REVIEW® of Ophthalmology

January 2012 • revophth.com

Improve Your Toric Success Rate P. 26

Bringing Monofocal IOLs into Focus P. 34

EHR Computing: In-house or in the Cloud? P. 22

LOTEMAX® OINTMENT

(loteprednol etabonate ophthalmic ointment) 0.5%

POWER IN A PRESERVATIVE-FREE OINTMENT

LOTEMAX® ointment is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

- In 2 phase 3, randomized, multicenter, double-masked, parallel-group, 4-week, clinical safety and efficacy evaluations of LOTEMAX® ointment (loteprednol etabonate ophthalmic ointment) 0.5% vs vehicle (mineral oil and white petrolatum) for the treatment of inflammation and pain following cataract surgery (N=805), LOTEMAX® ointment demonstrated statistically significant resolution of anterior chamber cells and flare* (24-32% vs 11-14%) and pain (73-78% vs 41-45%) vs vehicle at post-operative day 8[1,2]

*Cell count 0 and no flare.

Important Risk Information about LOTEMAX® ointment

- LOTEMAX® ointment, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures
- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for 10 days or longer, IOP should be monitored
- Use of corticosteroids may result in posterior subcapsular cataract formation and may delay healing and increase the incidence of bleb formation after cataract surgery. The initial prescription and renewal of the medication order beyond 14 days should be made by a physician only after examination of the patient with the aid of magnification
- Corticosteroids may increase the hazard of secondary ocular infections. If pain, redness, itching or inflammation becomes aggravated, the patient should be advised to consult a physician. If signs and symptoms fail to improve after 2 days, the patient should be reevaluated. Fungal culture should be taken when appropriate
- Patients should not wear contact lenses during their course of therapy with LOTEMAX® ointment. LOTEMAX® should not be used in children following ocular surgery as it may interfere with amblyopia treatment. LOTEMAX® is not indicated for intraocular administration
- The most common ocular adverse event, reported in approximately 25% of subjects in clinical studies, is anterior chamber inflammation. Other common adverse events, with an incidence of 4-5%, are conjunctival hyperemia, corneal edema, and eye pain. Many of these events may have been the consequence of the surgical procedure

Please see the Brief Summary of the LOTEMAX® ointment full prescribing information on the reverse side.

References: 1. LOTEMAX ophthalmic ointment Prescribing Information, April 2011. **2.** Comstock TL, Paterno MR, Singh A, Erb T, Davis E. Safety and efficacy of loteprednol etabonate ophthalmic ointment 0.5% for the treatment of inflammation and pain following cataract surgery. *Clin Ophthalmol.* 2011;5:177-186.

For product-related questions and concerns, call **1-800-323-0000** or visit **www.bausch.com**.

BAUSCH + LOMB

Lotemax® Ointment
loteprednol etabonate
ophthalmic ointment, 0.5%

Bausch & Lomb
Lotemax®
loteprednol etabonate
ophthalmic ointment 0.5%

Brief Summary: Based on full prescribing information revised April 2011

1 INDICATIONS AND USAGE

LOTEMAX® ointment is a corticosteroid indicated for the treatment of post-operative inflammation and pain following ocular surgery.

4 CONTRAINDICATIONS

LOTEMAX ointment, as with other ophthalmic corticosteroids, is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.

5 WARNINGS AND PRECAUTIONS

5.1 Intraocular pressure (IOP) increase

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for 10 days or longer, IOP should be monitored even though it may be difficult in children and uncooperative patients.

5.2 Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

5.3 Delayed healing

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids.

The initial prescription and renewal of the medication order beyond 14 days should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

5.4 Bacterial infections

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated

5.5 Viral infections

Employment of a corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and may exacerbate the severity of many viral infections of the eye (including herpes simplex).

5.6 Fungal infections

Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use. Fungal culture should be taken when appropriate.

5.7 Contact Lens Wear

Patients should not wear contact lenses during their course of therapy with LOTEMAX ointment.

5.8 Amblyopia

LOTEMAX (loteprednol etabonate ophthalmic ointment), 0.5% should not be used in children following ocular surgery. Its use may interfere with amblyopia treatment by hindering the child's ability to see out of the operated eye (see Pediatric Use, 8.4).

5.9 Topical ophthalmic use only

Lotemax is not indicated for intraocular administration.

6 ADVERSE REACTIONS

Adverse reactions associated with ophthalmic steroids include elevated intraocular pressure, which may be associated with optic nerve damage, visual acuity and field defects, posterior subcapsular cataract formation, secondary ocular infection from pathogens including herpes simplex, and perforation of the globe where there is thinning of the cornea or sclera.

The most common ocular adverse event reported at approximately 25% in subjects in clinical studies with Lotemax ointment was anterior chamber inflammation. Other common adverse events, with an incidence of 4-5%, were conjunctival hyperemia, corneal edema, and eye pain. Many of these events may have been the consequence of the surgical procedure. The only non-ocular adverse event occurring at ≥ 1% was headache (1.5%).

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic effects: Pregnancy Category C.

Loteprednol etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic (increased incidence of meningocele, abnormal left common carotid artery, and limb flexures) when administered orally to rabbits during organogenesis at a dose of 3 mg/kg/day (150 times the maximum daily clinical dose), a dose which caused no maternal toxicity. The no-observed-effect-level (NOEL) for these effects was 0.5 mg/kg/day (25 times the maximum daily clinical dose). Oral treatment of rats during organogenesis resulted in teratogenicity (absent innominate artery at ≥ 5 mg/kg/day doses, and cleft palate and umbilical hernia at ≥ 50 mg/kg/day) and embryotoxicity (increased post-implantation losses at 100 mg/kg/day and decreased fetal body weight and skeletal ossification with ≥ 50 mg/kg/day). Treatment of rats with 0.5 mg/kg/day (25 times the maximum daily clinical dose) during organogenesis did not result in any reproductive toxicity. Loteprednol etabonate was maternally toxic (significantly reduced body weight gain during treatment) when administered to pregnant rats during organogenesis at doses of ≥5 mg/kg/day.

Oral exposure of female rats to 50 mg/kg/day of loteprednol etabonate from the start of the fetal period through the end of lactation, a maternally toxic treatment regimen (significantly decreased body weight gain), gave rise to decreased growth and survival, and retarded development in the offspring during lactation; the NOEL for these effects was 5 mg/kg/day. Loteprednol etabonate had no effect on the duration of gestation or parturition when administered orally to pregnant rats at doses up to 50 mg/kg/day during the fetal period.

LOTEMAX should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.

8.3 Nursing Mothers

It is not known whether topical ophthalmic administration of corticosteroids could result in sufficient systemic absorption to produce detectable quantities in human milk. Systemically administered steroids appear in human milk and could suppress growth, interfere with endogenous corticosteroid production, or cause other untoward effects. Caution should be exercised when LOTEMAX ointment is administered to a nursing woman.

8.4 Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

LOTEMAX (loteprednol etabonate ophthalmic ointment) 0.5% should not be used in children following ocular surgery. Its use may interfere with amblyopia treatment by hindering the child's ability to see out of the operated eye.

8.5 Geriatric Use

No overall differences in safety and effectiveness have been observed between elderly and younger patients.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, and Impairment of Fertilty

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in a chromosome aberration test in human lymphocytes, or *in vivo* in the single dose mouse micronucleus assay. Treatment of male and female rats with up to 50 mg/kg/day and 25 mg/kg/day of loteprednol etabonate, respectively, (2500 and 1250 times the maximum daily clinical dose, respectively) prior to and during mating did not impair fertility in either gender.

17 PATIENT COUNSELING INFORMATION

17.1 Risk of Contamination

Patients should be advised not to touch the eyelid or surrounding areas with the tip of the tube. The cap should remain on the tube when not in use

Patients should be advised to wash hands prior to using LOTEMAX ointment.

Do not use if tamper evident skirt is visible on bottom of cap.

17.2 Contact Lens Wear

Patients should also be advised not to wear contact lenses during their course of therapy.

17.3 Risk of Secondary Infection

If pain, redness, itching or inflammation becomes aggravated, the patient should be advised to consult a physician.

MANUFACTURER INFORMATION

Bausch & Lomb Incorporated

Tampa, Florida 33637 USA

9243500

CME

SAVE THE DATE

3rd Annual

MANAGING GLAUCOMA:
BEYOND INTRAOCULAR PRESSURE

April 19, 2012

Conrad Chicago
521 North Rush Street
Chicago, IL 60611
Hotel #: (312) 645-1500

Program Chair:

Robert N. Weinreb, MD
Distinguished Professor and Chairman of Ophthalmology
Morris Gleich Chair
Director, Shiley Eye Center
Director, Hamilton Glaucoma Center
University of California San Diego

Agenda and Additional Faculty to Follow

ACCREDITATION STATEMENT: This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of the Institute for the Advancement of Human Behavior (IAHB) and *Review of Ophthalmology*®/Jobson Medical Information LLC. The IAHB is accredited by the ACCME to provide continuing medical education for physicians.

CREDIT DESIGNATION STATEMENT: The IAHB designates this live activity for a maximum of *5 AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

3 Ways to Register!

① Online: **www.revophth.com/GlaucMgmt2012**

② Call: **(877) 451-6512**

③ Email: **ReviewMeetings@Jobson.com**

Jointly Sponsored by

REVIEW® of Ophthalmology

IAHB
Institute for the Advancement of Human Behavior

Supported by an Independent Educational Grant from Allergan, Inc.

ALLERGAN

REVIEW NEWS
Volume XIX • No. 1 • January 2012

Academy and FDA Announce Plan to Tally TASS Incidence

The American Academy of Ophthalmology will team with the Food and Drug Administration on a program to help ophthalmologists reduce Toxic Anterior Segment Syndrome, a rare, but potentially sight-stealing complication of cataract surgery. As a part of the FDA's Proactive TASS Program, the AAO will help to create a physician registry to track TASS occurrences. The registry, which is currently in a pilot stage, will assist the FDA in determining the cause of the condition in order to prevent future outbreaks.

Currently, the identification of TASS outbreaks is dependent on surgeons and surgical centers keeping detailed records of all products and equipment used during cataract surgery. However, this can be cumbersome and underreporting is suspected. The new online reporting mechanism will be housed with the AAO-sponsored registry for Physician Quality Reporting System, a system that ophthalmologists use regularly, making reporting more convenient.

The AAO will serve as a consultant in the program, helping to determine the data to be collected and to recruit cataract surgeons to participate. The academy also will be involved in the analysis of the data collected at the end of the pilot to determine if changes are needed prior to the creation of a permanent registry.

The academy's efforts are part of a broader FDA program that is one of the first proactive surveillance programs to monitor the multiple medical devices used in cataract surgery and to aid in early identification of a national TASS outbreak. The FDA will use the pilot to develop the permanent registry that can be used by regulatory agencies as well as clinicians. The registry will provide a better understanding of factors present in the development of adverse events and outbreaks in patients who have received intraocular lenses.

Nanoparticles May Work to Deliver Drugs

Hitching a ride into the retina on nanoparticles called dendrimers offers a new way to treat age-related macular degeneration and retinitis pigmentosa, say investigators at the Mayo Clinic, Wayne State University and Johns Hopkins. Their study shows that steroids attached to the dendrimers target the damage-causing cells associated with neuroinflammation, leaving the rest of the eye unaffected and preserving vision. The findings appear in the journal *Biomaterials*.

Dry AMD and RP are caused by neuroinflammation, which progressively damages the retina and can lead to blindness. "There is no cure for these diseases," says Mayo Clinic ophthalmologist Raymond Iezzi, MD, a lead author of the study. "An effective treatment could offer hope to hundreds of millions of patients worldwide."

Dr. Iezzi and fellow principal author Rangaramanujam Kannan, PhD, an ophthalmology professor at the Wilmer Eye Institute of Johns Hopkins, developed an intracellular, sustained-release drug delivery system. The research, conducted in part at Wayne State University's Kresge Eye Institute with collaboration from Wayne State's College of Engineering and Ligon Research Center of Vision, tested the dendrimer delivery system in rats that develop neuroinflammation.

The target was microglial cells, inflammatory cells in charge of cleaning up dead and dying material in the eye, Dr. Iezzi says. When activated as "trash collectors," the cells cause damage via neuroinflammation. The microglial cells gobble up the dendrimers, and the drug then shuts down the cells' activity.

"Surprisingly, the activated microglia in the degenerating retina appeared to eat the dendrimer selectively, and retain them for at least a month. The drug is released from the dendrimer in a sustained fashion inside these cells, offering targeted neuroprotection to the retina," Dr. Kannan says.

The treatment reduced neuroinflammation in the rat model and protected vision by preventing injury to photoreceptors in the retina. Though the steroid offers only temporary protection, the treatment as a whole provides sustained relief from neuroinflammation.

Seizure Drug Could Retard Tumors' Spread

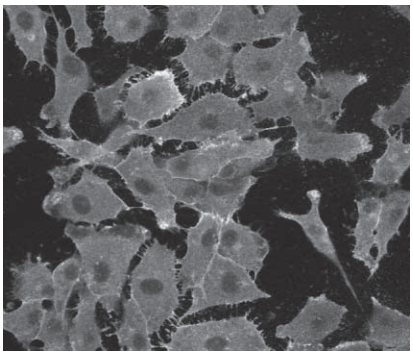
A drug commonly used to treat seizures appears to make eye tumors less likely to grow if they spread to other parts of the body, according to researchers at Washington University School of Medicine in St. Louis. Their findings are available online in the journal *Clinical Cancer Research*.

Uveal melanoma can be very aggressive and metastasize from the eye to other organs, especially the liver. "Melanoma in general, and uveal melanoma in particular, is notoriously difficult to treat once it has metastasized and grown in a distant organ," says principal investigator J. William Harbour, MD. "We previously identified an aggressive class 2 molecular type of uveal melanoma that, in most cases, already has metastasized by the time the eye cancer is diagnosed, even though imaging the body can't detect it yet. This microscopic amount of cancer can remain dormant in the liver and elsewhere for several years before it begins to grow and becomes lethal."

Once this happens, the prospects for survival are poor, according to Dr. Harbour, the Paul A. Cibis Distinguished Professor of Ophthalmology and Visual Sciences and professor of cell biology and of molecular oncology.

Dr. Harbour's new study shows that drugs known as histone deacetylase (HDAC) inhibitors alter the conformation of the DNA of the aggressive form of uveal melanoma, which changes the way key genes are expressed, rendering the tumor cells less aggressive.

"We looked at uveal melanoma cells in the laboratory and in an animal model, and we found that HDAC inhibitors can block the growth and proliferation of tumor cells," he says. "HDAC inhibitors appear to reverse the aggressive molecular signature that we had identified several years ago as a marker for metastatic death. When we look at aggressive melanoma cells under the microscope after treatment with HDAC inhibitors, they look more like normal cells and less like tumor cells."



Aggressive uveal melanoma cells carry the "class 2 signature," meaning they are likely to spread outside of the eye.

Because HDAC inhibitors already are on the market, Dr. Harbour says he thinks it may be possible to quickly begin testing the drugs in patients with aggressive forms of uveal melanoma.

The drugs have relatively mild side effects that are not as severe as those seen in patients undergoing chemotherapy. One HDAC inhibitor, for example, is the anti-seizure drug valproic acid. Its most common side effect is drowsiness, which is typical of all HDAC inhibitors.

Clinical trials of HDAC inhibitors could begin in the next six to 12 months. Already, other researchers have applied for funding to begin testing an HDAC inhibitor called SAHA (suberoylanilide hydroxic acid) in patients with metastatic uveal melanoma.

"I think this is a reasonable place to start in the challenging effort to improve survival in patients with metastatic uveal melanoma," Dr. Harbour says. "I suspect that the best role for HDAC inhibitors will be to slow or prevent the growth of tumor cells that have spread out of the eye but cannot yet be detected. This might lengthen the time between the original eye treatment and the appearance of detectable cancer in the liver and elsewhere."

Like the chicken pox virus that lives for years in nerve cells without affecting health, Dr. Harbour says treatment with HDAC inhibitors may allow patients with aggressive melanomas to live for many years without any detectable spread of their disease.

Dr. Harbour and his colleagues previously developed a screening test to predict whether the cancer would be likely to spread to the liver and other parts of the body. The test is helpful because although less than 4 percent of patients with uveal melanoma have detectable metastatic disease, up to half will eventually die of metastasis even after successful treatment of the tumor with radiation, surgery, or, in the worst cases, removal of the eye.

Tumors that tend to remain contained within the eye are called class 1 uveal melanomas. With a needle biopsy, doctors can quickly determine whether a tumor is likely to be a class 1 cancer or whether it carries a molecular signature that identifies it as a high-risk, class 2 melanoma. Dr. Harbour's team developed a test to identify the class 2 molecular signature, and that test is now being used around the world to detect the aggressive form of uveal melanoma.

CMS Rule Would Make Payments Transparent

The Centers for Medicare & Medicaid Services has proposed a rule that will increase public awareness of financial relationships between drug and device manufacturers and certain health-care providers. This is one of many steps under the Affordable Care Act designed to increase transparency in the health-care system, which can lead to better care at lower costs, the agency says.

The proposed rule would require

manufacturers of drugs, devices, biologicals and medical supplies covered by Medicare, Medicaid or the Children's Health Insurance Program to report to CMS payments or other transfers of value they make to physicians and teaching hospitals. The proposed rule would also require manufacturers and group purchasing organizations to disclose to CMS physician ownership or investment interests.

This increased transparency is intended to help reduce the potential for conflicts of interest that physicians or teaching hospitals might face as a result of their relationships with manufacturers.

Drug and biologic manufacturers, medical device or supply manufacturers and GPOs would be affected by the new reporting requirements. These organizations, as well as the physicians and teaching hospitals, would have an opportunity to review and correct information prior to its publication.

The ACA provides that violators of the reporting requirements will be subject to civil monetary penalties (CMPs), capped at $150,000 annually for failing to report, and $1 million for knowingly failing to report.

CMS is proposing that data collection will not begin on Jan. 1, 2012 and that manufacturers and GPOs do not need to begin data collection until final regulations are issued. Depending on the timing of the final rule, CMS is proposing that manufacturers and GPOs will be required to submit a partial year on March 31, 2013. Once the data has been submitted, CMS will aggregate manufacturer submissions at the individual physician and teaching hospital level, provide them with a 45-day period to confidentially review and, if necessary, correct the data, and make the data publicly available by Sept. 30, 2013.

CMS will accept comments on the proposed rule until Feb. 17, 2012, and will respond to them in a final rule to be published in 2012. REVIEW

REVIEW Editorial Board

Contributors

Advisory Board

Jobson Publishing Group

PRESIDENT & PUBLISHER **RICHARD D. BAY**

BUSINESS OFFICES
11 CAMPUS BOULEVARD, SUITE 100
NEWTOWN SQUARE, PA 19073
SUBSCRIPTION INQUIRIES (877) 529-1746
(USA ONLY); OUTSIDE USA, CALL (847) 763-9630

BUSINESS STAFF
SALES MANAGER, NORTHEAST,
MID ATLANTIC, OHIO
JAMES HENNE
(610) 492-1017 JHENNE@JOBSON.COM

SALES MANAGER, SOUTHEAST, WEST
MICHELE BARRETT
(610) 492-1014 MBARRETT@JOBSON.COM

CONFERENCE/MEETINGS DIRECTOR
KIMBERLY MCCARTHY
(610) 492-1045 KMCCARTHY@JOBSON.COM

CLASSIFIED ADVERTISING
(888) 537-4858

DIRECTOR OF PUBLISHING OPERATIONS
CASEY FOSTER
(610) 492-1007 CFOSTER@JOBSON.COM

PRODUCTION MANAGER
SCOTT TOBIN
(610) 492-1011 STOBIN@JOBSON.COM

SUBSCRIPTIONS
$63 A YEAR, $99 (U.S.) IN CANADA,
$158 (U.S.) IN ALL OTHER COUNTRIES.
SUBSCRIPTIONS E-MAIL: **RHSUBS@HALLDATA.COM**
CIRCULATION E-MAIL: **RHSUBS@HALLDATA.COM**

CIRCULATION
PO BOX 2026, SKOKIE, IL 60076
(877) 529-1746
OUTSIDE USA: (847)763-9630
FAX: (847)763-9631

SENIOR CIRCULATION MANAGER
ANTHONY GUADAGNINO
(212) 219-7870 aguadagnino@jobson.com

CHIEF OPERATING OFFICER
JEFF MACDONALD

CEO, INFORMATION GROUP SERVICES
MARC FERRARA

VICE PRESIDENT, HUMAN RESOURCES
LORRAINE ORLANDO

CORPORATE PRODUCTION DIRECTOR
JOHN ANTHONY CAGGIANO

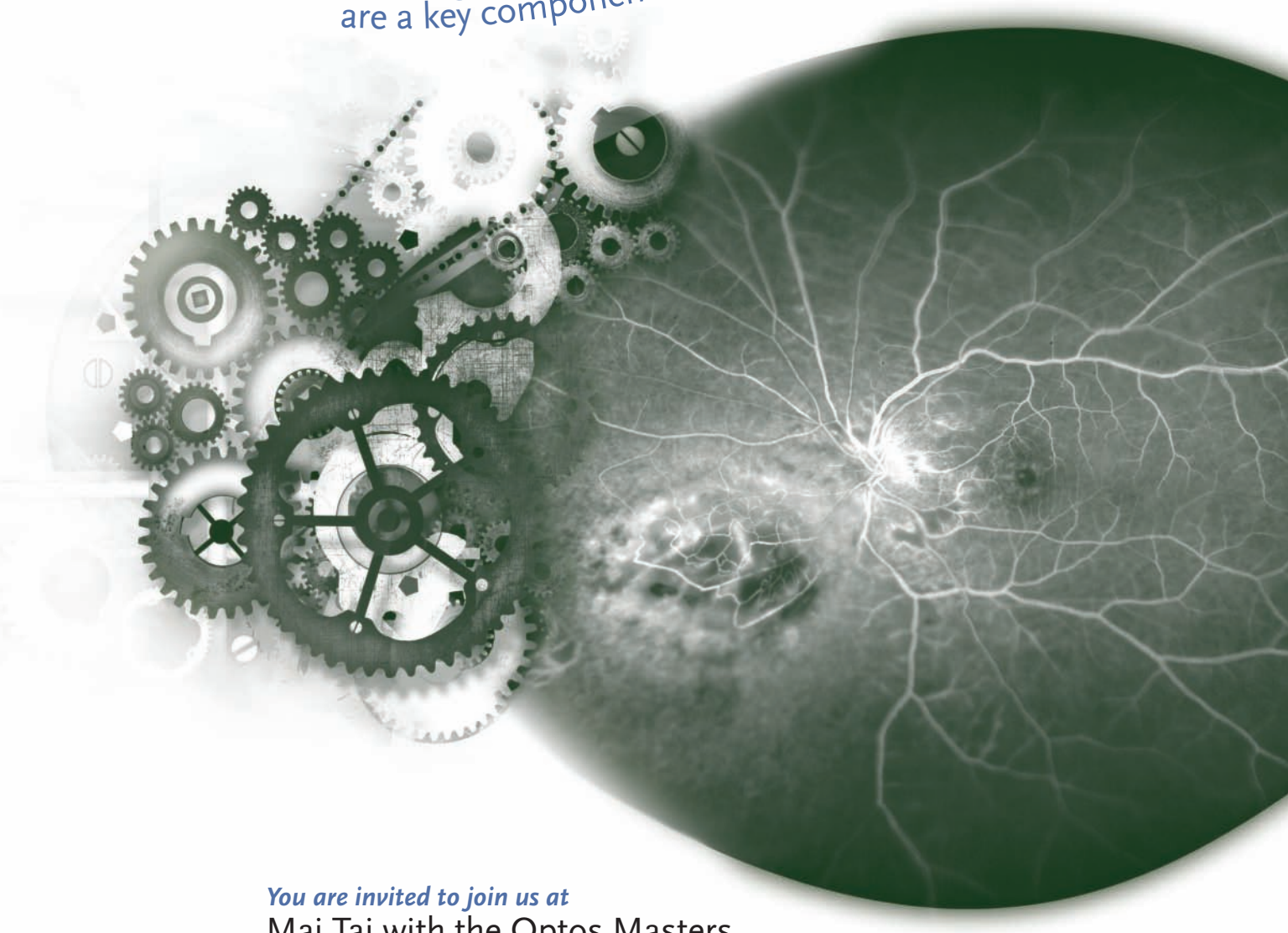
VICE PRESIDENT, CIRCULATION
EMELDA BAREA

jmi

100 Avenue of the Americas
New York, NY 10013

REVIEW OF OPHTHALMOLOGY (ISSN 1081-0226) is published monthly, 12 times per year by Jobson Publishing, LLC. 100 Avenue of the Americas, New York, NY 10013-1678. Jobson Publishing, LLC, a wholly-owned subsidiary of Jobson Medical Information LLC. Periodicals postage paid at New York, NY and additional mailing offices. Postmaster: Send address changes to Review of Ophthalmology, PO Box 2026, Skokie, IL 60076, USA. Subscription Prices: US One Year $63.00, US Two Year $112.00, Canada One Year $99.00, Canada Two Year $181.00, Int'l One Year $158.00, Int'l Two Year $274.00. For subscription information call (877) 529-1746 (USA only); outside USA, call (847) 763-9631. Canada Post: Publications Mail Agreement #40612608. Canada Returns to be sent to Bleuchip International, P.O. Box 25542, London, ON N6C 6B2.V

The inner workings of the periphery
are a key component of your treatment.



