score worse than 0.05. This may not be the case for patients with moderate BCVA loss who suffer secondary RGC loss due to optic-nerve swelling, revealing a possible therapeutic window for FC," explains co-author Solon Thanos, MD, Institute of Experimental Ophthalmology. Prof. Thanos suggests that the pronounced long-term effect of FC on visual acuity found in the study could be attributed to early and prolonged treatment at a dose higher than previously tested.

Big-City Dwellers Court Dry Eye

Residents of major cities with high levels of air pollution have an increased risk of dry-eye syndrome, according to a study presented at the AAO meeting that examined the health records of 606,708 U.S. veterans. The researchers suggest that environmental manipulations should be considered as part of the overall control and management of patients with dry eye.

Those living in areas with high levels of air pollution had the highest magnitude of increased risk for dry eye, at an incidence rate ratio of 1.4. Most metropolitan areas, including New York City, Chicago, Los Angeles and Miami showed relatively high prevalence of dry eye (17 to 21 percent) and high levels of air pollution.

Additionally, the risk of dry eye was 13 percent higher in ZIP codes in high altitude areas. Higher humidity and wind speed were inversely associated with the risk of DES when controlled for air pollution and other weather conditions. The research findings suggest that primary-care physicians and eye-care professionals should be aware of the association between environmental conditions and dry eye, and elicit an environmental history when assessing patients with dry eye. REVIEW

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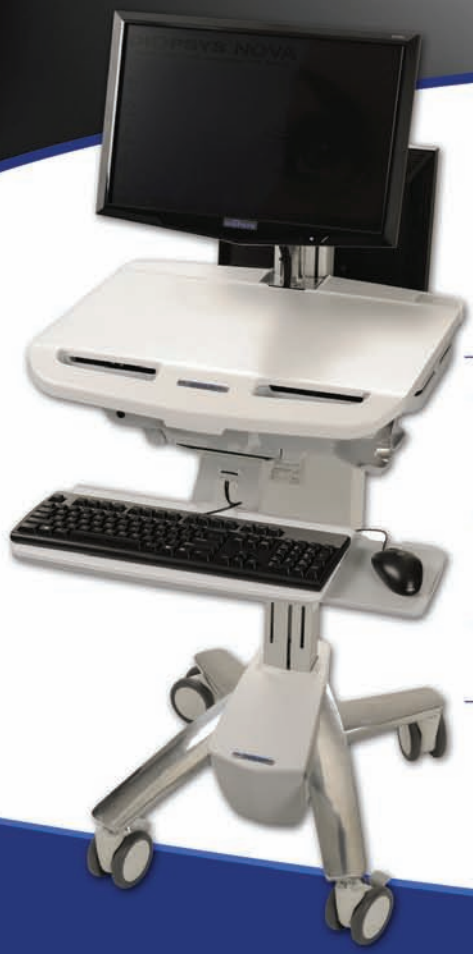

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Departments

Cover Focus

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Program Times
Saturday, February 15, 2014
7:30am-4:30pm
Reception to follow

Sunday, February 16, 2014
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Don't Be Your Father: Retire to, Not From

As someone who harbors a fantasy of actually retiring one day and whose most obvious pastime is making mistakes, I am unavoidably drawn to something that has become a cottage industry: articles about the mistakes we make in preparing for retirement. Did you know that 7 million baby boomers will retire in the time it takes to read this sentence? I think I read that somewhere, but I could be mistaken.

Our readers are not unlike the rest of society in that a significant percentage are nearing retirement age. Many of the articles that you encounter today touch on the same financial shortfall that marks physicians' preparedness as that of the rest of us. In April, the AMA Insurance Agency released a survey revealing that nearly half of the physician respondents consider themselves behind in preparing for the financial future of themselves and their families. There is more than enough financial advice out there for us to add to it, so we won't.

Our two feature articles this month cover many of the top-level concerns that need to be addressed when making the transition from active practice to ... whatever the heck else you decide to do.

Physicians have an additional burden the rest of us don't. Unquestionably, there is a lot of heavy lifting to be done in leaving an ophthalmology practice, and Chris Kent's article on p. 22 provides an excellent starting point. Before weighing you down with that, we thought it would be nice to start with proof that it can be done, and Walt Bethke does so in his article on p. 34.

There's another equally important but less-often discussed aspect of retirement prep for physicians. I could be mistaken about this part as well, but my impression is that we differ from our parents' generation in that today we retire *to*. Our parents (OK, usually our fathers) retired *from*. The actuarial tables say most of us will have another couple of decades in this next phase of the ride.

A surgeon whose opinion I trust recently told me that one of the "dirty little secrets" in ophthalmology is this: In the push to get through medical school, residency, the grind of setting up a practice and the increasing challenge of keeping it all going while devoting time to raising a family, too many ophthalmologists either wait too long, don't make or just don't have the time to simply consider, let alone prepare for, what they might do with themselves once that happy day finally arrives when they lay their burden down.

Don't be that person. With any luck, you've got a whole other act to get through before the final curtain. Learn your lines.

A very happy holiday season to all of you. See you in 2014.

ADVERTORIAL

By Karl G. Stonecipher, MD

Ophthalmic Antibiotic Use in the Real World

The more you understand about pathogens, the better able you'll be to combat them in practice.

Methicillin-resistant *Staphylococcus aureus* (MRSA) was described in 1961 not long after the introduction of methicillin.[1] Since that time, it has spread worldwide, and its prevalence has increased in both healthcare and community settings. In 2005, there were an estimated 478,000 hospitalizations with a diagnosis of *S. aureus* infection in U.S. hospitals.[2] Of these, roughly 278,000 were related to MRSA.[2]

The emergence of multidrug-resistant Gram positive pathogens, including MRSA, is a big concern for today's practicing ophthalmologists. And, in fact, studies have shown that MRSA has become increasingly resistant to multiple antibiotics, but before we take a closer look at any data, I would like to first share some general thoughts about ocular infection.

A Few Tips on Ocular Infection

I recommend checking out your local hospital's microbial resistance patterns, and I usually do this once a year to find out what drugs work on what bugs. Although this provides systemic information and may not always apply to ophthalmology, it allows us to create a picture of the surrounding milieu of microbial infections that we are seeing.

Because there is variation from state to state and country to country, it's very necessary to evaluate your patient population. And, always be cautious about the following four particular groups of patients:

- ***Group 1:*** *healthcare workers.* Doctors, nurses, radiology technicians and candy stripers, to name a few, walk the halls of hospitals and are exposed to more virulent bugs than the average person. Also in this group are nursing home workers and patients who live or work in an environment prone to exposure to multidrug resistant bacterial infections.
- ***Group 2:*** *animal husbandry workers.* Those in this line of work are involved in the care and breeding of domestic animals such as cattle, hogs, sheep and horses. As such, they often deal with a variety of antibiotics and thus expose themselves to more resistant bacteria based on the use and abuse of antibiotics in this industry.
- ***Group 3:*** *preachers, priests, pastors and the like.* This patient population is one we least expect, but makes the most sense. These individuals shake more hands, visit more hospitals and nursing homes, and stop in to hug each and every one of those new additions to the congregation more than anybody I know.
- ***Group 4:*** *patients with ocular surface disease or meibomian gland dysfunction.* Because these patients already live with a compromised ocular surface, they can also be prone to infection.

The latest trend data from the ARMOR and Ocular TRUST studies make it clear that bacteria are a moving target because resistance patterns change among drugs and drug classes.[3,4] For those of us ophthalmologists who started practicing before fluoroquinolones were on the market, I think this means a bit more. Previously, when we dealt with complicated infections, we were forced to refer patients to an academic center or have the local formulating pharmacy make an ophthalmic drop based on our culture reports. If the culture did not grow any bacteria, we were forced to take a "shotgun" approach, which means we used the strongest drugs we had available to cover as many groups of pathogens that we could without focusing treatment toward a particular microbe. But today, we have more choices, and based on those choices, we can make educated decisions on how to treat ophthalmic infections. Let's see what the ARMOR and Ocular TRUST studies teach us about antibiotics in the real world.

Put Your TRUST in Research

The first Ocular TRUST (for Tracking Resistance in the U.S. Today) study looked at the antimicrobial susceptibility of a variety of organisms commonly seen in ophthalmology (actual ocular isolates) to azithromycin, ciprofloxacin, gatifloxacin, levofloxacin, moxifloxacin, penicillin, tobramycin, trimethoprim and polymyxin B.[3]

Ocular Trust 2[5] showed that the fluoroquinolones were similar in their activity against methicillin-susceptible strains of *Staphylococcus aureus*, which were 89% to 93% susceptible. It also showed us that tobramycin and trimethoprim showed *in vitro* activity against methicillin-sensitive *S. aureus* (MSSA), which were more than 95% susceptible. Unfortunately, 54% of the *S. aureus* isolates were methicillin-resistant (MRSA). These strains of MRSA showed resistance to multiple drugs, including penicillin, azithromycin, polymyxin B, tobramycin and disappointingly, the fluoroquinolones. However, MRSA still showed high rates (95%) of susceptibility to trimethoprim.

Among the coagulase-negative staphylococci (CoNS) isolates tested in Ocular TRUST 2, methicillin-resistant phenotype (MRSE) was less susceptible to all antimicrobi-

als compared to the methicillin-susceptible phenotype (MSSE).[5] CoNS susceptibility profiles were the same for all the tested fluoroquinolones, again regardless of generation.

Arm Yourself with Information

Resistance to one or more antibiotics is prevalent among ocular bacterial pathogens.[4] The ARMOR study is our latest addition to the spectrum of surveillance studies prospectively following the ocular microbial world. The first ARMOR analysis included 200 *S. aureus* and 144 CoNS ocular isolates collected from 34 centers across the United States that were submitted for laboratory evaluation of minimum inhibitory concentration (MIC).

MICs were determined by microbroth dilution for 200 *S. aureus*, 144 CoNS, 75 *Streptococcus pneumoniae,* 73 *Haemophilus influenzae* and 100 *Pseudomonas aeruginosa* isolates.[4] A large proportion of *S. aureus* and CoNS isolates were resistant to oxacillin/methicillin, azithromycin or fluoroquinolones; 46.5% of *S. aureus*, 58.3% of CoNS, 9.0% of *P. aeruginosa* and 9.3% of pneumococcal isolates were nonsusceptible to two or more antibacterial drug classes.[4] Only 2.7% of *H. influenzae* isolates were nonsusceptible to one of the agents tested.[4] Methicillin-resistant staphylococci were statistically more likely (all $p<.0038$) to also be resistant to fluoroquinolones, aminoglycosides and macrolides.

This study also revealed that close to 40% of the *S. aureus* ocular isolates were MRSA and fluroquinolone-resistant and that more than 50% of the CoNS were MRSE, with more than 40% of those isolates being fluroquinolone-resistant. It—and other studies—indicate that even newer fluoroquinolones have largely lost activity against resistant organisms.[4,6,7]

In a presentation at the 2011 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting by Haas et al., 57% of ocular CoNS isolates were methicillin-resistant and 40% of the ocular CNS isolates were not susceptible to ciprofloxacin.[6] Fifty percent of ocular *S. aureus* isolates were MRSA and 40% of ocular *S. aureus* isolates were not susceptible to ciprofloxacin.[6]

For the fourth consecutive year, ARMOR study participants collected bacterial isolates of known ocular pathogens and subjected them to antibiotic susceptibility testing. The 2012 data set included 456 isolates of *S. pneumoniae*, *S. aureus*, CoNS, *P. aeruginosa* and *H. influenzae* from 25 sites across the United States and these were compared to the results from the three previous years.[7] Study authors reported that resistance rates have remained relatively stable over the four-year period. However, several bacterial isolates demonstrated resistance to many common antibiotics. For example, more than 33% of *S. aureus* and CoNS isolates were resistant to three or more antibiotics, especially MRSA and methicillin-resistant CoNS isolates that were multi-drug resistant more than 73% of the time.[7] MIC_{90} (MIC inhibiting the visible growth of 90% of all isolates) values were compared for all organisms, showing that some of the agents tested had better activity than others.

After accounting for annual fluctuations, overall resistance rates generally did not show substantial changes over the four-year study period. However, a number of isolates were resistant to commonly used ophthalmic antibiotics. Multi-drug resistance was especially prevalent among the MRSA and MRCoNS isolates. Therefore, the authors concluded that continued vigilance is warranted to monitor the contribution of resistant isolates to the pathogen population. Additionally, the information from the ARMOR studies highlights the importance of considering antibiotic potency and current resistance trends when making therapeutic decisions.

Another report from the 2013 ARVO annual meeting stated that more than 33% of *S. aureus* and CoNS isolates were resistant to three or more antibiotics. Methicillin-resistant isolates of *S. aureus* (MRSA) and CoNS (MRCoNS) were predominantly multi-drug resistant (>73%). Compared to the three previous years, non-susceptibility rates were similar and the new data set reduced some of the fluctuation seen over the previous years.

So, to bring this discussion full circle, how do we reach our ultimate goal of minimizing/avoiding postoperative infections and ensuring excellent outcomes?

Simple Steps for Success

Below are some pointers I follow in my practice. Perhaps they will also serve you well.

While we might feel pressure to use more generic ocular formulations, this is one situation in which you shouldn't cave simply to save a patient some money. Microbes are a moving target, as I explained earlier. You need to change with them, which means using antimicrobial therapy that a pathogen is susceptible to.

With special populations (i.e., healthcare workers, animal husbandry workers, preachers, priests, and patients with ocular surface disease or meibomian gland dysfunction), which I mentioned earlier, I add an additional antibiotic with a combination of polymixin B/trimethoprim sulfate being my first choice. This generic antibiotic has good coverage, as evidenced by both the ARMOR and TRUST studies. If the patient has a sulfa allergy, then I will chose gentamicin primarily because although used extensively in years past, it is rarely used today.

One last comment: we are responsible for our patients. Therefore, we must diligently seek the technology to help improve outcomes. Just as importantly, we must also monitor patients to help prevent any potential complications.

Dr. Stonecipher is a clinical assistant professor of Ophthalmology at the University of North Carolina and medical director of TLC Laser Eye Centers in Greensboro. He also serves on the editorial boards of several scientific journals.

1. Barber M. Methicillin-resistant staphylococci. J Clin Pathol 1961; 14:385.
2. Klein E, Smith DL, Laxminarayan R. Hospitalizations and deaths caused by methicillin-resistant Staphylococcus aureus, United States, 1999–2005. Emerg Infect Dis. 2007;13(12):1840-6.
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7. Haas W, Deane J, Morris TW, Sahm DF. Antibiotic Resistance Surveillance of Ocular Pathogens-four years of ARMOR Study Results. Poster presented at: The 2013 Association for Research in Vision and Ophthalmology Annual Meeting; May 7, Seattle, WA, Poster 2904-B0273.

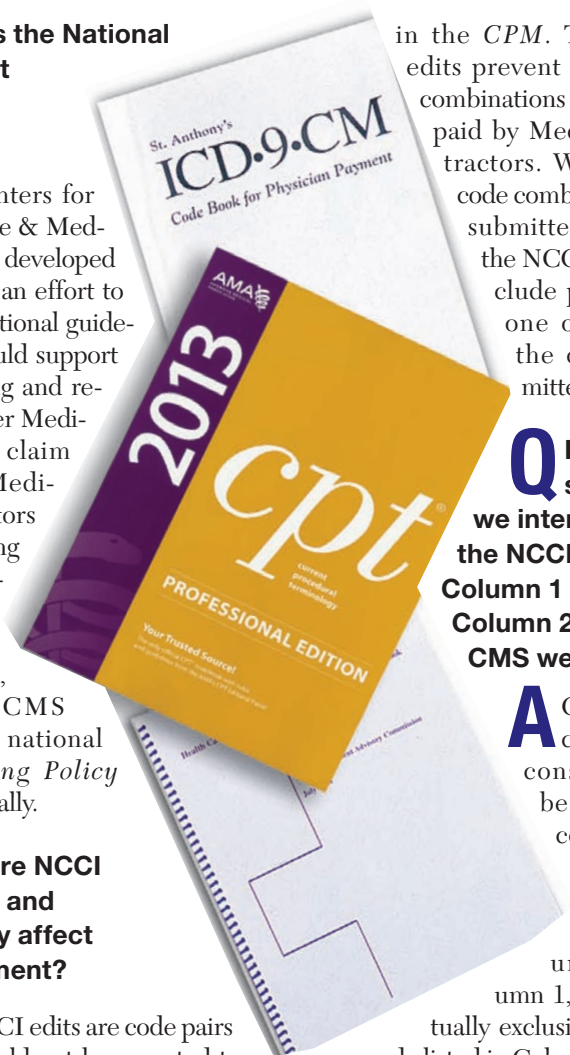
Donna McCune, CCS-P, COE, CPMA

Understanding NCCI Edits and Bundles

For proper reimbursement, it's necessary to know which codes cannot be submitted together and how to use modifer -59.

Q What is the National Correct Coding Initiative?

A The Centers for Medicare & Medicaid Services developed the NCCI in an effort to encourage national guidelines that would support correct coding and reduce improper Medicare Part B claim payments. Medicare contractors began applying the NCCI edits on claims beginning January 1, 1996, and CMS updates the national NCCI *Coding Policy Manual* annually.



Q What are NCCI "edits" and how do they affect reimbursement?

A The NCCI edits are code pairs that should not be reported together for a range of reasons explained in the *CPM*. The NCCI edits prevent these code combinations from being paid by Medicare contractors. When these code combinations are submitted together, the NCCI edits preclude payment of one or more of the codes submitted.

Q How should we interpret the NCCI table, Column 1 and Column 2, on the CMS website?

A Column 2 codes are considered to be incidental components of the procedure described under Column 1, or are mutually exclusive with the code listed in Column 1. Medicare only reimburses the procedure code in Column 1. The service(s) in Column 2 are fragments and not separately reimbursed. An example of an edit would be as follows:

Column 1	Column 2
66984 (Cataract removal w/IOL)	67010 (Anterior vitrectomy)

Anterior vitrectomy is bundled with cataract removal with an intraocular lens. Only the Current Procedural Terminology code 66984 is eligible for reimbursement if both codes are submitted on the same date of service.

Q What happened to the Mutually Exclusive edits file previously posted as part of the NCCI edit file?

A CMS changed the format of the NCCI edits beginning with the April 2012 version. The Mutually Exclusive edits were combined in the Column 1/Column 2 edits, frequently called "bundles." CMS explained that this did not eliminate the mutually exclusive concept or delete the mutually exclusive codes; the files were simply combined to create one file. The new file contains the Column 1 and Column 2 edits,

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reflecting those codes that cannot be submitted together.

Q Is there a way to override the edit and permit payment of both procedures?

A Yes. You may use modifier -59 when a procedure or service includes two or more CPT codes that are bundled together in the NCCI edits, yet circumstances support separate charges. Keep in mind that this is not common. Modifier -59 may not be used to override the NCCI edits just because each procedure has a distinct indication and is preplanned: "Use of modifier -59 ... does not require a different diagnosis for each HCPCS/CPT code procedure/surgery. Additionally, different diagnoses are not adequate criteria for use of modifier -59. The codes remain bundled unless the procedures/surgeries are performed at different anatomic sites or separate patient encounters."

Q When is it appropriate to break an NCCI edit with modifier -59?

A The CPT manual defines modifier -59 as a "Distinct Procedural Service" and explains: "Modifier -59 is used to identify procedures or services, other than E/M services, that are not normally reported together but are appropriate under the circumstances. Documentation must support a different session, different procedure or surgery, different site or organ system, separate incision or excision, separate lesion, or separate injury (or area of injury in extensive injuries) not ordinarily encountered or performed on the same day by the same individual."

For example, in your office you examine a patient with uncontrolled open-angle glaucoma and perform gonioscopy at the same time. You schedule her for laser trabeculoplasty at the hospital later the same day. During the laser trabeculoplasty, you use a goniolens to perform the treatment. In the NCCI edits, 92020 (gonioscopy) is bundled with 65855 (laser trabeculoplasty). Your claim will append modifier -59 to the 92020 performed in the office due to different sessions on the same day (an office session and a hospital session), but not to the use of a goniolens during the treatment.

Q Are there any other edits that affect Medicare reimbursement?