You are invited to join us at

Mai Tai with the Optos Masters

a presentation and discussion of interesting case studies.

Moderator: Paul Tornambe, MD, FACS
Date: Monday, January 16, 2012
Time: 2:00pm – 3:30pm
Location: Grand Wailea Resort Hotel & Spa, Plumeria 1 & 2

See Optos at Hawaiian Eye 2012, booth #11

200Tx™ ultra-widefield retinal capture

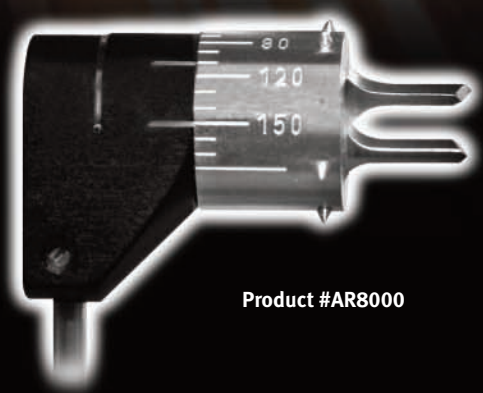
A comprehensive view of the periphery has a lot to offer your practice. Quick and noninvasive, a single 200Tx™ ultra-widefield retinal image with fluorescein angiography can scan up to 200° or 82% of the retina. The result is a picture that provides more insights for your diagnosis and treatment decisions. If you're looking for guidance, the 200Tx is the technology to turn to.

To see more, visit **optos.com/ophthalmology.**

optos® Ophthalmology
Building *The* Retina Company

Introducing the Devgan Axis Marker...

Now the only thing slowing you down is the morning commute.



Product #AR8000

The Devgan Axis Marker improves efficiency by taking corneal toric IOL marking out of the operating room and moving it preoperatively to the slit lamp. Simply clip the marker into a standard tonometer housing unit and rotate to the patient's designated axis. Reference grips along the side of the instrument match up with the toric calculator and help to ensure accurate positioning. Since the marks are made with the patient sitting up, cyclorotation is not an issue.

The Devgan Technique uses anterior stromal puncture marks that typically last two weeks. Every purchase of a Devgan Axis Marker includes instructions and cystotomes to help you get started.

Visit www.accutome.com/DevganAxisMarker for more information

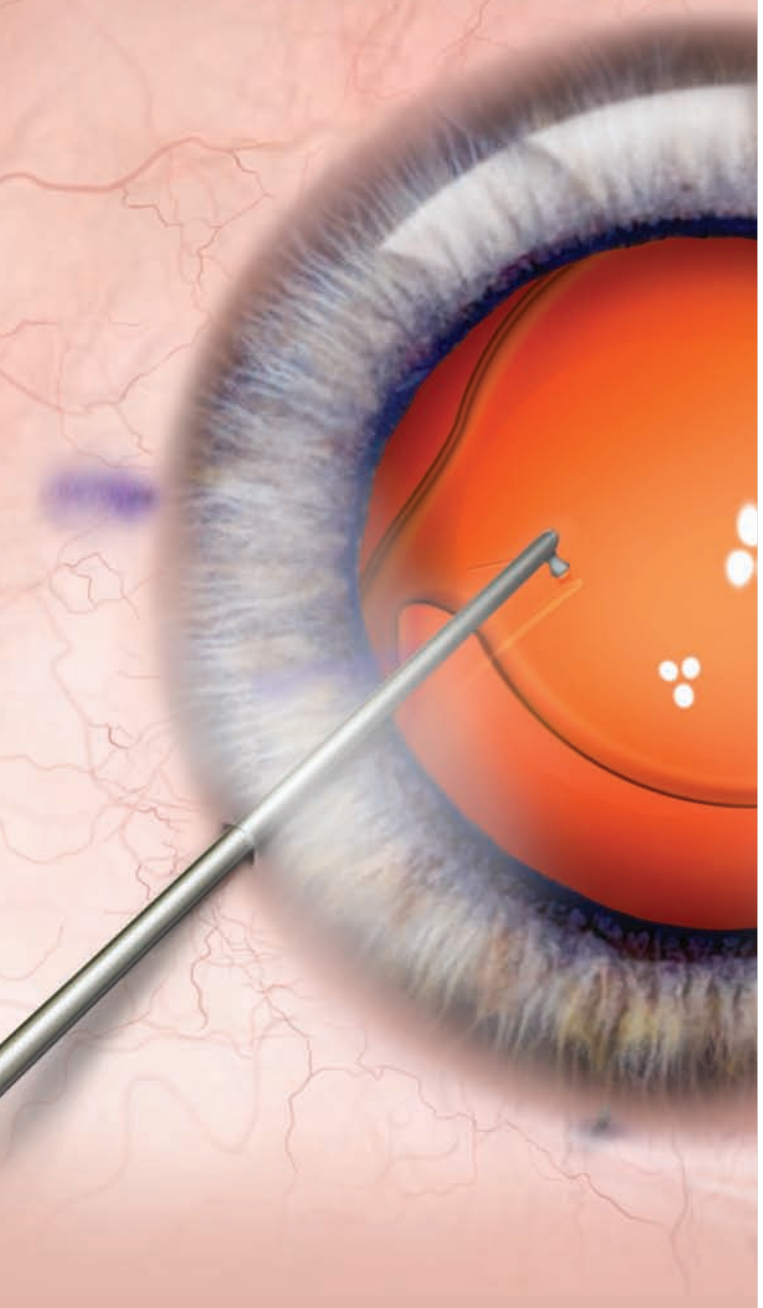
Visit Us At Hawaiian Eye Booth 508

ACCUTOME®
"Where The Difference Is Visible"

3222 Phoenixville Pike, Malvern, PA 19355 USA • 800-979-2020 • 610-889-0200 • FAX 610-889-3233 • www.accutome.com

REVIEW of Ophthalmology

January 2012 • Volume XIX No. 1 | revophth.com

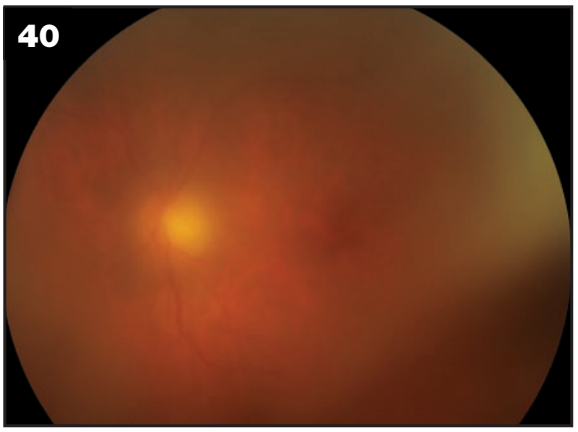


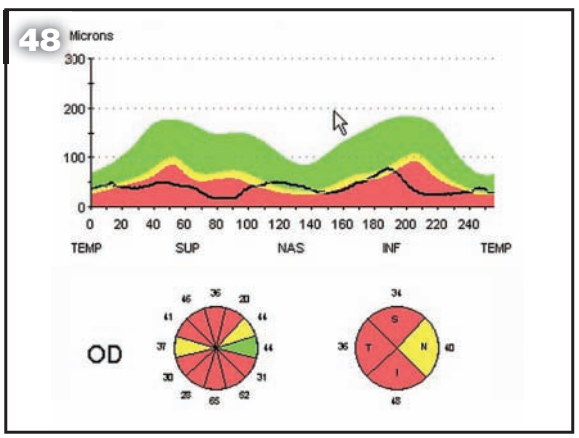
Cover Focus

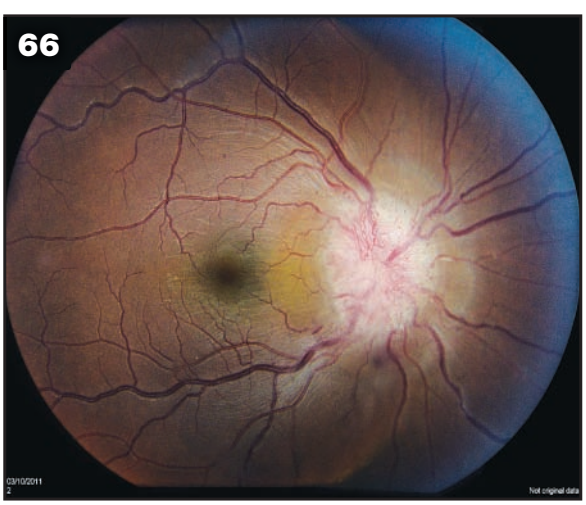
Feature Articles

Cover illustration Mark Erickson, jirehdesign.com

Departments







KNOWING THE OSMOLARITY OF A PATIENT'S TEARS IS ESSENTIAL

in a number of clinical settings

CONTACT LENS
Ensure the compatibility and comfort of contact lens materials.

GLAUCOMA
Measure the impact of chronic preservative use in glaucoma patients.

REFRACTIVE SURGERY
Identify patients with DED and guide pre- and post-surgical treatment to improve outcomes.

CATARACT
Improve outcomes and manage expectations following surgery.

GENERAL PRACTICE *Diagnose with confidence, manage therapy, improve compliance, enhance patient education.*

Ask us about **FREE** use of a TearLab
with a test card commitment.

For more information, call
1-855-TearLab (832-7522)
or visit @ www.tearlab.com

TearLab®

CE | FDA 510(k) Cleared (k083184) | | 920109 REV A

SUPERIOR IMAGING MADE EASY

HD Slit Lamp Camera

Change your slit lamp from the ordinary to the extraordinary with Woodlyn's new High Definition Digital Slit Lamp Camera. Not only does it offer every aspect of digital imaging technology needed to optimize the examination, it also provides images which aid in the documentation and diagnosis of the patient. In addition it helps to visually educate the patient on problematic areas and keeps a history of yearly exams to follow diagnostic progression. The digital imaging is processed in real time immediately capturing full color ocular photos. Its superior quality in high resolution allows the images to be: enlarged, enhanced, segmented and stored.

Authorized Dealer

ULTRAVISION™

Combine The Power of Woodlyn's HD Slitlamp Camera With The Most Versatile Solution For Acuity, Imaging, EMR & Patient Consultation. All This On One Screen.

Package Price

$8995.00

Call Us For Details.

WOODLYN

woodlynintl.com | (847) 952 8330 facebook.com/woodlynintl

REVIEW of Ophthalmology

Don't Be Driven To iDistraction

In the protean world of medical technology, there are few areas of greater and more rapid flux than mobile technology. Reflective of the society at large, physicians, especially younger ones, are in thrall to their handheld devices for both personal and, increasingly, clinical uses.

As often happens at the leading edge of any developing story, it can be difficult to be sure what's real, what's hype, and when and how you need to actually adapt your thinking or your routines to assure that you're up with the times.

I thought it was notable that the venerable *Journal of the American Medical Association* recently announced a new feature: QR codes that allow readers using handheld devices to go from specific articles in the publication to videos and other complementary content online. Great idea. But that same week saw a CNN report on QR codes citing a survey of college students, the demographic you'd most expect to be in tune with new technology. While 80 percent of respondents owned a smartphone and recognized a QR code, just 20 percent knew how to navigate one; and 75 percent felt they'd be unlikely to use one in the future.

Ophthalmologists have a longstanding reputation not just for embracing but driving development of new technology. At the iTunes store alone, there are already more than 80 apps specific to ophthalmology, and there will probably be more by the time I finish this column. It's probably safe to speculate that ophthalmologists as a group are ahead of the curve in terms of adoption of this technology.

While the National Transportation Safety Board made the top of the news this month by proposing a ban on handheld devices while driving, a *New York Times* article got less attention but might be more instructive to physicians incorporating these devices into practice.

It's an old lesson but worth repeating as any new technology emerges. There is nothing inherently good or bad about new tech; it depends on how it's used.

The *Times* article makes the point that beepers, phones and multitasking have long been part of medical practice. The difference today is a matter of degree and the level to which younger doctors grew up accustomed to being constantly connected and doing too many things at the same time. It details some scary trends including a rise in texting and shopping (!) in the OR and other distractions by surgical staff and even surgeons.

The *Times* has to sell papers, so what you choose to believe is your call. But there is a valuable lesson in the article and it's a simple one: Is your new tool enhancing or hindering your interaction with your patient?

As Doctors Use More Devices, Potential for Distraction Grows. NY Times, Dec. 14, 2011.


Fine-tuning WaveTec's In-the-OR Aberrometer

The ORA system that's replacing the ORange has multiple improved features and appears to produce better outcomes.

Christopher Kent, Senior Editor

As cataract surgeons manage more previous refractive surgery and toric intraocular lens patients, patient expectations for "perfect" outcomes continue to rise. One of the technologies attempting to address these realities has been WaveTec Vision's ORange intraoperative wavefront aberrometer, which lets the surgeon fine-tune spherical and astigmatic lens choices by measuring the refraction when the eye is aphakic and checking the refraction after the new lens is implanted.

WaveTec Vision is currently preparing to replace existing ORange instruments with a new, more advanced version of the instrument known as the Optiwave Refractive Analysis system, or ORA. Here, two surgeons who have had the opportunity to use the new instrument share their insights regarding the differences between the ORange and ORA devices, and discuss how much the upgrade is affecting their outcomes.

Improved Optics

Shamik Bafna, MD, director of cornea services at the Cleveland Eye Clinic in Ohio, one of the demo sites for the ORA, has been using the new device for about four months. He notes that the new model includes a number of major changes. "First, the light source is different," he says. "Where the ORange used a laser light to take the readings, the ORA uses a super luminescent light-emitting diode, or SLED. WaveTec found that this light source produces a much sharper fringe pattern, allowing readings to be more accurate. Second, the company has improved the overall optics by switching to aspheric lenses, which allow the light to be transmitted more accurately."

Robert Weinstock, MD, director of cataract and refractive surgery at the Eye Institute of West Florida in Largo, Fla., used the ORange instrument for several years and has been using the ORA for a few months. To evaluate repeatability, his group has been taking two or three measurements rather than one, particularly when measuring aphakic eyes. Dr. Weinstock says the improved optics in the ORA have indeed improved repeatability. "With the ORange, we could see a quarter to a half-diopter spherical equivalent difference between one reading and the next," he says. "With the ORA, we're seeing less than a 0.12-D difference in spherical equivalency for aphakic refractions, three readings in a row."

Dr. Weinstock says this also seems to be resulting in better outcomes. "We've been checking our patients at one day and one week, and they've been right on target," he says. "The ORange was already helping me tremendously, but I think this is going to be an additional step towards increased accuracy and predictability."

Dr. Bafna adds that in his experience, the ORA is able to measure a greater number of problematic patients than the ORange. "If the system has difficulty taking a measurement, it puts up a red flag, meaning it was unable to capture a reading," he explains. "I find that with the ORA, I'm seeing that red flag less often."

Improved User Interface

Dr. Bafna notes that some changes in the ORA will be immediately obvious to the user. "Those changes include what WaveTec is calling the

wide field of view capture," he says. "The ORange system screen only displayed a fringe pattern indicating the quality of the data capture; you didn't see the eye. With the ORA, the screen also shows the eye while the data is being captured, making it possible to note potential problems. If the eye isn't centered or the speculum is pushing on the eyeball, which can raise intraocular pressure and alter the data, you can do something about it and avoid an aberrant reading."

"The ORA's graphical user interface is much more sophisticated and polished," observes Dr. Weinstock. "The screen includes a full-field view of the eye, taken with an infrared camera. That's important because if the cornea dries out or gets mucusy or the chamber collapses, your reading won't provide usable data. You can't always pick that up just from seeing the little bull's-eye reticle. Also, the new video display helps guide your centration and alignment."

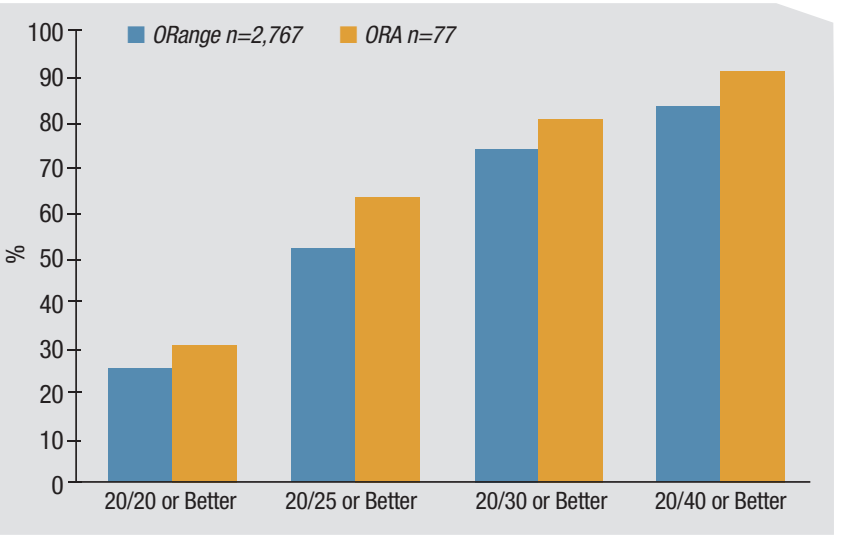
Other Improvements

Drs. Bafna and Weinstock note several other changes for the better:

• ***On-demand reticle.*** "One big thing we were missing with the ORange was some guidance," says Dr. Weinstock. "Now they've built a reticle into the software. Once you take a reading, you can press a button on the device and a reticle appears in front of one of your eyes through the microscope. You can use the hash marks on the reticle to align a toric lens or place an LRI correctly and make it the right length. The reticle looks like it's sitting on the eye."

• ***Improved algorithms.*** Dr. Bafna says that when he first got the ORange, he was not happy with it. "The numbers seemed inconsistent," he says. "However, over time, WaveTec improved the algorithms. Today, I'm a big proponent of this technology, and with the ORA, they've improved the algorithms even further."

Uncorrected Distance Visual Acuity One Month Postop



"As with any biometry device, different formulas work better for different types of eyes," notes Dr. Weinstock. "Traditionally, we've measured axial length and K-values and plugged them into the various formulas. If someone has a really long eye, you might use a Holladay II formula; if some has a short eye you might use a Haigis or SRKT formula. The ORA has its own set of proprietary formulas that it uses to calculate lens power selection for a particular eye, and it weighs the aphakic refraction and a vergence formula, in addition to K-values and axial length. Those proprietary formulas are based on the large amount of data collected from users of the ORange instrument.

"If you have a post-myopic-LASIK eye, for example, you hit a button on the ORA and tell it that; then it will use a slightly different formula to calculate the lens power," he continues. "Likewise for a hyperopic LASIK eye, or a very long or short eye. And the company continues to refine the formulas and update them as more cases are done." (According to the company, the software has optimized lens constants for about 95 percent of all IOLs currently in use.)

• ***One-step data capture.*** "Using the ORange was a two-step process," notes Dr. Bafna. "First you had to make sure everything was in focus; then you'd tell the machine to capture the data. The ORA does all of this in one step, which saves time."

• ***Help with marketing to patients.*** According to the company, the ORA comes with a kit that includes access to a user website with tools designed to help practices explain the technology to patients.

Rolling Out Soon

WaveTec plans to upgrade current owners of an ORange device to the ORA by the middle of 2012. The ORA system will cost about $40,000 with a monthly subscription fee of $3,000, allowing for unlimited use. The ORA systems will start shipping after the first of the year. REVIEW

Dr. Weinstock has received consultation honorariums from WaveTec, but has no financial interest in the company or either instrument. Dr. Bafna has no financial ties to the company or either instrument.

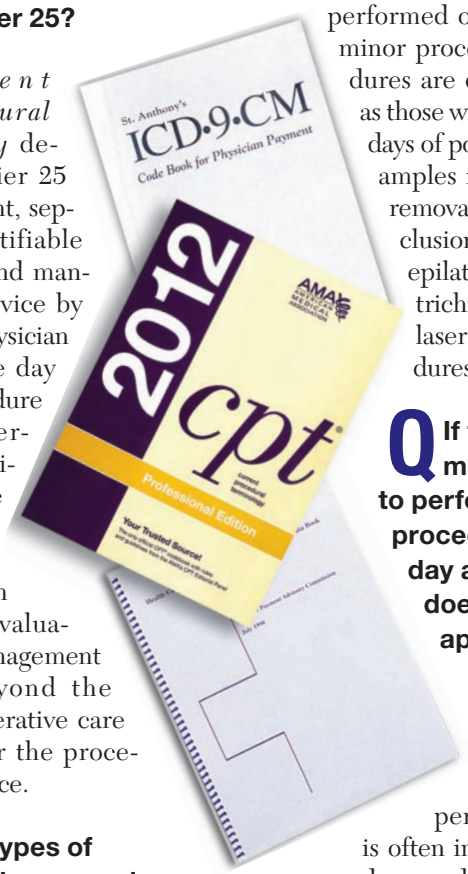
Donna McCune, CCS-P, COE

Redefinitions Increase The Use of Modifier 25

The redefinition of some surgeries from major to minor procedures has led to an increase in the use of modifier 25.

Q What is the definition of modifier 25?

A *Current Procedural Terminology* defines modifier 25 as "Significant, separately identifiable evaluation and management service by the same physician on the same day of the procedure or other service." It indicates that the patient's condition required an additional evaluation and management service beyond the usual preoperative care provided for the procedure or service.



Q What types of procedures require the use of modifier 25?

A Modifier 25 should be appended to an exam (992xx or 920xx) or consultation (9924x) when a separately identifiable service has been performed on the same day as a minor procedure. Minor procedures are defined by Medicare as those with zero (0) or ten (10) days of postoperative care. Examples include foreign body removal (65222), punctal occlusion with plugs (68761), epilation for correction of trichiasis (67820) and the laser and injection procedures listed below.

Q If the physician makes the decision to perform a minor procedure on the same day as the office visit, does modifier 25 apply to that visit?