A Yes. On April 1, 2013, Medicare Administrative Contractors implemented new billing edits that cause denials of some claims that were previously paid. These new edits are under the auspices of the contractor for the NCCI, Correct Coding Solutions, LLC. Known as Medically Unlikely Edits, they are automated prepayment edits designed to prevent inappropriate reimbursement: "An MUE is a maximum number of Units of Service (UOS) allowable under most circumstances for a single Healthcare Common Procedure Coding System/Current Procedural Terminology (HCPCS/CPT) code billed by a provider on a date of service for a single beneficiary."

Q Are Medically Unlikely Edits new?

A No. However, while MUEs were inaugurated in 2007, CMS only implemented the date of service MUE on April 1, 2013. "The total units of service (UOS) from all claim lines for a HCPCS/CPT code with the same date of service will be summed and compared to the MUE value." The DOS MUEs look at the entire claim, while ordinary MUEs look at individual lines on a claim one at a time.

Q Is the MUE table on the CMS website and how should we interpret it in the context of DOS MUEs?

A Yes, the MUE table is a separate file on the CMS website and is located with the NCCI edit table. For example, the MUE table presents as follows:

HCPCS / CPT CODE	MUE VALUES
67820 (Correction of trichiasis, epilation by forceps only)	1

The MUE value of "1" indicates that the payer expects this service on one claim line on any given date of service. Therefore, if the patient has lashes epilated from the two upper eyelids, the claim will only be paid if filed on one line as 67820-50 with units "1." If filed on two lines with RT and LT modifiers, the remittance advisory for this claim will process and pay line one and deny line two because it exceeds the Medically Unlikely Edit for 67820, which is set at "1" unit of service. An appeal of this claim would eventually get it paid, once the biller learns how to use modifier -50 (bilateral procedure) instead of two lines or "2" units.

Q How often are these edits updated and/or revised?

A Both the NCCI edits and MUEs are updated and/or revised on a quarterly basis. Billers should check the CMS website quarterly to stay on top of any revisions that may affect their claims. REVIEW

Ms. McCune is vice president of the Corcoran Consulting Group. Contact her at DMcCune@corcoranccg.com.

To the Editor:

I read with concern your latest article on "Reimbursement Issues with Lasering Floaters" in the October 2013 issue. While the reimbursement issues may be accurate, the practice of lasering floaters is typically not practiced and is considered reckless by vitreoretinal surgeons at any respected institution that I am aware of. I have personally seen patients lasered for "floaters" who had diffuse macular laser scars that narrowly missed the fovea. Further, to state that surgical treatment "is the exception and not the rule" for debilitating vitreous opacities is completely untrue, again, according to any major training institution to which I have ever been exposed.

To publish this article may influence those with less experience (i.e., non-vitreoretinal surgeons) to consider this method of treatment that, again, is considered unsafe by most retinal specialists and largely unproven. Readers may best be served by articles on reimbursement for procedures that are less controversial and more routinely practiced.

Leon Charkoudian, MD
Wilmington, N.C.

Author response

Thank you for your letter expressing concerns about my recent Medicare Q&A column. The purpose of this column is to present coding and reimbursement issues and not state opinions regarding the service itself. We do not assert to physicians how to care for patients. It would not be appropriate for us to do so. The article does state that this procedure is rare and that little data exists to support the success of the procedure at this time. We worked hard to present the information in a balanced manner appreciating the varied opinions regarding this treatment.

The following resources were used to develop this information:

1. Ocular Surgery News, YAG Laser offers safe option for floaters, March 15, 2007.
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We hope you will consider the article as an educational piece on coding and reimbursement and not as an endorsement for this procedure.

Donna M. McCune, CCS-P, COE, CPMA, Vice President, Corcoran Consulting Group.

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Refractive Surgery and EMRs: Missing Links

How a surgeon overcame the challenge of a lack of connectivity between his devices and his medical records system.

Brian Will, MD, Vancouver, Wash.

Imagine spending thousands of dollars and untold hours installing a new electronic medical records system in your practice only to realize that the assurances that the system would connect to all your devices were either not accurate or downright false. We were faced with this prospect after we created a custom management information system at our practice and were astonished that the interface necessary to connect our computers to our excimers, femtosecond lasers, topographers and wavefront imagers didn't actually exist. Instead, we were expected to print out paper reports from these devices and then manually scan them in, one by one—a tedious prospect fraught with opportunities for mistakes. In response, we rolled up our sleeves and used a mix of off-the-shelf hardware and in-house software to rig our devices with the ability to send their information directly into the patients' digital records. Here's how we did it.

The Problem With Scanning

Relying on a tech to manually scan reports into our system was a non-starter for us for a couple of reasons. First, we didn't want just a picture of the report. To be worth anything for outcomes analysis, we actually wanted all of the hundreds of data points and metrics the report contains, such as refraction data, pupil size, flap thickness, Zernike coefficients and keratometry readings. An electronic scan gives us none of this.

Second, EMR companies expect the tech to be responsible for locating and manually moving the scanned report into the proper patient folder in the EMR system. This is ridiculous given the capabilities of modern computing technology, and is particularly egregious because it's only a matter of time before the tech makes a mistake and places a vital report in the wrong patient folder, effectively losing the data forever and violating HIPAA by burying one patient's information in another patient's medical report.

Once a report is scanned in, some practices might try to use optical character recognition to "read" the letters and numbers in an attempt to extract them for analysis, calculation of percentages, etc. Though traditional OCR is an elegant concept, it has several limitations. First, in most cases OCR is not 100-percent accurate in recognizing letters, numbers and symbols. For our purposes, where we're dealing with surgical lasers that actually treat patients, even 99-percent accuracy isn't good enough. Second, some fonts used by printers use the same symbol for different characters. For example, the Arial font frequently used in medical reporting uses the same symbol for an uppercase "I" that it uses for a lowercase "l." This would wreak havoc as you try to get your system to perform a mathematical outcomes analysis of your LASIK patients. Finally, OCR typically works in a setting in which the data you need is always found in the same data field in the printed report. However, some reports, such as those produced by AMO's excimer laser, for example, print similar data in different locations. Such a situation wouldn't work well with traditional OCR.

Our Solution

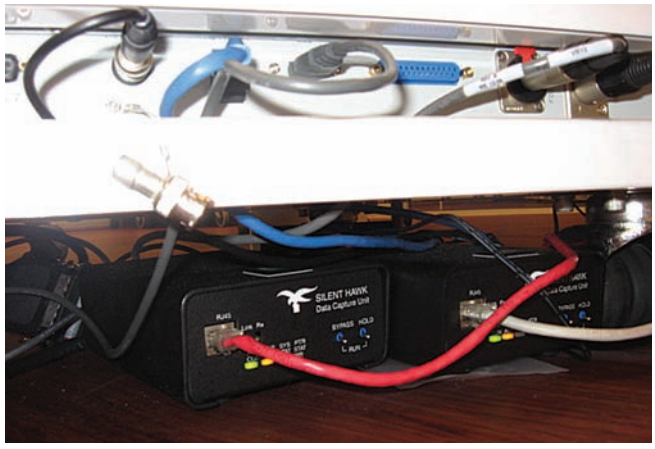
The first part of our device connectivity system consists of a small (3 x 4 x 6 inch) data-capture device from a company called JADTech (Torrance,

This article has no commercial sponsorship.

Calif.). The device slides underneath our lasers and refractive diagnostic equipment and patiently waits for the user to hit the "print" command. When this is done, the JADTech device emulates a printer and reads the streamed printer control language that the computer would use to print something on paper.

The second part of the system is the extraction of the vital patient data from the PCL code. We had special software written that takes the PCL and extracts all the pertinent data from it and then formats it instantly into commonly used formats such as tab-delimited, comma-separated and the format mandated by the Digital Imaging and Communications in Medicine, or DICOM, standard. Therefore, once the report file is captured, key data is extracted and used to name the file. The software then automatically imports the extracted data into the appropriate data tables in the database, creates a database link to the now uniquely named report and moves it into the correct patient folder in the EMR. This is all accomplished within seconds of the technician pressing the print button on the device console.

Perhaps more important, both the image of the report and the extracted data are immediately available in the patient record, accessible to any device connected to our data cloud. This is opposed to waiting for your tech to get around to printing out the paper report then walking over to the scanner to scan it into the system, and then hoping he names it properly, all during a very fast-paced, hectic clinic day. Also, without this system, a tech would need to type critical data such as the WaveScan refraction, pupil diameter and keratometry values into the EMR, introducing a source of error. With the system, however, a user can simply click the mouse and import this data into the exam record.



The data capture device slides beneath the diagnostic or surgical device and captures patient report data when the print button is used.

System Benefits

In addition to the basic benefit of instantly filing the data in the patient record and in a format that we can analyze afterward, we've built other features into it that are mandatory in a medical practice.

• ***Security.*** Some connectivity solutions used with EMR systems use a universal serial bus interface. The risk with USB is that it allows bidirectional data transfer, meaning that hackers could use it to insert viruses or malware into the excimer or femtosecond laser. Iranian scientists learned about the hazards of USB bidirectionality the hard way when a USB device was used to insert the infamous Stuxnet worm onto their uranium enrichment centrifuges, crippling their nuclear program.

Though we're unlikely to encounter a virus as formidable as Stuxnet in our practice, we can't compromise patient safety with the connectivity devices we use. So, we've elected to use a device that uses both hardware and software firewalls that make data transfer backward from our network to our laser systems impossible. In fact, the same security device is actually used in U.S. nuclear missile silos and nuclear reactor facilities. Also, if we need to transfer any data captured by our device to a remote location outside of our secure network, the software has a built-in method for 256-bit encryption so the data can be safely emailed or securely moved to the cloud.

• ***Always on.*** Our system runs on any enterprise-level server and is always on. It is operational across any local area network or wide area network and will also operate using a secure virtual private network. The peripheral hardware attached to each laser or diagnostic device is also operating 24/7. In more than two years of operation, none of the peripheral devices has failed or required rebooting.

• ***Universal connectivity.*** We wanted our solution to work for every device that we encountered in our clinic and surgical suites. With the device that we elected to use, we can use the identical hardware and software to connect to anything ranging from so-called "legacy" systems (i.e., old, outdated hardware) that are common in medical settings, to state-of-the-art diagnostic or surgical devices.

Though we can interface with most devices, we can't yet interface with the Alcon WaveLight excimer laser, the Alcon/WaveLight FS200 femtosecond laser for flap creation or the Ziemer Femto LDV femtosecond laser. However, if and when we are able to install the system in a beta site with these instruments, we'd be able to capture the data from those devices, as well.

• ***Scalable.*** We have two office locations, so we needed a system that could be used reliably at both sites. With the system we selected we can connect anywhere from 1 to 99 peripheral data capture devices to a single server that is running the core

(continued on page 68)

Creating a Smooth Path to Retirement

Christopher Kent, Senior Editor

This transition can be fraught with peril if undertaken with little thought. Here's how to do it right.

As the proverb says, all good things must come to an end. Endings, of course, can be difficult, and retiring from practice is no exception. Making this transition go smoothly—without undue stress or disappointment, and without causing grief for those with whom you work—requires planning, a good attitude and a basic understanding of the challenges you're likely to face. The challenges involved vary somewhat depending on the practice situation from which you're retiring (e.g., solo vs. group practice), but many of the issues are the same.

Here, three consultants and an experienced practice administrator share their advice regarding: planning your transition; dealing with a major life change at the psychological level; finding a buyer for a practice; making the transition as painless as possible for those with whom you work; being realistic about the value of your practice; dealing with (and protecting) your patients; and finding a replacement doctor (when necessary).

Planning for the Change

"The number one pitfall in the process of transitioning from active practice, which I see repeatedly, is that physicians do not plan their transition early enough," says Bruce Maller, founder, president, and chief executive officer of BSM Consulting. "If you wait until the last year or two to start planning, odds are good that things will not work out particularly well. Things might work out OK if you have no interest in seeing your practice continue, but most of the practitioners I work with feel a sense of purpose and see their practice as a legacy with value. They want to see their practice continue, both for the good of their patients and the good of those working in the practice. For that to happen, you have to be planning much further ahead than a year or two."

Craig N. Piso, PhD, a psychologist and organizational development consultant with a focus in ophthalmology, notes that planning is essential. "Retiring is a tough thing to do, even if you're well-prepared. And if you're not prepared—if you haven't done any planning—you won't have confidence about the changes you're making. In some cases, this results in a doctor avoiding retirement altogether. A lot of ophthalmologists end up working longer than they ever dreamed, and sometimes they can't even explain why they're still working."

How far ahead should you plan your transition? "I normally advise my cli-

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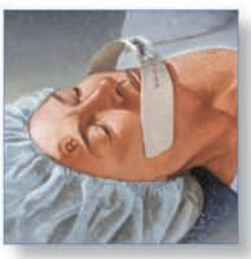

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ents to think about transition planning between three and 10 years before the date that they plan to start the transition," says Mr. Maller. "If you're part of a group practice, the group probably has a plan specifying how partners can transition from full-time work into retirement, and that plan probably states how much advance notice you need to provide. In that situation you might be able to get away with planning your transition three to five years ahead of the date you want to move out. But if you're on your own, you need to plan with a longer-term time horizon. You need to have enough time to do it right."

In addition to planning early, the following strategies can help make your retirement transition go smoothly (both at the personal and business level):

• ***Let your goals for the practice drive your transition process.*** "Five or 10 years ahead of your anticipated retirement date, you need to really think about what your goals are—your goals should drive the process," says Mr. Maller. "For example, you might want to optimize the worth of your practice, bring in an associate or make sure your practice continues after you leave. You need to be clear on those goals. Otherwise the process will become reactive: 'Oh, I'm a year away, I'll just hang up my gloves and in the meantime I'll try to sell my practice to a group in town.' If you go that route you're limiting your options, and the likelihood of a favorable outcome is significantly diminished. If you want to see something happen in the future, whether it's selling your practice for as much a possible or giving your practice to the next generation, those goals should drive your plans."

• ***Have a written plan.*** "There are so many moving parts to this that you don't want to forget anything important," says Corinne Z. Wohl, MHSA, COE, administrator at Delaware Ophthalmology Consultants, who has been in health-care management for more than 25 years. "Write down your plan, step by step. What do you need? What are your concerns? How are you going to address each of them?"

• ***Get specific about your dreams, goals and aspirations.*** "It's important for you to determine what your dreams are," says Dr. Piso. "I recommend that people write down their dreams and goals for this year and for the long term. Then, start crafting that into a retirement plan, not just a financial plan, but plans centering on the things you'd love to do, the lifestyle you'd like to be living."

"Like many surgeons, ophthalmologists tend to rely on their own thinking .... Don't be afraid to get help from someone with expertise in this kind of change."
—Craig N. Piso, PhD

"Make sure you have something to do in retirement," adds Mark E. Kropiewnicki, JD, LLM, an attorney with Health Care Law Associates and a consultant with the Health Care Group, both in Plymouth Meeting, Pa. "You can't just go and sit on your rear end. Many people die soon after they retire; some become different, less effective and vibrant than they were before. You need to retire to something—a hobby, a business, becoming a consultant, volunteering—because you'll get tired of playing golf pretty quickly. Furthermore, if you have a spouse and no project to keep you busy, you'll get tired of each other pretty quickly, even though you love each other."

• ***Don't be afraid to get help planning the transition.*** "Doctors often don't make use of the expertise that's out there to help guide and coach them when planning for major changes and transitions," says Dr. Piso. "There are consultants who are expert at the technology of making major life or practice changes, who can assist with both the tangible and intangible variables that must be taken into account.

"Like many surgeons, ophthalmologists tend to rely on their own thinking," he continues. "They're used to being the smartest man or woman in the room. So when they start thinking about things outside of their area of expertise, such as the technology of change and planning for retirement, they rely on their own guidance. But these are things for which ophthalmologists are not usually trained, and that can lead to less-than-ideal choices that undermine the transition to retirement, and get things off on the wrong foot. So don't be afraid to get help from someone with expertise in this type of change."

• ***Think strategically, not tactically.*** "Strategic planning means focusing on the longer-term, broader view about positioning your practice for future success," explains Mr. Maller. "Tactics, in contrast, are the things you do to achieve those goals. In my experience, physicians are very good at thinking tactically, but they seldom think strategically. I think it's because a surgeon's job is very tactical: 'You have a problem, I'll fix it.' That's how surgeons are trained, how they're wired, and they are very good at that. But if you ask them to think more broadly about something like their business or retirement, many of them find that hard to do. Fortunately, most physicians are incredibly bright, so when I take the time to point them in that direction, they get the idea quickly."

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• ***If you're looking for a replacement, one year might not be enough time.*** "I think it's getting harder and harder to recruit doctors, although it may depend on what part of the country you're in," says Ms. Wohl. "It often takes more than a year to find the right doctor for your practice. You should take that into account when planning your retirement."

• ***In a group practice, learn from other doctors' retirement experience and make changes right after they've gone.*** "We always learn something when a doctor goes through the retirement process," says Ms. Wohl. "Sometimes when an owner retires, we find that we need to make significant changes in how the compensation formula works. When someone else has just retired is a good time to reevaluate shareholder agreements and compensation formulas; any problems are clear, but emotions are low because usually no one else is on the verge of retiring. It's harder to fix problems when you're in the middle of the process yourself."

• ***Make sure your practice's retirement protocol hasn't been sitting in a file unchanged for years.*** With circumstances in the world rapidly changing, a plan set up 10 or 20 years ago may not be as applicable as it used to be. "You may not realize it until you start to implement it," says Ms. Wohl. "At that point, it's too late. Ideally you should look at your official retirement protocol periodically. Of course, in the real world doctors often don't because they're more focused on day-to-day challenges."

• ***Remember that the best-laid plans may have to be altered due to circumstances beyond your control.*** Being flexible can preserve your peace of mind if things don't go the way you planned. "In the past five years, I've known several doctors who had planned to retire who ended up staying on longer than they had anticipated because of the changes in their portfolios in 2008," says Ms. Wohl. "When they finally retired, they wished they'd been able to do so earlier, but sometimes you have to adapt to unexpected circumstances. If this is the case, focusing on things that do make you happy while still working may relieve some of the stress that comes from the change in plans."

Dealing With Change

One of the biggest issues a surgeon must deal with when getting ready to retire, according to Dr. Piso, is the difficulty all human beings have making significant changes in life or career. "Even when people want to change, and it's under their control and in their own best interest, they still often fail to make the changes," he says. "An ophthalmologist's career is the result of a huge amount of investment at the front end, including college, medical school, residency, all the effort required to pay back loans, and the work required to get established successfully in a solo or group practice or become entrenched in an academic system, as well as earning the respect of your colleagues. To reach a point at which you've mastered your craft may require doing thousands and thousands of procedures. After all of that up-front investment, it's hard to let go. Some may feel that they haven't gotten the return on their investment that they deserved. Others simply haven't done the planning that would enable them to more easily make the transition."

Dr. Piso observes that it's always easier to stay with something that's become comfortable than to risk moving to something new and different. "As author Jim Collins says in his book *Good to Great*, good is the enemy of great," he says. "In other words, when things are good enough, we settle. We prefer to remain comfortable rather than deal with the discomfort of embracing change. And there's the rub, because if we don't muster our courage and tolerate the discomfort of going through transition, we never make the changes that allow us to be our best, or to have new experiences that might bring us great joy. We settle for what we currently have. The discomfort of making a transition—especially when you haven't done any planning—is the biggest obstacle to entering what could be a wonderful time of your life."

Dr. Piso says that three things can help us avoid falling into this trap. "The first thing to do is simply accept the reality that nothing in life is permanent," he says. "Generally, ophthalmologists find that their surgical skills are the first thing to go. Hands tremble, vision starts to fade. So the first task is to accept that no matter how great your career is, there will come a time when you have to hang up your gloves.

"Second, it helps to have an enlightened understanding of the process of change," he continues. "We usually think of a change as going from point A to point B, but it's much more realistic to think of this journey as A to B to C, where B is the transition, which is a thing unto itself. In this case, your career is point A and retirement is point C. B is the transition between those two, and transition can be tough because that's when you change your habits, lifestyle, schedule, identity and professional activities. Thinking of the process this way helps make it go more smoothly because you're seeing it more realistically.

"Third, it's important to realize that the energy you need to deal with the stress of making a transition comes from a psychological, emotional standpoint; it comes from the generation of hope," he says. "When we have hope, we're energized. It's that energy that enables us to keep moving forward and make the changes and endure the difficulties we may encounter in transition.

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"There are two primary sources for that hope," he continues. "One is having goals that are personally important and meaningful to us, such as retiring to doing something different that we really care about. The other is having confidence that we can make the transition successfully. That partly comes from doing our homework about the details of the new situation we hope to create, such as understanding the budget of retirement life, sources of revenue and expenses; but it also comes from having confidence that we're going to be psychologically and emotionally strong enough to let go of the past and enter new territory and a new lifestyle. When people have hope, both because they've planned for tangible concerns like money and budgets and because they have faith in their ability to deal with change, they have the energy they need to make the transition successfully."

The Challenge of Slowing Down

Many ophthalmologists would prefer to make the retirement transition more slowly; instead of simply calling it quits one day, they aim to cut back on their workload gradually. "In the real world, at least based on my experience, most doctors don't just work full time and then abruptly stop working," notes Mr. Maller. "Most choose—or would like to be able to choose—to start the process by slowing down." Dr. Piso agrees, noting that gradual change is generally much more manageable psychologically and emotionally than abrupt change.

Slowing down can make the psychological transition easier, but it can also complicate the last years of practice enormously, depending on the physician's circumstances. "It's a lot easier to slow down in a group practice than a solo practice," notes Mr. Kropiewnicki. "Today we see many solo ophthalmologists age 60 or 65 hoping to sell their practice and continue working for the buyer. They often underestimate how difficult this is to do.

"[Slowing down] is probably the biggest mistake people make when they're looking to sell. A buyer, whether a group or individual, is looking for a viable practice .... You need to maintain your income and keep your patients coming in as long as possible."
—Mark Kropiewnicki

"For example, assume I'm in a solo practice wanting to sell to you," he continues. "My practice is making a decent amount of money. You've been in practice for a couple of years working for someone else; now you move into my area and you're interested in buying my practice. My goal is to sell the practice and continue to make some money; your goal is essentially to slip into my shoes and make the same amount of money I do. The problem is, how can we work out a deal that will allow you to buy the practice and have enough net income to pay me for the purchase of the practice, pay me to continue to work in the practice and put some money in your pocket so you can live? It's almost impossible to do.

"On the other hand, if the buyer is a group practice it could work out," he says. "A group practice with three or four doctors and a young guy that's coming up to speed could buy my practice, allowing me to slow down and take an extra day or two off. They can make money by taking the work that I don't want to do anymore, including surgeries. We're seeing a lot of that sort of deal, but selling to a solo doctor is considerably harder."

In fact, if you're hoping to sell your practice, slowing down may be exactly the wrong thing to do. "This is probably the biggest mistake people make when they're looking to sell," says Mr. Kropiewnicki. "You may be 60 years old and not wanting to work so hard, so you start cutting back from five days a week to four, and then three and a half. But a buyer, whether a group or an individual, is looking for a viable practice. If you're spending $300,000 for overhead and only putting $100,000 into your pocket, buyers are not going to be interested. And once patients start going somewhere else because you're cutting back on your hours, there's no effective way to get them back. So you need to maintain your income and keep your patients coming in as long as possible.

"The same thing applies to doing surgery," he continues. "If you're still doing the surgeries you can just transition them all to the guy or group that buys your practice. But if you start referring your surgeries to someone else before you sell, you may have a problem convincing the buyer to proceed."

Even if slowing down is a viable option in your specific situation, advance planning is crucial. "It requires very effective planning to be able to make a change of this magnitude gradually," says Dr Piso. "If you cut back to part-time or try out a change in schedule and lifestyle without careful planning, it may not go smoothly. It's easy to take that as evidence that you're going down the wrong path. In fact, it may very well be the right path—just the wrong way of trying to get there."

"The concept of slowing down has strategic implications for the practice

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that that doctor is a part of, so even this level of change calls for planning far in advance to avoid compromising the needs of the practice," agrees Mr. Maller. "In my experience, the people you work with will be very reasonable if you give them enough time to manage the change. If you don't give them much time and you force them into a corner where you're simply telling them what you're going to do, they'll become unreasonable. That rarely works.

"For a solo practitioner, switching to part-time work may require bringing in a younger partner to carry some of the workload," he adds. "This also requires advance planning, and equally important, transparency. You have to be completely open and honest with the younger doctor about your plans, so he or she can plan accordingly."

Finding a Practice Buyer

If a part of your retirement plan involves selling your solo practice, that process can involve pitfalls of its own. These strategies can help avoid disappointments and misfires:

• ***Be realistic about the value of your practice.*** Mr. Maller says a common mistake he sees solo ophthalmologists make when preparing to retire is having an unrealistic sense of what their practice is worth. "Many surgeons expect that when they retire they're going to get some significant bolus of cash or consideration for their practice, but when the time comes they find out that this isn't realistic," he says. "They may find that there aren't any buyers for the practice; the big group in town they thought might buy the practice is not particularly interested—certainly not at the price the doctor assumed the practice was worth.

"Don't let the value tail wag the dog," he continues. "The practice has been very good to you over the past 35 years; you've made a lot of money and done extremely well. Don't assume there's this residual value in your practice that you're going to cash in. That's just not real-world.

"Ultimately, the real value of your practice is the patient list and patient records, and technically, you don't own the patient records," he points out. "You're simply functioning as a custodian. When you're transitioning out of practice, it makes more sense to think about finding a capable person or group who can take over as custodian of your patients—as opposed to, 'I own these 20,000 patient charts, somebody should pay me several hundred thousand dollars for them.' That's just not realistic."

• ***If you're a solo practice hoping for a solo buyer, make sure you advertise.*** "Any potential buyers in your area probably have a restrictive covenant that's going to prevent them from buying your practice," notes Mr. Kropiewnicki. "So your buyer will most likely be someone from another part of the country who's interested in working in your area. Few young doctors coming out of training are looking to buy a practice; it's usually doctors who have been working for several years who have just decided to make a move. You have to advertise to make that happen."

• ***Don't get too focused on one specific way of selling your practice.*** "I'm a firm believer that it doesn't hurt to talk to almost everybody; you never know where the right deal is going to come from," says Mr. Kropiewnicki. "Be open to alternatives. If you're looking at a group buying you, it's basically going to be one your competitors, whether friendly or not. Or a group in the next town over might be looking to make inroads in your community.

"One possibility that's becoming more common is having a hospital buy your practice," he continues. "Hospitals are looking for this type of arrangement a little bit more than in the past. It may be that there aren't many ophthalmologists in the area, so the hospital wants to make sure you stick around for a couple of years until they can recruit another ophthalmologist to come to the area.

"In those cases you probably won't get top dollar for your practice, but it gives you a nice place to land and continue to work; and you also (hopefully) have someone else who will be responsible for of all the changes that are needed from a standpoint of billing, EMR and regulatory requirements," he says. "In fact, that's the reason many older doctors are looking to move on; they have no desire to get into electronic records just to avoid penalties, or to deal with all the regulatory stuff."

• ***If your solo practice doesn't attract a buyer, consider simply working another year or two.*** "Some doctors want to start slowing down, but nobody wants to buy them, and they don't want to work for someone else; they've been doing things their way and don't want to have to deal with it," says Mr. Kropiewnicki. "In many cases, the value of their practice isn't huge—maybe only $300,000 or $400,000. In that situation, rather than trying to sell it, just work for another year or two. If you're making $300,000 a year, another couple of years will earn you as much money as you would have from selling the practice. Then, if you want to slow down, work another year making $250,000, another year making $200,000, and another making $150,000.

"By then you'll probably be looking to get out, because at some point you're working more to pay the overhead than to put money in your pocket," he adds. "But I've seen doctors do it that way. They're not making a lot of income, but they're happy. Some patients will leave, but if you're not worried about selling that's not a bad thing. You can continue to work and make money."

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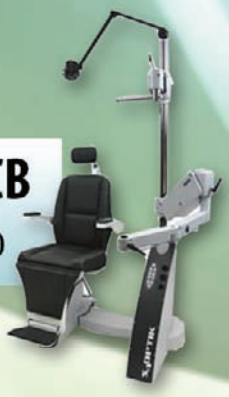

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Protecting Patients and Staff

A doctor's retirement will obviously affect many others, including staff and patients. It's important to think carefully about how to ensure your patients' ongoing care, and in some cases, how to encourage them to continue coming to the practice (if the practice will continue after you've retired). Similarly, it behooves a retiring doctor to mitigate the potential negative impacts retiring can have on employees.

Probably the most important advice here is to not overlook these concerns. Mr. Maller notes that when doctors start thinking about retirement, they tend to be a little self-centered in how they view the world. "Doctors often don't think enough about what's best for their patients and their employees," he says. "I don't mean to imply that they don't care; I don't think that's the case. They simply don't think this way.

"If you run a business for 30 or 35 years, your patients and the people working for you are integral to that business," he says. "You need to do the right thing for them. You need to make sure your patients have continuity of care, and your employees are not left hanging. Thinking about these issues is hard for many doctors, who are so focused on the finish line that they lose some perspective. Thinking about others first changes your view of the process and how you go about it. That's actually another reason to be realistic about the value of your practice."

One of the most important things you can do to minimize the potential negative impact of leaving is to not wait until the last minute to inform your staff. "This is somewhat practice-dependent, but I'm a big advocate for educating and engaging staff sooner, not later, about your plans," says Mr. Maller. "Of course, you don't want to scare off the staff and have them think, 'Oh, he's quitting, I need to find another job.' Nevertheless, when communicating with them, be honest. Tell them you're thinking about transitioning over the next several years and you're starting to get a little bit more serious about that, but you want them to know that you're going to do everything in your power to do this in an orderly fashion so that if they choose to stay with the practice they'll always have a job. Tell them that you're grateful for their help and loyalty and the wonderful job they've done with your patients, and that your goal is to perpetuate the practice into the future.

> *"Retirement should be a prospect that you get excited about, and one that is envisioned as another rewarding part of your life, not a sign that your life is over."*
> *—Craig N. Piso, PhD*

"If you're part of a group, you may need to consult with the other partners about how you handle this," he continues. "But if it's just you in a solo practice, I think it's best to treat the staff as adults and have adult conversations about your plans. Just do it in a way that doesn't create fear or anxiety, but instead portrays a positive, hopeful future for them.

"I've seen situations in which a doctor knows that on a certain date he'll be leaving the group, but he doesn't want to tell anyone, patients or staff, until the week before he leaves," he adds. "That doctor is putting his interests ahead of what's best for the group, and I do not advocate that. A doctor in this position may say he doesn't want to upset anyone, but it's far more upsetting to leave in this manner."

Once your staff knows you're retiring, some will probably want to jump ship before the retirement date arrives. If that's the case, you may want to incentivize important staff members to stick around. "If you're selling a practice, you'll typically end up telling your staff a month or two ahead of time," says Mr. Kropiewnicki. "If it's two months and someone you need is not going to be kept on after the sale, or they decide to retire, you may want to give that person an incentive to stick around until the bitter end.

"First of all, if an employee is being terminated, make sure he knows that he'll be able to collect unemployment because he's not being terminated as a result of any wrongdoing," he continues. "And if you need him to stick around, perhaps to keep billing and collecting up to the end (or even a bit beyond), offer him a bonus for staying. This might be a month or even two months or more of extra pay. Sometimes you need to throw some money at it to make it work; otherwise you'll have to try to hire someone to fill in for two months, which is hard to do."

Another issue is managing your patients as you approach retirement. If you want your patients to continue coming to the practice after you depart, you need to give careful thought to what you say to them about your departure. Ms. Wohl notes that in her multi-doctor practice retiring doctors are coached about this. "It makes a difference when you verbally pass the patient on to a real doctor with a name, instead of just telling patients that you'll be retiring in a year and asking them to call and be scheduled with someone else," she says. "We coach the doctor to say something like: 'When you come back, I'd like you to see Dr. Jones; she's been a great col-

league of mine for many years, and I think you'll really like her.' He can even introduce Dr. Jones if she happens to be nearby."

You should also coach your staff about how to handle making appointments, taking telephone calls and answering questions about your retirement. "You want to be sure your staff also says the right things," Ms. Wohl advises. "It's very easy for a patient to decide to try a practice that's closer to her home if the doctor she likes is leaving. We try to keep patients attached to the practice by making them feel wanted and doing a personal handoff. Your staff should be coached to say something that indicates you're hoping the patient will see your colleague, whom you trust and respect and with whom you believe the patient will be very comfortable. It should be a nurturing, personalized handoff."

Finally, if you're closing a solo practice, get someone else to take your patient records. "Most states require you to keep your records for a number of years," notes Mr. Kropiewnicki. "In a group practice, that's already taken care of. If you're solo, where are you going to keep them? Your basement or attic? It's better if you can find somebody that's willing to take them. You can tell your patients that the other doctor now has their records, which they can get from him if they don't choose to see him."

A Great Transition

Clearly, retiring from practice deserves careful thought and planning. Most people only get one chance to do it right, so finding and taking good advice is worthwhile. "If you follow guidelines like those we've been discussing, you're much more likely to be able to transition on your terms, in a way you can be proud of, and in a way that will help ensure that the legacy you've created through your career will continue," says Mr. Maller.

Having the right attitude is also key. "Retirement should be seen as a new section of your life, not just some kind of endgame," says Dr. Piso. "Retirement can be seen as an empowering opportunity to bring in the return on investment generated by a successful career. It should be a prospect that you get excited about, and one that is envisioned as another rewarding part of your life, not a sign that your life is over. It should be an opportunity to do things you've always wanted to do. Then someday when you die you won't do so with a sense of regret for things not done, but a sense of contentment about a life well-lived." REVIEW

How to Stage Your Second Act

Walter Bethke, Managing Editor

These physicians' stories prove that you can still lead a purposeful, fulfilling life post-retirement.

F Scott Fitzgerald once wrote, "There are no second acts in American lives." Though pundits and scholars debate what he exactly meant, one popular reading of his quote is that once we carve a name for ourselves in a particular field of endeavor, for good or ill, that's what will define us, that's our one shot. From there, we spiral inevitably downward into the third act, the falling action, the denouement, the decline. Many people, both physicians and nonphysicians, feel the same way about retirement. They look on it as an end to the legitimate life they've lived and the start of a prison sentence of boredom and frustration. It doesn't have to be this way, though. Here, ophthalmologists who've retired from clinical and surgical practice tell how they flipped open the pages of their life's script and wrote a new second act, and retired happy.

Easy Does It

Retired ophthalmologists say that, when it came time to say goodbye to ophthalmology, a gradual disengagement was better than an abrupt break.

"I'd espouse tapering off, rather than going full-bore and then immediately stopping," says W. Banks Anderson Jr., MD, who treated patients at the Duke Medical Center for 40 years, eventually becoming vice-chair of the ophthalmology department. "In my case, I first gave up OR surgery when I turned 70. Though this was stressful, there were benefits to it: For one, you're not on the call schedule anymore, so you're not wedded to your phone or pager; and, two, if you operate on someone and then go on a trip, you have to make sure you arrange for someone to see them if they have a problem in your absence. It hangs over your head.

"So, I continued with my clinical practice for four years, and then, eventually, for the fifth year, I cut out Fridays," Dr. Anderson continues. "I gradually gave up my office practice until retiring completely at age 75. I feel this gradual retirement is wiser than just quitting, because it acclimates you to not being in the office every day."

David Miller, MD, had a fruitful career in ophthalmology, serving as chief of ophthalmology at Beth-Israel Deaconess Medical Center in Boston and helping pioneer the use of viscoelastics, namely Healon, in cataract surgery. After 20 years at the hospital, though, he decided it was time to slow down. "For me, it was gradual," he says. "I went from full-time academic as head of the eye unit to private

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practice with some former cornea students of mine. At that point, I was in my 60s and I only came in one or two days a week. That was very healthy. I never felt as if I were swimming alone somewhere."

Though connections with family and friends are important in retirement, physicians say it's the activities that you connect with during your work years, the ones you think about as you rush home on Friday afternoon, that make retirement something to look forward to. Here are some ways ophthalmologists have found fulfillment in their post-work years.

Dr. Anderson's Violin

Music has always been a part of Dr. Anderson's life, though it wasn't until he lost it that he realized how important it was to him.

"I started playing violin in grammar school, and continued playing through high school," Dr. Anderson says. "In my last two years of prep school, however, I learned to play lacrosse, a game few folks knew how to play back then. Then, at Princeton, lacrosse took up an awful lot of time, and I didn't play the violin." He still kept it with him wherever he went, like an old friend that he didn't talk to much anymore but couldn't dismiss. "I didn't play it much in medical school, except around Christmas," he recalls. "Then I got married and started a practice. Basically, I didn't play the violin for 30 years."

Then, he came home one day to find that his house had been robbed—his old violin was gone. "When you play an instrument, you spend an awful lot time with it," he says. "And then, when it goes out of your life, even if you haven't been playing it, you get a grief reaction. I found myself feeling that I didn't want to be without a violin, so I got a new one. Then, I felt that I sounded so much better with my new violin that I started playing again."

Years later, fate intervened again.

Verena Mosenbichler-Bryan,t PhD

W. Banks Anderson Jr., MD, (center, wearing glasses) plays two concerts a year with the Duke Medicine Orchestra.

This time, though, it was in his favor. "Around the time I was retiring completely from ophthalmology, the Duke Medical Center started up the Duke Medicine Orchestra," he says. Dr. Anderson saw his chance to take the hobby that had given him so much pleasure during his years of clinical practice and turn it into something more in his retirement. He now plays second violin in the DMO. "We play two concerts a year," he says. "The last one was Dvořák's New World Symphony. We're now practicing Tchaikovsky's Symphony Number 6, Pathétique, two pieces by our conductor's husband, and a piece for a brass choir—something without strings."

Being reunited with his love of music has taught Dr. Anderson something that he thinks other physicians could learn, also. "Cultivate your interests before you retire," he says. "Don't isolate yourself in medicine 24/7."

Keeping a Hand in Things

Some folks retire from ophthalmology and find that the thing that brings them fulfillment is … more ophthalmology. Here is how two physicians stayed involved in medicine while still making time for themselves.

Retinal specialist Thomas Aaberg retired as chair of Emory Eye Center in 2009 at age 73, after having served on the faculty since 1988, but he never stopped thinking about helping patients. "For me, the great benefit of medicine is the people and trying to help them," he says. "And I found I can do that as a voluntary physician." He keeps up his licensure, and currently volunteers at two hospitals, Grady Hospital in Atlanta, Ga., his home state, and McCall Memorial Hospital in McCall, Idaho, where he and his wife spend their summers.

"I knew Grady Hospital well because it's a part of our teaching system at Emory," Dr. Aaberg says. "At Grady, we had always relied on community physicians to come in and oversee things and be available for questions from the residents. So, it was a natural move for me to go there once I retired.

"McCall, Idaho, is a small town in the mountains," Dr. Aaberg continues. "When I went there, I found that the hospital had no ophthalmologists so, as a volunteer, I take care of ophthalmic cases that come in. I handle cases such as corneal foreign bodies, subconjunctival foreign bodies and lacerations in the cornea or sclera that aren't full-thickness and don't require repair in the OR. The hospital has good slit lamps, good ultrasound and some other facilities. However, you don't want to work on someone who was in a car accident with a huge stellate laceration that requires a microscopic closure—they just don't have that equipment. They also don't have vitrectomy equipment or big dollar items, so we have to send those cases down the canyon to Boise. However, with me there, the other physicians know they're not sending down cases unnecessarily—it's a long drive down the canyon with one eye patched."

Dr. Aaberg says one of the surprise benefits of volunteering is that he's no longer on the clock; he can take as much time as he wants with a patient, and the patients love it. "I volunteered at my son's practice for a while in Grand Rapids, Michigan, and, after I left, he would have to see the patients I had seen and they'd be disappointed," he recalls with a chuckle. "My son came to me after and said, 'Dad, you

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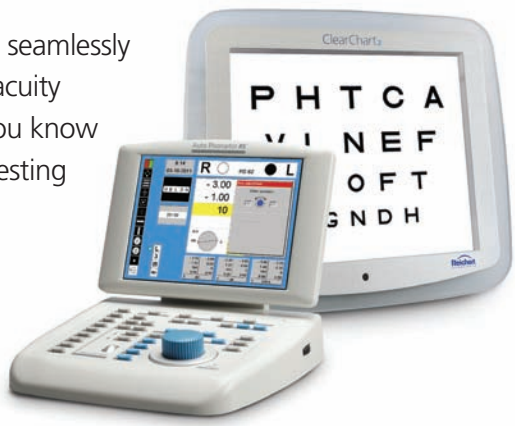

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shouldn't have spent that much time talking with patients because now they expect that of me.' It was devastating for the other doctors to hear the patients say, 'When's that other doctor coming back? That older doctor, I want to see the older doctor."