A Not always. Unlike major surgeries (those with a 90-day postop period), the office visit is often included with a minor procedure and not separately billable. CPT states that, "this modifier is not used to report an E/M service that resulted in a decision to perform surgery." In addition, the *Medicare Claims Processing Manual*, Chapter 12, §40.2A4 states, "where the decision to perform the minor procedure is typically done immediately before the service, it is considered a routine preoperative service and a visit or consultation is not billed in addition to the procedure."

Q If the patient has two different diagnoses being addressed, is it appropriate to bill the office visit with modifier 25?

A Yes. If the patient does have more than one problem being addressed at the visit, it is appropriate to use different diagnoses on the claim. However, it is not required that two different diagnoses exist. The CPT definition of modifier 25 specifically states, "different diagnoses are not required for reporting of the E/M services on the same date."

Q If only one diagnosis exists, how do we determine when to bill the visit as well as the procedure?

A The CPT definition says that a separately identifiable service must be provided. If the physician has to cope with more than one

Classic IOP reduction in a preservative-free form

For topical beta-blocker patients at risk for preservative toxicity, why add insult to injury?

- In a large clinical study in which patients were switched from a preserved to a preservative-free beta blocker, there was significant improvement in signs and symptoms of preservative toxicity on the ocular surface[1]
  - A significant reduction ($p<0.0001$) in all ocular signs and symptoms, including pain and discomfort, was seen in patients who were switched to a preservative-free formulation.[1]

INDICATIONS AND USAGE

Preservative-free TIMOPTIC® in OCUDOSE® is indicated in the treatment of elevated intraocular pressure in patients with ocular hypertension or open-angle glaucoma. Preservative-free TIMOPTIC® in OCUDOSE® may be used when a patient is sensitive to the preservative in Timoptic (timolol maleate ophthalmic solution), benzalkonium chloride, or when use of a preservative-free topical medication is advisable.

IMPORTANT SAFETY INFORMATION

Timoptic is contraindicated in patients with: bronchial asthma; a history of bronchial asthma; severe chronic obstructive pulmonary disease; sinus bradycardia; second or third degree atrioventricular block; overt cardiac failure; cardiogenic shock; hypersensitivity to any component of this product.

This drug is absorbed systemically. The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. Severe respiratory or cardiac reactions, including death, have been reported following systemic or ophthalmic administration of Timolol maleate. Timoptic should be used with caution in patients with cerebrovascular insufficiency.

The most frequently reported adverse experiences have been burning and tinging upon instillation.

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

Reference 1: Jaenen N, Baudouin C, Pouliquen P, et al, Ocular symptoms and signs with preserved and preservative-free glaucoma medications. *Eur J Ophthalmol.* 2007;17(3):341-349

IOP=intraocular pressure

TIMOPTIC® in OCUDOSE®
(TIMOLOL MALEATE 0.5% OPHTHALMIC SOLUTION) (DISPENSER)

ATON PHARMA ATON Pharma, a Division of Valeant Pharmaceuticals North America LLC Bridgewater, NJ 08807 OCU049-1111ROPH

Brief Summary of Prescribing Information

ATON PHARMA

PRESERVATIVE-FREE STERILE OPHTHALMIC SOLUTION
in a Sterile Ophthalmic Unit Dose Dispenser

TIMOPTIC®
0.25% AND 0.5%
(TIMOLOL MALEATE OPHTHALMIC SOLUTION)
in OCUDOSE®
(DISPENSER)

CONTRAINDICATIONS

Preservative-free TIMOPTIC in OCUDOSE is contraindicated in patients with (1) bronchial asthma; (2) a history of bronchial asthma; (3) severe chronic obstructive pulmonary disease (see WARNINGS); (4) sinus bradycardia; (5) second or third degree atrioventricular block; (6) overt cardiac failure (see WARNINGS); (7) cardiogenic shock; or (8) hypersensitivity to any component of this product.

WARNINGS

As with many topically applied ophthalmic drugs, this drug is absorbed systemically.

The same adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions and cardiac reactions, including death due to bronchospasm in patients with asthma, and rarely death in association with cardiac failure, have been reported following systemic or ophthalmic administration of timolol maleate (see CONTRAINDICATIONS).

Cardiac Failure

Sympathetic stimulation may be essential for support of the circulation in individuals with diminished myocardial contractility, and its inhibition by beta-adrenergic receptor blockade may precipitate more severe failure.

In Patients Without a History of Cardiac Failure continued depression of the myocardium with beta-blocking agents over a period of time can, in some cases, lead to cardiac failure. At the first sign or symptom of cardiac failure, Preservative-free TIMOPTIC in OCUDOSE should be discontinued.

Obstructive Pulmonary Disease

Patients with chronic obstructive pulmonary disease (e.g., chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease (other than bronchial asthma or a history of bronchial asthma, in which TIMOPTIC in OCUDOSE is contraindicated [see CONTRAINDICATIONS]) should, in general, not receive beta-blockers, including Preservative-free TIMOPTIC in OCUDOSE.

Major Surgery

The necessity or desirability of withdrawal of beta-adrenergic blocking agents prior to major surgery is controversial. Beta-adrenergic receptor blockade impairs the ability of the heart to respond to beta-adrenergically mediated reflex stimuli. This may augment the risk of general anesthesia in surgical procedures. Some patients receiving beta-adrenergic receptor blocking agents have experienced protracted severe hypotension during anesthesia. Difficulty in restarting and maintaining the heartbeat has also been reported. For these reasons, in patients undergoing elective surgery, some authorities recommend gradual withdrawal of beta-adrenergic receptor blocking agents.

If necessary during surgery, the effects of beta-adrenergic blocking agents may be reversed by sufficient doses of adrenergic agonists.

Diabetes Mellitus

Beta-adrenergic blocking agents should be administered with caution in patients subject to spontaneous hypoglycemia or to diabetic patients (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Beta-adrenergic receptor blocking agents may mask the signs and symptoms of acute hypoglycemia.

Thyrotoxicosis

Beta-adrenergic blocking agents may mask certain clinical signs (e.g., tachycardia) of hyperthyroidism. Patients suspected of developing thyrotoxicosis should be managed carefully to avoid abrupt withdrawal of beta-adrenergic blocking agents that might precipitate a thyroid storm.

PRECAUTIONS

General

Because of potential effects of beta-adrenergic blocking agents on blood pressure and pulse, these agents should be used with caution in patients with cerebrovascular insufficiency. If signs or symptoms suggesting reduced cerebral blood flow develop following initiation of therapy with Preservative-free TIMOPTIC in OCUDOSE, alternative therapy should be considered.

Choroidal detachment after filtration procedures has been reported with the administration of aqueous suppressant therapy (e.g. timolol).

Angle-closure glaucoma: In patients with angle-closure glaucoma, the immediate objective of treatment is to reopen the angle. This requires constricting the pupil. Timolol maleate has little or no effect on the pupil. TIMOPTIC in OCUDOSE should not be used alone in the treatment of angle-closure glaucoma.

Anaphylaxis: While taking beta-blockers, patients with a history of atopy or a history of severe anaphylactic reactions to a variety of allergens may be more reactive to repeated accidental, diagnostic, or therapeutic challenge with such allergens. Such patients may be unresponsive to the usual doses of epinephrine used to treat anaphylactic reactions.

Muscle Weakness: Beta-adrenergic blockade has been reported to potentiate muscle weakness consistent with certain myasthenic symptoms (e.g., diplopia, ptosis, and generalized weakness). Timolol has been reported rarely to increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.

Information for Patients

Patients should be instructed about the use of Preservative-free TIMOPTIC in OCUDOSE.

Since sterility cannot be maintained after the individual unit is opened, patients should be instructed to use the product immediately after opening, and to discard the individual unit and any remaining contents immediately after use.

Patients with bronchial asthma, a history of bronchial asthma, severe chronic obstructive pulmonary disease, sinus bradycardia, second or third degree atrioventricular block, or cardiac failure should be advised not to take this product. (See CONTRAINDICATIONS.)

Drug Interactions

Although TIMOPTIC (timolol maleate ophthalmic solution) used alone has little or no effect on pupil size, mydriasis resulting from concomitant therapy with TIMOPTIC (timolol maleate ophthalmic solution) and epinephrine has been reported occasionally.

Beta-adrenergic blocking agents: Patients who are receiving a beta-adrenergic blocking agent orally and Preservative-free TIMOPTIC in OCUDOSE should be observed for potential additive effects of betablockade, both systemic and on intraocular pressure. The concomitant use of two topical beta-adrenergic blocking agents is not recommended.

Calcium antagonists: Caution should be used in the coadministration of beta-adrenergic blocking agents, such as Preservative-free TIMOPTIC in OCUDOSE, and oral or intravenous calcium antagonists, because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension. In patients with impaired cardiac function, coadministration should be avoided.

Catecholamine-depleting drugs: Close observation of the patient is recommended when a beta blocker is administered to patients receiving catecholamine-depleting drugs such as reserpine, because of possible additive effects and the production of hypotension and/or marked bradycardia, which may result in vertigo, syncope, or postural hypotension.

Digitalis and calcium antagonists: The concomitant use of beta-adrenergic blocking agents with digitalis and calcium antagonists may have additive effects in prolonging atrioventricular conduction time.

CYP2D6 inhibitors: Potentiated systemic beta-blockade (e.g., decreased heart rate, depression) has been reported during combined treatment with CYP2D6 inhibitors (e.g., quinidine, SSRIs) and timolol.

Clonidine: Oral beta-adrenergic blocking agents may exacerbate the rebound hypertension which can follow the withdrawal of clonidine. There have been no reports of exacerbation of rebound hypertension with ophthalmic timolol maleate.

Injectable epinephrine: (See PRECAUTIONS, General, Anaphylaxis)

Carcinogenesis, Mutagenesis, Impairment of Fertility

In a two-year oral study of timolol maleate administered orally to rats, there was a statistically significant increase in the incidence of adrenal pheochromocytomas in male rats administered 300 mg/kg/day (approximately 42,000 times the systemic exposure following the maximum recommended human ophthalmic dose). Similar differences were not observed in rats administered oral doses equivalent to approximately 14,000 times the maximum recommended human ophthalmic dose.

In a lifetime oral study in mice, there were statistically significant increases in the incidence of benign and malignant pulmonary tumors, benign uterine polyps and mammary adenocarcinomas in female mice at 500 mg/kg/day (approximately 71,000 times the systemic exposure following the maximum recommended human ophthalmic dose), but not at 5 or 50 mg/kg/day (approximately 700 or 7,000 times, respectively, the systemic exposure following the maximum recommended human ophthalmic dose). In a subsequent study in female mice, in which postmortem examinations were limited to the uterus and the lungs, a statistically significant increase in the incidence of pulmonary tumors was again observed at 500 mg/kg/day.

The increased occurrence of mammary adenocarcinomas was associated with elevations in serum prolactin which occurred in female mice administered oral timolol at 500 mg/kg/day, but not at doses of 5 or 50 mg/kg/day. An increased incidence of mammary adenocarcinomas in rodents has been associated with administration of several other therapeutic agents that elevate serum prolactin, but no correlation between serum prolactin levels and mammary tumors has been established in humans. Furthermore, in adult human female subjects who received oral dosages of up to 60 mg of timolol maleate (the maximum recommended human oral dosage), there were no clinically meaningful changes in serum prolactin.

Timolol maleate was devoid of mutagenic potential when tested *in vivo* (mouse) in the micronucleus test and cytogenetic assay (doses up to 800 mg/kg) and *in vitro* in a neoplastic cell transformation assay (up to 100 mcg/mL). In Ames tests the highest concentrations of timolol employed, 5,000 or 10,000 mcg/plate, were associated with statistically significant elevations of revertants observed with tester strain TA100 (in seven replicate assays), but not in the remaining three strains. In the assays with tester strain TA100, no consistent dose response relationship was observed, and the ratio of test to control revertants did not reach 2. A ratio of 2 is usually considered the criterion for a positive Ames test.

Reproduction and fertility studies in rats demonstrated no adverse effect on male or female fertility at doses up to 21,000 times the systemic exposure following the maximum recommended human ophthalmic dose.

Pregnancy: Teratogenic Effects — Pregnancy Category C.: Teratogenicity studies with timolol in mice, rats and rabbits at oral doses up to 50 mg/kg/day (7,000 times the systemic exposure following the maximum recommended human ophthalmic dose) demonstrated no evidence of fetal malformations. Although delayed fetal ossification was observed at this dose in rats, there were no adverse effects on postnatal development of offspring. Doses of 1000 mg/kg/day (142,000 times the systemic exposure following the maximum recommended human ophthalmic dose) were maternotoxic in mice and resulted in an increased number of fetal resorptions. Increased fetal resorptions were also seen in rabbits at doses of 14,000 times the systemic exposure following the maximum recommended human ophthalmic dose, in this case without apparent maternotoxicity.

There are no adequate and well-controlled studies in pregnant women. Preservative-free TIMOPTIC in OCUDOSE should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Nursing Mothers: Timolol maleate has been detected in human milk following oral and ophthalmic drug administration. Because of the potential for serious adverse reactions from timolol in nursing infants, 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: Safety and effectiveness in pediatric patients have not been established.

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

ADVERSE REACTIONS

The most frequently reported adverse experiences have been burning and stinging upon instillation (approximately one in eight patients).

The following additional adverse experiences have been reported less frequently with ocular administration of this or other timolol maleate formulations:

BODY AS A WHOLE: Headache, asthenia/fatigue, and chest pain.

CARDIOVASCULAR: Bradycardia, arrhythmia, hypotension, hypertension, syncope, heart block, cerebral vascular accident, cerebral ischemia, cardiac failure, worsening of angina pectoris, palpitation, cardiac arrest, pulmonary edema, edema, claudication, Raynaud's phenomenon, and cold hands and feet.

DIGESTIVE: Nausea, diarrhea, dyspepsia, anorexia, and dry mouth.

IMMUNOLOGIC: Systemic lupus erythematosus.

NERVOUS SYSTEM/PSYCHIATRIC: Dizziness, increase in signs and symptoms of myasthenia gravis, paresthesia, somnolence, insomnia, nightmares, behavioral changes and psychic disturbances including depression, confusion, hallucinations, anxiety, disorientation, nervousness, and memory loss.

SKIN: Alopecia and psoriasiform rash or exacerbation of psoriasis.

HYPERSENSITIVITY: Signs and symptoms of systemic allergic reactions including anaphylaxis, angioedema, urticaria, and localized and generalized rash.

RESPIRATORY: Bronchospasm (predominantly in patients with preexisting bronchospastic disease), respiratory failure, dyspnea, nasal congestion, cough and upper respiratory infections.

ENDOCRINE: Masked symptoms of hypoglycemia in diabetic patients (see WARNINGS).

SPECIAL SENSES: Signs and symptoms of ocular irritation including conjunctivitis, blepharitis, keratitis, ocular pain, discharge (e.g., crusting), foreign body sensation, itching and tearing, and dry eyes; ptosis; decreased corneal sensitivity; cystoid macular edema; visual disturbances including refractive changes and diplopia; pseudopemphigoid; choroidal detachment following filtration surgery (see PRECAUTIONS, General); and tinnitus.

UROGENITAL: Retroperitoneal fibrosis, decreased libido, impotence, and Peyronie's disease.

The following additional adverse effects have been reported in clinical experience with ORAL timolol maleate or other ORAL beta blocking agents, and may be considered potential effects of ophthalmic timolol maleate: *Allergic:* Erythematous rash, fever combined with aching and sore throat, laryngospasm with respiratory distress; *Body as a Whole:* Extremity pain, decreased exercise tolerance, weight loss; *Cardiovascular:* Worsening of arterial insufficiency, vasodilatation; *Digestive:* Gastrointestinal pain, hepatomegaly, vomiting, mesenteric arterial thrombosis, ischemic colitis; *Hematologic:* Non-thrombocytopenic purpura; thrombocytopenic purpura; agranulocytosis; *Endocrine:* Hyperglycemia, hypoglycemia; *Skin:* Pruritus, skin irritation, increased pigmentation, sweating; *Musculoskeletal:* Arthralgia; *Nervous System/Psychiatric:* Vertigo, local weakness, diminished concentration, reversible mental depression progressing to catatonia, an acute reversible syndrome characterized by disorientation for time and place, emotional lability, slightly clouded sensorium, and decreased performance on neuropsychometrics; *Respiratory:* Rales, bronchial obstruction; *Urogenital:* Urination difficulties.

Distributed by:
ATON Pharma,
a Division of Valeant Pharmaceuticals North America LLC
Madison, NJ 07940

Manufactured by:
Laboratories Merck Sharp & Dohme-Chibret
63963 Clermont-Ferrand Cedex 9, France

Issued April 2009

OCU049-1111ROPH

occurrence of the same problem but do so in different ways, then the visit and the procedure are billable. For example, your patient presents with two chalazions: a large one on the right eye, and a small one on the left eye. You incise and drain the larger one, and treat the small one with medications and warm compresses. Both the exam and the minor procedure carry the same diagnosis (i.e., 373.2). The exam would be filed with modifier 25 and the procedure would be modified with RT to designate right eye.

Q When is it inappropriate to use modifier 25 to file separately for the exam and the procedure?

A If the only purpose of the exam is preoperative care, or to determine the need to proceed with the procedure, then a claim for an office visit with modifier 25 would not be appropriate. For example, your patient was last seen six weeks ago and received her third intravitreal injection to her left eye. Examination today will determine whether a fourth injection is needed now or can be postponed. OCT of the left eye demonstrates progressive exudative AMD. You proceed with the injection to the left eye based on these findings. Your examination of the fellow eye is unremarkable and noncontributory. The decision for minor surgery does not, in itself, support the use of modifier 25.

Q Why are payers interested in modifier 25 usage?

A There are several reasons why payers, especially Medicare contractors, are interested in physician claims using modifier 25. The Office of Inspector (OIG) 2011 General Work Plan included "Evaluation and Management Services During Global Surgery Periods" as a target for scrutiny. Its 2012 Work Plan continues to include this issue. OIG expects to determine if the number of E/M services provided during the global surgery period has changed since the global surgery concept was developed in 1992. The 2012 OIG Work Plan also includes a new investigation of E/M claims with modifiers during the global surgery period that resulted in payment, citing that prior OIG work found inappropriate payments. It should be noted that in 2005, the OIG published a report indicating that 35 percent of claims filed in 2002 with modifier 25 did not meet the requirements. They instructed Medicare contractors to pay attention to this issue. Minimal reviews occurred immediately following the OIG's request. The 2011 and 2012 OIG Work Plans seem to have resurrected the effort.

When to Use Modifier 25

Here is an example of when you should use modifier 25:

- Your patient with systemic lupus erythematosus is being followed for potential toxicity due to Plaquenil therapy. The patient also complains today of a foreign body sensation OU that has not responded to artificial tears. You diagnose keratoconjunctivitis sicca, recommend continuation of tears and insert punctal plugs in the lower puncta. Submit an office visit with modifier 25 along with the minor procedure.

In contrast, you should not use modifier 25 when:

- Your patient presents with continued dry-eye complaints after a trial of artificial tears. You recommend and insert punctal plugs. Do not use modifier 25; file for minor procedure only.

Q Are the Recovery Audit Contractors (RAC) interested in this issue?

A Yes, all four RAC organizations list on their websites that evaluation and management services during the global surgery periods for both major and minor procedures are under review.

Q How frequently do ophthalmologists use modifier 25?

A Data from the Centers for Medicare & Medicaid Services indicates that ophthalmologists utilized modifier 25 on 9 percent of office visits submitted in 2009 (the most recent data available at this time). It is one of the most frequently used modifiers in ophthalmology and its use continues to grow.

Q Is there a particular reason for the increased utilization of modifier 25?

A Yes. Some surgical procedures have been redefined from major procedures to minor procedures in the past few years. For example, laser trabeculoplasty (65855) is a minor procedure; it was previously a major procedure. As of January 1, 2011, laser peripheral iridotomy (66761) also became a minor procedure. Both procedures have 10 postop days. Intravitreal injections (67028) have grown to be the second most frequently performed surgical service in ophthalmology. This procedure is also a minor procedure with zero postop days. When physicians file for an office visit on the day of these procedures, modifier 25 is required. REVIEW

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

EHR Computing: In-house or in the Cloud?

Michelle Stephenson, Contributing Editor

Several factors need to be considered when deciding where to store your patients' data.

Cloud computing is not new, and most of us use these services every day. For example, many e-mail services (Yahoo mail, Gmail, Hotmail) and information-sharing services (Google Docs) operate in the cloud. True cloud computing allows users to access information over the Internet from any computer with an Internet browser.

Although no electronic health record vendors in ophthalmology are currently offering true cloud computing, they do offer a Web-hosted option. "People put a lot of things in the bucket of cloud computing, including 'Web-hosted,' where the EHR application resides remotely on the EHR vendor's servers and can be accessed by practices over the Web using a remote desktop client of some sort," says Mary Ann Fitzhugh, vice president of marketing, Compulink Business Systems.

With the Web-hosted option, the application is running on servers located in a secure data center rather than in the ophthalmologist's office. Users then access the application through a Web browser or by special-purpose client software provided by the vendor. The vendor is responsible for backing up the data and managing the server, including all updates to the software. The vendor is also responsible for providing secure, HIPAA-compliant storage of all patient data.

A key benefit of implementing EHR as a cloud solution is simplicity. Vendor management of the server reduces the need for offices to have dedicated IT expertise and the cost associated with that support. Hosted solutions also simplify access, providing users with the ability to access patient data when they are outside of the office. Other benefits include improved reliability, system availability, ease of adding new users and security.

However, while cloud computing sounds like a good way to reduce the overall IT complexity of implementing EHRs, several factors need to be taken into consideration when deciding whether to bring your EHR systems in-house or to choose a web-hosted option. The size and location of your practice and your financial situation are two important factors to consider.

Cost

When weighing the options, ophthalmologists need to determine which one makes sense financially. With the in-house (client-server) option, the product is purchased up-front, it is set up in the ophthalmologist's office, and the office is responsible for backing up the data and maintaining the server.

#1 PRESCRIPTION ALLERGY EYE DROP[1]

Zero-itch Starts Here

Once Daily Pataday™ (olopatadine hydrochloride ophthalmic solution) 0.2%

Prescribe the Number One prescription allergy eye drop to Start and Finish the day with Zero-itch.[1,2]

- Start: As soon as 3 minutes following allergen challenge, 60% of patients achieved Zero-itch*†
- Finish: At 16 hours, 60% of patients had Zero-itch*‡

INDICATION AND DOSING

PATADAY™ Solution is a mast cell stabilizer indicated for the treatment of ocular itching associated with allergic conjunctivitis. The recommended dose is one drop in each affected eye once a day.

IMPORTANT SAFETY INFORMATION

PATADAY™ Solution is for topical ocular use only. It is not for injection or oral use.

To prevent contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep the bottle tightly closed when not in use.

PATADAY™ Solution should not be used to treat contact lens-related irritation. The preservative in PATADAY™ Solution, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses should be instructed to wait at least ten minutes after instilling PATADAY™ Solution before they insert their contact lenses.

Symptoms similar to cold syndrome and pharyngitis were reported at an incidence of approximately 10%.

For additional information about PATADAY™ Solution, please refer to the brief summary of prescribing information on the following page.

*Post-hoc analysis of combined data from two studies using a contralateral conjunctival allergen challenge (CAC). Based on a scale of itching scores of 0-4, with 0 as no itching and 4 as severe itching. Ocular itching was evaluated 3 minutes after allergen challenge at onset and at 16 hours.

†(N=85; 95% CI=48.8, 70.5) ‡(N=82; 95% CI=48.3, 70.4)

References: 1. IMS Health, IMS National Prescription Audit™, August 2010 to February 2011, USC 61500 OPHTH ANTI-ALLERGY. **2.** Data on file.

Alcon®

With the Web-hosted option, ophthalmologists pay a monthly fee for these services.