For ophthalmologists who'd rather retire from the clinical end of things but still keep a hand in research, one possible route is to become a consultant to industry. This is the path that Perry Binder, MD, took.

Like other doctors who find fulfillment in retirement, Dr. Binder had set the stage during his practice years by serving eight years in academic medicine, running a private ophthalmic research lab for 25 years, and then operating a clinical practice while doing consulting on the side for 11 years. "I found if companies like what you have to say, they ask you to be a member of their advisory board," he says. "Then, in 2008, I gave my partners six months' notice that I was going to be departing and, in 2009, I entered the third phase of my career: corporate ophthalmology." His time in corporate ophthalmology was busy. "At that time I was medical monitor for AMO, and I also became medical monitor for AcuFocus," he says. "Then, I developed software for analyzing outcomes which was purchased by Accelerated Vision, a company from Kansas City, which then hired me as a consultant. A company called Stroma invited me to be a consultant for them, as well." Dr. Binder resigned from AMO in August of 2013.

Dr. Binder says that, if consulting seems like a good fit for a physician, he or she should start working toward it now. "If you haven't done consulting work in the past and are now retired, you don't have much to offer them that they can't get on their own. But if you have done consulting in the past, then maybe clean up your resume and come up with a very specific, positive plan for a given project or product. Some of these jobs still exist. You just have to get a good match."

Arts and Literature

Like Dr. Anderson with his music, some ophthalmologists find that, in retirement, they finally have the time they need to throw themselves into their artistic pursuits.

Edward L. Shaw, MD, had been interested in art ever since his grandfather would take him to the museums in his hometown of New York City, but he says it was solidified in college when he took a course in art history. "Then, during my career in ophthalmology, I was fortunate to be able to travel and lecture at many foreign meetings," he says. "I was therefore able to explore art in many countries, especially Italy, England and France." After retiring, he relocated to Los Angeles and visited its museums. He knew what he wanted to be: a docent at the Getty Museum.

After proving his worth in an interview process, Dr. Shaw was selected for the program and began training that continues to this day. This constant education is what he loves about it. "You always train," he says. "I'm still training, and doing research on different objects. That's part of the reason I like it—it doesn't stop."

The other part he likes about being a docent at the Getty Museum is the teaching, the passing on of his knowledge to the next generation of art lovers. "We teach, mostly to children," he says. "We usually find out what schools are coming and the ages of the students, and then try to be age-specific with what we select." He adds that his love of art, and growing knowledge, has made his personal trips to museums both here and abroad more rewarding. "The beauty of what I'm doing now is that when I go to Italy, the more I know about the art the more I can enjoy the trip," he says. "I just keep going and going—I'm driving my wife crazy, but that's a different story."

Once Boston's Dr. Miller left his practice, he began to have thoughts of betrayal and murder. That is, he began writing plays. "My wife, Renee, is an actress, and I got interested in writing plays after attending her performances," he says. "I realized I enjoyed writing fiction, but I wasn't really good enough to write a novel. But I realized I could tell fictional stories in a play, because there the actors and the director do a lot for you."

Owing partly to the scientist in him, Dr. Miller enjoys writing plays about actual figures from history, playing "what if" with their lives. He's written plays about such luminaries as Sir Arthur Conan Doyle, Shakespeare and John Tyndall. "Tyndall was a physicist in the 19th century and considered by many to be the father of the concept of global warming," he says. "But as I researched him, something very interesting turned up: His wife murdered him. She supposedly accidentally gave him a double dose of his sleep medicine and wasn't tried for the crime. However, when I looked up the medicine, I determined that a double or even quadruple dose couldn't kill a person. No one noticed that, so I thought it would help in writing a play."

Though his protagonists are larger-than-life, his productions are more humble, and Dr. Miller likes it that way. "First, we'll put it on in our living room for some neighbors," he says. "Our complex has a meeting room that holds about 50 people, so we might put the play on there. If I'm lucky, we might get a space at the local Brookline Library that holds 100 people."

His wife usually plays the lead female role, and she recruits her acting friends to fill out the rest of the cast. Everyone has fun and works hard, especially Dr. Miller, who polishes his work constantly. In life, as in his work, he's never found it that hard to imagine a second act. "I get a big kick out of it," he says. "And, after the production's done, it's time to think of writing another play!" REVIEW

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CATT: Some Questions Answered, Some Remain

Clinicians face a complex algorithm when choosing an optimal anti-VEGF regimen. Here is what several recent studies found.

Nathan C. Steinle, MD, Dilsher S. Dhoot, MD, Alessandro A. Castellarin, MD, and Robert L. Avery, MD, Santa Barbara, Calif.

The Comparison of Age-related macular degeneration Treatments Trial was a groundbreaking clinical study that redefined comparative-effectiveness research.[1] As with any exceptional trial, CATT answered many questions while raising others.

This article will review the findings of CATT and compare them with several similar studies that looked at various anti-VEGF treatment alternatives in patients with AMD.

CATT Background

In CATT, 1,185 patients with neovascular AMD were assigned at enrollment to one of four treatment groups defined by dosing regimen (monthly versus as-needed) and drug (bevacizumab versus ranibizumab) with monthly review.[2] At year one, patients initially assigned to monthly dosing were reassigned randomly to monthly versus as-needed treatment, without changing the drug utilized. Treatment consisted of 0.5-mg ranibizumab or 1.25-mg bevacizumab.

Overall, at both one and two years, ranibizumab and bevacizumab had

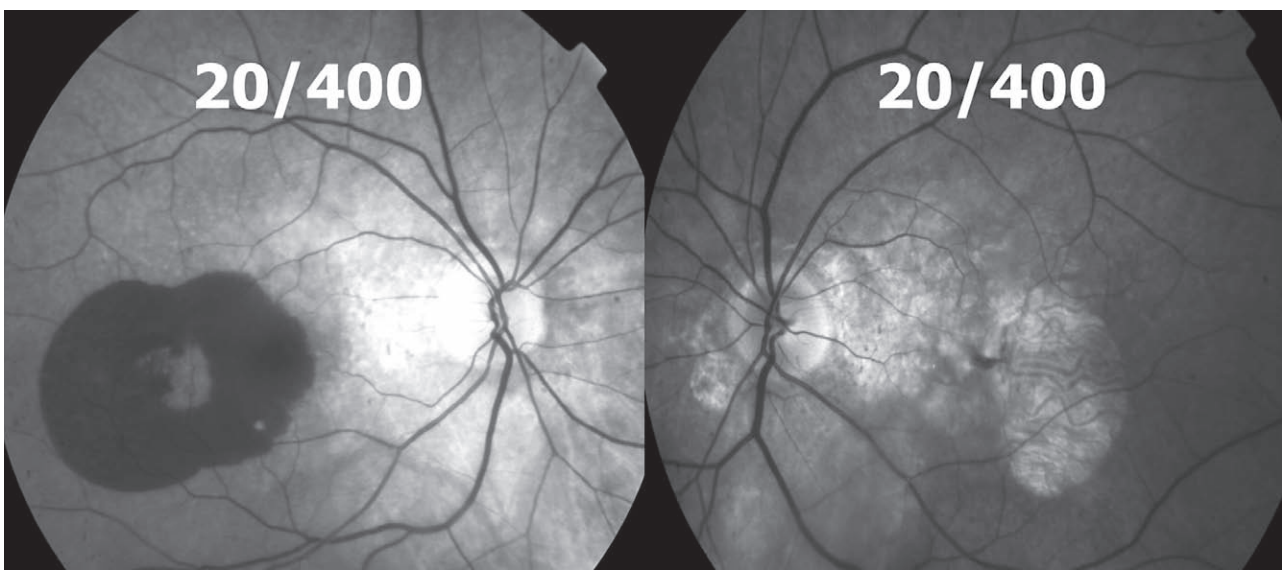

Figure 1. A 79-year-old female presents with a macular hemorrhage in her right eye. The patient is functionally monocular secondary to a longstanding macular scar in her left eye from past exudative age-related macular degeneration.

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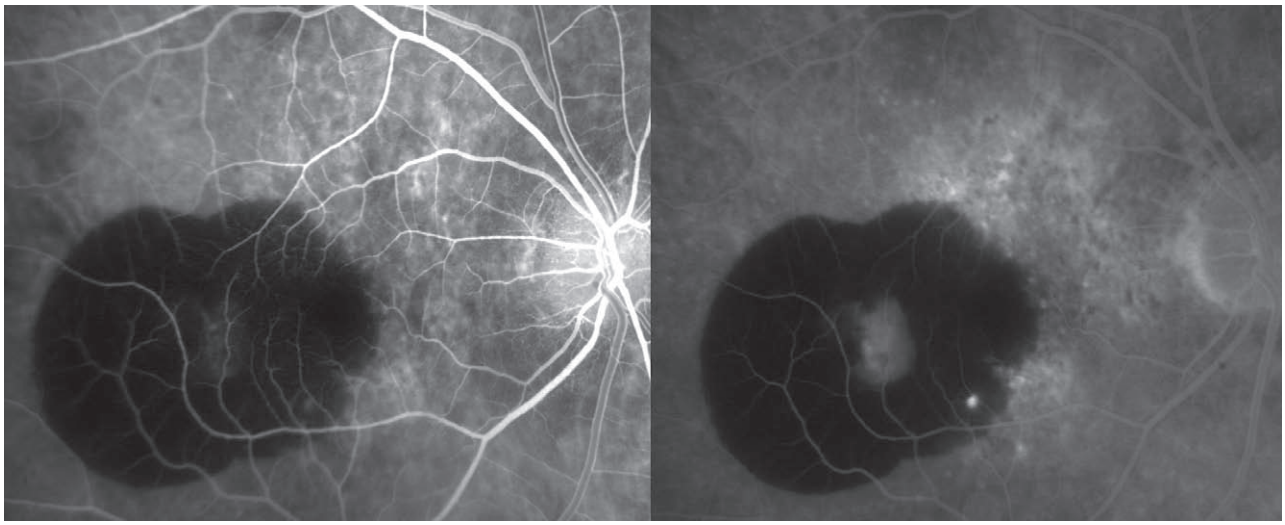


Figure 2. Early- and late-phase fluorescein angiogram images reveal a macular hemorrhage with active choroidal neovascularization.

similar beneficial effects on visual acuity when the dosing regimen was the same. At two years, the mean gains in visual acuity between the two drugs were within 1.4 letters. Collectively, at two years, 60 percent or more of the patients in all groups had 20/40 vision or better. Subtle differences were detected in year two between dosing regimens: the as-needed dosing of either drug at two years produced 2.4 letters less mean gain versus monthly dosing (p=0.046). The greatest difference in mean gain in visual acuity was between ranibizumab monthly and bevacizumab as-needed (3.8 letters).

Other Trials

Other recent clinical trials provide insight into optimal treatment strategies for neovascular AMD. The alternative treatments to Inhibit VEGF in Age-related choroidal Neovascularization, or IVAN, randomized trial performed in the United Kingdom with 610 participants revealed that the comparison by drug was inconclusive; at one year bevacizumab was neither inferior nor equivalent to ranibizumab using a 3.5-letter limit.[3] At one year, the mean difference between ranibizumab and bevacizumab was two letters in favor of ranibizumab. When IVAN examined dosing strategies, discontinuous treatment was equivalent to continuous treatment at one year. The discontinuous treatment group in IVAN received three loading injections before moving to as-needed treatments, but if there was any leakage, the patient received another cycle of three doses given monthly. At the two-year primary outcome in IVAN, neither the drug nor treatment regimen comparison was conclusive.[4]

In another clinical trial comparing bevacizumab and ranibizumab for neovascular AMD, MANTA, the Multicenter Anti-VEGF Trial in Austria, 321 patients were randomized to as-needed treatment with ranibizumab versus bevacizumab following three initial monthly injections. Note that all patients were treated with baseline as-needed protocols, as there were no monthly treatment arms in MANTA. The top-line results for MANTA showed that bevacizumab was equivalent to ranibizumab for visual acuity at all time points over one year.[5] In MANTA, the mean increase of visual acuity at 12 months in the bevacizumab group was 4.9 letters while the ranibizumab group gained 4.1 letters (p=0.78). Thus, MANTA (as opposed to CATT and IVAN) showed a slightly favorable trend toward bevacizumab (although not statistically significant).

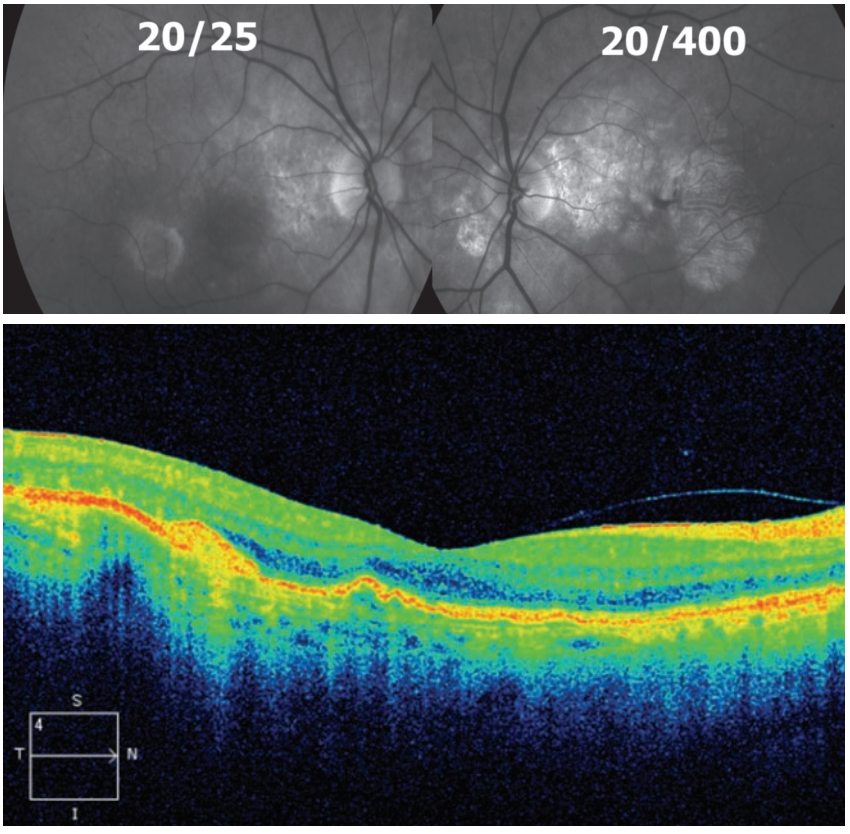
The Groupe d'Evaluation Francais Avastin versus Lucentis for neovascular AMD (GEFAL) study examined 501 patients in France.[6] In this study comparing bevacizumab and ranibizumab, an as-needed dosing regimen was initiated following three loading doses, and patients were followed for one year. In GEFAL, at the 12-month primary endpoint, the two drugs were equivalent for visual acuity.

In contrast to CATT, these three other comparative studies performed three loading doses in their respective as-needed treatment arms, whereas the as-needed treatment arm in CATT did not require loading doses. One of the more disappointing outcomes of the CATT year-two results centered on the reassignment of monthly treatment patients to as-needed treatment in the second year of the study (the same drug was utilized for both years). Study patients treated monthly in year one demonstrated very little carry-over protection when treatment was switched to as-needed dosing in year two. With

either drug, switching to as-needed dosing after one year of continuous monthly treatments produced a mean 2.2-letter decrease. This decline in year two resulted in mean visual acuity virtually equal to that produced with as-needed dosing for the full two years. These results suggest that it is necessary to continue treating monthly in order to preserve any gains achieved with a baseline monthly dosing protocol, as any switch to as-needed dosing will likely lead to a small loss of vision.

This absence of carry-over protection calls into question the common practice of delivering three scheduled monthly injections for new onset exudative AMD patients before switching to as-needed dosing (i.e., utilizing a dosing schedule similar to the PrONTO protocol).[7] If CATT demonstrated that monthly treatment in year one provided no additional benefit when patients were switched to as-needed dosing in year two, it is questionable as to why three initial monthly injections provide any added stability versus baseline as-needed dosing.

In CATT, there were more patients with dry optical coherence tomography imaging at the end of year two in the monthly treated groups than the as-needed treated groups. The monthly ranibizumab treated group had the highest proportion of patients with no fluid on OCT. In IVAN, at both one and two years, the mean foveal retinal thickness did not differ significantly between ranibizumab and bevacizumab. However, the patients receiving continuous treatment had significantly reduced mean foveal retinal thickness versus discontinuous treatment. In MANTA, there were no significant differences in the decrease of retinal thickness between ranibizumab and bevacizumab. The role that thinner, drier OCT results may play in geographic atrophy formation remains to be determined.



Figures 3 & 4. The same patient as shown in the previous images, after one year of monthly ranibizumab intravitreal injections. The visual acuity in the right eye improves to 20/25 and the optical coherence tomograph shows a dry macula. CATT, and other ongoing comparative trials, continue to elucidate optimal dosing strategies for intravitreal pharmacotherapy in exudative AMD.

Adverse Events

One of the most vigorously debated aspects of CATT was the safety of serial intravitreal anti-VEGF injections. Rates of death and arteriothrombotic events were similar for both ranibizumab and bevacizumab. At two years, 5.3 percent of ranibizumab-treated patients and 6.1 percent of bevacizumab-treated patients had died (p=0.62). Meanwhile, 4.7 percent of ranibizumab-treated patients and 5.0 percent of bevacizumab-treated patients experienced arteriothrombotic events (p=0.89). However, interestingly, the overall number of serious adverse events was significantly higher in bevacizumab-treated patients (p=0.004). This finding had been reported in year one[8] and remained in year two with a similar cumulative risk ratio of 1.30. The patients that were treated monthly had lower serious systemic adverse events rates than patients treated with as-needed dosing.

In IVAN, there was no statistical difference at one year between treatment regimens in the number of serious systemic adverse events. Numerically, there were more serous systemic adverse events in the bevacizumab group than the ranibizumab group, but this difference did not reach statistical significance (p=0.25). In IVAN, in contrast to

CATT, at one year there was a lower rate of arteriothrombotic events or heart failure in participants receiving bevacizumab (p=0.03), but no difference between treatment regimens was found (p=0.34). In year two of IVAN, the rate of arteriothrombotic events or heart failure was no longer significantly different between drugs. However, year two of IVAN did reveal an increased risk of systemic SAEs and death with discontinuous treatment, including a twofold increase in mortality (p=0.01). MANTA reported that neither the total number of adverse events nor the number of adverse events in any specific subgroup was significantly different between ranibizumab or bevacizumab. Finally, GEFAL revealed a higher number of systemic serious adverse events in the bevacizumab arm, but this increased number was not statistically significant.

Overall, all four trials found systemic adverse events to be higher in bevacizumab treated patients (although only CATT was statistically significant), but none of the studies has found bevacizumab use to be a significantly higher risk for arteriothrombotic events (as noted earlier, in IVAN, bevacizumab actually showed a lower rate of arteriothrombotic events or heart failure compared to ranibizumab at year one, but this finding was no longer significant at year two).

Other Issues

IVAN was the only one of the four major comparative trials that measured serum VEGF levels. At one year, serum VEGF was significantly lower with bevacizumab (p<0.0001) and higher with discontinuous treatment (p=0.004). At year two, there was a consistent further drop in serum VEGF for both drugs. As more data is collected, concerns of systemic VEGF suppression with intravitreal bevacizumab may alter the future use of bevacizumab in AMD and other ophthalmic disease states such as retinopathy of prematurity.[9-11]

With an approximately 40-fold difference in cost per dose between ranibizumab and bevacizumab, CATT estimated the two-year drug cost per patient to vary from $705 in the bevacizumab as-needed group to $44,800 in the ranibizumab monthly treatment group. IVAN also showed that bevacizumab was less costly than ranibizumab in both the continuous and discontinuous regimens. IVAN reported that the main cost for ranibizumab arms was drug cost (85 percent of costs), whereas for bevacizumab it was treatment administration and monitoring costs (64 percent of costs).