"You never really buy the product. It makes the up-front installation setup less expensive and easier because you don't have to go out and buy a server, install a server, and then worry about how to support that server," explains Jim Messier, vice president of sales and marketing, Medflow, Inc.

For smaller practices especially, this option makes sense. The larger the practice, the less sense it makes to go to a cloud environment, according to Mr. Messier.

For the client-server option, the up-front fee is typically $35,000, and there is a low monthly fee that is paid to the software company for monthly expenses. With the Web-hosted option, the monthly fee is typically $650 to $800 for as long as you use the product.

"You've got to really look at the numbers. In a hosted environment, you are not going to have to make the investment to purchase the server hardware or the third-party software. There is savings on the initial purchase, but if you look at things over a five-year and a 10-year period, at about five years, you break even. If you just look at paying $35,000 up-front versus $800 a month, anyone would go for the $800 solution, but you are not purchasing it for just one month. An EHR is a long-term commitment of five, seven or 10 years," Mr. Messier says.

For smaller practices that may not have an internal IT expert, there may be additional financial benefits. "The biggest advantage of the Web-hosted option is that it gets you out of the IT business," Ms. Fitzhugh says. "With the software and the servers located in your office, you're going to need the IT expertise to maintain and manage those resources. You're going to be responsible for managing everything from complex data backup plans to ensuring you can pass a data security audit. With Web-hosting, all of this is your vendor's problem to solve."

Additionally, in a hosted environment, the vendor is responsible for all computer updates. "When a manufacturer changes or updates a piece of software, it either sets up something where you download the data or it sends you a CD," says Kevin Corcoran, an ophthalmology practice management consultant based in San Bernardino, Calif. "You have to do all of the computers in your office one at a time in the client-server model. In the cloud, all of the software is updated at once by someone else. All updates will be done for you, saving you time and money. Also, if your practice grows, it's a lot easier to add new computers to your office if you operate in the cloud than if you have to buy hardware and install it."

Security

Security is a concern with both options and needs to be taken into account. If the server is in your office, you have better control over who has access to the data, and you can access the data anytime. "If it's in the cloud, who has it, where is it, and who might be looking at it? That's the extreme, but it's also reality," Mr. Messier says.

Mr. Corcoran agrees, noting that physicians are giving up control of their data: "Now that your data is on someone else's computer, can you guarantee security? Clearly, that's a big concern. If you have a disagreement with the vendor, will they snip the umbilical cord, and you will lose access to your data. What if you don't pay someone, for example? Do they hold you hostage by saying, 'If you want your data, pay our bill?' "

Of course, data may not be secure in the ophthalmologist's office, either. Mr. Corcoran knows cases where one partner in a multi-physician practice stole another physician's data. There have also been instances where a server is destroyed and the backup system fails.

When it comes to data safety and security, there are no true guarantees if you do it yourself.

The Pros and Cons

There are several drawbacks to the client-server model, especially for smaller practices, according to Michael Chiang, MD, who is professor of ophthalmology and medical informatics at the Casey Eye Institute at Oregon Health and Science University and chair of the AAO Medical Information Technology Committee. One of the difficulties of implementing EHRs for small practices is that they may not have the technical resources or infrastructure to implement these systems, and they may not have an IT person to maintain the system. "For smaller practices, you could make the argument that cloud-based systems really make sense because the implementation is simple. For true cloud-based systems, you only need a computer and good web access," he says.

While servers are not large, they are not easy to keep in-house. "For example, you have to make sure that the area is physically secure, meaning that someone can't just walk in and steal data from the machine or inadvertently place corrupted files on the machine," Dr. Chiang says. "Additionally, the servers need to be physically secure in the sense that if there is a flood or a fire or some other type of disaster, the machine must be protected as much as possible. For example, it has to be mounted somewhere safe."

Additionally, all data must be backed up. "If the machine crashes in the middle of the day, there must be a redundancy mechanism so that you don't have to close the office," he adds. "There also needs to be a backup mechanism so that, if the machine breaks or if the room floods, you have a copy of everything at an off-site location to prevent permanent loss of data."

Servers must also be kept in a controlled environment. Because they generate heat, they must be stored in rooms that are temperature-controlled. Particularly if your practice is located in an older building, ventilation and air conditioning modifications may be required. "All of those things can be really time-consuming and expensive," says Dr. Chiang. "That is difficult for any practice, but especially smaller practices that may have limited space and limited resources. Operating in the cloud gives others the responsibility of handling those things for you."

There are several drawbacks to computing in the cloud, also. Although the hosting companies guarantee functionality and reliability, there have been cases where cloud-based servers have crashed. For example, in April 2011, thousands of businesses and major websites crashed after an Amazon cloud failure. "A lot of people, including large corporations, used this cloud-based system for their storage," Dr. Chiang says. "When that crashed, people weren't able to get access to their data and were taken off-line for a while. No system is 100-percent bulletproof."

Including client-server models. During Hurricane Katrina, hospitals were flooded, and many patients' paper-based medical records were destroyed. "That case demonstrated a major benefit of EHRs because VA patients who had their data stored in EHRs had their data backed up off-site and were able to get back to normal medical care within a few days," he adds.

Ms. Fitzhugh adds that ophthalmology is a particularly difficult specialty for Web-based solutions because of the complexity of the ophthalmic environment. "Just trying to integrate all of the diagnostic equipment with the EHR software over the Web can be challenging; some equipment simply cannot be supported," she says. "Additionally, pushing images back and forth into the cloud requires network bandwidth that offices might not have available locally. Ultimately, I think everyone wants everything to be in the cloud because that will relieve practices from needing IT expertise and maintaining all these servers on the premises, but the technology needed to support pure cloud is not quite ready for prime time."

Mr. Messier notes that EHRs are only as good as their weakest link, which is often the Internet connection in Web-hosted situations. "Connections are getting better and better," he says, "and they are certainly better than they were 10 years ago, but they are the weak link. Ophthalmologists need a fast connection and some type of backup connection that is in place so that if the primary goes down, they are still able to function in their offices."

He notes that an upgraded Internet connection is often not considered in the cost analysis, but it should be. "In eye care, even if you are a one-doctor practice, you are probably going to have between three and seven pieces of diagnostic equipment, so in order for you to have a fully functional EHR, you need to have that diagnostic information and those images internal to your charting. The challenge there is, in a cloud environment, we need to be able to take that information and store it to the server. You have to have the bandwidth to be able to upload this information and the modality to store it onto the server so that you can walk into the exam room, look at those images, and be able to make your treatment decisions without any hesitation and without any delay," he says.

While there are many considerations when choosing between the client-server model and the Web-hosted model, the cloud is the way of the future. "The trend is clearly toward the cloud," says Mr. Corcoran. "Not everybody is sold on the idea, but I wouldn't be spending lots of money on servers if I was the CEO of a physician practice management company." REVIEW

37 Ways to Get Great Outcomes with Torics

Christopher Kent, Senior Editor

Surgeons share their experience and offer strategies for making the most of these intraocular lenses.

The use of toric intraocular lenses in cataract surgery is steadily increasing, and as happens with any new technology, plenty of "tricks of the trade" are still being discovered. (For example, a study just published in October found that if you can't exactly match the cylinder-correcting power of the toric IOL to the corneal astigmatism, better outcomes are achieved by using a lower rather than higher cylinder value.[1])

Here, seven experienced surgeons share their insights into every aspect of implanting toric lenses, from measuring, marking and patient management to implanting the lenses on the correct axis and correcting any problems that turn up postop.

Measuring and Marking

Possibly the most crucial part of the procedure is determining the axis of astigmatism as accurately as possible. This is scarcely a foolproof process, but a number of strategies can help:

• ***Get K-readings from multiple sources.*** "If you get manual Ks and use that as the gold standard, that's fine—if your technician is perfect," notes James A. Davison, MD, FACS, who practices at the Wolf Eye Clinic in Marshalltown and West Des Moines, Iowa. "Unfortunately, no one is perfect. So you want to confirm that the manual Ks are pretty close to some other method. We get K-readings from manual keratometry, automated keratometry and computerized video keratography (such as the TMS-2 from Tomey) or computerized tomography (such as the Pentacam). If the IOLMaster indicates that astigmatism is present and the patient is interested in receiving a toric lens, we go ahead and do the CVK or the Pentacam." Dr. Davison's favorite device for this purpose is the Pentacam. "The Pentacam takes a great picture of the front surface of the cornea and provides a nice visualization of where the axis of the astigmatism is," he says.

Stephen S. Lane, MD, medical director at Associated Eye Care in St. Paul, Minn., and adjunct clinical professor of ophthalmology at the University of Minnesota, notes that his team takes as many as five different measurements to determine the magnitude and axis of the astigmatism. "We use manual and automated keratometry and topography, including measuring with the Lenstar and IOLMaster," he says.

• ***Remember that not all K-readings are created equal.*** John Berdahl, MD, corneal, refractive and glaucoma surgeon at Vance Thomp-

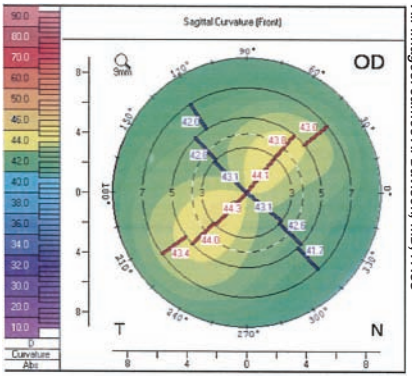
son Vision in Sioux Falls, S.D., and assistant clinical professor at the University of South Dakota, agrees that using multiple sources for your measurements is crucial, but emphasizes that topography is especially important. "The tricky part with toric IOLs is getting reliable keratometry measurements," he says. "Anterior topographers do the best job of quantifying the axis and magnitude of anterior corneal astigmatism."

"The IOLMaster is a great product, but may not be the best for identifying the exact orientation of the axis of astigmatism," notes Dr. Davison. "It's great for determining the average K-value and the power of the implant, but you shouldn't use the IOLMaster for determining the axis. That's one reason Alcon's instructions say to use manual keratometry for that purpose."

Dr. Berdahl agrees. "The IOLMaster takes six data readings and extrapolates from that data," he says. "It wasn't designed to provide incredibly accurate astigmatism measurements. So you should probably put a little less weight on that device than on something like a topography unit, which will give you much more precise astigmatism readings."

• ***Be wary of disagreement between measuring instruments.*** "Part of the goal of taking multiple readings with different instruments is to see whether all of the readings are within 10 degrees of each other," says Dr. Davison. "I like to see whether the manual Ks are close to the Pentacam Ks. If they're not within 10 degrees, we go back and take the Pentacam picture again and do the manual Ks again. We may end up having to do this on a different day, because by the time I see everything the patients usually have had drops in their eyes. But it's really important to get the axis right."

"If there are discrepancies between the readings, I tend to rely on manual or automated keratometry for the magnitude of the astigmatism, and topography for the axis," says Dr. Lane. "Usually three or four of the five measurements will agree. If only one disagrees, I treat it as an outlier and exclude it."



All images: James A. Davison, MD, FACS

A Pentacam sagittal curvature image of an anterior corneal surface shows regular astigmatism of about 1 D with the steep axis at about 45 degrees.

"If the measurements we get with different instruments are out of agreement by more than 10 degrees, I start to be leery about using a toric lens, especially if the patient has a large amount of astigmatism," says Dr. Berdahl. "If the alignment of a toric lens is off by 10 degrees, it loses 30 percent of its effect. That's not a big deal with low-power toric lenses, but in a large diopter lens like a T-9, that's almost 1.5 D of cylinder."

• ***Use the most comprehensive topographic algorithm.*** David F. Chang, MD, clinical professor at the University of California, San Francisco, and in private practice in Los Altos, Calif., notes that he uses the topographic function that computes the astigmatic axis and magnitude from the entire area within the 3-mm optical zone, rather than the function that uses the simK measurements taken only at the edge of the optical zone. "Looking only at the keratometric points on the edge of the 3-mm optical zone might cause you to underestimate corneal toricity that is greater closer to the visual axis," he explains.

• ***If you're using video keratography, use the highest resolution.*** "This will allow you to see the orientation of the astigmatism a lot more clearly," notes Dr. Davison.

• ***Consider manually checking the Pentacam numbers for further confirmation.*** "I learned this strategy from Warren Hill," explains Dr. Davison. "He looks at the Pentacam numbers, but he also puts the Pentacam picture up and draws a line through the picture identifying the axis based on what he sees, to make sure it's close to what the Pentacam's numbers say."

Pitfalls to Avoid

Many factors can interfere with an accurate measurement. A few to watch out for:

• ***Mark the eye while the patient is upright.*** "If you don't, the eye may rotate when the patient lies down, and you'll end up not aligning the lens to the intended axis," says Dr. Berdahl.

• ***Be on the lookout for dry eye.*** "Dry eye can alter the keratometry value," notes Dr. Berdahl. "Usually you can see on topography that the corneal surface isn't pristine, and there are plenty of other clues that the ocular surface isn't as stable as it should be. For example, if a person is blinking a lot and having a hard time when you do the manifest refraction, that a clue. If there's a difference between your IOLMaster Ks and your topography Ks, that's a clue. We need to be diligent about investigating these signs to avoid ending up placing the toric lens on the wrong axis."

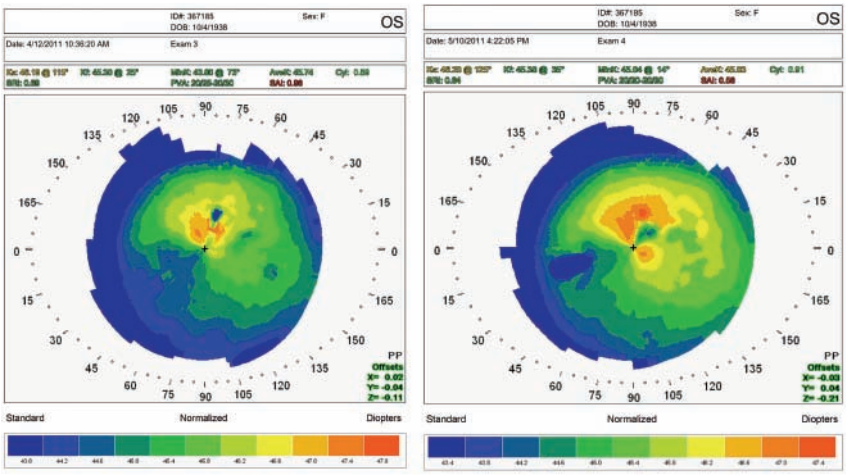
• ***Ask whether the patient wears contact lenses.*** Dr. Davison notes that a patient may wear contact lenses part-time and neglect to mention it. "Contact lenses change the shape of the corneal surface," he points out. "When a cataract patient comes in, you may not be thinking about contact lenses as you would with a LASIK patient. But if you don't ask about

contact lenses, you might proceed and get the wrong numbers, leading to a poor result because the cornea was deformed from the contact lens wear. So be sure to ask."

• ***Make sure your technicians have the patient's head aligned correctly when they record the topography or keratometry.*** "After identifying the axis for the toric IOL from our keratometry or topography, we take a lot of effort to properly mark the axis prior to surgery," says Dr. Chang. "Typically, we sit the patient upright and make ink marks denoting a reference such as the 180-degree axis. However, we're trusting that the patient's head was properly aligned when our technicians recorded the topography or keratometry. This is another potential source of error."

• ***Even if you use advanced intraoperative technology, take preop measurements.*** Dr. Lane uses WaveTec's ORange system, as well as other high-tech systems like the Surgery Guidance System from SensoMotoric Instruments in Germany, which takes a preop photograph of the eye and then overlays a digital reticle during surgery that moves with the eye. Nevertheless, he says he still takes preop measurements in the traditional way. "In theory it isn't necessary," he notes, "but I have to be prepared to finish the case if the power goes out or an instrument suddenly fails to work. Additionally, when the measurement from the intraoperative instruments agrees with the preoperative measurements it's very reassuring that we've chosen the proper IOL."

• ***Remember that the spherical component is important, too.*** "Even if you place the correct lens exactly on-axis, missing the spherical component will produce a poor outcome," says Dr. Davison. "Let's say you have a patient with a T-7 lens who starts off with 4 D of astigmatism. If you get it down to 0.25 D, that's great—unless the final spherical equivalent is -0.75 D. In that case, the patient still won't see very well at distance."



Computerized videokeratoscopy images of corneal anterior basement membrane dystrophy showing irregular astigmatism. Note the fluctuation in appearance from one month to another (left-right). In this situation, surgeons recommend caution about choosing to implant a toric IOL.

• ***Make it your goal to minimize all variables.*** Dr. Davison notes that while a single variable being slightly off might not have a serious impact on the visual outcome, multiple variables being slightly off all in the same direction could add up to trouble. "Let's say you had a poor K-reading from your technician," he says. "Then suppose you had a poor reference mark because the patient's head was tilted. Then let's suppose your axis marker was slightly bent, or you didn't have your circular degree marker in the center of the eye. Then let's say you put the lens in and it wasn't quite perfect because of parallax; the eye wasn't looking exactly at the microscope filament and it was off-center a little bit.

"If you take all those errors and add them up, that's a lot of opportunity for things to be off," he says. "In some cases, those kinds of errors might cancel each other out. But if they all happen to shift in the same direction, the cumulative effect could result in a substantial error in your placement."

• ***Make sure patient expectations are reasonable.*** "We make sure our patients understand that with toric lenses—and even with monofocal lenses—we try to get a perfect result, but we hardly ever hit the center of the bull's-eye," says Dr. Davison. "Even with all of these technologies, these are still imperfect procedures. So, our focus is on getting as close to perfect as possible. We even put that in the consent form."

Is This Eye a Good Candidate?

When an eye is not average in some respect, a toric IOL could be contraindicated or require special consideration.

• ***If you choose to use a toric when a topographic bow tie is regular but asymmetric, warn the patient that the correction won't be perfect.*** "In this situation you're going to get some correction of the astigmatism, but because of the asymmetry the result may not be perfect," says Dr. Davison. "Unfortunately, patients are expecting perfection more and more, even if you don't charge them very much."

• ***Think twice if a patient has corneal anterior basement membrane dystrophy.*** "These patients

can have variable vision and variable astigmatic axes," notes Dr. Davison. *(See example, facing page.)* "They're not only irregular but asymmetric as well. That's a problem you can't make better with a toric IOL."

Dr. Berdahl notes that in some cases, however, a toric lens might be a worthwhile option. "If the anterior topography looks good, even though the patient has ABMD, I'd consider a toric lens," he says. "If the anterior topography is irregular, then I'd do a PTK first to smooth it out."

Dr. Davison notes that if the patient has a substantial toric surface underneath the corneal anterior basement membrane dystrophy, he might consider a toric. "A toric might actually be able to make the patient's vision a little bit better," he adds. "But I've spent half an hour talking to patients like this, and they still don't appreciate that their result would have been worse without the toric lens. All they care about is whether they see well; if they don't see well, they don't care why—especially when they've paid extra money. So it's best not to promise something that you won't be able to deliver. For that reason, I'm not likely to recommend the toric for one of these patients, unless he really, really understands the situation."

• ***If the patient has keratoconus, consider waiting for cross-linking availability.*** "I'm worried that the keratoconus will progress," says Dr. Berdahl. "I'd prefer to cross-link the cornea first to get it stabilized. Without that, the astigmatism could change, or the patient could end up needing a corneal transplant. If he does, you'll be doing a corneal transplant on top of a lens that has astigmatic correction built in, and things will get complex. I would consider implanting a toric in specific cases, but I'd prefer to do corneal cross-linking first. At this point, it looks like cross-linking will be approved in the United States soon, so I'd advise the patient to wait for that."

Choosing the Lens

Power and axis aren't the only considerations to weigh when making your final lens choice.

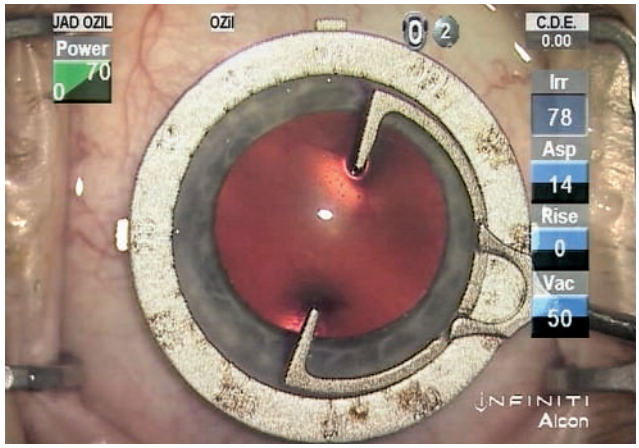
• ***Consider slightly undercorrecting with-the-rule keratometric astigmatism and fully correcting—or slightly overcorrecting—against-the-rule keratometric astigmatism.*** "We're not measuring posterior corneal astigmatism, which probably accounts for the astigmatic discordance between the pseudophakic keratometry and refraction that we often see," notes Dr. Chang. "Typically, in our cataract population, posterior corneal astigmatism adds against-the-rule cylinder. This would explain why many pseudophakic patients with 0.75 D of with-the-rule cylinder have no astigmatism in their refraction, and why some patients with spherical keratometry have 1 D of against-the-rule astigmatism in their refraction.

"For this reason, with toric IOLs I slightly undercorrect with-the-rule keratometric astigmatism and fully correct, or slightly overcorrect, against-the-rule keratometric astigmatism," he says. "For example, if the patient has 1.75 D of with-the-rule astigmatism on keratometry, I'd implant a T3 Acrysof toric, but for 1.75 D against-the-rule, I'd probably use a T5. We definitely don't want to flip the axis with our toric IOL."

• ***Factor in lens asphericity when dealing with patients who've had hyperopic LASIK.*** "Surgeons are careful about using the Alcon toric IOL in patients who've had hyperopic LASIK because the Alcon torics introduce negative spherical aberration to compensate for the positive spherical aberration of the normal cornea," explains Dr. Davison. "Hyperopic LASIK also introduces negative spherical aberration, so using the Alcon toric adds the two negative asphericities together, creating a greater negative spherical aberration than would otherwise be intended.

"However, if you don't use the toric IOL in that situation, you'll be leaving the patient with the far more significant lower-order astigmatism aberration," he continues. "That residual will be a lot more obvious to the

patient than the less-significant residual higher-order spherical aberration. In general, I think it's more important to fix the lower-order aberrations than the higher, so if someone has had hyperopic LASIK but has substantial keratometric astigmatism, I'd offer him a toric lens because his uncorrected vision will be much improved with the astigmatism corrected."



A Graether Half Circle Axis Marker (ASICO) being used to mark a left eye at approximately 162 degrees.

• ***Know how much surgically induced astigmatism you're creating.*** Dr. Berdahl notes that having accurate data about this can make a difference in your outcomes. "The bigger the incision you use, and the more centrally located that incision, the more astigmatism it will induce," he points out. "That may alter your surgical plan, and perhaps the outcome." (All of the manufacturers' calculators ask the surgeon to enter the expected amount of surgically induced astigmatism.)

• ***If you use the Alcon toric, be especially careful with the initial alignment.*** "The exact alignment of the Alcon toric lens is very important since it is more difficult to rotate than the Staar toric lenses," says James P. Gills, MD, founder and director of St. Luke's Cataract & Laser Institute, and clinical professor of ophthalmology at the University of South Florida. "The Alcon toric is difficult to rotate because of the lens construction and the tackiness of the lens material to the capsule. However, I use the Alcon Toric because the bi-asphericity of this lens provides better optical results. Also, the fact that the Alcon torics are less likely to rotate could be of benefit once the lens is correctly positioned."

In the OR

Placing the toric lens correctly can be as challenging as measuring the axis. These strategies can help:

• ***Mark the axis of astigmatism twice; once in the exam room, and again in the OR prior to surgery using a surgical keratometer.*** "This is a simple way to ensure the accuracy of your reference marks," says Dr. Gills.

Dr. Davison agrees. Preop, he prefers to simply mark the 6 o'clock axis at the limbus. "Once in surgery, I use a two-part axis determiner to place the astigmatic axis at the correct orientation," he says. "I also reinforce the marks using a Weck-Cel sponge that I mark with ink, so the marks don't fade away during the surgery."

• ***Consider using bimanual surgery.*** "When implanting a toric lens, we maintain the anterior chamber with an irrigation cannula through one paracentesis and position the lens with a hook through the other paracentesis," says Dr Lane. "There are other approaches favored by different surgeons, such as positioning with one hand using the irrigation/aspiration tip. But I find this method to be the fastest, easiest and least invasive way to do it."

• ***Try alternate methods for locating the axis.*** Hyo-Myung Kim, MD, PhD, at the Korea University College of Medicine in Seoul has developed a method for identifying the axis for toric IOL implantation on the eye that requires no special instrumentation. Dr. Kim takes a photograph of the anterior segment; he uses the photograph to identify the desired axis marking points, as well as nearby conjunctival blood vessels that can be used as reference points. He then calculates the precise distance from the reference points to the axis marking points. Once in the OR, he uses calipers to locate the axis marking points on the eye relative to the reference vessels.

In a recent study involving 40 eyes of 20 patients, researchers compared Dr. Kim's method to two conventional techniques in which the patient was marked while seated at the surgical table or in front of a slit lamp. Dr. Kim's method was more accurate than either conventional method by a small but statistically significant amount.[2]

"This approach has several advantages," says Dr. Kim. "We don't need any special instruments to mark the axis, and we don't have to spend time marking the eye before surgery. Taking the photograph is a very simple process. And, our method appears to give us more accurate results." (Dr. Kim notes, however, that mydriatics mixed with vessel constrictors can make identification of the reference vessels more difficult. He suggests preoperatively selecting an additional landmark near the limbus as an alternative reference point in case any problem arises.)

• ***When initially implanting the lens, leave it about 20 degrees shy of the final orientation.*** This will allow you to very carefully move it to its precise alignment as a separate step, say our surgeons.

• ***Try to rotate the lens after insertion to identify potential postop rotation problems.*** "A technique

The First Breakthrough in Subjective Refraction in 80 Years

Vmax Vision PSF Refractor™ is the answer!

The wait to replace the oldest instrument in your office is over. Vmax Vision proudly introduces the new PSF Refractor™ with proprietary Point Spread Function (PSF) technology which provides 5X greater accuracy than the phoropter and enables you to:

- Refine refraction to 0.05 D – neutralizing wavefront aberrations
- Obtain final and reliable results with the PSF Refractor™
- Provide high acuity nighttime vision subjectively – a real solution to nighttime driving problems
- Delegate refraction. It has never been easier. Learn in a few hours and be proficient in a few days
- Increase ROI with higher profit margin on exceptional products
- Differentiate your practice and Wow your patients

Maximize your patients' vision. The free-form individualized premium Encepsion™ Lenses are optimized when paired with the high fidelity PSF refraction.

The PSF Refractor™ is the missing link of your cutting edge practice. Call Vmax Vision at 888.413.7038 for an in-office demonstration today. Or, for more information, visit www.VmaxVision.com.

vmax™
VISION, INCORPORATED

1.888.413.7038
info@vmaxvision.com
www.vmaxvision.com

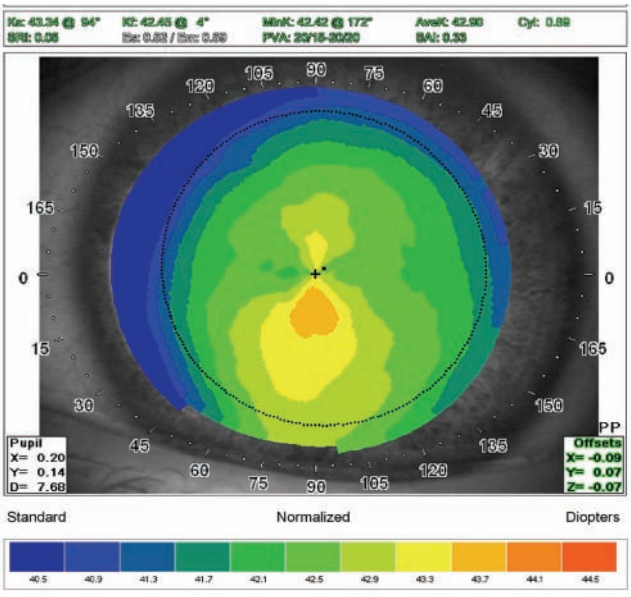
I follow is to try to rotate the lens both clockwise and counterclockwise immediately after insertion," says Catherine T. Fitzmorris, MD, who practices at Gulf South Eye Associates in Metairie, La. "This helps me identify cases which are more likely to rotate postoperatively."

• ***Be sure to remove all of the viscoelastic from behind the lens.*** "This enables the lens to tack itself down to the capsular bag, making it less likely to rotate," says Dr. Berdahl.

• ***Take special care with long eyes receiving low-dioptric-powered lenses, especially with vertical orientation.*** In this situation, Dr. Davison notes that postop rotation is more likely because the lens is standing on one haptic. "In that situation, gravity wants to rotate the lens so it's not standing on a single point," he explains. "It's inherently more stable when it's supported by two horizontal points.

"A few years ago I published a paper with Art Weinstein," he continues.[3] "We found that for powers from 6 to 10.5 D, 3.4 percent of the lenses fell off the vertical axis and rotated significantly; 1.4 percent of 11 to 15.5 D lenses, and 0.5 percent of 16 to 20.5 D lenses also rotated significantly off their intended axis. In contrast, lenses with a power of 21 D or higher didn't rotate at all. So when the eye is really long, postoperative rotation is more of a concern, especially when the lens is oriented vertically."

To proactively prevent that rotation, Dr. Davison suggests two strategies. "First, consider making the standard 2.4-mm-width incision's shelf a little longer," he says. "Usually my shelf is about 1.7 mm; in this situation I might make it almost 2 mm. I want to make sure that I can stromal hydrate the incision without overinflating the eye and the capsular bag. Second, make sure you remove all viscoelastic from in front of and behind the lens. If you leave any viscoelastic and you overinflate the eye, the lens is more likely to rotate afterwards, especially in really long eyes when the lens is placed vertically."



Computerized videokeratoscopy image of a cornea post-hyperopic LASIK. Hyperopic LASIK induces negative spherical aberration, so if the toric IOL also adds negative spherical aberration the surgeon must weigh that against the positive visual effect of eliminating the astigmatism.

• ***In the case of a radial capsule tear, you can probably leave the lens in.*** "Many surgeons believe that an anterior radial tear is a contraindication for a toric lens, so if a tear occurs, they might not implant one; or, if implanted already they might try to remove the lens and replace it with something else," says Dr. Davison. "Even if a posterior tear is discovered after the lens is in, you don't have to remove it; you can leave it in as long as you orient it properly and capture the optic anterior to the anterior capsule remnant created by an intact capsulorhexis. In fact, if you try to take it out, you're probably going to make the situation worse. You'll create more tears or other problems. Then where do you put the next lens? Even if you're forced to leave the lens with an imperfect alignment, leaving it may still be better than trying to take it out. You can correct some residual problems from an imperfect alignment with LASIK—assuming that the cornea has enough tissue."

• ***Intraoperative aberrometry can help, especially with unusual eyes.*** Dr. Berdahl has used the ORange device for several years. "It's especially useful in situations where the eye is very long or short," he says. "For example, I had a patient who was a +12 hyperope prior to cataract surgery. We were going to implant a 34-D multifocal lens, plus a 3-D piggyback. However, when I did the aphakic measurement, it called for a 34-D lens—not the equivalent of a 37-D lens. So I ended up only implanting the 34-D lens, and the outcome was right on the money. If I had followed my preop IOL calculations, we would have ended up leaving him a 2- to 3-D myope."

Dr. Berdahl adds that this technology is also helpful when implanting a Crystalens. "Sometimes the Crystalens has a tendency to vault a little anteriorly," he says. "If you have a more myopic reading with the ORange device after implanting the lens, you can go back in and tap the lens posteriorly. I'm now getting much more appropriate and consistent results with the Crystalens."

• ***In some situations a capsular tension ring may help.*** "If the patient is a very high myope with a large capsular bag, I'll occasionally use a capsular tension ring to try to prevent any lens rotation and make sure the lens is in the best possible location,"

says Dr. Berdahl. "I haven't seen clinical data proving that this helps, but anecdotal reports suggest that it does."

• ***Triple-check everything at the end of surgery.*** "Once the eye is returned to normal pressure, it's important to confirm that everything is correct with at least two other people who are present in the OR," says Dr. Davison. "Everybody looks at the paper and the video screen one last time. We make sure we used the right lens. And it's especially important to confirm the axis, because believe it or not, you can get tired or mixed up and put the lens on the wrong axis. We sometimes even get the axis marker out again to inspect, just to make sure. If you triple-check and confirm with others, it's almost always fine."

Resolving Problems Postop

Lens rotation after surgery only happens in a small percentage of cases, but when it does, these steps can help ensure an appropriate remedy.

• ***If the postop refraction isn't perfect, use trial lenses and a lensometer to determine whether lens rotation is to blame.*** "With the use of toric IOLs that correct large amounts of astigmatism, even a small amount of rotation can cause an unusual refraction," notes Dr. Fitzmorris. "One way to verify that the refraction is secondary to rotation of the lens is to use trial lenses and an auto lensometer.

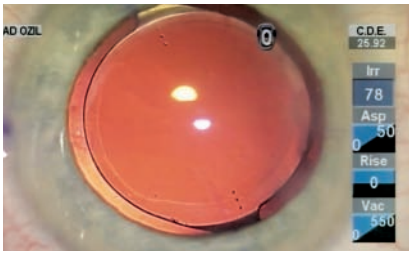
"For example," she continues, "suppose you were trying to correct 4 D of cylinder at 90 degrees. Take a +4-D lens and place it on the automatic lensometer, aligned at the 90-degree mark. Now, suppose the toric lens you implanted actually oriented at 95 degrees, postop. Take a -4 D cylindrical lens from the trial lens set and orient it at the 95 degree meridian over the +4-D lens already on the automatic lensometer. The resulting neutralization of the two lenses will tell you what your postop refraction should have been as a result of the rotation.

"You can compare this reading to your actual postop refraction," she concludes. "If it matches, the lens rotation is the source of the imperfect outcome. If not, something else is amiss, and an IOL exchange may be necessary."

• ***If the eye has residual astigmatism postop, consult the calculator at*** astigmatismfix.com ***for advice on the best way to proceed.*** Use of this calculator, created by Dr. Berdahl, is free. "You can put a lens in exactly where you want it to be but have residual astigmatism because of posterior corneal curvature, or because you have more surgically induced astigmatism than you expected, or because the preop Ks weren't good enough," explains Dr. Berdahl. "What should you do? Our calculator takes the patient's manifest refraction and the current lens and location and tells you how much effect rotating the lens will have. This will give you a good sense of whether it's worth it to go back in and rotate the lens or not."

• ***If you have to rotate a misaligned implant, you don't need to mark the patient preoperatively.*** "Make a note of the rotation axis at the slit lamp and use that exact axis as a reference point intraoperatively," advises Dr. Fitzmorris.

• ***If you need to reorient a toric lens late, keep the bottle height low.*** "This will usually happen in long eyes, so it's important to lower the bottle height to about 50 cm above the eye," says Dr. Davison. "If you go in with a high bottle height you'll overexpand the eye, hurting the patient and causing the lens to move posteriorly. Then it may be unreachable with the silicone tip, which you want to use to suction onto the anterior IOL surface so you can rotate the lens. So, lower the bottle, then take out all of the viscoelastic and use stromal hydration on the incision so you don't overinflate the eye or the bag. Even during the primary procedure, it's helpful to lower the bottle height for final orientation in long eyes." (Dr. Davison adds that he's never had a toric lens go out of position a second time after late re-orientation.)



An intraoperative photograph shows a toric IOL with good alignment and fairly symmetrical anterior capsule optic overlap.

An Option Worth Offering

"Toric intraocular lenses are a fabulous technology," says Dr. Davison. "It amazes me that people are still reluctant to use it. I think they may have had negative experiences with multifocal lenses, which are much more finicky and require everything else to be perfect to achieve good results. With toric lenses, if you simply follow the cookbook and do the right thing, you're going to get good results and have happy patients." REVIEW

Dr. Davison is a paid consultant for Alcon; Dr. Lane is a consultant for SMI in Germany, Alcon and WaveTec Vision. Dr. Chang is a consultant for Alcon; his fees are donated to the Himalayan Cataract Project and Project Vision. Drs. Berdahl, Gills and Fitzmorris have no financial ties to any technology discussed.

1. Felipe A, Artigas JM, Díez-Ajenjo A, et al. Residual astigmatism produced by toric intraocular lens rotation. Journal of Cataract & Refractive Surgery 2001;37:10:1895-1901
2. Cha D, Kang SY, Kim SH, Song JS, Kim HM. New axis-marking method for a toric intraocular lens: mapping method. J Refract Surg. 2011;27:5:375-9.
3. Davison JA, Weinstein AJ. Three strategies for reorienting AcrySof toric IOLs. Cataract & Refractive Surgery Today 2010;10:1-4.
4. Visser N, Berendschot TJM, Bauer NJC, et al. Accuracy of toric intraocular lens implantation in cataract and refractive surgery. J Cataract Refract Surg 2011; 37:1394-1402.

Bringing Monofocal IOLs into Focus

Walter Bethke, Managing Editor

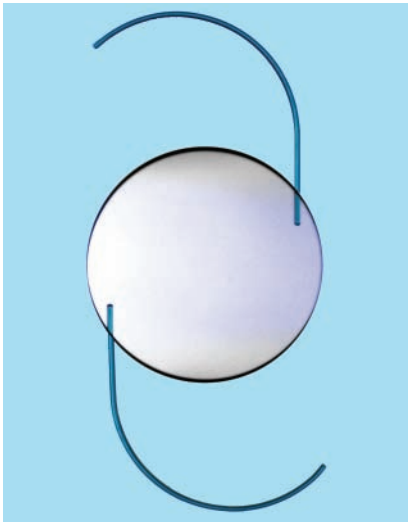
The most recently approved crop of monofocal lenses has features worth exploring, say surgeons.

The products that make the biggest promises get the most attention, as anyone who has marveled at the amount of information generated about multifocal and accommodating IOLs can attest. That being the case, in cataract surgery, monofocal intraocular lenses are so ubiquitous they're almost taken for granted, yet they're the lenses most of the patients who need cataract surgery are likely to get. Since 2010, four new monofocal intraocular lenses have been introduced in the United States, and surgeons have been gradually amassing experience with them, getting a feel for how to put their features to use in the operating room. Here, several surgeons experienced in the use of these IOLs discuss the new devices.

Aaren Scientific's EC-3 Lenses

Aaren's Enduring Clarity line of lenses is composed of two models, the EC-3 and the EC-3 Precision Aspheric Lens. Both are three-piece lenses made of a hydrophobic acrylic, with a square-edged optic to reduce the incidence of posterior capsule opacification. They each have a 6-mm optic and come in powers ranging from +4 to +34 D in 0.5-D increments.

According to the company, the bi-sign aspheric lens uses two different curvatures within the lens itself in order to balance out aberrations in the lens with misalignment, large pupils and different corneal shapes. The lens produces spherical aberration of an opposite sign in the central 3-mm zone vs. that in the periphery outside the central zone. The lens's maker says that by having both positive and negative asphericity within the lens, it may be less impacted by a misalignment than if the asphericity was all one sign. "The lens balances out the aberrations so, in the presence of a



Aaren Scientific

Aaren's EC-3 PAL lens's design may be less affected by tilt and decentration.

NEW

CVSi21 *CVS-PC*

Lombart's CVSi21 And CVS-PC Computerized Vision Systems

Now you have a choice of operating systems when you buy the Lombart CVS computerized vision systems.

The CVSi21 utilizes the Apple Macintosh computer, renowned for its stability. This all inclusive unit incorporates a High Quality LCD flat panel 21" monitor and CPU in a compact one-piece system that mounts easily to the wall.

The CVS-PC utilizes a 19" Dell all-in-one PC and is designed for those who prefer a Windows based °operating system in a more economical unit

56 Button Remote provides direct access to all charts and allows you to rapidly navigate through an infinite number of chart combinations giving you unprecedented selection, efficiency and control.

Exclusive Software features a wide range of popular optotypes required in today's practice environment. *Standard optotypes include:* Snellen Letters, Tumbling E, Landolt Rings, Numbers, HOTV, Crowding Bars, Children's Charts, Red/Green Testing, ETDRS and Contrast Testing.

Customize Your System by adding your own videos and images for patient education and fixation.

Enhanced Remote Features facilitate operation and include:

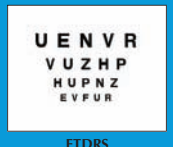
- Random Character Generation
- Single Letter Isolation
- Vertical & Horizontal Line Isolation
- 4-Dot & Fixation Tests
- Built-in Video Clips for Child Fixation
- Easy Retrieval of Images for Patient Education

Snellen Chart


Patient Education


Children's Charts


Disparity



ETDRS


Video

(1-800-566-2278)

Call 1-800-Lombart

Or Your Local Lombart Representative.

Corporate Office - 5358 Robin Hood Road, Norfolk, VA 23513-2430
757-853-8888 | FAX 757-855-1232 | 800-566-2278 | 800-446-8092
www.lombartinstrument.com

ATLANTA•BALTIMORE/WASHINGTON D.C.•BOSTON•BOYNTON BEACH/MIAMI•BRADENTON•CHARLOTTE
CHICAGO•CINCINNATI•DALLAS•DENVER•DETROIT•GREENSBORO•HOUSTON•KANSAS CITY•KNOXVILLE•LOS ANGELES
MINNEAPOLIS•NEW JERSEY/NEW YORK•NORFOLK•PORTLAND•SACRAMENTO•SAN DIEGO•SAN FRANCISCO

lens misalignment or tilt, you'll find a more consistent image quality, contrast sensitivity and expanded depth of focus," says Kim Dyer, marketing manager for Aaren.

Venice, Fla., ophthalmologist P. Dee G. Stephenson took part in the Food and Drug Administration trial of the lens, and was pleased with how it performed. "Effective lens position is one of our big enemies when it comes to outcomes," she says. "So, the asphericity characteristics of the lens are a big deal, because we don't want to induce aberrations."

In the multicenter FDA study, 354 subjects received the EC-3 lens in one eye and another monofocal in the fellow. At a year, 99 percent had a best-corrected vision of 20/40 or better. The most frequent adverse event was a 2-percent incidence of secondary surgical intervention for the following reasons: open operative sideport incision to relieve elevated intraocular pressure (0.6 percent); lens removal (0.6 percent); retinal detachment repair (0.3 percent); piggyback lens procedure (0.3 percent) and epi-retinal membrane removal (0.3 percent). There was also a 1.1-percent incidence of cystoid macular edema in the study. Dr. Stephenson says her EC-3 patients are two years postop now and have no lens glistenings that some surgeons might be concerned about when considering an acrylic lens.

Dr. Stephenson says the three-piece design can be a boon to surgeons. "Being a three-piece lens is a big benefit," she says. "Since it's three-piece, this means if this is the go-to lens for a surgeon, she doesn't need to have another lens around as a backup. She can use this lens and, after choosing the proper power, put it in the sulcus if she tears the bag since it's not a one-piece." In the study, the lens went through an average incision size of 2.9 mm.

"I was a silicone lens person for a long time," Dr. Stephenson says. "So for me to try an acrylic lens was a big deal. In my arm of the EC-3 study, I inserted a silicone, three-piece, fourth-generation silicone IOL in the other eye of each of the 26 patients I operated on. I was surprised that the EC-3 performed as well as the three-piece silicone lens."

Alcon's High-correction Torics

Though many surgeons have been pleased with the AcrySof toric IOL, they been somewhat restricted by the limited range of correction the lenses had been approved for. This changed with the approval of the AcrySof IQ Toric for high ranges of correction. Specifically, this acrylic, single-piece lens is newly approved to treat corneal astigmatism ranges of 2.57 to 3.07 D (T6 model), 3.08 to 3.59 D (T7), 3.6 to 4.1 D (T8) and 4.11 D and higher (T9).

"The interesting thing is that people in the United States were interested in getting access to the high end of the toric correction range, but the majority of patients who would need a toric lens fall in the range of toric lenses that we've had available for a long time," says Richard Tipperman, MD, assistant surgeon at the Cataract and Primary Eye Care Service at Wills Eye Institute. "However, a lot of the advantage of the expanded toric range is that the idea of treating higher levels of astigmatism seems to make more sense to surgeons just starting with the technology. It might not make a lot of sense to some people to use a lens to treat 1 or 1.25 D of astigmatism. However, they know that if a patient has 2 to 4 D of astigmatism, if it's left untreated the uncorrected vision is going to be very poor. So, for almost all surgeons, using the higher power toric intuitively makes more sense, and they're more comfortable using it for that.

"The one thing a surgeon may encounter on occasion with higher power torics that isn't always an issue with lower power toric lenses is the potential for 'flipping' or overcorrecting a patient," Dr. Tipperman continues. "The way the lenses work, for every 10 degrees they're off axis, you lose a third of the effect of the implant until, at 30-degrees misalignment, they're effectively neutral in terms of astigmatism correction. But, if you implant a T3 toric, the lowest power available in the United States, and overcorrect the patient by 50 percent, the patient will only have 0.5 D of induced astigmatism 90 degrees away from where it was originally. However, if you do this with a T8 or T9, the patient will have 1.75 to 2 D of astigmatism oriented 90 degrees away from the original astigmatism, and that will be very manifest to him. So, it's crucial that the axes line up." *(For a discussion of the finer points of implanting torics, see "37 Ways to Get Great Outcomes with Torics," on p. 26.)*

In the clinical study of the AcrySof toric, almost 90 percent of the lenses didn't rotate or rotated only 5 degrees or less. However, Dr. Tipperman says there are situations where rotation can occur spontaneously. "Some surgeons have a feeling that very high myopes with very large anterior segments and very large capsular bags are at risk for spontaneous rotation," he says. "In light of this, when faced with patients who are very nearsighted or who have high axial lengths, there are surgeons who will counsel them preoperatively, saying, 'Look, this is the best lens for your nearsightedness and astigma-

Laser Refractive Cataract Surgery is Now a Reality with Alcon's LenSx® Laser.

Cataract Surgery Will Change in a Femtosecond.

With Alcon's LenSx® Laser, the Possibilities Have Just Begun.

Delivering the precision of a femtosecond laser to Refractive Cataract Surgery, the LenSx® Laser is designed to reproducibly perform many of the most challenging aspects of traditional cataract surgery. Creating highly reproducible capsulotomy, lens fragmentation and all corneal incisions including arcuate incisions with image-guided surgeon control, Alcon's LenSx® Laser is Putting the Future in Motion.

CAUTION: United States Federal Law restricts this device to sale and use by or on the order of a physician or licensed eye care practitioner. United States Federal Law restricts the use of this device to practitioners who have been trained in the operation of this device.

Please see adjacent page for brief summary information.

The LenSx® Laser is indicated for use in patients undergoing cataract surgery for removal of the crystalline lens. Intended uses in cataract surgery include anterior capsulotomy, phacofragmentation, and the creation of single plane and multiplane arc cuts/incisions in the cornea, each of which may be performed either individually or consecutively during the same procedure.