Endophthalmitis developed in 11 patients in CATT (0.06 percent of injections, 11/18, 509 injections), with four cases utilizing ranibizumab and seven cases utilizing bevacizumab (p=0.38). In 10 of these 11 cases, the patient was enrolled in a monthly treatment protocol. The greater number of injections seen in monthly treatment leads to a greater risk of endophthalmitis. At one year, IVAN reported one case of severe uveitis, MANTA reported no cases of endophthalmitis, and GEFAL reported two culture-negative endophthalmitis cases that developed in a single patient. In clinical practice, the common use of compounding pharmacies in the preparation of bevacizumab, among other medications, is also of concern and has recently received much attention in the lay media.[12]

With the recent addition of aflibercept, clinicians now have several reasonable treatment options for exudative AMD. The ideal treatment regimen remains unknown. Nearly all trials to date have examined either a monthly regimen or a modified as-needed approach. In clinical practice, many clinicians employ a treat-and-extend protocol, though it has the least evidence of comparative efficacy. As we move forward with our collective decision-making, clinicians will continue to balance optimal visual acuity results, maintaining a fluid-free retina without atrophy, treatment burden, systemic risks and cost in a complex decision algorithm. CATT has clarified many of our decisions while at the same time introducing new variables for future investigation. REVIEW

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Rethinking Conventional Wisdom on Amblyopia

A series of studies has changed the way we treat amblyopia and offered new hope for young patients with the condition.

Dorothy H. Hendricks, MD, Wilmington, Del.

The Pediatric Eye Disease Investigator Group was formed in 1997. A collaborative network that is funded by the National Eye Institute, PEDIG is dedicated to facilitating multicenter research in eye disorders that affect children. There are more than 100 participating sites with more than 200 pediatric ophthalmologists and pediatric optometrists in the network. One of the major focuses has been the evaluation of different treatment modalities for amblyopia. The results of their Amblyopia Treatment Studies have revolutionized the treatment of amblyopia.

Amblyopia was selected because it is the most common cause of monocular vision loss in children. Amblyopia is unilateral, or less commonly bilateral, reduced visual acuity that is not due to any structural aspect of the eye or visual pathway. Major causes of amblyopia include anisometropia, strabismus and visual deprivation.

Standard treatment practices for amblyopia include spectacle correction, occlusion therapy and atropine penalization. In the past, patients were typically treated with full-time occlusion therapy. Lack of compliance with this standard treatment practice was a common problem. The PEDIG amblyopia treatment studies sought to determine if other alternatives were effective.

Atropine vs. Patching

The first of the amblyopia studies was a randomized trial of atropine versus patching for the treatment of moderate amblyopia, which was defined as vision of 20/40 to 20/100 in children age 3 to 7. The results of this study found that atropine and patching produced similar improvements in vision. Although both treatments were well-tolerated, the atropine treatment did have a slightly higher degree of acceptability on a parental questionnaire. More patients in the atropine group had a reduction in visual acuity of the sound eye at six months; however, this finding did not persist with further follow-up.[1] In addition, some of these children were enrolled in a subsequent study to determine the visual acuity at age 10. After six months of treatment in either the atropine or patching group, further treatment was determined at the discretion of the ophthalmologist. This study found that at age 10, the improvement in the vision in the amblyopic eye was maintained and that the outcome was similar regardless of initial treatment with atropine or patching.[2]

Amblyopia Treatment Studies involving members of the Pediatric Eye Disease Investigator Group have revolutionized the treatment of the condition.

Atropine Regimens

Since the first PEDIG study found that atropine was comparable to patching therapy for the treatment of amblyopia, the next study addressed the question of atropine frequency. The PEDIG investigators conducted a randomized clinical trial comparing

daily atropine to weekend atropine in patients with moderate amblyopia, defined as vision 20/40 to 20/80, in children less than 7 years of age. The study found that in approximately half of patients, in both groups, the vision improved to either 20/25 or better than or equal to the vision in the sound eye.[3] The PEDIG group then investigated whether weekend atropine could be beneficial in cases of severe amblyopia, defined as vision of 20/125 to 20/400. For this trial, in contrast to other amblyopia treatment studies, the subjects included children age 3 to 12 years of age. In the younger group of children ages 3 to 6, subjects were randomized to weekend atropine with a plano lens or weekend atropine and full-spectacle correction. The results showed similar levels of improvement in both groups. The older children in this study, ages 7 to 12, were randomized to either weekend atropine or two hours of daily patching. While there were similar levels of improvement in the vision of the amblyopic eye, the improvement was significantly less than the results for the younger subjects.[4]

Full-time vs. Part-time Patching

The PEDIG network also sought to determine the necessity of the typically prescribed full-time patching regimens. In a randomized trial they compared full-time, or all but one hour per day, to six hours of patching per day in children younger than 7 years of age with vision in the range of 20/100 to 20/400. Fortunately for patients, they found that both treatment protocols produced similar improvements in vision.[5]

Next, they looked at the treatment of moderate amblyopia, defined as vision in the range of 20/40 to 20/80, to determine if two hours of patching was as effective as six hours per day in children younger than 7. The results of this study showed that two hours per day produced similar improvements in visual acuity when compared with six hours per day in children with moderate amblyopia.[6] This change in treatment has had a major impact on families struggling to patch their children.

Near vs. Distance Activities

At one time, it was commonly accepted that near activities produced better results than distance activities when performing patching for the treatment of amblyopia. PEDIG investigators conducted a randomized trial to determine if this was true. Children age 3 to 7 with amblyopia ranging from 20/40 to 20/400 were randomized to two hours of patching per day with near versus distance activities. Results showed similar improvements in vision in both groups.[7]

At one time, it was commonly accepted that near activities produced better results than distance activities when performing patching for the treatment of amblyopia. PEDIG investigators conducted a randomized trial to determine if this was true. ... Results showed similar improvements in vision in both groups.

Refractive Correction

Investigators were also curious if spectacle correction alone, without patching, could be enough to treat anisometropic amblyopia. Results of this trial showed that in one-third of 3- to 7-year-old children with untreated anisometropic amblyopia, resolution of amblyopia occurred with refractive correction alone. Children with moderate amblyopia, vision in the range of 20/40 to 20/100, were more likely to have resolution of amblyopia, while children with denser levels, on average, had a three-line improvement in visual acuity.[8] This result has had a major impact on treatment and significantly reduced families' patching burden.

Investigators also found that optical correction alone resulted in improvement in vision for patients with combined strabismic-anisometropic amblyopia. In fact, one-quarter of children did not require any further amblyopia treatment.[9]

Older Children

Typically, amblyopia has been thought of as a disease that can be treated until approximately the age of 9, and if not diagnosed and treated by this age, permanent vision loss results. The PEDIG investigators performed a randomized trial to determine if treatment in older children could be beneficial. In the 7- to 12-year age group, children were randomized to optical correction in combination with patching two to six hours per day or optical correction alone. In this group, 53 percent of children in the treatment group responded compared with 25 percent of those provided with only optical correction.[10] In addition, 82 percent

of patients age 7 to 12 years maintained an increase in visual acuity one year after cessation of treatment other than glasses correction.[11] In the 13- to 17-year age group, participants were randomized to optical correction combined with two to six hours of patching per day and atropine or optical correction alone. In this age group, the response rate was the same in both groups, indicating little benefit to treatment in older children. The study did find that children who had never been treated in the past showed some improvement with amblyopia treatment.[10] The results of this study bring hope to families whose children were either non-compliant with treatment when younger or not detected until an older age.

Given that there was benefit to treating children age 7 to 12 years, investigators questioned whether success was equal with patching and atropine. A randomized trial comparing two hours of patching per day to weekend atropine in children age 7 to 12 with moderate amblyopia, vision 20/40 to 20/100, was performed. The results showed similar levels of improvement with both treatment options.[12]

Future Studies

PEDIG currently has a number of trials under way as well. Fifteen-year follow-up will be available in the near future for the Atropine vs. Patching study. One current study will compare the efficacy and safety of oral levodopa and patching versus oral placebo and patching for amblyopia in children 7 to <13 years old. Another will evaluate the effectiveness of increasing prescribed patching treatment from two to six daily hours after visual acuity has stabilized with initial treatment and amblyopia is still present. Other related studies named on the PEDIG website include:

Atropine versus patching has been studied in several recent trials.

- A Randomized Trial of Bilateral Lateral Rectus Recession versus Unilateral Lateral Rectus Recession with Medial Rectus Resection for Intermittent Exotropia;
- Glasses versus Observation for Moderate Hyperopia in Young Children;
- Pediatric Cataract Surgery Outcomes Registry;
- Effectiveness of Home-Based Therapy for Symptomatic Convergence Insufficiency;
- Data Collection for Esotropia Treated with Botulinum Toxin-A Injection; and
- A Randomized Clinical Trial of Observation versus Occlusion Therapy for Intermittent Exotropia.

These studies revolutionized the treatment of amblyopia. Previously, families faced full-time occlusion therapy for their child. Today, they may only need spectacle correction alone as curative treatment. For patients who do require treatment, results can be obtained with either two hours of daily patching or weekend atropine treatment. In addition, these studies have also shown that improvements can still be made in older children up to the age of 12, and even in older children who have never been treated previously. Pediatric ophthalmologists and patients' families are anxiously awaiting the results of the current trials, which may have an equally profound impact on our understanding of amblyopia. REVIEW

... these studies have also shown that improvements can still be made in older children up to the age of 12, and even in older children who have never been treated previously.

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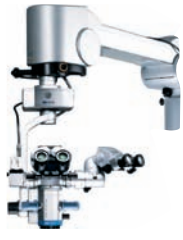

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Cool Opportunities to Modulate Nociception

A breakdown of the corneal nerves, how they're stimulated and how dry eye, trauma and contact lenses affect them.

Mark B. Abelson, MD, CM, FRCSC, FARVO, and Daniel Gamache, PhD, Andover, Mass.

Few things can grab and hold your attention like a foreign object that finds its way onto the surface of your eye. The combination of pain, itch and the flood of tears screams out the message, "Pay attention to me!" with enough force to rival even the loudest of overtired 2-year-olds. When the offending eyelash is removed, we're left with a sense of relief combined with a reminder of the cornea's mighty sensory defenses. This month we'll consider aspects of ocular surface sensory function including physiology, pathology and the future of potential therapeutic interventions.

Wiring the Ocular Surface

The cornea is one of the most densely innervated tissues in the human body. Stimulation of afferent nerve endings can elicit a collection of protective reflex responses including blinking, tearing or gross motor movements such as flinching.

The endings originate from cell bodies in the ipsilateral trigeminal ganglion; these nerve endings project via the ophthalmic nerve, which is composed of multiple axonal fibers including the high speed, myelinated A-delta fibers and the larger, slower-conducting C fibers. In the cornea, nerves bifurcate and project toward the corneal surface through the basal and more superficial layers of the corneal epithelium. These endings are the nerve fingertips, transducing mechanical, chemical and thermal inputs into an integrated neural output directing appropriate tearing and blink responses.

A number of recent studies have compiled confocal images of the ocular surface to map the overall pattern of corneal innervation. In one study, cholinesterase staining revealed perforation sites at which nerves crossed through Bowman's membrane prior to their final bifurcation and projection into the epithelial layer; these sites were relatively diffuse in the central cornea (20 to 30 sites), and more common in the mid-peripheral cornea (130 to 160 sites).[1] The density of this corneal neuropil fluctuates according to the overall health of the ocular surface.

The nerve cells that comprise this sensory network are heterogeneous. Polymodal nerves, which constitute approximately 70 percent of the total nerves in the cornea, are activated by mechanical, chemical and/or thermal stimuli.[2] Another 20 percent of corneal sensory nerve cells respond exclusively to mechanical inputs such as physical displacement, and the remaining 10 percent are sensitive only to the sensation of cold. In addition to their role in detecting environmental threats, the sensory nerves of the cornea are a vital part of basal tear-film regulation. This role is demonstrated in patients with familial dysautonomia (Riley-Day syndrome), a genetic disorder in which parts of the autonomic nervous system, including corneal sensory nerves, fail to develop normally.[3] These patients exhibit a congenital corneal anesthesia, and suffer from severe dry eye due to lack of tear production. Thus the concept of a nociceptor, or nerve that senses pain, is more about how these specific sensory inputs are interpreted and utilized than it is about the specific stimuli to which each responds.

Like nociceptors in other tissues, corneal nerves respond in a graded fashion that is proportional to the stimulus, and this response can be enhanced by repeated stimuli in a process referred to as sensitization. Unlike other nociceptors, however, those in

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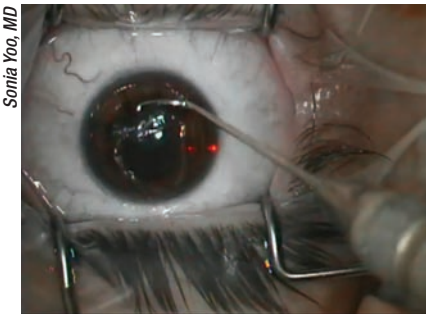
the cornea have an inherently lower activation threshold and so will trigger afferents with stimuli that would not activate receptors in other tissues.[4] Changes associated with sensitization can include a further reduced threshold for activation, increased magnitude in response, or both. Altered responsivity of nociceptors can establish a hyperalgesic state in which neurons are spontaneously active and sensitive to stimuli that are not considered to be noxious. Sensitization most typically occurs as a consequence of tissue injury and inflammation, and can occur within minutes of an initial offense.[5]

Sensory Transduction

The high density and heterogeneity of nociceptors in the cornea underlie an exquisite ability to respond to diverse environmental stimuli of varying intensities. Sensory activation requires simultaneous participation of multiple nerve ending response elements including ion channels, g-proteins and other intracellular signaling molecules. The key transducers of sensory stimuli are the non-specific cation channels (also called transient receptor potential channels, or TRPs). There are 28 human TRP genes, and the sensitivity to thermal, mechanical and chemical stimuli displayed by individual nerve endings is, in large part, a reflection of their specific TRP channel repertoire.[4] Stimulus-dependent TRP channel opening causes local membrane depolarizations that are amplified and propagated by voltage-gated sodium channels (NAV) from the nerve terminals toward the nerve cell bodies, and from there on to the CNS.

The TRP channel family includes receptors for capsaicin, menthol and mustard oil, and while responses to these compounds are more pharmacological than physiological, there is an inherent logic to the revelation that the menthol receptor, TRPM8, is the initial sensory moiety responsible for



Sonia Yoo, MD

Like LASIK, PRK traumatizes afferent sensory nerves in the cornea.

cold sensation. This receptor has recently been established as an exquisite sensor of ocular surface dryness, and plays a key role in the production of basal tears.[6] In particular, the TRPM8 variant expressed in the cornea is particularly sensitive to very small changes (±0.3 C) in surface temperature, and plays a key role in maintenance of tear-film homeostasis.[7] Basal tearing is dramatically diminished in TRPM8 knockout mice, and pharmacological modulation of the TRPM8 channel has also been shown to affect tearing.[8]

By monitoring subtle temperature changes, TRPM8 functions as a reporter of ocular surface hydration. During the interblink period, when the tear film evaporates, ocular surface temperature decreases approximately 0.3 C per second.[9] In addition, cold thermoceptors can be activated by hyperosmotic tears, which is relevant to interblink evaporative effects.[10] TRPM8 channels sense the temperature and osmotic changes, causing them to depolarize and send signals to the central nervous system that result in tear secretion by the lacrimal gland and goblet cells. Patients with reduced corneal innervation, either as a result of chronic inflammation or aging, are at greater risk of dry eye as the feedback from TRPM8-containing receptors diminishes.

Tearing in response to noxious stimuli is maintained in TRPM8 knockout mice, emphasizing the role of other types of ocular surface sensors in health and disease.[7] This returns us to the discussion of tissue injury, inflammation and nociceptor sensitization. When ocular surface drying is accompanied by proinflammatory mediator production by cells of the cornea and conjunctiva, the conscious perception of discomfort is set into motion by the collective contribution of nociceptors at various levels of sensitization and activity. Carlos Belmonte, MD, PhD, of Alicante, Spain, has proposed that dry eye is essentially a state of ocular surface pain and that corneal nociceptors are central to pathophysiology and probably disease management.[6,11] Polymodal neurons are the key participants in the discomfort associated with dry eye. TRPV1 and TRPA1 are cold transducers expressed on corneal polymodal neurons that inherently have higher thresholds for activation than TRPM8 channels. Therefore, noxious cold or hyperosmolarity are required to activate these channels and send signals to the brain that are perceived as ocular surface discomfort.

The Impact of Inflammation

Ocular surface cells, and inflammatory leukocytes that invade the tissue in disease states, produce mediators that can influence sensory neurons. Corneal sensory neurons exhibit a property termed plasticity, alluding to their ability to adapt to local conditions. Receptors for inflammatory mediators such as prostaglandins and bradykinin mediate the sensitization of nociceptors during tissue injury. Inflammation-induced sensory neuron changes include increased expression of transducing components within nerve ending membranes as well as enhanced signaling upon stimulation.[1] In addition, neuronal sensitivity is modulated by density and localization of transducers within membrane lipid rafts, post-translational glycosylation and kinase-dependent phosphorylation.

Direct damage to sensory neurons,

as occurs during corneal surgical procedures, also elicits sensitization in association with nerve regenerative processes. PRK and LASIK directly traumatize corneal sensory afferent nerves and also induce inflammatory responses that alter the reactivity of neurons. PRK can produce severe ocular pain and hypersensitivity to normally non-noxious stimuli as in the frequently reported incidence of photophobia. It has been shown that neurons injured following PRK exhibit sustained spontaneous activity and are hypersensitive.[13] LASIK produces similar responses and the resultant hypersensitivity is often perceived as a sensation of dryness. The extent of nerve damage after LASIK is likely independent of flap location due to the uniform distribution of nerves in the cornea.[1,2]

The plasticity of corneal sensory neurons is not only characterized by the ability to increase in sensitivity but also to decrease in sensitivity to stimulation. For example, corneal sensory neurons have been shown to adapt to stimulation in contact lens wearers.[14] Lens wear stimulates mechanical nociceptors as well as polymodal sensors. Approximately half of contact lens wearers have been reported to exhibit dry-eye symptoms as a result of stimulation of these sensory transducers.[15] Mechanical contact and hypoxia-induced proinflammatory mediator production contribute to this discomfort during contact lens wear. While contact lens wear is another example of corneal nerve sensitization, adaptive desensitization to particular stimuli in a subgroup of contact lens wearers reflects the complex dynamics of ocular surface sensations.[14]

A New Therapeutic Target

It's clear that the vital role of corneal sensory function, together with the impact of inflammation on sensory neuron function, suggest that modulators of nociceptors could present a number of therapeutic opportunities. The broadest spectrum ophthalmic anti-inflammatory agents available are the corticosteroids, which have side effects that limit their use in chronic conditions. Alternatively, non-steroidal anti-inflammatory drugs are frequently used successfully post-surgery, but these drugs target only prostaglandin synthesis; other mediators are unaffected. Strategies that directly target corneal nociceptors and their transducers may provide improvements in ocular surface pain management.

Effects achieved with the TRPV1 agonist capsaicin provide evidence that analgesia can be achieved by targeting the nerve directly. Capsaicin initially causes pain via its TRPV1 agonist properties, but sustained channel opening with long exposures ultimately leads to cytotoxicity due to excessive calcium influx. This cytotoxicity results in analgesia due to the death of the sensory neuron. SYL1001 (Sylentia SA), a short interfering RNA (siRNA) targeted at the TRPV1 channel, is in early clinical development for the treatment of dry-eye discomfort. Other studies suggest that TRPM8 may be an attractive target for pain management.[16] The rationale for this target is derived from the analgesic properties of menthol, a known TRPM8 agonist. This approach remains speculative since menthol has agonist activity at other TRPs, and can produce a hyperalgesic state at high concentrations. Low concentrations of menthol can induce tearing, which is consistent with the above discussion of the role of TRPM8 in basal tear secretion.[17] Therefore, TRPM8 is a particularly attractive target for dry eye due to the potential combined effects on both discomfort and tear secretion.

Our own experiences tell us that corneal sensory inputs operate with exquisite responsiveness. The molecular mechanisms behind the cornea's ability to sense and respond to sensory input are being elucidated. The ability to selectively manipulate individual components of this response system has the potential to provide life-changing opportunities for therapeutic advances. TRP channels appear to be a central factor in the signaling pathways initiated by corneal insult and leading to a compensative response. The trick will be to untangle the many subtleties of TRP channel variants and their signaling co-conspirators. Until then, keep the artificial tears handy. REVIEW

Dr. Abelson is a clinical professor of ophthalmology at Harvard Medical School. Dr. Gamache is director of ophthalmic pharmaceuticals market research at Market Scope LLC.

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Macular Damage: The Diagnostic Missing Link

Clinicians seldom look for early damage in the macula, but recent work indicates that such damage can indeed be there.

Donald C. Hood, PhD, New York

The macula, the central ±8 degrees of the retina, is essential for everyday vision. This is the part of the retina we use to read, see details and recognize a face; it's the only part of the retina in which our vision is in sharp focus (assuming our refractive acuity is good). If a few-degree section of your retina located away from the macula were excised, you might not even realize it was missing. But if a segment of that size were removed from your central fovea at the center of your macula, you'd be devastated. Your vision would drop precipitously; you wouldn't be able to see details, read or recognize many familiar things.

Despite the visual importance of the macula, ophthalmologists seldom focus on this region when looking for signs of early glaucoma. However, the work done by our group has demonstrated that early glaucomatous damage can and does occur in this area, and the most commonly used visual field test—the 24-2 test—misses most of this damage.

Consider Figure 1A (facing page). This shows a fundus view of the retina of the right eye, with the optic disc on the right, and with two overlays: an optical coherence tomography map showing the thickness of the retinal ganglion cell layer, and dots representing the locations of the retinal ganglion cells tested by the 24-2 visual field test. In this map, dark red indicates a thick ganglion cell layer; dark blue indicates a thin ganglion cell layer. The black circle has a radius of 8 degrees, which encompasses just about all of the red and yellow on the map.

That area represents less than 2 percent of your retina, but it contains more than 30 percent of your ganglion cells. That's where the action is, and that's the area you want to preserve. (It's worth noting that the thinness in the center is the result of all non-receptor cells being pushed to the side; the center area is packed with receptors, providing the detailed vision we experience at the fovea.) The points that are tested in the 24-2 test—not counting the one point that's right in the center—miss this region of high ganglion cell density. Furthermore, even within the central ±8 degrees the 24-2 only tests four points.

Our research is now showing that considerable damage due to glaucoma can occur within the area bounded by those four points. This can be seen in Figure 1B, which shows the retinal ganglion cell damage (thinning) in this eye due to glaucoma. The fact that early damage can occur in this area means that in some patients the results of a 24-2 visual field test may appear normal or only reveal a couple of trouble spots—but if you did a finer test like the 10-2 visual field, you'd find clear abnormalities.

Why the Macula Is at Risk

Currently, the damage caused by glaucoma is generally presumed to begin at the optic disc, creating arcuate visual defects because of the way the ganglion cell fibers travel to the disc. Up until now, early glaucomatous damage in the macula has not been seen as an issue by many ophthalmologists. That's partly because not everyone believes that early damage is likely to occur there; but equally important, the parts of the optic disc thought of as most vulnerable to glaucoma, where

This article has no commercial sponsorship.

glaucomatous damage is generally believed to originate, are its superior and inferior quadrants. The fibers in those vulnerable quadrants were typically assumed to be associated with the classic arcuate defects seen clearly on the 24-2 test. (In fact, the 24-2 test was designed to pick up that kind of damage.)

What our work has demonstrated is that large sections of the inferior macula—within the ±8 degree region—are, in fact, associated with fibers entering the optic disc in the vulnerable inferior quadrant, not in the relatively damage-immune temporal quadrant that you would expect to be associated with the macula. This explains why macular damage from glaucoma should not be a surprise, and why it often appears as what my colleague Robert Ritch, MD, who first alerted me to this damage, refers to as a comma. They are just very tight arcuates close to fixation. (Also, the fact that the fibers in question originate in the inferior macula explains why these small macular defects tend to appear in the superior visual field, which of course is flipped relative to the physical location on the retina.)

In other words, the lower half of the macula is just as vulnerable to damage occurring in the inferior disc as we have traditionally assumed the inferior retina outside the macula to be. That means we need to be looking there for damage.

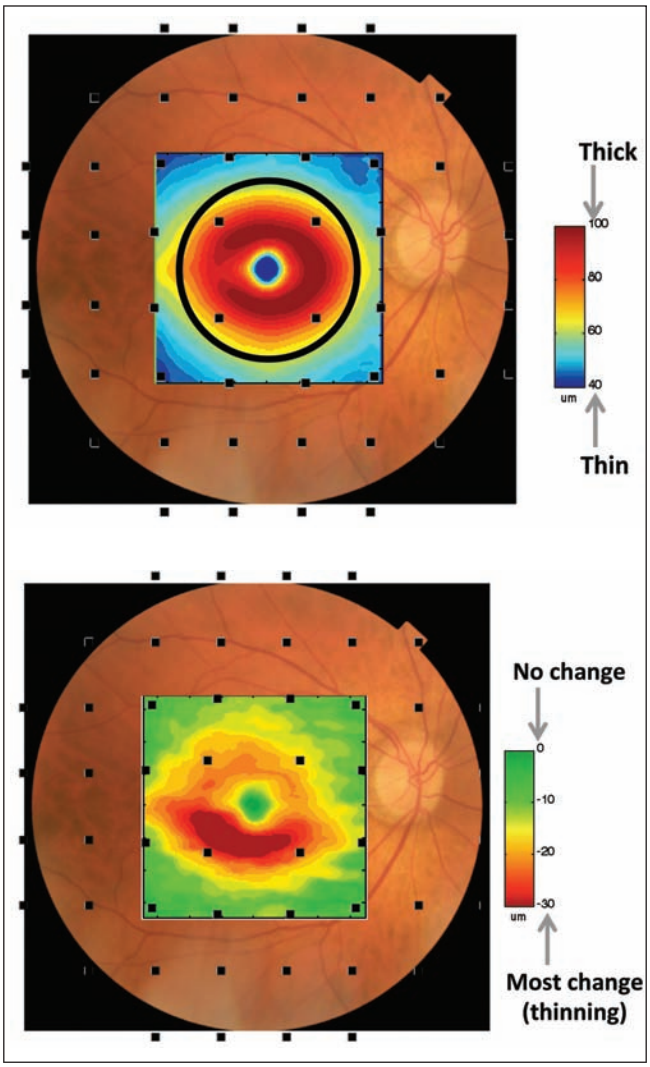


Figure 1A (top): Fundus view of a retina, overlaid with an OCT map of the thickness of the retinal ganglion cell layer and dots representing the locations tested by the 24-2 visual field test. Figure 1B (bottom): The same retina with an overlay showing RGC layer thinning; the thinning falls inside the area tested by the 24-2. Such damage would be revealed by the 10-2 visual field test. (Modified from Hood DC, et al. Glaucomatous damage of the macula. Prog Retin Eye Res 2013;32:1-21. Used with permission.)

Some ophthalmologists perform the 10-2 if they notice a suspicious point on the 24-2, or if the patient has a vague complaint about having trouble seeing, or notes that his contrast is not as good as it used to be. But for many ophthalmologists, the 10-2 test is reserved for following advanced glaucoma cases, where the damage is so extensive that the 24-2 is largely useless and they're trying to determine what vision is left. In fact, the 10-2 test is helpful when it's used early in the disease. It can indeed reveal damage that would not be evident from a 24-2 test.

Adding OCT to the Mix

I'm a firm believer in scanning glaucoma suspects with OCT and comparing the results to the patient's visual fields. In my lab we routinely perform OCT and visual field tests on all patients suspected of having glaucoma or neuro-ophthalmological problems. Then, we compare the results.

The beauty of looking at them together is that they're different kinds of tests that produce complementary data, with different kinds of variability and problems. One is a structural, anatomical test; the other is a behavioral/functional test. Also, if one test doesn't produce useable data, the other probably will. Some patients, for example, have a hard time doing visual fields and produce variable results, but we can usually get a good OCT scans from those individuals.

The other advantage of using them together is that they're both topographical, spatial tests. That means you can compare the data and see whether the abnormalities that appear in one are also evident in the other at the corresponding location. This is a far better way to detect a problem than just accepting a report that says one area is statistically normal (coded as green on summary

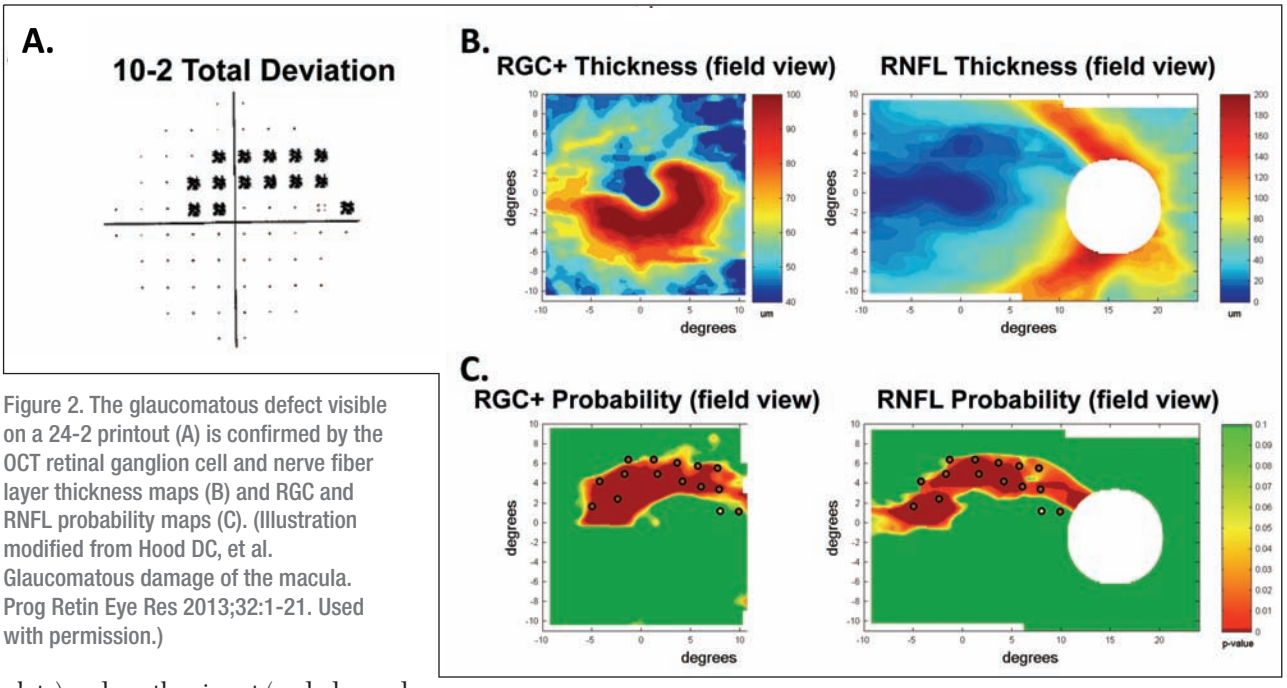


Figure 2. The glaucomatous defect visible on a 24-2 printout (A) is confirmed by the OCT retinal ganglion cell and nerve fiber layer thickness maps (B) and RGC and RNFL probability maps (C). (Illustration modified from Hood DC, et al. Glaucomatous damage of the macula. Prog Retin Eye Res 2013;32:1-21. Used with permission.)

plots) and another is not (coded as red on summary plots).

For example, consider Figure 2. Here, the defect visible on the 10-2 printout (2A) is confirmed by the retinal ganglion cell thickness map from the OCT (2B, left panel), and the OCT retinal ganglion cell probability map (2C, left panel) confirms that this area is statistically abnormal. The same kind of comparison can also be done using the OCT measurements of the retinal nerve fiber layer (2B and 2C, right panels). This damage might have been missed, and certainly would have been underestimated, if the patient only took the 24-2 visual field test.

In some cases, having the two tests to compare elevates something that looks insignificant to something of concern. In a case like this, the visual field may only have a few marginally abnormal points and many doctors would not be concerned. The same might be true of the OCT by itself. But when both show damage in the same location, it suggests that there may indeed be a problem.

It wouldn't be unreasonable to ask: Why not just scan these patients with the OCT? We're currently doing a prospective study asking that question: If you just did the OCT, how often would you have to do a visual field to make the best diagnosis? There's no question that in many cases you can make your diagnosis just using OCT. However, that strategy will not work 100 percent of the time. Furthermore, if you want to follow the patient, the functional measure—the visual field—is typically going to be closer to the patient's complaint. For screening purposes you might be able to just use the OCT and save some time by not doing the visual field. But there is a point to doing both in the clinic, and many ophthalmologists are doing exactly that.

Despite the advantages of OCT, there are some serious concerns surrounding interpretation of the results. Most ophthalmologists are very busy; they just want to know: Is the result normal or abnormal? This is understandable, and the manufacturers are trying to respond to this need by developing reports that can make interpretation easier, highlighting more of the subtle information the scans contain. In the meantime, we can make sure that young ophthalmologists receive more training in how to read the scans. Also, most ophthalmologists should have someone they can rely on, as needed, to help interpret OCT scans. The reality is that OCT scans are just as complicated as MRI scans, and ophthalmologists would benefit from having the equivalent of a radiologist to help interpret them.

Points to Remember

With this information in mind, here are some strategies that will help enhance your ability to detect early glaucomatous damage:

• ***If your patient has any complaints of hazy vision or difficulty reading, or if you do a 24-2 visual field and find even one suspicious spot in the middle, perform a 10-2 visual field.*** The macula is often damaged in early glaucoma, and signs of this can easily be missed if you don't run the 10-2 test. (In general, it would be even better to perform a visual field test

that combines the best of the 24-2 and 10-2 test patterns.)

• ***Be aware that the macula can have diffuse damage.*** We now have clear OCT evidence for something that's been in the literature for some time. In addition to the macula often having early local defects, the macula can also have very subtle but significant diffuse damage throughout. This damage is easy to miss. It's visible on the 10-2 visual field, but clinicians often dismiss that evidence because it could be due to a small pupil or cataracts. For that reason, the best way to confirm it is with macular OCT.

• ***If you're going to look at a circumpapillary retinal nerve fiber report, know which areas are most important.*** Scrutinize the region of the temporal portion of the inferior quadrant of the disc for local thinning. This is where you will find damage associated with small arcuate defects in the upper visual field of the macula. We call this relative small, about 35-degree region the macular vulnerability zone. Damage in that area will affect the macula and have a major impact on vision.

• ***With OCT, look at more than just the retinal nerve fiber layer profiles or the summary information.*** Ophthalmologists often just look at the circumpapillary plot or some simple summary of the plot on the routine reports. However, if that appears normal, it doesn't mean that the macula is healthy. To be complete, compare the abnormal regions of the retinal ganglion cell plot to abnormal regions on the 10-2 visual field (as in Figure 2).

• ***When checking the circumpapillary plot, also check the underlying scan.*** Every manufacturer includes the scan on which the circumpapillary plot is based, although in some reports it's too small to be of much use. The reason for looking at this scan is that it will tell you whether the circumpapillary information can be trusted. In particular, make sure that the machine's software is accurately marking the edges of the retinal nerve fiber layer. If not, the circumpapillary information is flawed and you'll need to redo the scan or hand-correct the lines placed by the algorithm.

I wouldn't suggest replacing the 24-2 test with the 10-2 ... In fact, damage may first appear at either location. Sometimes a patient will produce a normal 24-2 and an abnormal 10-2; sometimes it will be the other way around. So, you really need both types of information.

• ***Realize that getting maximum information from OCT scans requires expertise.*** You can't just look at the summary circles on these reports with their red or green regions and expect to find all the signs of damage that the scans might reveal to an experienced eye. To really take advantage of this technology, you should either devote some time and energy to learning to interpret the scans or find someone who has experience reading them that you can turn to for help when faced with a challenging case.

• ***When checking the circumpapillary plot, ask yourself whether it agrees with what you're seeing on the visual field.*** There should be some agreement between them, especially if the damage is clear. If there's any doubt, then go to the retinal ganglion cell thickness scan and superimpose it on the visual field to see whether there's agreement.

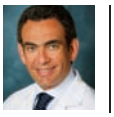
Clinical Realities

Although ophthalmologists are increasingly adding OCT to their glaucoma work-ups, the idea of doing a second visual field test (the 10-2) is not always well-received. That's not surprising, given the heavy patient load most ophthalmologists manage today; performing an extra visual field test takes extra time. I wouldn't suggest replacing the 24-2 test with the 10-2; after all, damage can and does appear farther from the fovea. In fact, damage may first appear at either location. Sometimes a patient will produce a normal 24-2 and an abnormal 10-2; sometimes it will be the other way around. So, you really need both types of information.

The ideal solution would be to modify the 24-2 test pattern so that it has extra points in the center. At least one manufacturer has already done this; the Octopus machine from Haag-Streit has a test that includes those extra points. But most of the machines in clinical use are Zeiss machines. It isn't that hard to modify the test, and I suspect Zeiss is working on making an alternative test pattern available.

In the meantime, you should at least be doing a 10-2 test if you have any concern whatsoever. And, if possible, use your OCT to enhance and confirm the information you gain from the visual fields. REVIEW

Dr. Hood is a professor of visual sciences in ophthalmology and James F. Bender Professor of Psychology at Columbia University in New York City.



Malpractice: How to Stay Out of Court

There are steps you can take before and after surgery to minimize your risk of an unhappy patient who decides to sue.

Walter Bethke, Managing Editor

For many refractive surgeons, finding themselves in a courtroom for malpractice may make them feel as if they've already lost; the entire process maligns their name, impugns their skills, drains them of money and saps them of energy. However, despite the best intentions, malpractice suits can occur. Here, experts in litigation and managing risk outline steps you can take in all phases of the doctor/patient interaction to minimize your risk of being dragged into the courtroom.

Advertising Issues

How you represent the procedure in your ads or on your website can expose you to risk later, experts say.

"Advertising was one of the big issues in a case I tried in May of this year," says C. Greg Tiemeier, a medical malpractice defense attorney in Denver. "The plaintiff had a Consumer Protection Act claim, focused on the absence of a discussion on my client's web page about any of the refractive procedure's risks other than a general statement. We wound up winning on the consumer protection claim largely because the plaintiff's expert's advertising was just as optimistic as the defendant's in terms of not really discussing the risks of the procedure. My advice would be to list the procedure's risks if you list its benefits, which goes along with instructions from a joint paper by the FTC, AAO and ASCRS. You can point out, in a realistic fashion, that the risks are pretty remote and that the patients are mostly satisfied.

"Another aspect to note is that a lot of surgeons use patient testimonials in ads or on their websites," Mr. Tiemeier continues. "Know though, that, as far as the FTC and a jury are concerned, what you say on your site—whether it's from your or your patient's mouth—is going to be attributed to you."

The Preop Process

You can either increase or decrease your risk of a lawsuit at different stages of the preoperative evaluation and informed consent process. Here are key aspects to be mindful of.

• ***Patient expectations and personality.*** Hans Bruhn, senior risk management specialist at the Ophthalmic Mutual Insurance Company, says it's important to make sure the patient is coming for the procedure for the right reasons. "Try to get at what the motivating factors are for the patient," he says. "Some think their whole life will change after refractive surgery and that, for instance, the perfect spouse will now be accessible to them if they have the procedure. This is unrealistic. Effective surgeons ask patients: 'What is your lifestyle? What do you do? What are your hobbies? And what you expect to be different, if anything, in those dimensions of your life after the procedure?' Clarify where a patient's expectations are unreasonable and have the courage to say, 'You're a candidate for the procedure but I don't think you're right for it because your expectations are out of sync. I respectfully decline to perform it.' "

Mr. Bruhn says that some physicians will alter the consent form to make sure the patient knows the possible effects of the procedure. "Some physicians will put a line next to key paragraphs for the patient to place his initials," he says. "This gives the patient a moment to really pause and consider what he's embarking on. Another technique is to have the patient hand write a statement to the effect, 'I have been

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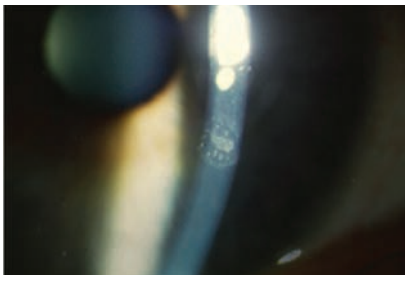
informed of the possible results and risks of the procedure.' "

Risk experts say that it might help to screen patients with personalities that might predispose them to fixating on negative aspects of the procedure. "The majority of refractive malpractice cases that I get are from patients who either have a history of depression or anxiety disorders," says Mr. Tiemeier. "I think it's worthwhile to have a question about what medications the patient is taking on the consent form, and if the patient indicates he's taking anti-anxiety or anti-depressant medication, it might behoove you to have a two or three-minute discussion with him on why he's on them, how long he's been taking them and how severe his condition is. Also, I see stock questionnaires in offices all the time that ask, 'Would you call yourself a perfectionist?' and 'Do you tend to be unhappy when things don't go exactly as planned?' If a patient answers yes to these, it warrants a brief discussion in which you inform him that he has to understand his vision won't necessarily be perfect. For example, if he's a rigid contact wearer, inform him that LASIK won't make his vision as good as it is with RGPs." In some perfectionist cases, experts say it might be better not to operate.