For Important Safety Information and Full Directions for Use, please reference the LenSx® Laser Directions for Use.

To learn more about LenSx® Laser technology for Laser Refractive Cataract Surgery, visit lensxlasers.com.

LenSx® LASER

Putting the Future in Motion

Alcon®

tism. However, you're aware that you have an unusual, very large eye. So, though this lens works well for everybody most of the time, even in highly nearsighted people, there's a very small chance it will shift for you. If it does, though, there's a way we can fix that."

Hoya Optics iSymm Lens/iSert

The clear (as opposed to containing a yellow chromophore) iSymm IOL and the iSert pre-loaded inserter were actually marketed by Hoya for more than a year before the FDA requested that they be removed from the market in June 2011, pending the results of additional testing. Since then, the company has submitted that data, and signs look positive for the lens regaining its marketing status before February 2012, so it's worth it for U.S. surgeons to be reacquainted with the IOL before it hits the market again. (The yellow version of the lens is currently available for sale.)

The iSymm is an aspheric, hydrophobic acrylic lens with a unique haptic design. "It's truly a one-piece product, but it sometimes is miscategorized as a three-piece," avers Jake Vander Zanden, president of Hoya's operations in the Americas. "We have a PMMA haptic on the lens, but I call it a one-piece because we use a chemical bonding process to join the haptics to the acrylic optic. We lathe cut the optics and then tumble polish them to give them a good finish. The advantage of using PMMA for the haptics is that they're a little stiffer than acrylic, which helps guarantee the lens's placement in the eye."

The -18 µm of negative asphericity in the lens is a product of a design Hoya calls the Aspheric Balanced Curve. In a lens with ABC, the central asphericity isn't large enough to adversely affect visual quality when the lens is perfectly centered, yet can maintain the beneficial aspheric effect on vision with decentrations of up to 0.5 mm, the company says. In the periphery of the lens, the design resembles other negative aspheric IOLs.

The iSymm is intended to come preloaded in an injector system to decrease the amount of manipulation necessary to implant it. The lens and injector together are known as the iSert. "The benefit of preloading is that it's done in an all-automated manufacturing process," says Mr. Vander Zanden. "Because it's truly preloaded, we think it's a safer system because no one touches the lens before it's in the patient's eye. It's always enclosed in the system, decreasing the likelihood of sterility issues, lens damage and exposure to contaminants that might cause toxic anterior segment syndrome. It also cuts out a lot of prep time by eliminating staff involvement in preparing the injector." The iSert is designed to deliver the lens through a 2.2-mm incision.

Mr. Vander Zanden is optimistic about the FDA process. "We went to an independent lab and had the tests that the

FDA required done again," he says. "We've submitted the data and are now waiting for the FDA to give final comments and approval."

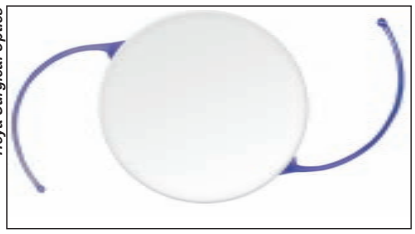
Lenstec's Softec HD

The Softec HD is a hydrophilic acrylic lens (26 percent water content) with an aspheric optic that offers powers in increments of 0.25 D in a certain power range [+18 to +25 D]. It is a clear lens, without any blue-blocking chromophore.

Majid Moshirfar, MD, of the Moran Eye Center at the University of Utah, says the lens has some features that set it apart from other monofocals. "The main reason I like to use it is because it's got relatively the same design as other lenses we've worked with—one-piece acrylic—but I can order it in 0.25-D steps in certain ranges," he says. "So, when it comes to the total magnitude of error or the spherical equivalent after surgery, I may be able to get patients closer to emmetropia with this lens because of these smaller increments. For instance, if I do two or three A-scans and the lens I need is 19.2, I can use a 19.25-D lens; I'm not forced to choose between a 19-D and a 19.5-D lens. At the end of the day, the most important optical error is the spherical equivalent, because the closer you get to plano, the better the result will be." The lens is also available in whole diopter powers from +5 to +36 D and in 0.5-D increments between +10.5 and +29.5 D.

Dr. Moshirfar says that the lens can easily go through a 2.2- or 2.4-mm incision, though many surgeons use a 2.8-mm incision. "The process of folding it will be familiar to surgeons who've been working with these one-piece gummy lenses or one-piece acrylic lenses," Dr. Moshirfar says. "There's no real learning curve in terms of centration in the eye. As a hydrophilic lens, it's got very good biocompatibility and has less of a chance of getting cloudy

Hoya Surgical Optics



The iSymm lens's PMMA haptics are chemically bonded to the acrylic optic.

and developing glistenings, though at the same time it's more resilient as you touch, manipulate and fold it. As it unfolds inside the eye, you don't see creases in it."

The other unique aspect of the Softec HD is its bi-aspheric design. "It has a symmetrical, bi-convex pattern from the anterior surface on one side to the posterior surface on the other," explains Dr. Moshirfar. "Because of this, it's a bit more forgiving when it comes to tilt, decentration and in terms of not creating coma or higher-order aberrations by itself. It has zero asphericity in total, meaning it doesn't have a plus or minus magnitude on its own."

After evaluating the lens's specifications, some surgeons might question the optic size of 5.5 mm. Dr. Moshirfar understands this concern, but doesn't think it's warranted. "First, if you're a surgeon used to doing a large capsulorhexis, I don't think this will be any different for you. But if you're used to making your capsulorhexis in the range of 5 mm or so, you may not have a problem with this because it's still going to be completely covered 360 degrees around; the anterior capsule is still going to cover the IOL optic. I haven't had photopsia issues, and I think it's because of the lens's symmetrical design, its water content and the fact that it's more forgiving when it comes to tilt and decentration in the bag."

Lenstec

The Softec HD comes in 0.25-D power increments for powers from +18 to +25 D.

Coming Attractions

Lens companies also have some designs that are either about to be studied in the United States or are already approved internationally and may arrive here in the future. Here is a rundown:

In September of 2011, Bausch + Lomb released the enVista hydrophobic acrylic IOL in Europe. The lens uses the company's aberration-neutral Advanced Optics design in a material the company says is free of glistenings.

Rayner, which introduced the C-flex IOL in the United States in 2007, has a toric IOL that's available internationally, the T-flex. The T-flex is available in standard astigmatism power ranges of +1 to +6 D. Also, in December 2011, the company received European approval for the Sulcoflex Multifocal Toric lens, which is designed to supplement a lens already in the bag in cases of unsatisfactory postop results.

For its part, Abbott Medical Optics launched the Tecnis Toric one-piece lens in Europe in 2011. The Tecnis Toric IOL has five models that are designed to treat different amounts of cylinder, from 0.69 D up to 2.74 D as measured at the corneal plane. The company says it's currently working toward FDA approval of the lens in the United States.

Considering the lenses that have been recently approved and those in the pipeline, Dr. Moshirfar appreciates having so many options. "I think we should try to use all of the various platforms so we can learn from each of them," he says. REVIEW


Diagnosis & Treatment of Intraocular Lymphoma

A look at the distinct clinical features that help to establish the diagnosis and guide treatment of these malignancies.

Mary E. Turell, MD, Arun D. Singh, MD, Cleveland

Intraocular lymphomas are rare malignancies that display a wide array of clinical manifestations; therefore diagnosis can be challenging. Almost all intraocular lymphomas are non-Hodgkin's lymphomas and the vast majority are of B-cell origin. Further confusion has arisen from the various nomenclature and classification schemes that have historically been used to describe this heterogeneous group of tumors. Many experts now group these entities based upon their site of ocular involvement and whether the disease is primary or secondary.

Using this scheme, the intraocular lymphomas can be subdivided into: primary vitreoretinal lymphoma; primary uveal lymphoma; and secondary intraocular manifestations of systemic lymphoma *(See Table 1)*. Each form has distinct clinical features that help to establish the diagnosis and to guide treatment.

Primary Vitreoretinal Lymphoma

Primary vitreoretinal lymphoma (PVRL) is a variant of primary central nervous system lymphoma (PCNSL), which is generally an aggressive, diffuse large B-cell malignancy associated with poor prognosis.[1] The age-adjusted incidence of PCNSL in the Unites States is approximately

RC Eagle, MD

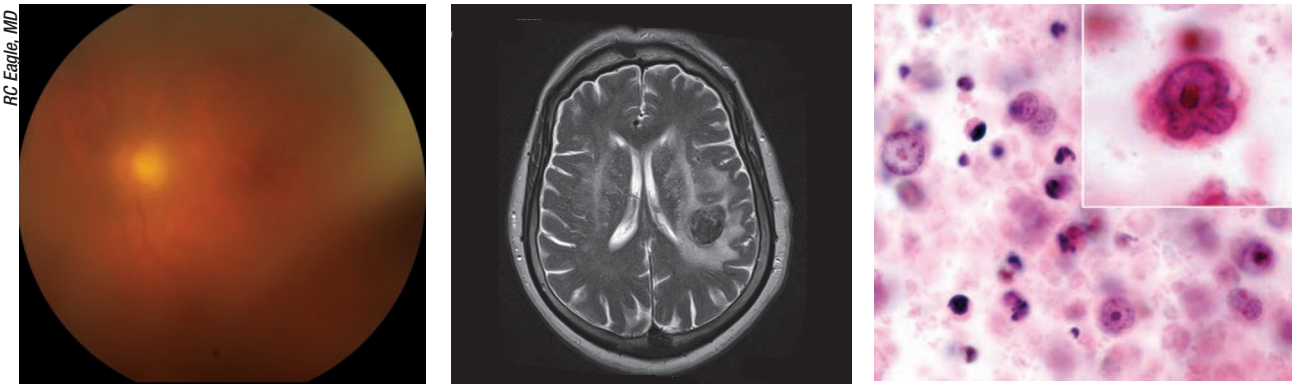


Figure 1. A 69-year-old woman presented with decreased visual acuity and floaters. Left: On dilated fundus examination, vitreous haze and vitreous cellular condensations were observed. Center: Magnetic resonance imaging of the brain showed increased T2 signal intensity in a periventricular distribution and a heterogeneous mass in the left temporoparietal region consistent with primary central nervous system lymphoma (PCNSL) with vitreoretinal involvement. Right: A representative vitrectomy sample reveals large atypical lymphocytes, necrotic lymphoid cells and nuclear debris consistent with PVRL. Inset demonstrates characteristic nuclear membrane protrusions and a prominent nucleolus. Main figure, Millipore filter, hematoxylin and eosin, original magnification × 250.

This article has no commercial sponsorship.

Table 1. Features of Various Types of Intraocular Lymphoma

Lymphoma	Epidemiology	Laterality	Symptoms	Clinical Features	Subtype	Morphology
Primary Vitreoretinal Lymphoma	50-70 years	Frequently bilateral	Decreased vision Floaters	Vitreous cells Retinal/choroidal infiltrates CNS involvement	DLBCL	Large cells Minimal cytoplasm Prominent nucleoli
Primary Uveal Lymphoma	M>F 50-70 years	Usually unilateral	Decreased vision Metamorphopsia	Clear vitreous Diffuse choroidal thickening Exudative retinal detachment	EMZL	Small centrocyte-like cells with variable plasmacellular differentiation
Secondary Intraocular Lymphoma	Variable	Unilateral or bilateral	Decreased vision	Variable: Choroidal thickening Iris infiltrates Pseudohypopyon Vitreous cells	Dependent on systemic NHL	Similar to systemic NHL

M: males, F: females, DLBCL: diffuse large B-cell lymphoma, EMZL: extranodal marginal zone lymphoma, NHL: non-Hodgkin's lymphoma

4.8 per million population, however, the exact incidence of PVRL is unknown.[2] The association between PVRL and PCNSL is variable, with CNS disease manifesting prior to, following or occurring simultaneously with ocular presentation. Approximately 25 percent of patients with PCNSL will have concomitant PVRL.[3] In contrast, 56 to 85 percent of individuals with PVRL ultimately develop central nervous system involvement.[4-7] In immunocompetent individuals, the peak incidence of PVRL is between the fifth and seventh decade, although disease may occur at a younger age in the immunocompromised population.

Symptoms and Clinical Findings

Individuals may be asymptomatic, however the majority present with painless decrease in vision or floaters.[6] Asymptomatic patients are often diagnosed when ophthalmic screening is performed in the setting of known PCNSL. The clinical findings are bilateral in 80 percent of cases, but are frequently asymmetric.[4] The hallmark of PVRL is the presence of fine vitreous cells *(See Figure 1)* and subretinal pigment epithelium deposits *(See Figure 2)*. When present, focal, multifocal or diffuse retinal, choroidal or chorioretinal infiltrates are considered essentially pathognomonic.[8] Anterior segment findings can occur including keratic precipitates, iris nodules, aqueous cells and flare, but are non-specific.[9] Other less-commonly reported features include: perivasculitis;[6] retinal artery occlusion;[11] exudative retinal detachment;[12] multifocal "punched-out" lesions at the level of the RPE;[13] and optic atrophy.[14]

Diagnostic Evaluation

Diagnostic evaluation should begin with a thorough history that explores not only ocular symptoms, but also changes in cognitive functioning, neurological decline and risk factors for immunocompromise. Due to the high correlation between PVRL and PCNSL, all patients diagnosed with ophthalmic disease should undergo systemic evaluation by an experienced oncologist. Recommended testing includes gadolinium-enhanced MRI of the brain and spinal cord, CSF studies, complete blood count and HIV testing, when appropriate.

In the setting of existing PCNSL, the diagnosis of PVRL with classic clinical findings is straightforward and biopsy of an ophthalmic site is unnecessary. In the absence of prior CNS disease, biopsy remains the gold standard. Several techniques exist including vitreous biopsy, retinal biopsy and subretinal biopsy. Proper surgical techniques and handling of the sample are critical, as aspirates are generally of low cellularity, and fragile lymphoma cells are prone to lysis during collection. For vitreous biopsy, an undiluted sample of approximately 1 to 2 mL is collected prior to the start of the infusion.[15] Next, a second diluted vitreous specimen using gentle vitreous cutting is obtained.[16] The vitreous cassette may be submitted as a third sample.[17] Specimens should be delivered to the laboratory, without fixative, within one hour of surgery.[15] PVRL cells are typically two to four times larger than normal lymphocytes, are pleomorphic and have scant cytoplasm.[18] The nuclei may be round, oval or indented, with conspicuous nuclear membranes, occasional fingerlike protrusions, and multiple, prominent, eccentrically located nucleoli. Mitoses are frequently observed.[19]

As vitreous biopsy is not diagnostic in all cases, supplemental techniques can be helpful in confirming

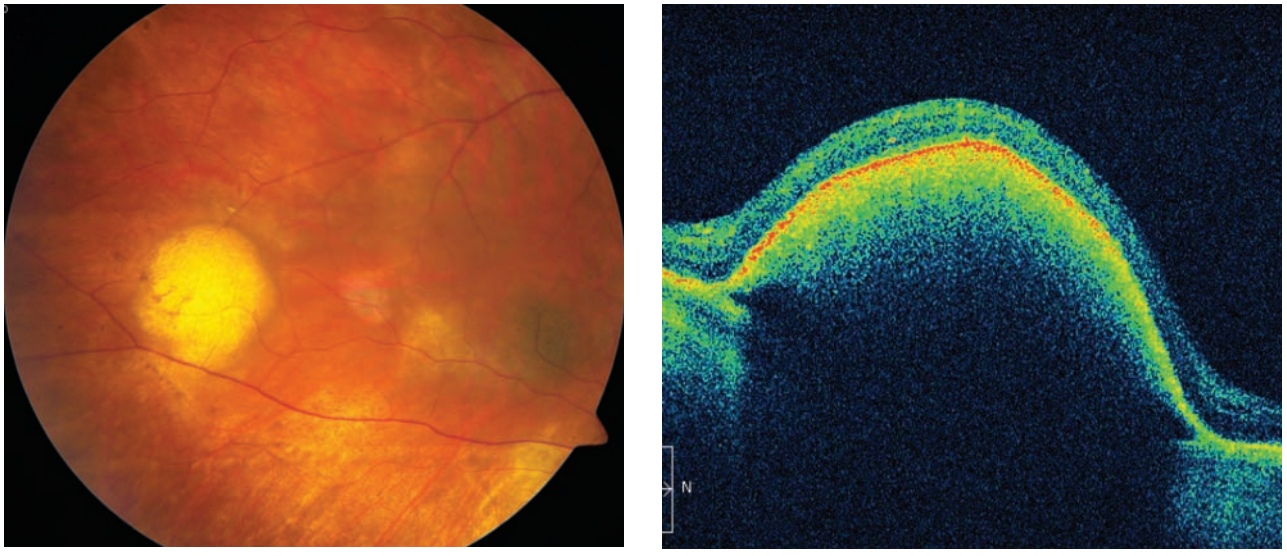


Figure 2. A 53-year-old woman with bilateral PVRL was treated with external beam radiotherapy and intravitreal methotrexate. Left: Two years later, she developed recurrence in the right eye manifesting as a dome-shaped, subretinal white deposit temporal to the macula. Right: OCT confirmed the subretinal pigment epithelial location of this lesion.

the diagnosis. Immunohistochemistry is useful for identifying markers for leukocytes (CD45), B-cells (CD20, CD79a, PAX-5), T-cells (CD45RO), and macrophages (CD68).[15] Clonality can be established using antibodies directed against κ and λ light chains.[17,18] Flow cytometry provides a means of quantitatively assessing the proportion of cells that demonstrate these markers. Polymerase chain reaction gene rearrangement studies can detect monoclonality of the heavy chain variable (V), diversity (D), and joining (J) immunoglobulin gene segments.[20] Measurement of IL-6 and IL-10 in aqueous or vitreous fluid can facilitate diagnosis, although an elevated IL-10/IL-6 ratio is not specific for PVRL.[21]

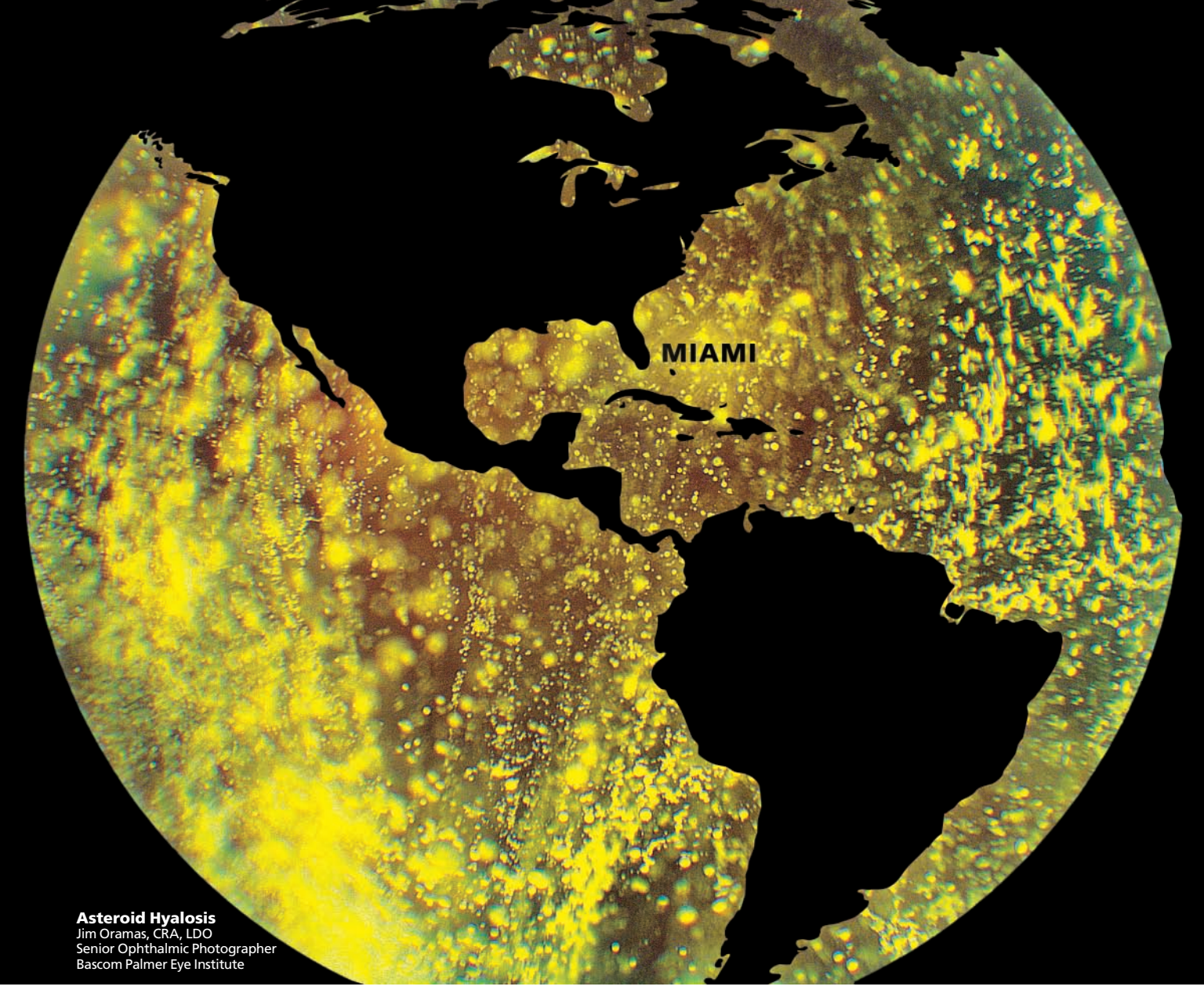
Differential Diagnosis

Delay in diagnosis of PVRL is common, as non-specific ophthalmic manifestations can masquerade as inflammatory, other neoplastic and infectious etiologies. In one series of 32 patients with histologically confirmed PVRL, the average interval between the onset of ocular symptoms and diagnosis was 21 months.[7] The differential diagnosis includes: sarcoidosis; syphilis; tuberculosis; birdshot retinochoroidopathy; multifocal chorioretinitis; acute posterior multifocal placoid pigmentary epitheliopathy; serpiginous choroiditis; and punctate inner choroidopathy.[22] When infiltrative subretinal or choroidal lesions are present, neoplasms such as choroidal metastases and amelanotic melanoma should be considered. In immunocompromised individuals, infectious diseases such as acute retinal necrosis, cytomegalovirus, toxoplasmosis and pneumocystis choroiditis should be considered.

Treatment

Consensus guidelines for treatment of PVRL have not been firmly established and depend upon patient factors as well as local expertise. When disease is unilateral and limited to the eye, local delivery of intravitreal methotrexate or rituximab has been shown to be effective and well-tolerated.[23,24] The largest reported series treated with intravitreal methotrexate (400 mg in 0.1 ml of 0.9% sodium chloride) included 44 eyes in 26 patients using an induction-consolidation-maintenance regimen. Clinical remission was achieved in all cases following an average of 6.4 injections with 95 percent of eyes requiring 13 injections or less.[25] None of the patients developed relapse after a follow-up period ranging from 41 to 107 months.[25] The most commonly reported ocular side effects included cataract, conjunctival hyperemia and transient keratopathy.[24] Early evidence suggests that rituximab may have fewer side effects and require fewer injections to achieve remission, however further investigation on larger numbers of patients is required.[23] Large retrospective studies have shown that while ocular treatment appears to improve local control, there is no proven survival benefit of ocular therapy.[26]

Prior to acceptance of intravitreal chemotherapy, bilateral external beam radiotherapy was widely used. EBRT remains an important therapy, particularly in patients with bilateral involvement, for those who may not tolerate intravitreal chemotherapy, and in individuals who find it difficult to return for multiple injections. Irradiation doses have varied, with an average dose of approximately 40 Gy given in fractions of 1.5 to 2.0 Gy.[27-30] Response to radiation and relapse rates are variable. In one series of 21 eyes in 12 patients, initial treatment included EBRT and sys-



Asteroid Hyalosis
Jim Oramas, CRA, LDO
Senior Ophthalmic Photographer
Bascom Palmer Eye Institute

THE EYES OF THE WORLD ARE ON MIAMI FOR BASCOM PALMER'S 50TH ANNIVERSARY SCIENTIFIC MEETING - February 2 - 4, 2012

50 YEARS OF VISION
Bascom Palmer Eye Institute
Second to None

Bascom Palmer Eye Institute is celebrating 50 years as a leader in the diagnosis and treatment of eye diseases. To mark this milestone anniversary, Bascom Palmer is hosting a 3-day scientific symposium and CME conference, featuring more than 180 of the world's most renowned ophthalmic specialists. It's an unprecedented opportunity to learn about the latest research and most advanced medical and surgical treatment options, directly from the doctors who helped develop them.

Bascom Palmer Eye Institute
UNIVERSITY OF MIAMI HEALTH SYSTEM

Contact: Continuing Medical Education • 305-326-6110 • bascompalmercme@miami.edu • bascompalmer.org

BEST HOSPITALS
U.S.News & WORLD REPORT
HONOR ROLL
2011-12

WE'RE CHANGING THE WAY

PATIENTS WITH VISION IMPAIRMENT ENVISION THEIR FUTURE

The Louis J. Fox Center for Vision Restoration of UPMC and the University of Pittsburgh—a joint program of the UPMC Eye Center and the McGowan Institute for Regenerative Medicine—is the first national, comprehensive, and multidisciplinary research and clinical program dedicated to ocular regenerative medicine. Our ophthalmologists and researchers focus on the discovery of new treatments for blindness and impairment through tissue regeneration, enhancement, transplantation, and technology. We're working hard to improve the quality of life for the millions of people affected by vision loss, so that we can all see a brighter future. Snap the code and learn more at **UPMCPhysicianResources.com.**

UPMC LIFE CHANGING MEDICINE

UPMC is affiliated with the University of Pittsburgh School of Medicine.

temic chemotherapy (six patients), systemic chemotherapy alone (four patients), EBRT alone (one patient), and no treatment (one patient). No ocular recurrence was observed in those receiving EBRT after a follow-up of four to 58 months (average of 18 months). Two patients who received chemotherapy but no EBRT developed ocular relapse at a follow-up time of 14 and 31 months.[30] Radiation-related side effects included optic neuropathy, retinopathy, conjunctivitis, dry eyes, cataracts and glaucoma.[31] In most cases, EBRT is reserved for individuals under age 65 years due to the high incidence of neurotoxicity in elderly individuals.

In patients with coexisting PCNSL, the majority are currently treated with high-dose intravenous chemotherapy. Methotrexate (8g/m^2) is most commonly used, either as a single agent or as part of a combination regimen. In a large, multicenter, retrospective study of 221 immunocompetent patients with PCNSL with ocular involvement, the median progression-free survival and overall survival were 18 and 31 months, respectively.[26]

Primary Uveal Lymphoma

The primary uveal lymphomas can be further subdivided into choroidal, iridal and ciliary body lymphomas. Primary choroidal lymphoma accounts for the majority of cases and is generally a low-grade B-cell lymphoma with a prolonged benign course. These tumors are morphologically and genetically similar to extranodal marginal zone lymphoma (EMZL) found elsewhere in the body. Primary iridal lymphomas may be of either B-cell or T-cell origin. The incidence of primarily iridal and ciliary body lymphoma is unknown, as these tumors have only been described in a handful of case reports. The discussion that follows pertains to primary choroidal lymphoma; while also rare, there are approximately 70 to 80 case reports in the literature.[32]

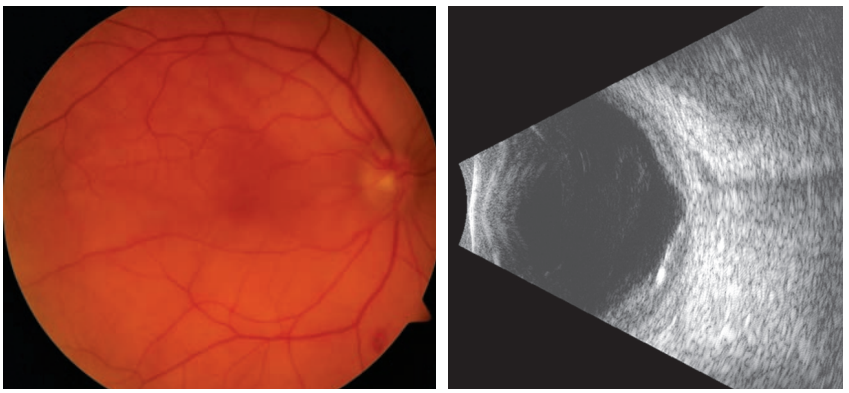


Figure 3. A 70-year-old woman noted painless, decreased vision in the right eye. Fundus examination (left) revealed unilateral diffuse, ill-defined choroidal thickening in the posterior pole extending into the macula of the right eye. B-scan ultrasonography (right) demonstrated diffuse thickening of the choroid. Subsequent choroidal biopsy revealed extranodal marginal zone lymphoma (MALT type).

Symptoms & Clinical Findings

Primary choroidal lymphoma is predominantly a unilateral process that most commonly affects men in the fifth to seventh decade. Initial symptoms may include recurrent episodes of painless, blurred vision and metamorphopsia secondary to exudative retinal detachment affecting the fovea.

When the disease is advanced, patients may develop pain and severely reduced vision due to secondary angle-closure glaucoma and extensive retinal detachment, respectively. When extraocular extension is present, proptosis and diplopia may occur. A classic feature is the presence of solitary or multiple yellow, creamy choroidal infiltrates *(See Figure 3)*. Notably, the vitreous remains clear with the absence of cellular reaction. Ultimately, diffuse thickening of the uveal tract develops and is often associated with exudative retinal detachment. In some cases, there may be episcleral extension appearing as a non-mobile orange to yellow or "salmon" patch.

Diagnostic Evaluation

Several imaging techniques are useful for establishing the diagnosis. B-scan ultrasonography typically reveals choroidal thickening with low echogenicity. Both computed tomography and magnetic resonance imaging of the globes confirm choroidal thickening with a corresponding decrease in the size of the vitreous cavity. Calcification is absent. Fluorescein angiography demonstrates early hypofluoresence with multiple foci of hyperfluorescence and staining in the late phase. Biopsy of episcleral tumor nodules and choroidal aspirates may also aid in the diagnosis.

Histopathologically, the features of primary choroidal lymphoma are similar to EMZL located elsewhere in the body. The cells are generally of the centrocyte-like, monocytoid and plasmacytoid type. Dutcher bodies, or collections of intranuclear immunoglobulin, can often be observed. Immunohistochemistry confirms the expression of B-cell antigens (CD20 and CD79a). Gene rearrangement studies or flow cytometry support the clonality and neoplastic nature of these B-cells.

Differential Diagnosis

The differential diagnosis of prima-

ry choroidal lymphoma includes diffuse uveal melanoma, uveal effusion syndrome, posterior scleritis and uveal metastases. Diffuse uveal melanoma can usually be distinguished based upon its pigmented appearance, vascularity, disturbance of the RPE and faster growth rate.[33] Uveal effusion syndrome is often bilateral and has associated dilated episcleral vessels, vitreous cells and "leopard spot-like" changes in the RPE. Fluorescein angiography does not generally demonstrate leakage.[32] Posterior scleritis occurs more frequently in women, is associated with autoimmune disease and demonstrates high internal reflectivity with the classic "T-sign" on B-scan ultrasonography. In the majority of uveal metastases, a prior history of malignancy can be elicited. Additionally, B-scan ultrasonography usually demonstrates medium internal reflectivity and fluorescein angiography reveals widespread leakage in the late phase.

Treatment

Before initiating localized treatment for primary choroidal lymphoma, it is essential to perform systemic studies to exclude the possibility of systemic lymphoma with uveal involvement. Recommended studies include CT of the chest and abdomen, complete blood count and serum protein electrophoresis.[34] Once disease is confirmed to be limited to the choroid, management consists of low-dose EBRT administered over several fractions.[34] Primary choroidal lymphoma typically follows a less-aggressive course than primary vitreoretinal lymphoma. In 13 eyes with biopsy proven primary choroidal lymphoma, subsequent systemic lymphoma developed in two cases (three and seven years after the initial diagnosis).[35] This underscores the importance of staging at the time of diagnosis and periodic systemic surveillance.

Intraocular Manifestations of Systemic Lymphoma

Intraocular lymphoma secondary to disseminated systemic lymphoma most commonly affects the choroid. For this reason, secondary lymphoma can have a similar clinical appearance to primary choroidal lymphoma.[36] Rarely, a spread to the retina *(See Figure 4)* without choroidal infiltration can occur.[36] Other exceptional presentations of secondary intraocular lymphoma include pseudohypopyon and iris infiltration.[37,38] While exceedingly rare, iridal lymphoma secondary

to systemic non-Hodgkin's lymphoma is more common than primary iridal lymphoma.[32] The most common subtype of systemic lymphoma that affects the eye is diffuse large B-cell lymphoma. This is followed by multiple myeloma, extramedullary plasmacytoma, lymphoplasmocytic lymphoma/immunocytoma and marginal zone B-cell lymphoma (MALT lymphoma).[36] The morphologic and immunophenotypic features of secondary choroidal lymphoma bear resemblance to its primary systemic counterpart. Staging evaluation and close collaboration with an experienced oncologist are critical in the management of patients with systemic lymphoma with intraocular involvement. REVIEW

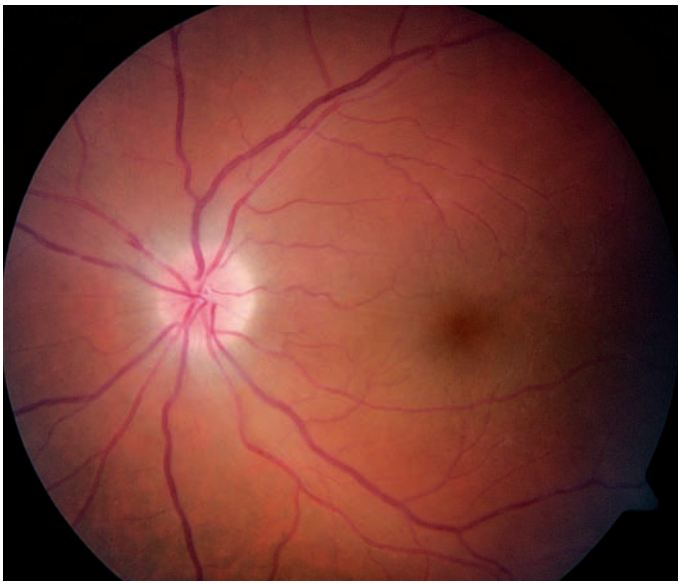


Figure 4. A 36-year-old man with a history of large B-cell testicular lymphoma presented with painless, decreased vision. On dilated fundus examination, vitreous cells and mild disc edema with a superonasal nerve fiber layer hemorrhage were noted. Atypical cells were present in the cerebrospinal fluid compatible with secondary central nervous system and vitreoretinal involvement of systemic non-Hodgkin's lymphoma.

Drs Turell and Singh are at the Cole Eye Institute, Cleveland Clinic. Contact Dr. Singh at the Department of Ophthalmic Oncology, Cole Eye Institute, Cleveland Clinic, 9500 Euclid Ave., Cleveland, OH 44195. Phone: (216) 445 9479; fax: (216) 445 2226; e-mail: singha@ccf.org.

Image credit, Figure 1. Reproduced with permission from Singh AD, Lewis H, Schachat AP. Primary lymphoma of the central nervous system. Ophthalmol Clin North Am 2005;18:199–207.

1. Pe'er J, Hochberg FH, Foster CS. Clinical review: Treatment of vitreoretinal lymphoma. Ocul Immunol Inflam 2009;17(5):299-306.
2. Olson JE, Janney CA, Rao RD, Cerhan JR, Kurtin PJ, Schiff D, et al. The continuing increase in the incidence of primary central nervous system non-Hodgkin lymphoma: a surveillance, epidemiology, and end results analysis. Cancer 2002;95(7):1504-10.
3. Hochberg FH, Miller DC. Primary central nervous system lymphoma. J Neurosurg 1988;68(6):835-53.
4. Peterson K, Gordon KB, Heinemann MH, DeAngelis LM. The clinical spectrum of ocular lymphoma. Cancer 1993;72(3):843-9.
5. Cassoux N, Merle-Beral H, Leblond V, Bodaghi B, Milea D, Gerber S, et al. Ocular and central nervous system lymphoma: clinical features and diagnosis. Ocul Immunol Inflam 2000;8(4):243-50.
6. Char DH, Ljung BM, Miller T, Phillips T. Primary intraocular lymphoma (ocular reticulum cell sarcoma) diagnosis and management. Ophthalmology 1988;95(5):625-30.
7. Freeman LN, Schachat AP, Knox DL, Michels RG, Green WR. Clinical features, laboratory investigations, and survival in ocular reticulum cell sarcoma. Ophthalmology 1987;94(12):1631-9.
8. Gass JD, Sever RJ, Grizzard WS, Clarkson JG, Blumenkranz M, Wind CA, et al. Multifocal pigment epithelial detachments by reticulum cell sarcoma. A characteristic funduscopic picture. Retina 1984;4(3):135-43.
9. Rajagopal R, Harbour JW. Diagnostic testing and treatment choices in primary vitreoretinal lymphoma. Retina 2011;31(3):435-40.
10. Fredrick DR, Char DH, Ljung BM, Brinton DA. Solitary intraocular lymphoma as an initial presentation of widespread disease. Arch Ophthalmol 1989;107:395-7.
11. Gass JD, Trattler HL. Retinal artery obstruction and atheromas associated with non-Hodgkin's large cell lymphoma (reticulum cell sarcoma). Arch Ophthalmol 1991;109:1134-9.
12. Michelson JB, Michelson PE, Bordin GM, Chisari FV. Ocular reticulum cell sarcoma. Presentation as retinal detachment with demonstration of monoclonal immunoglobulin light chains on the vitreous cells. Arch Ophthalmol 1981;99:1409-11.
13. Lang GK, Surer JL, Green WR, Finkelstein D, Michels RG, Maumenee AE. Ocular reticulum cell sarcoma. Clinicopathologic correlation of a case with multifocal lesions. Retina 1985;5(2):79-86.
14. Purvin V, Van Dyk HJ. Primary reticulum cell sarcoma of the brain presenting as steroid-responsive optic neuropathy. J Clin Neuro-ophthalmol1984;4(1):15-23.
15. Coupland SE. Vitreous biopsy: Specimen preparation and interpretation. Monogr Clin Cytol. 2012;21:61-71. Epub 2011 Oct 18.
16. Margolis R, Brasil OF, Lowder CY, Singh RP, Kaiser PK, Smith SD, et al. Vitrectomy for the diagnosis and management of uveitis of unknown cause. Ophthalmology 2007;114:1893-7.
17. Yeh S, Weichel ED, Faia LJ, Albini TA, Wroblewski KK, Stetler-Stevenson M, et al. 25-Gauge transconjunctival sutureless vitrectomy for the diagnosis of intraocular lymphoma. Br J Ophthalmol 2010 May;94(5):633-8.
18. Farkas T, Harbour JW, Davila RM. Cytologic diagnosis of intraocular lymphoma in vitreous aspirates. Acta Cytol 2004 Jul-Aug;48(4):487-91.
19. Whitcup SM, de Smet MD, Rubin BI, Palestine AG, Martin DF, Burnier M, Jr., et al. Intraocular lymphoma. Clinical and histopathologic diagnosis. Ophthalmology 1993;100:1399-406.
20. Chan CC, Gonzales JA. Classification of lymphomas. Primary Intraocular Lymphoma. 1 ed. Hackensack, NJ: World Scientific Publishing Co. Pte. Ltd.; 2007.
21. Akpek EK, Maca SM, Christen WG, Foster CS. Elevated vitreous interleukin-10 level is not diagnostic of intraocular-central nervous system lymphoma. Ophthalmology 1999;106:2291-5.
22. Singh AD, Lewis, H, Schachat, AP, Peereboom D. Lymphoma of the retina and CNS. In: Singh A, Damato, BE, Pe'er J, Murphree AL, Perry, JD, editor. Clinical Ophthalmic Oncology. Philadelphia, PA: Saunders Elsevier Inc.; 2007. p. 372-7.
23. Kitzmann AS, Pulido JS, Mohney BG, Baratz KH, Grube T, Marler RJ, et al. Intraocular use of rituximab. Eye (Lond). 2007;21(12):1524-7. Epub 2007/04/28.
24. Smith JR, Rosenbaum JT, Wilson DJ, Doolittle ND, Siegal T, Neuwelt EA, et al. Role of intravitreal methotrexate in the management of primary central nervous system lymphoma with ocular involvement. Ophthalmology 2002;109:1709-16.
25. Frenkel S, Hendler K, Siegal T, Shalom E, Pe'er J. Intravitreal methotrexate for treating vitreoretinal lymphoma: 10 years of experience. Brit J Ophthalmol 2008;92(3):383-8.
26. Grimm SA, McCannel CA, Omuro AM, Ferreri AJ, Blay JY, Neuwelt EA, et al. Primary CNS lymphoma with intraocular involvement: International PCNSL Collaborative Group Report. Neurology 2008;71(17):1355-60.
27. Margolis L, Fraser R, Lichter A, Char DH. The role of radiation therapy in the management of ocular reticulum cell sarcoma. Cancer 1980;45(4):688-92.
28. Hormigo A, Abrey L, Heinemann MH, DeAngelis LM. Ocular presentation of primary central nervous system lymphoma: Diagnosis and treatment. British J Haematol 2004;126(2):202-8.
29. Isobe K, Ejima Y, Tokumaru S, Shikama N, Suzuki G, Takemoto M, et al. Treatment of primary intraocular lymphoma with radiation therapy: A multi-institutional survey in Japan. Leuk Lymphoma 2006;47(9):1800-5.
30. Berenbom A, Davila RM, Lin HS, Harbour JW. Treatment outcomes for primary intraocular lymphoma: Implications for external beam radiotherapy. Eye (Lond). 2007;21(9):1198-201.
31. Jahnke K, Thiel E, Abrey LE, Neuwelt EA, Korfel A. Diagnosis and management of primary intraocular lymphoma: An update. Clin Ophthalmol 2007;1(3):247-58.
32. Coupland SE. Uveal Lymphoproliferative Tumors. In: Singh AD, Damato B, Pe'er J, Murphree AL, Perry JD, editors. Clinical Ophthalmic Oncology. Philadelphia, PA: Elsevier, Inc; 2007. p. 316-21.
33. Font RL, Spaulding A, Zimmerman L. Diffuse malignant melanoma of the uveal tract: A clinicopathological report of 54 cases. Trans Am Acad Ophthalmol Otolaryngol. 1968;72:877-95.
34. Augsburger JJ, Greatrex KV. Intraocular lymphoma: Clinical presentations, differential diagnosis and treatment. Trans Pa Acad Ophthalmol Otolaryngol 1989;41:796-808. Epub 1989/01/01.
35. Coupland SE, Foss HD, Hidayat AA, Cockerham GC, Hummel M, Stein H. Extranodal marginal zone B cell lymphomas of the uvea: an analysis of 13 cases. Journal Pathol 2002;197(3):333-40.
36. Coupland SE, Damato B. Understanding intraocular lymphomas. Clin Exp Ophthalmol 2008;36(6):564-78.
37. Shakin EP, Augsburger JJ, Eagle RC, Jr., Ehya H, Shields JA, Fischer D, et al. Multiple myeloma involving the iris. Arch Ophthalmol 1988;106:524-6.
38. Tranos PG, Andreou PS, Wickremasinghe SS, Brazier JD. Pseudohypopyon as a feature of multiple myeloma. Arch Ophthalmol 2002;120:87-8.


Is Imaging Ready for Clinical Practice?

A surgeon with extensive experience using these technologies makes the case that it is.

By Christopher Kent, Senior Editor

Technology is changing rapidly, and one of the benefits of that change has been a steady improvement in surgeons' ability to image and analyze structural change in the eye.[1] This is significant, because imaging technology can detect and quantify structural information that would otherwise require very specific training and experience for a surgeon to uncover—if the information could be detected at all. Comparing serial simultaneous stereoscopic optic disc photographs remains the gold standard for detecting glaucoma progression via structural change. However, this isn't widely done in clinical practice. It's time-consuming, and the stereoscopic cameras needed to obtain this type of photograph are not widely available. Furthermore, not many of today's surgeons have the training to expertly examine the photographs.

Fortunately, computer-guided digital technologies such as optical coherence tomography and confocal scanning laser ophthalmoscopy have steadily become more sophisticated, making it possible to monitor, quantify and analyze the eye in ways that would have been impossible a few years ago.

Evolving Clinical Analysis

Robert N. Weinreb, MD, distinguished professor and chair of ophthalmology at the University of California San Diego and director of both the Shiley Eye Center and the Hamilton Glaucoma Center at UCSD, believes that imaging technology has reached the point at which it deserves to be an integral part of glaucoma management.

"Traditionally, the clinical approach to managing glaucoma has been to examine for progression or to stage the disease, and then base our treatment on a prediction of the patient's probable loss of function," he says. "Until recently, we've detected progression largely using event-based analysis. Such an approach looks for a progression milestone—i.e., the event. For example, we might use the technology to determine whether an observed loss of neuroretinal rim is outside of two standard deviations found in a normative database. Or, we might seek to ascertain whether the mean deviation in a visual field has worsened by a certain amount.

"Another promising approach that's recently become practical with structural imaging is to measure the rate of change in a given measurement," he continues. "That allows us to estimate the likelihood and expected severity of an individual's functional loss. This type of analysis, which bears some resemblance to monitoring visual fields, is referred to as trend-based analysis."

Dr. Weinreb cites a recent study that used OCT to evaluate retinal nerve fiber layer thickness in 116 eyes over a period of five years, using Zeiss's guided progression analysis system.[2] "The data showed that this was an effective way to identify individuals exhibiting progressive loss, as well as to determine their rate of loss," he says. "Notably, the group of subjects identified by this method only slightly overlapped those showing progression by visual field analysis."

Benefits of Imaging

Dr. Weinreb notes that imaging technology offers a number of significant advantages as a tool for

managing glaucoma:

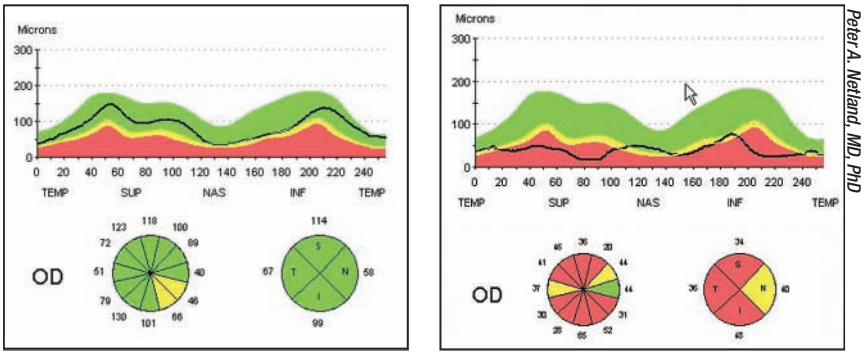
• ***Today's imaging technology allows expert examination by non-experts.*** "For example, several studies have demonstrated that digital analysis of serial confocal scanning laser ophthalmoscopy images compares favorably with expert comparison of serial optic disc stereophotographs," he says. "In one study this technology performed at least as well for detecting optic nerve changes caused by experimentally induced IOP increases in monkey eyes as glaucoma specialists evaluating photographs.[3] Two other studies also found reasonable agreement between CSLO images analyzed with proprietary software and analysis of optic disc photographs."[4,5]

• ***Image acquisition is relatively easy***. "Ease of image acquisition is valuable because ease of use allows more frequent scanning, which is important for determining the rate at which the disease is progressing," he points out. "The more frequently you conduct exams, the better your estimates of the rate of change."