• ***Informed consent.*** Ectasia and dry eye remain big items that should always be mentioned in the informed consent process. "Overall, the number of LASIK lawsuits is down," says Mr. Tiemeier. "I think doctors have gotten a lot better with patient screening, particularly with respect to ectasia. However, it remains an issue because a few studies have found that you can't always predict it. Consequently, informed consent becomes key. A consent form should include the risk of ectasia, if it's not already part of it, because it's a big ticket item that will likely lead to a corneal transplant postop, at least until we get approval of corneal cross-linking. And, in my experience, the need for a transplant has been a trigger for lawsuits over and over again."



A mention of epithelial ingrowth is especially helpful on consent forms for LASIK retreatments, experts say.

Mr. Tiemeier says that, when checking for ectasia risk, it's not so much what new imaging technology you have, but that you properly use whatever devices you do have and then pay close attention to the results. "It doesn't do any good if you use the latest corneal diagnostic imaging device to screen for ectasia but don't really look at the results and analyze them effectively," he says. "The 'standard of care' is a legal doctrine, not a medical one, and it is what I can get six jurors to believe it is based on the testimony of experts. I've had two trials where jurors believed 32-incision RK was within the standard of care, for instance. In the end, you have to have a reasonable basis for what you do in terms of what is in the patient's best interest. I've been able to win cases where I think some surgeons would say the care was not within the appropriate standards, but I proved that the doctor had a reasonable basis for doing what he did."

Dry eye is another post-LASIK issue that can lead to problems. "Some surgeons think of dry eye as a transient condition that's no big deal," says Mr. Tiemeier. "They believe you put in some over-the-counter artificial tears and the patient is fine. But patients don't look at it that way. In fact, dry-eye complaints were involved in almost every refractive surgery lawsuit I've defended. Dry eye is overwhelmingly the most common complaint. However, dry eye is something I don't think many doctors discuss much with patients preoperatively, but I think they would be better off if they did. In my opinion, based on the multitude of ophthalmology and refractive surgery cases I've tried, informed consent isn't just a shield that we use at trial. It's the kind of thing that, if done right, will keep the doctor out of the courtroom."

Mr. Bruhn also says to consider the possibility of needing the patient's consent for ancillary procedures that might be necessary if the primary one can't proceed. "A patient might go in for a LASIK but, due to some situation that arises during surgery, another procedure needs to be done instead," he explains. "The question is, did you advise the patient that you may have to do a different procedure and get consent for that once you get in there? That could be a point of risk, and the patient might allege that no consent was obtained for the other procedure."

Postop Care

Finally, a surgeon can put himself at risk postop if he doesn't respond appropriately to a patient who is become non-compliant and/or foul-tempered.

"Is the patient not coming in for his postop visits, becoming a no-show?" asks Mr. Bruhn. "Is he not complying with his postop drops? If this is occurring, you have to follow-up with him. The patient/doctor relationship is based on mutual trust. If that's broken by this behavior, or if the patient makes an aggressive statement such as, 'I'm going to sue you'—admittedly that's overt—you have to take note. You may have to decide if you want to terminate the relationship. It might be best to say, 'We don't seem to be on the same page, so it might be best for you to find someone who you are comfortable with. And, if you don't get this appropriate care, then X, Y or Z can occur.' You can then provide resources the patient can use to find another physician." REVIEW

Prostaglandins Deepen Upper Eyelid Sulcus

Researchers in Tokyo retrospectively compared 250 eyes of 250 patients administered one of five types of prostaglandin eye drops to determine the frequency of appearance of upper eyelid sulcus deepening, finding that upper eyelid sulcus deepening most frequently occurred with bimatoprost usage.

Study participants were diagnosed with primary open-angle glaucoma or ocular hypertension. Five healthy patients were included as controls. One eye of each patient was treated with one of the following prostaglandin eye drops for > three months: latanoprost; travoprost; tafluprost; bimatoprost; and isopropyl unoprostone. A single-lens reflex camera was used to photograph open eyelids. Three ophthalmologists independently judged the appearance of the deepened upper eyelid sulcus in the photographs by comparing the right and left eyes. A subjective self-reported questionnaire was also administered.

Upper eyelid sulcus deepening was objectively (photograph) and subjectively (questionnaire) noted as follows: latanoprost, 24 percent and 12 percent; travoprost, 50 percent and 24 percent; tafluprost, 18 percent and 10 percent; bimatoprost, 60 percent and 40 percent; and unoprostone, 8 percent and 10 percent. It occurred more frequently (objectively and subjectively) in the bimatoprost group than in the latanoprost, tafluprost and unoprostone groups ($p<0.001$).

J Glaucoma 2013;22:626-631.

Inoue K, Shiokawa M, Wakakura M, Tomita G.

DME Patients Report Improved Vision After Ranibizumab

Research from Australian, Canadian and European outpatient retina practices supports benefit from ranibizumab or ranibizumab plus laser treatment for patients with diabetic macular edema and provides vision-related, patient-reported outcome evidence that mirrors visual acuity outcomes.

Patients 18 years or older (n=345) with type 1 or 2 diabetes and visual impairment due to DME were enrolled in a Phase III, double-masked, 12-month study to determine the impact of intravitreal ranibizumab, 0.5 mg, compared with laser on patient-reported visual function. Patients were randomized to ranibizumab plus sham laser (n=116), ranibizumab plus laser (n=118) or sham injections plus laser (n=111). Ranibizumab and sham injections were given for three consecutive months, then as needed; laser plus sham treatment was given at baseline and then as needed. Outcomes were measured by National Eye Institute Visual Functioning Questionnaire 25 (NEI VFQ-25) scores at baseline, three and 12 months for patients receiving one or more study treatments with one or more post-baseline NEI VFQ-25 assessments and last observation carried forward for missing data.

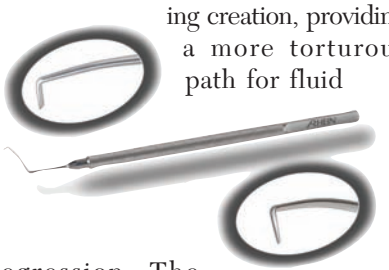
Mean baseline NEI VFQ-25 composite scores were 72.8, 73.5 and 74.1 in the ranibizumab, laser and ranibizumab plus laser groups. At 12 months, the mean composite scores (95 percent CIs) improved by 5 (ranibizumab vs. laser, 2.6 to 7.4; $p=0.01$ vs. laser) and 5.4 (ranibizumab plus laser vs. laser alone, 3.3 to 7.4; $p=0.004$ vs. laser) from baseline in the ranibizumab and ranibizumab plus laser groups, respectively, compared with 0.6 (-1.8 to 3) for the laser group. Near activities scores improved by 9 (ranibizumab vs. laser, 5 to 13; $p=0.01$) and 9.1 (ranibizumab plus laser vs. laser, 5.6 to 12.6; $p=0.006$) compared with 1.1 (-3 to 5.2) for the laser group, whereas distance activities score improved by 5.3 (ranibizumab vs. laser, 1.8 to 8.9; $p=0.04$) and 5.6 (ranibizumab plus laser vs. laser, 2.3 to 9; $p=0.03$) compared with 0.4 (-3.1 to 3.8) for the laser group. Patients with better baseline visual acuity or lower central retinal thickness had greater improvements with ranibizumab treatment compared with laser in composite and some subscale scores compared with patients with worse visual acuity or higher central retinal thickness.

JAMA Ophthalmol 2013;131: 1339-1347.

Mitchell P, Bressler N, Tolley K, Gallagher M, et al.

New Line of Rhein Knives and Chopper

Rhein Medical has launched its new line of reusable or disposable knives. The knives have special glass handles that can withstand an autoclave. The blades are super sharp, and consist of keratomes, limited-depth and paracentesis blades. The keratomes include parallel and trapezoidal configurations, and incorporate Rhein's patented 3-D design. The 3-D feature causes the incision to contort during creation, providing a more torturous path for fluid egression. The result is a better self-sealing incision. Packaged six per box, the knives can be reused over and over. The trapezoidal keratomes have a special mark exactly 2 mm from the distal segment to assist the surgeon in incision construction. Competitively priced, the new blades will reduce your operating costs significantly, with improved results, the company says.



Rhein also introduced its new Nichamin Femto Chopper, developed in coordination with Louis D. Nichamin, MD. The unique distal tip is specifically designed to fit into femto laser-created cleavage planes. The tip angulation and bend promote effortless separation of laser-fragmented sections; a special ergonomic design facilitates intraocular manipulation and helps to prevent instability from sideport leakage, enhancing anterior chamber stability. The reusable, autoclavable chopper is guaranteed for life and available for a no -obligation surgical evaluation.

Contact Rhein Medical for information on either product at (727) 209-2244.

Tomey Unveils RC-800 AutoRefractor/Keratometer

Tomey has launched its RC-800 AutoRefractor/Keratometer. The device features a color touch screen with auto shot function and a high-speed printer. The intuitive touch-screen operation measures not only refraction and keratometry but also the diameter of the cornea and pupil. The company reports the device is vastly more affordable and equivalently accurate to other competitive models.

For refraction, fogging is applied automatically for each measurement for more accurate results. And keratometry measurements provide enough information for contact lens fitting. For information call 1 (888) 449-4045 or visit tomeyusa.com.

Haag-Streit Teams with Sony To Produce High-def, 3D Surgery

Haag-Streit USA will begin offering Sony Electronics' medical grade 3D video camera, video recorder and displays with Haag-Streit USA's line of surgical microscopes. The high-definition, medically compliant equipment is designed to enable surgeons and clinicians to capture, record and display 3D video in the operating room, providing the ability to share the procedure in 3D in real time and for playback later.

The equipment, specifically designed for ophthalmic and neurosurgery applications, includes the MCC-3000MT camera that can be easily mounted on most surgical microscopes, and the new HVO-3000MT recorder designed to record surgical footage in 3D. Together with the LMD-2451MT 24-inch display and the LMD-3251MT 32-inch display, this system is the ideal solution for recording and displaying microsurgery procedures in 3D, the company says. For information, visit haag-streit-usa.com or sony.com/3dforsurgery. REVIEW

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Decreased vision follows a recent history of sinusitis, fever, headache and other symptoms in a healthy, young patient.

Nika Bagheri, MD

Presentation

A 21-year-old Caucasian female presented to the Wills Retina Service with a three-day history of bilateral decreased vision, worse in the right eye. She denied any flashes, floaters, or associated complaints. Three weeks prior she had an episode of sinusitis treated with amoxicillin for 10 days as an outpatient. One week prior she developed high fevers to 103 F, severe headache, retrobulbar ache, neck pain and stiffness, nausea and vomiting, confusion, diffuse myalgias and a bilateral lower extremity nontender papular erythematous rash. At a community emergency department she was rehydrated, given Benadryl, and a lumbar puncture was performed, which ruled out bacterial meningitis. She was discharged on azithromycin and her systemic symptoms and fever resolved prior to her presentation to the Wills Retina service.

Medical History

Past ocular history was unremarkable and past medical history was significant for migraine headache and Lyme disease, which was previously treated. Immunizations were up to date. Her only medication was an oral contraceptive. Family history was notable for a maternal grandmother with multiple sclerosis. She denied any sick contacts, recent travel and bug or animal bites. She has two indoor dogs and cats and two indoor cats and works at a veterinary clinic. She lives in a university dormitory. She denied any history of sexually transmitted infections, or alcohol or IV drug use.

Examination

Uncorrected visual acuity was count fingers and 20/30 in the right and left eye, respectively, without improvement on pinhole. The right pupil was sluggish, with an afferent pupillary defect, and the left was briskly reactive. Motility was full and intraocular pressure was within normal limits in both eyes. Confrontation visual fields were limited by visual acuity on the right, but full in the left eye. Slit-lamp exam was notable for fine, nongranulomatous, keratic precipitates bilaterally, 1+ anterior cell and flare in the right eye, and trace cell and flare in the left eye. Posterior exam revealed 1+ anterior vitreous cell and macular edema in the right eye, and optic disc edema in both eyes. A diffuse periphlebitis was present bilaterally but worse on the right, and multiple, white-centered retinal hemorrhages were seen in the periphery bilaterally *(See Figure 1)*. Neurologic exam was unremarkable.

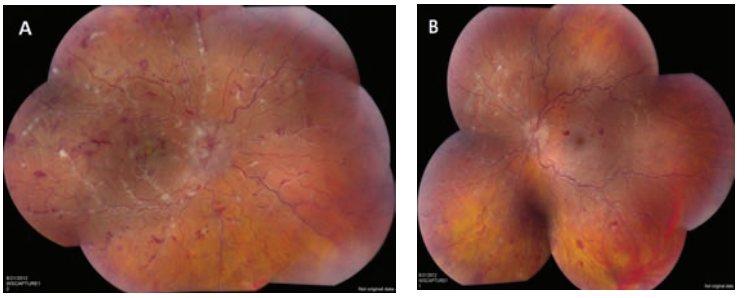

Figure 1. Fundus photos revealing: A) optic disc edema, macular edema, severe diffuse periphlebitis and white-centered retinal hemorrhages OD; B) less-severe optic disc edema, periphlebitis and white-centered retinal hemorrhages OS.

What is your differential diagnosis? What further workup would you pursue? Please turn to p. 66

Diagnosis, Workup and Treatment

The patient underwent further imaging to characterize the retinal pathology. Fluorescein angiography showed hyperfluorescence of the disc and retinal veins consistent with leakage and staining *(See Figure 2)*. Optical coherence tomography demonstrated significant macular edema in the right eye and a normal macula in the left eye *(See Figure 3)*. The patient was admitted to the internal medicine service at Thomas Jefferson University Hospital for a comprehensive systemic workup including Infectious Disease and Rheumatology consults as well as neuroimaging. She was empirically started on IV ceftriaxone. A brain MRI showed scattered subarachnoid hemorrhages in the bifrontal region with subtle, likely reactive, leptomeningeal enhancement, bilateral optic disc prominence and enhancement and normal optic nerves *(See Figure 4)*. A stat Neurology consult was obtained, deep vein thrombosis prophylaxis was discontinued, and empiric acyclovir and methylprednisolone 1 gram IV daily were initiated.

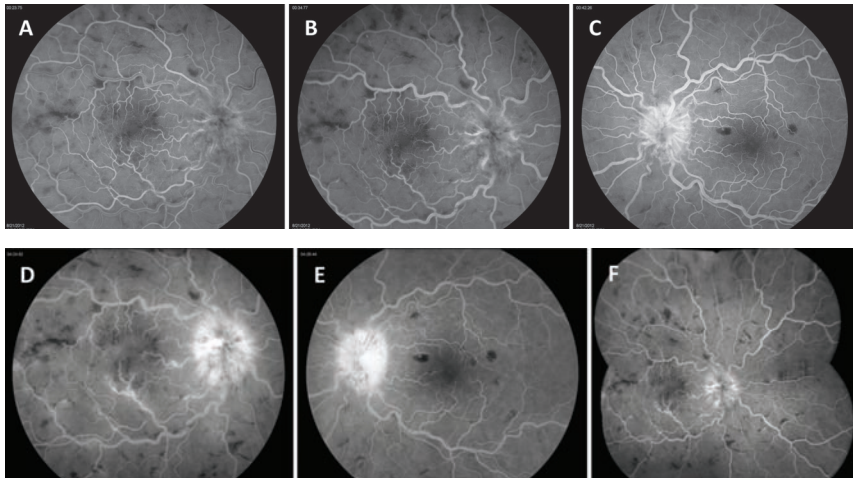

Figure 2. Fluorescein angiography revealing A) normal filling OD; B and C) leakage and staining of venules (sparing the arterioles) OU; D and E) disc and vessel leakage and staining OU; and F) absence of vessel occlusion OD.

The patient's complete metabolic panel and complete blood count were normal except for elevated platelets of 458. Her CSF studies from the community ED showed increased leukocytes with elevated neutrophils at 40 percent, 25 erythrocytes, absent xanthochromia, normal protein and slightly elevated glucose at 76. CSF gram stain and bacterial cultures were negative.

Given the patient's history, exam and risk factors, a broad workup was initiated to rule out human immunodeficiency virus; tuberculosis; Lyme disease; syphilis; cat scratch disease; toxoplasmosis; human herpes virus 6; cytomegalovirus; Epstein-Barr virus; west Nile virus; Rickettsia panel; ehrlichia and anaplasmosis; sarcoidosis; rheumatoid arthritis; systemic lupus erythematosus; antiphospholipid antibody syndrome; small vessel vasculitides such as Wegener's granulomatosis; and blood and urine cultures.

Throughout her hospital stay the patient remained asymptomatic except for her decreased vision. MRA imaging ruled out aneurysm and CNS vasculitis. Her workup was notable for Lyme studies that showed IgG reactive, and 1 of 3 IgM bands reactive, which was considered negative for re-infection. She was positive for Toxoplasma IgG but negative for IgM, ANA positive (1:40, homogenous staining), and her erythrocyte sedimentation rate was 45. All other investigations were normal. With negative viral studies, acyclovir was stopped.

Per Rheumatology, an associated

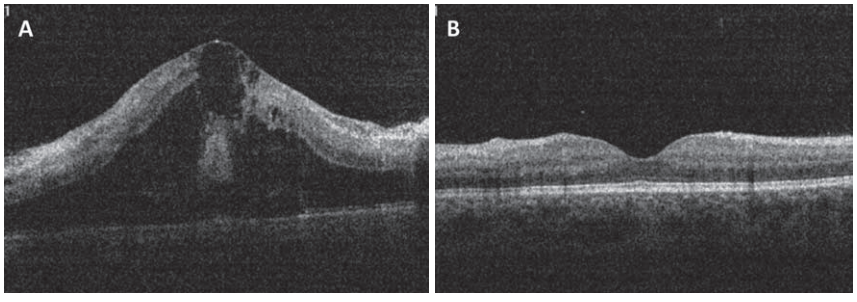

Figure 3. Macular OCTs showing A) macular edema OD, B) normal macula OS.

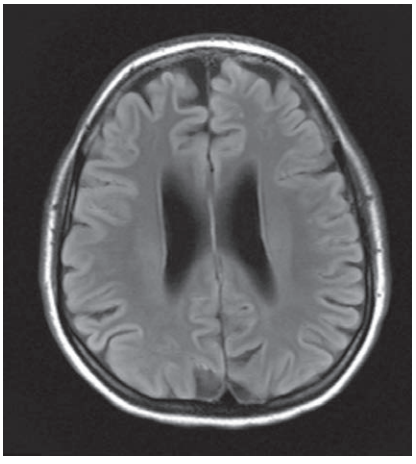

Figure 4. MRI with scattered bifrontal subarachnoid hemorrhages.

auto-immune disorder was unlikely. Per Infectious Diseases, the patient's workup was most consistent with aseptic meningitis. She received full pulse of three days of IV methylprednisolone followed by a tapering dose of oral prednisone. She was discharged on IV ceftriaxone to complete a 14-day course.

After two weeks her fundus exam showed significant improvement with less disc edema, less macular edema in the right eye, substantial decrease in perivenous sheathing, and resolution of the white-centered retinal hemorrhages peripherally. One month after presentation she was doing well with complete resolution of macular edema in her right eye. Her visual acuity improved to 20/100 in the right eye and 20/20 in the left eye. She was continued on a prednisone 40 mg daily taper. She was diagnosed as secondary frosted branch periphlebitis with prominent disc edema in a patient with aseptic meningitis.

Discussion

Frosted branch angiitis (FBA), or acute frosted retinal periphlebitis, is a rare clinical entity first described in the Japanese literature in 1976 in a 6-year-old child with idiopathic bilateral retinal periphlebitis.[1] The severe sheathing of retinal vessels created the appearance of frosted tree branches. Fewer than 60 cases have been reported in the world literature, and the majority of cases (75 percent) are from Japan.[2]

The use of the term FBA in the literature as both a clinical syndrome as well as a clinical sign prompted Robert C. Kleiner, MD, et al, to distinguish three different subgroups based on their etiology.[3] FBA can be classified as 1) primary idiopathic FBA; 2) secondary FBA due to infectious or auto-immune etiology; or 3) FBA in neoplastic processes.

The primary idiopathic form is the acute clinical syndrome comprised of young and otherwise healthy patients (10 to 30 years old) who typically present with bilateral visual loss and panuveitis.[2,3] These patients typically respond promptly and favorably to corticosteroid treatment. The pathogenesis of this idiopathic variety is unknown, but hypothesized to be an immune-mediated mechanism directed towards an inciting antigen in the eye, possibly triggered by a bacterial or viral infection.[2] Secondary FBA is associated with infectious diseases, including cytomegalovirus; tuberculosis; HIV, toxoplasmosis; Epstein-Barr virus; herpes simplex virus; varicella zoster virus; human T-lymphotropic virus; antistreptolysin-O; Coxsackie virus A10; adenovirus; measles and rubella; as well as with autoimmune diseases, including sarcoidosis; multiple sclerosis; lupus; Behçet's, and Crohn's disease.[2,4,5] In this subgroup, FBA is a clinical sign of underlying disease as opposed to a distinct clinical entity. The pathogenesis for infectious etiologies is thought to be due to viral antigens forming immune-complexes and depositing in retinal vessels. Immune complexes are similarly responsible in autoimmune disorders.[4] Frosted branch-like angiitis comprises patients affected by lymphoma and leukemia, in whom the pathology is thought to be caused by infiltration of retinal vessels with malignant cells.[2]

FBA is a clinical diagnosis. It is associated with acute visual loss, and mild anterior segment inflammation may be present. Posterior segment inflammation is always severe with thick white vascular sheathing and retinal edema on ophthalmoscopy.[6] Veins are affected more so than arteries. Retinal exudates and hemorrhages are present. Fluorescein angiography shows normal venous flow in the early phases, and dye leakage from sheathed vessels in the late phase with optic disc hyper fluorescence.[6] Importantly, there are no signs of vessel occlusion or stasis. Visual field testing shows restriction or relative central defects thought to result from macular edema.[7] Electrophysiology has shown a reduction in amplitudes of the electroretinogram, electrooculogram and visually evoked response.[7] Most patients have been treated with systemic steroids, with favorable visual recovery.

Our case is consistent with FBA due to aseptic meningitis. A letter to the editor of the *European Journal of Neurology* described a case of FBA associated with aseptic meningitis in 2000.[8] This is the only other documented case of FBA associated with aseptic meningitis. Our case is unique, however, given the very prominent disc edema and scattered subarachnoid hemorrhages on presentation. Significant disc edema in the setting of FBA should prompt neuroimaging to rule out intracranial pathology. REVIEW

The author would like to thank Michael Dollin, MD, of the Retina Service for his time and assistance in preparing this case report.

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7. Watanabe Y, Takeda N, Adachi-Usami E. A case of frosted branch angiitis. Br J Ophthalmol 1987;71:553-558.
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REVIEW | Technology Update

(continued from page 21)

software. The server does not even need to be located locally, as the capture system will readily communicate across a WAN or VPN, thereby markedly reducing expensive hardware or software costs.

• ***OR friendly.*** Some connectivity systems we had looked at require a computer workstation, keyboard, mouse and monitor for each device that requires data capturing, including laser systems in your OR. This requirement quickly creates an unwieldy, unworkable workspace that's cluttered with 110-volt wiring and cables and monitors that interfere with iris recognition capture. Our small capture device fits on the laser or other device and is connected to the network with one Category 5 cable, minimizing clutter.

• ***Helps make my results better.*** Once I began to collect the set of data from my lasers and preop equipment that I had been missing, I was able to create a program to analyze the numbers in ways I couldn't before. I was unable to analyze them previously due to the sheer magnitude of the task involved with manually inputting thousands of Zernike coefficients, wavefront capture diameters, Q-values (corneal asphericity) and other data points that were photographed in the clinical record but ultimately ignored because they couldn't be used for statistical queries. Now, though, equipped with this data from hundreds of patients, I can establish search parameters such as, "Every patient between -1 and -6 D with at least 0.5 D of astigmatism, keratometry between 45 and 47 and spherical aberration and coma terms greater than 0.3 µm," and the system will instantly give me their results. I can understand the complex relationships between vision metrics and my final results.

Being able to instantly record, sort and analyze surgical outcomes without the need for manual entry of data brings my refractive surgery practice closer to the evidence-based medicine ideal, which is the application of population-based vision outcomes data to the care of the individual patient. It's startling to think that, though we refractive surgeons routinely review sphere, cylinder and visual acuity data, when it comes to analyzing the clinical effects of higher-order aberrations like spherical aberration on lower-order aberrations like myopia, we have failed to derive a useable algorithm in more than 10 years. With a system like this, we will be able to see these relationships, and laser manufacturers may even be able to use what we learn to adjust how their lasers treat patients with certain combinations of HOAs and LOAs to optimize results. REVIEW

Dr. Will is in private practice. For surgeons interested in elements of the system and how they might apply to their instruments, he can be contacted at drwill@willvision.com.
A longer discussion of refractive surgery's MIS challenges appears on Review's *Web version of the article.*

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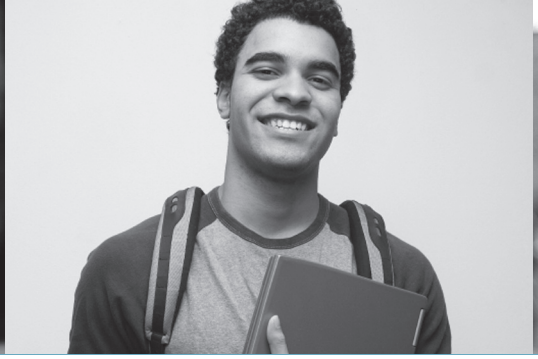


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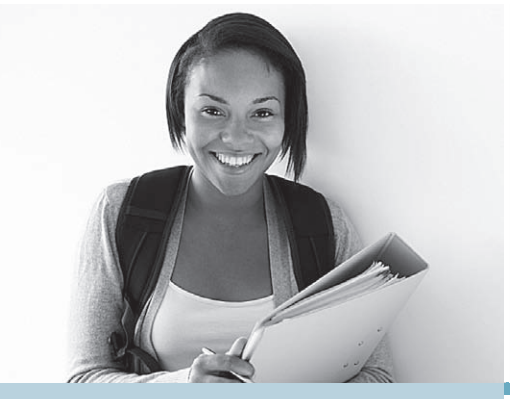

About Rick

Rick Bay served as the publisher of The *Review* Group since 1991.

To those who worked for him, he was a leader whose essence was based in a fierce and boundless loyalty.

To those in the industry and the professions he served, he will be remembered for his unique array of skills and for his dedication to exceeding the expectations of his customers, making many of them fast friends.

Scholarships will be awarded to advance the education of students in both ***Optometry*** and ***Ophthalmology***, and will be chosen by their school based on qualities that embody Rick's commitment to the profession, including integrity, compassion, partnership and dedication to the greater good.

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THE RICK BAY FOUNDATION
for Excellence in Eyecare Education

LUMIGAN® 0.01% AND 0.03%
(bimatoprost ophthalmic solution)

Brief Summary—Please see the LUMIGAN® 0.01% and 0.03% package insert for full Prescribing Information.

INDICATIONS AND USAGE

LUMIGAN® 0.01% and 0.03% (bimatoprost ophthalmic solution) is indicated for the reduction of elevated intraocular pressure in patients with open angle glaucoma or ocular hypertension.

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

Pigmentation: Bimatoprost ophthalmic solution has been reported to cause changes to pigmented tissues. The most frequently reported changes have been increased pigmentation of the iris, periorbital tissue (eyelid) and eyelashes. Pigmentation is expected to increase as long as bimatoprost is administered. The pigmentation change is due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. After discontinuation of bimatoprost, pigmentation of the iris is likely to be permanent, while pigmentation of the periorbital tissue and eyelash changes have been reported to be reversible in some patients. Patients who receive treatment should be informed of the possibility of increased pigmentation. The long term effects of increased pigmentation are not known.

Iris color change may not be noticeable for several months to years. Typically, the brown pigmentation around the pupil spreads concentrically towards the periphery of the iris and the entire iris or parts of the iris become more brownish. Neither nevi nor freckles of the iris appear to be affected by treatment. While treatment with **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution) can be continued in patients who develop noticeably increased iris pigmentation, these patients should be examined regularly.

Eyelash Changes: LUMIGAN® 0.01% and 0.03% may gradually change eyelashes and vellus hair in the treated eye. These changes include increased length, thickness, and number of lashes. Eyelash changes are usually reversible upon discontinuation of treatment.

Intraocular Inflammation: LUMIGAN® 0.01% and 0.03% should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Macular Edema: Macular edema, including cystoid macular edema, has been reported during treatment with bimatoprost ophthalmic solution. **LUMIGAN®** 0.01% and 0.03% should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Angle-closure, Inflammatory, or Neovascular Glaucoma: LUMIGAN® 0.01% and 0.03% has not been evaluated for the treatment of angle-closure, inflammatory or neovascular glaucoma.

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.

Use With Contact Lenses: Contact lenses should be removed prior to instillation of **LUMIGAN®** 0.01% and 0.03% and may be reinserted 15 minutes following its administration.

ADVERSE REACTIONS

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

In clinical studies with bimatoprost ophthalmic solutions (0.01% or 0.03%) the most common adverse reaction was conjunctival hyperemia (range 25%–45%). Approximately 0.5% to 3% of patients discontinued therapy due to conjunctival hyperemia with 0.01% or 0.03% bimatoprost ophthalmic solutions. Other common reactions (>10%) included growth of eyelashes, and ocular pruritus.

Additional ocular adverse reactions (reported in 1 to 10% of patients) with bimatoprost ophthalmic solutions included ocular dryness, visual disturbance, ocular burning, foreign body sensation, eye pain, pigmentation of the periocular skin, blepharitis, cataract, superficial punctate keratitis, periorbital erythema, ocular irritation, eyelash darkening, eye discharge, tearing, photophobia, allergic conjunctivitis, asthenopia, increases in iris pigmentation, conjunctival edema, conjunctival hemorrhage, and abnormal hair growth. Intraocular inflammation, reported as iritis, was reported in less than 1% of patients.

Systemic adverse reactions reported in approximately 10% of patients with bimatoprost ophthalmic solutions were infections (primarily colds and upper respiratory tract infections). Other systemic adverse reactions (reported in 1 to 5% of patients) included headaches, abnormal liver function tests, and asthenia.

Postmarketing Experience: The following reactions have been identified during postmarketing use of **LUMIGAN®** 0.01% and 0.03% in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to **LUMIGAN®** or a combination of these factors, include: dizziness, eyelid edema, hypertension, nausea, and periorbital and lid changes associated with a deepening of the eyelid sulcus.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C

Teratogenic effects: In embryo/fetal developmental studies in pregnant mice and rats, abortion was observed at oral doses of bimatoprost which achieved at least 33 or 97 times, respectively, the maximum intended human exposure based on blood AUC levels.

At doses at least 41 times the maximum intended human exposure based on blood AUC levels, the gestation length was reduced in the dams, the incidence of dead fetuses, late resorptions, peri- and postnatal pup mortality was increased, and pup body weights were reduced.

There are no adequate and well-controlled studies of **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution) administration in pregnant women. Because animal reproductive studies are not always predictive of human response **LUMIGAN®** should be administered during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: It is not known whether **LUMIGAN®** 0.01% and 0.03% is excreted in human milk, although in animal studies, bimatoprost has been shown to be excreted in breast milk. Because many drugs are excreted in human milk, caution should be exercised when **LUMIGAN®** is administered to a nursing woman.

Pediatric Use: Use in pediatric patients below the age of 16 years is not recommended because of potential safety concerns related to increased pigmentation following long-term chronic use.

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

Hepatic Impairment: In patients with a history of liver disease or abnormal ALT, AST and/or bilirubin at baseline, bimatoprost 0.03% had no adverse effect on liver function over 48 months.

OVERDOSAGE

No information is available on overdosage in humans. If overdose with **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution) occurs, treatment should be symptomatic.

In oral (by gavage) mouse and rat studies, doses up to 100 mg/kg/day did not produce any toxicity. This dose expressed as mg/m2 is at least 70 times higher than the accidental dose of one bottle of **LUMIGAN®** 0.03% for a 10 kg child.

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility: Bimatoprost was not carcinogenic in either mice or rats when administered by oral gavage at doses of up to 2 mg/kg/day and 1 mg/kg/day respectively (at least 192 and 291 times the recommended human exposure based on blood AUC levels respectively) for 104 weeks.

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

Bimatoprost did not impair fertility in male or female rats up to doses of 0.6 mg/kg/day (at least 103 times the recommended human exposure based on blood AUC levels).

PATIENT COUNSELING INFORMATION

Potential for Pigmentation: Patients should be advised about the potential for increased brown pigmentation of the iris, which may be permanent. Patients should also be informed about the possibility of eyelid skin darkening, which may be reversible after discontinuation of **LUMIGAN®** 0.01% and 0.03% (bimatoprost ophthalmic solution).

Potential for Eyelash Changes: Patients should also be informed of the possibility of eyelash and vellus hair changes in the treated eye during treatment with **LUMIGAN®** 0.01% and 0.03%. These changes may result in a disparity between eyes in length, thickness, pigmentation, number of eyelashes or vellus hairs, and/or direction of eyelash growth. Eyelash changes are usually reversible upon discontinuation of treatment.

Handling the Container: Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye, surrounding structures, fingers, or any other surface in order to avoid contamination of the solution by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

When to Seek Physician Advice: Patients should also be advised that if they develop an intercurrent ocular condition (e.g., trauma or infection), have ocular surgery, or develop any ocular reactions, particularly conjunctivitis and eyelid reactions, they should immediately seek their physician's advice concerning the continued use of **LUMIGAN®** 0.01% and 0.03%.

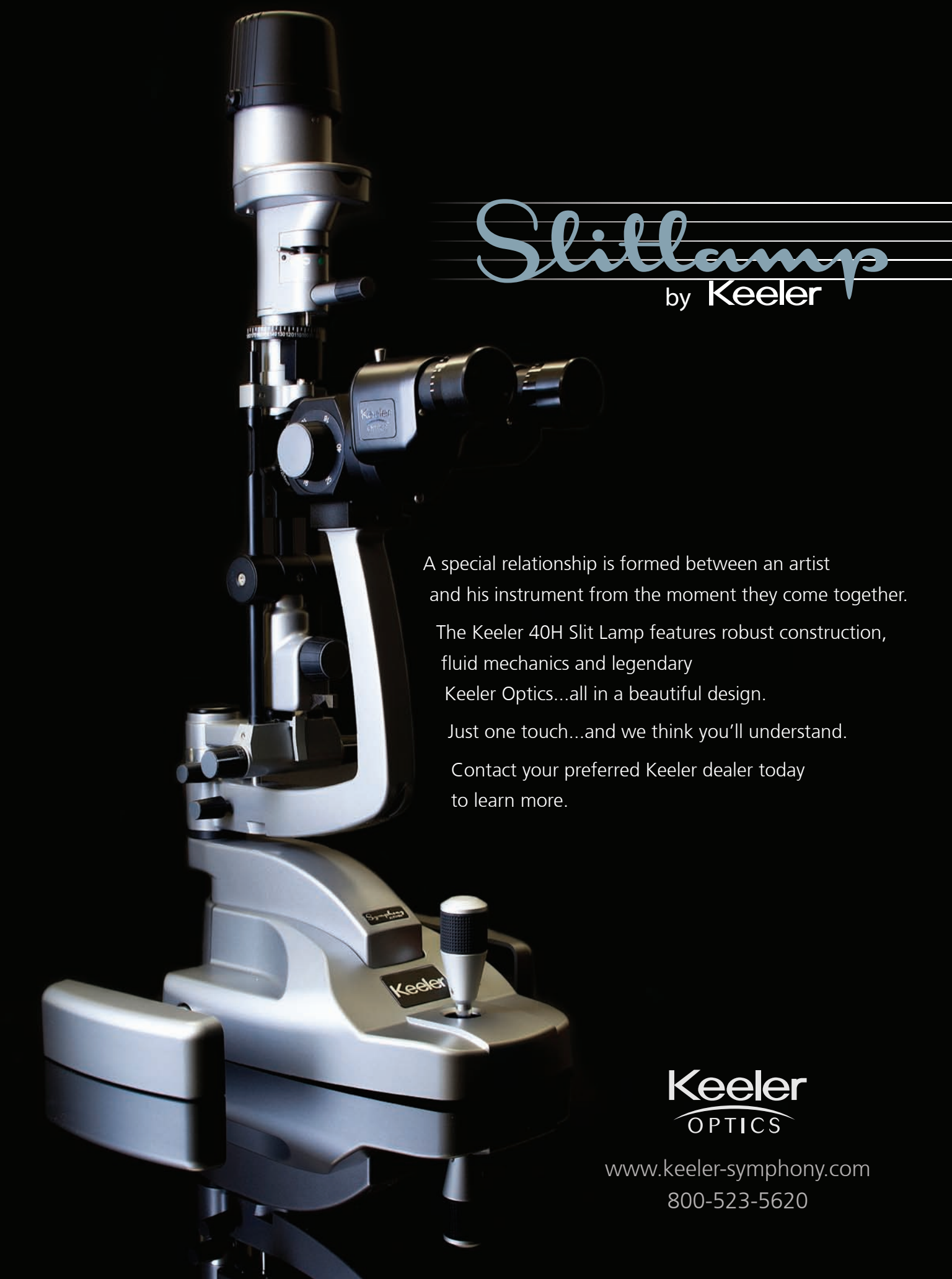
Use with Contact Lenses: Patients should be advised that **LUMIGAN®** 0.01% and 0.03% contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to instillation of **LUMIGAN®** and may be reinserted 15 minutes following its administration.

Use with Other Ophthalmic Drugs: Patients should be advised that if more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes between applications.

APC70EN12 based on 71807US13.

Rx only

ALLERGAN®


Slitlamp
by Keeler
A special relationship is formed between an artist
and his instrument from the moment they come together.
The Keeler 40H Slit Lamp features robust construction,
fluid mechanics and legendary
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For patients starting or changing PGA therapy

Drop IOP.
Keep monotherapy.

Indication: LUMIGAN® (bimatoprost ophthalmic solution) 0.01% is indicated for the reduction of elevated intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Important Safety Information

Warnings and Precautions: LUMIGAN® causes changes to pigmented tissues, mostly increased pigmentation of the iris, eyelid, and eyelashes as long as LUMIGAN® is administered. Iris color change may not be noticeable for several months to years. After discontinuation of bimatoprost, iris pigmentation is likely to be permanent, while eyelid and eyelash changes have been reported to be reversible in some patients. Patients should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

LUMIGAN® should be used with caution in patients with active intraocular inflammation (eg, uveitis) because the inflammation may be exacerbated. Macular edema, including cystoid macular edema, has been reported with LUMIGAN®. LUMIGAN® should be used with caution in aphakic patients, in pseudophakic patients with a torn posterior lens capsule, or in patients with known risk factors for macular edema.

Adverse Reactions: The most common (25%-45%) adverse event with LUMIGAN® was conjunctival hyperemia. Approximately 0.5% to 3% of patients discontinued therapy due to conjunctival hyperemia. Other common events (> 10%) included growth of eyelashes and ocular pruritus.

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

Write it RIGHT 0.01%

LUMIGAN® 0.01%
(bimatoprost ophthalmic solution) 0.01%