• ***Digital data is more easily analyzed.*** "The quantified nature of digital data is ideal for statistical analysis and comparison," notes Dr. Weinreb. "This is a key factor in our developing ability to calculate the rate of glaucoma progression, making it possible to predict which individuals are at the greatest risk of functional impairment and/or blindness."[2,6]

• ***Imaging provides an objective measure of progression.*** "When we examine a patient clinically, we may think the eye looks worse," he says. "Perhaps the rim is narrower, or the RNFL appears to be thinner. But with today's imaging technology we have objective, quantitative measures that studies are showing correlate well to disease progression."

Dr. Weinreb cites one recently published study that used Zeiss's Stratus OCT to obtain RNFL measurements in 253 eyes of 253 patients annually, while also obtaining visual fields and optic disc stereophotographs. Progression was detected with the visual fields using Zeiss's GPA software and by masked assessment of the stereophotographs by expert graders. The data showed that mean rates of change in average RNFL thickness were significantly higher in eyes that progressed, with a sensitivity of 77 percent and specificity of 80 percent.[7] "Notably, RNFL parameters were significantly better at discriminating progressed eyes than measurements of the optic nerve head or macular thickness," he adds.



Peter A. Netland, MD, PhD

A normative database can help identify the status of a patient's glaucoma. Left: a patient recently diagnosed. The black line, showing the classic double-hump pattern, is almost entirely within the normal (green) range. Quadrant analysis is largely within normal limits as well. Right: advanced glaucoma. Note the placement of the tracing line and quadrant colors indicating that the thickness falls outside of the normal range.

• ***Reproducibility is better than that obtained with clinical assessment of photographs, and better than the test-retest variability of most clinicians.*** Dr. Weinreb notes that this is true at least in part because digital data capture and analysis is non-subjective.

• ***Digital data is easily exported into electronic medical records.*** "This advantage is likely to become even more significant as medicine continues to move toward the paperless office," he points out.

• ***Imaging allows measurement of anatomical features that can't otherwise be measured.*** These include the lamina cribrosa and choroidal thickness, as shown in a recent study.[8] "Some of these regions are showing promise as bellwethers that may reveal glaucomatous damage early in the disease," he notes.

"For example, measuring the ganglion cell complex in the macula has turned out to be a very sensitive and specific test for glaucomatous damage," he says. (Retinal ganglion cells extend through three layers: the retinal nerve fiber layer; the ganglion cell layer; and the inner plexiform layer, which consists of the retinal ganglion cell dendrites.) "The reason for measuring the ganglion cell complex at the macula is that the retinal ganglion cells have the greatest density in this area, where they can be six cells deep. In fact, 50 percent of retinal ganglion cells are located in the central 4.5 mm around the macula. So even though the macula is a very small part of the retina, you can detect signs of change there with high sensitivity."

• ***Imaging allows earlier and more informed clinical decisions than simple clinical examination.*** "Thanks to steady improvements in instruments' speed of image capture and resolution, as well as improved software for data analysis, our ability to detect a problem early in the disease continues to improve, surpassing what

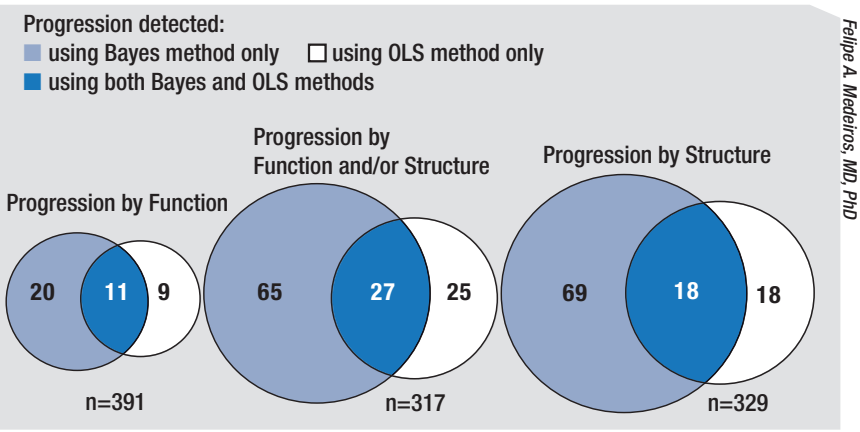
we can discover with a traditional examination," says Dr. Weinreb. "In some situations, detection of disease and/or progression via imaging may also be possible earlier than would be possible using visual fields."

Combining Data

Given that both structural and functional testing are valuable and appear to be largely complementary rather than redundant, a sensible next step in the evolution of glaucoma management is improving ophthalmologists' ability to monitor and combine both kinds of information. Dr. Weinreb points out that the first step along this road has already been taken by some companies; Zeiss's Cirrus HD-OCT, for example, now offers an automatically generated report that summarizes key data from the Humphrey Field Analyzer and Cirrus OCT. The report provides an overview of both structure and function status, so the clinician doesn't have to spend time looking for multiple reports. Optovue's RTVue OCT will soon be adding a similar feature presenting its data along with visual field data from Haag-Streit's Octopus or Oculus's Centerfield II perimeter. (Optovue is also developing software that will produce a map overlaying the two types of data.)

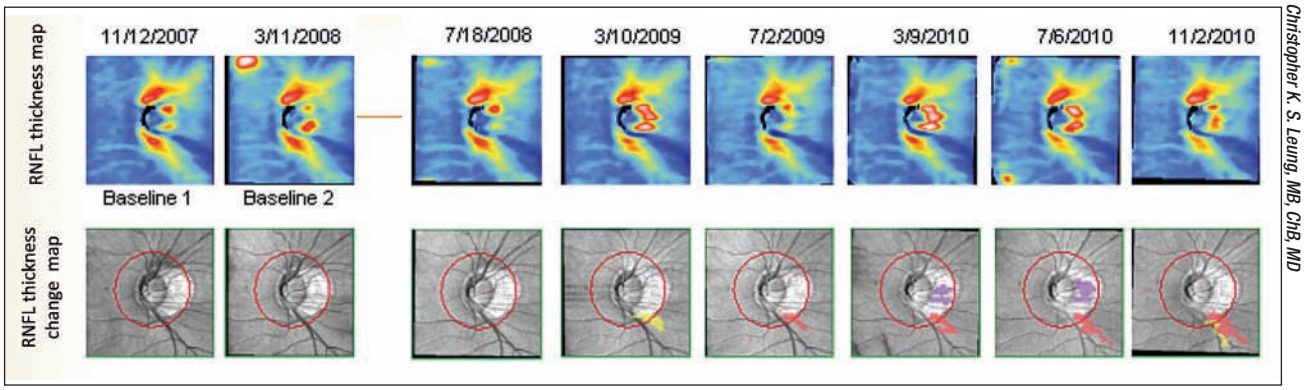
Taking this evolution even further, Dr. Weinreb notes that a recent paper by Felipe Medeiros, MD, PhD, at the UCSD, reported his use of a Bayesian hierarchical model to integrate rates of change from the visual field index (SAP) with average retinal nerve fiber layer thickness measurements made using scanning laser polarimetry with enhanced corneal compensation.[9] "The study included data from annual exams of 434 eyes included in the Diagnostic Innovations in Glaucoma Study," he says. "Dr. Medeiros compared this approach to analysis using the conventional method—ordinary least-squares regression. Although the approaches had equally good specificity when identifying healthy eyes—100 percent—the Bayesian method identified significantly more progressed eyes than the conventional method—22.7 percent vs. 12.8 percent ($p<0.001$). Furthermore, the Bayesian method identified a much greater proportion of the eyes that

Combining Structural and Functional Data



Felipe A. Medeiros, MD, PhD

New methods for combining structural and functional data are showing promise. In a recent study, a Bayesian hierarchical model used to integrate the two types of data identified significantly more progressed eyes than the ordinary least-squares regression method; it also identified many more than were identified via expert analysis of optic disc stereophotographs.[9]



Christopher K. S. Leung, MB, ChB, MD

In this Cirrus HD-OCT sequence, RNFL damage was evident before detectable visual field loss; an inferotemporal RNFL defect was observed in the thickness map in the presence of a normal visual field on 7/18/2008. Inferotemporal RNFL progression was detected on 3/10/2009 (yellow pixels in the RNFL thickness change map) and confirmed in subsequent visits (red pixels), while possible visual field progression wasn't noted until 11/2/2010 (EMGT criteria).

were categorized as progressing by expert analysis of optic disc stereophotographs than the OLS regression method did: 74 percent vs. 37 percent (p=0.001)."

Clearly, says Dr. Weinreb, combining structural and functional data holds promise as a resource for monitoring glaucoma progression.

Imaging Caveats

Of course, today's imaging technology is still far from perfect, and human error is still a factor during clinical use, so when using this technology it's important to be conscious of its limitations and the ways in which it can produce misleading data. Dr. Weinreb notes several important considerations:

• ***Imaging isn't 100-percent accurate.*** "For that reason, clinicians must take all available information into consideration, including functional measurements, and use their best clinical judgment to evaluate the information as a whole," he says.

• ***Assessment of scan quality is important.*** Dr. Weinreb notes that the best technology can still be undercut by artifacts, eye movement, corneal conditions and the like.

• ***Atypical patients may produce misleading data.*** "There are many atypical patients—particularly high myopes or patients with tilted discs—for whom you can't readily interpret the information these technologies are able to produce," he observes.

• ***Normative databases may not be representative of all patient populations.*** "A normative database from a European ancestry population is not necessarily relevant to a Japanese population," he points out. "Furthermore, normative databases are statistical in nature. That means there's always a low probability that a patient who is outside normal parameters according to the database really is normal, but happens to fall at the low end of the statistical distribution."

It's a Good Time to Start

Despite these limitations, Dr. Weinreb believes that the evidence has demonstrated that imaging technologies are ready for use in glaucoma clinical practice. "With all the new software that's available, including the ganglion cell complex analyses for diagnosis, trend analysis for progression and the ability to combine structural and functional testing, there's an opportunity to use

(continued on page 59)

PRK and CCL: Perfect Together?

Some think early keratoconus patients can benefit from simultaneous PRK and corneal cross-linking.

Walter Bethke, Managing Editor

For the past several years, there's been a growing interest in cross-linking corneas to strengthen them against the effects of ectasia and keratoconus, and many surgeons think it works well. Some surgeons, however, think it's capable of more, and have actually been combining it with simultaneous refractive laser procedures in an effort to not only stave off a corneal transplant, but maybe give a patient functional vision as well. Other physicians, though, think performing a refractive procedure that could weaken an already unstable cornea at the same time as a cross-linking procedure is ill-advised. Here's a look at the pros and cons of the approach.

The Combined Approach

The originator of the combined PRK/cross-linking procedure, Athens, Greece, surgeon John Kanellopoulos, says he started it to improve outcomes in these cross-linking patients. The process involves first performing a topography-guided PRK, followed by a 30-minute cross-linking treatment. "For any case of irregular astigmatism that suggests keratoconus in a patient who's under 35 years of age and who suggests a risk of progression, most surgeons internationally would agree that you'd cross-link the patient," he says. "We've found that by combining cross-linking with a conservative topographically guided ablation for normalization of the cornea, you get a more effective cross-linking effect and a significant improvement in visual rehabilitation."

Dr. Kanellopoulos says that he's been performing the procedure in this population of young keratoconic patients for almost seven years and has reduced the rate of corneal transplant in them by 80 percent. "After this protocol's employed, we don't need to perform a transplant if the total residual corneal thickness is 400 microns or more," says Dr. Kanellopoulos. "If the thickness is 350 microns or more, there's a 60-percent chance that a transplant won't be necessary."

Questioning the Combination

Ronald Krueger, MD, medical director of the refractive surgery department at the Cleveland Clinic's Cole Eye Institute, has been working with corneal cross-linking for several years now, mostly as a therapeutic treatment. "Though I'd say I'm more in favor of doing both at the same time, I understand the reasons why it might not be a good idea, too," he says.

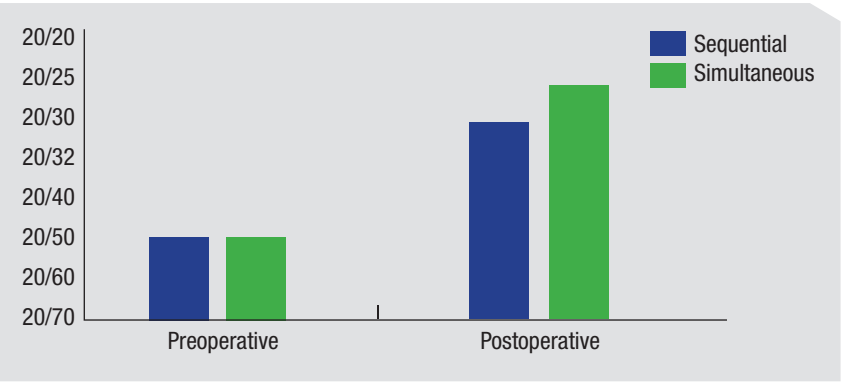
"The reason why it might not be ideal is the cross-linked eye is unstable for a while," Dr. Krueger continues. "This is because it's adjusting based on what the cross-linking has done. So there'd be cases where the surgeon would do PRK and flatten out the cornea and perform cross-linking and the patient would be doing well and would have a more balanced refraction. But then, over the course of months or years, the refraction drifts into farsightedness because the cornea keeps flattening beyond the initial treatment. That's because it was steep and irregular to begin with, and now that it's cross-linked, it's regularizing itself over a longer period of time. So the response after seeing that would be, 'Why not cross-link it first, let it stabilize, then do a PRK to get a more accurate refraction?' Though that's not a bad idea, the counter-argument to that is, 'What about the poor patient that has to undergo two separate procedures and

also has this lengthy period of time in between the procedures where he has to try to wear contacts or do something else like that which may not be working for him?' "

Dr. Kanellopoulos acknowledges that refractions are unpredictable in these patients, but says the procedure isn't aimed at providing the super-sharp vision that typical refractive surgery patients demand, and that he accounts for the potential unpredictability with his PRK nomogram. "The typical patient with oblique keratoconus would be something like +0.5 -3.5 at 80 degrees," he says. "By doing the treatment, the patient might end up -2 -0.5 at 80 degrees—so the patient might actually have an increase in myopia in this eye. However, more important, in this patient there would be a significant decrease in the irregular astigmatism. The best-corrected visual acuity might shift from 20/50 to maybe 20/20 or 20/25. That's where the added benefit is: He can now wear glasses and maybe soft contact lenses comfortably for the rest of his life."

As for how the nomogram helps facilitate this, he says the key is aiming low. "It's almost impossible to get consistent refractions in keratoconic eyes," Dr. Kanellopoulos says, "because the refractions tend to be irregular. So, even in cases where the patient's refractive error and corneal thickness would permit a full correction, we would discourage that. In our nomogram for these early keratoconic patients, we treat around 75 percent of the sphere, 70 to 75 percent of the cylinder, and keep the total ablation depth under 50 microns, anticipating that the cross-linking itself would induce some shift in the cornea. The predictability has actually rarely been an issue for us, and the only negative outcome would be to overcorrect a patient to a point that would necessitate a hyperopic correction. Even in such a case, you'd have to judge the overcorrection as well as the improvement in visual function. For instance, if you end up with a +0.5-D hyperope that's 20/20 with correction, but he started as a -1 myope with an astigmatism of -3 D and was 20/50 best-corrected, some would consider this a positive outcome."

Sequential vs. Simultaneous PRK and Cross-linking: BSCVA[1]



Dr. Kanellopoulos conducted a study comparing 127 eyes that underwent cross-linking in one visit and then PRK in a second visit six months later to 198 eyes that underwent both procedures on the same day.[1] At an average follow-up of three years, in the sequential group the mean uncorrected acuity improved from 0.9 ±0.3 logMAR (~20/160 Snellen) to 0.49 logMAR (~20/63), and mean best-corrected acuity from 0.41 logMAR (~20/50) to 0.16 logMAR (~20/30). Mean reduction in spherical equivalent refraction was 2.5 D, mean haze score was 1.2, and mean reduction in keratometry was 2.75 D.

In the simultaneous group, mean uncorrected vision improved from 0.96 logMAR (~20/200) to 0.3 logMAR (20/40), and mean best-corrected vision from 0.39 logMAR (~20/50) to 0.11 logMAR (~20/25). Mean reduction in spherical equivalent refraction was 3.2 D, mean haze score was 0.5, and mean reduction in K was 3.5 D. Endothelial cell count preoperatively and at last follow-up was unchanged ($p<0.05$) in both groups. Overall Dr. Kanellopoulos reports that the simultaneous group did better ($p<0.05$) in all fields evaluated, with improvement in uncorrected and best-corrected vision, a greater mean reduction in spherical equivalent refraction and keratometry and less corneal haze.

Opponents of a simultaneous approach also say that the refractive ablation takes away tissue that the surgeon could have used for cross-linking. "That's something to consider," says Dr. Krueger. "However, now we have adjuncts such as Dextran that can cause the cornea to swell a bit. Then, when it's swollen, you've made it thicker so it's still in a safe range to perform cross-linking. But if you adhere to a maximum ablation of 50 microns, you're actually not taking that much tissue away anyway. The rule is you need about 400 microns of native cornea to perform cross-linking, but that includes the epithelium and other layers."

Dr. Kanellopoulos intends to continue performing the procedure and studying the hundreds of cases he's already done over the long term. "The concern some voice about the potential adverse effect of the PRK procedure thinning the cornea is valid," he says. "But we've found the adverse effect is overshadowed by the improvement in visual function and the expansion of the area that can be cross-linked."

1. Kanellopoulos AJ. Comparison of sequential vs. same-day simultaneous collagen cross-linking and topography-guided PRK for treatment of keratoconus. J Refract Surg 2009;25:9:S812-8.

Acanthamoeba Creeps into the Light

Clearing up misconceptions about the *Acanthamoeba* infection in light of recent outbreaks.

Mark B. Abelson, MD, CM, FRCSC, FARVO, Ira Udell, MD, and James McLaughlin, PhD, Andover, Mass.

The past two decades have seen a series of microbial "epidemics" due to endemic protozoans in the genus *Acanthamoeba*. In the eye, these organisms can cause a keratitis which is difficult to diagnose, resistant to treatment and has the potential to be sight-threatening. While the infection caused by *Acanthamoeba* is often associated with contact lens use,[1] particularly in Western countries, a retrospective assessment of outbreaks suggests that there are a number of factors involved in the epidemiology of *Acanthamoeba* keratitis. In this month's column, we'll take a look at recent AK outbreaks, consider the relative importance of various factors implicated in these outbreaks, and discuss the latest approaches to AK diagnosis and treatment.

Acanthamoeba is one of the more abundant protozoa on earth.[2] Members of the genus *Acanthamoeba* have been isolated from soil, treated and untreated tap water, swimming pools, hot tubs and numerous other environments.[3] The protozoa's life cycle consists of an active, feeding trophozoite phase and a dormant, cyst phase. Formation of the cysts is activated by any of a number of unfavorable conditions including extremes of temperatures, pH or low humidity.[4] Surveys of water supplies and other environmental sources have identified several dozen species, but among these is one group (sometimes referred to as T4), which includes three or four species particularly associated with keratitis in humans. While it's not unusual for individuals to exhibit *Acanthamoeba*-specific antibodies, it's not clear why the rates of infection are so low, given the prevalence of the organism in the environment. Cases of central nervous system *Acanthamoeba*-mediated encephalitis, which are often fatal, appear to be the work of opportunistic pathogens as they occur primarily in immune-compromised patients.[3] In contrast, keratitis from an *Acanthamoeba* infection typically occurs in immune-competent individuals, so the precise mechanisms underlying *Acanthamoeba* virulence are unclear.[2-4]

Sources and Modes of Infection

AK was first documented in the United States in the early 1970s, and was traced back to ocular exposure to contaminated water. Information regarding the disease remained sparse, but the suggestion that the disease may be associated with contact lens use was established in the 1980s.[6] Initial studies blamed increased incidence on the use of "homemade" saline solutions by contact lens wearers; however, infection was later observed among lens wearers using store-bought multipurpose solutions. Most of these solutions are effective in killing *Acanthamoeba* trophozoites, but don't effectively kill cysts.[5]

Several spikes in the incidence of AK in the United States have been reported in the past two decades. The first outbreak was seen between 1985 and 1995 in Iowa towns served by the University of Iowa Hospitals and Clinics.[7] This increase was thought to be associated with flooding and subsequent water supply contamination.

A second spike in cases was reported between 2003 and 2006; this included significant increases in multiple geographic areas including Chicago, San Francisco, Boston and Philadelphia.[8,9] In Chicago, 63 reported cases in a period from 2004 to 2006 was greater than 10 times the rate previously seen in that area. Epidemiological research found that around half of all AK patients in the Chicago area outbreak had been using

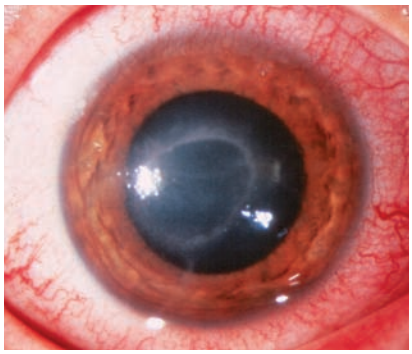
This article has no commercial sponsorship.

the same brand of a "no-rub" contact lens solution (Complete Moisture plus Multi-Purpose; AMO) for cleaning and storing their contacts.[9] This finding led to a Food and Drug Administration investigation and a voluntary recall by AMO. Subsequent studies have shown that contact solutions employing the "no-rub" approach to disinfection have minimal efficacy for killing *Acanthamoeba*, particularly when compared to hydrogen peroxide-based disinfection solutions.[10,11] An FDA workshop in 2009 recommended that, despite the low prevalence of AK, lens solution testing should include measurements of efficacy against *Acanthamoeba*.[12]

While the annual number of AK cases in the United States is certainly low relative to other types of ocular infections, historical approximations of ~250 cases per year are likely to be underestimates, based upon the difficulty of diagnosis and similarity to other forms of keratitis.[9] *Acanthamoeba* keratitis occurs at higher rates, and is not so closely associated with contact lens use in nations or regions where reliable water supplies are lacking. In these areas, the combination of poor water quality and inadequate medical resources also leads to poorer final visual outcomes of AK infections.[13]

Beyond Contact Lenses

Following the outbreaks in Chicago, the Centers for Disease Control and Prevention set up an informal network of hospitals, practitioners and public health officials to monitor the prevalence of the disease, as there were some doubts about actual versus reported rates of infection. Despite studies that showed a strong correlation between the AMO solution and the most recent outbreak, rates of reported AK did not decline following voluntary withdrawal of the solution from the market. This point is highlighted in a recent review article, which states that while the "role of contact lens solutions should not be minimized, it has become clear that other, more global risk factors likely underlie the most recent *Acanthamoeba* keratitis outbreaks."[14]



Some cases of *Acanthamoeba* keratitis present with ring-like stromal infiltrates composed of inflammatory cells.

At the same time, a number of studies showed that regardless of sources, *Acanthamoeba* were common contaminants of home water systems both in the United States and abroad.[15-18] In a recently published report, ~50 percent of the homes screened in an Ohio study were positive for *Acanthamoeba*.[16] Prevalence of the organism in community water supplies may also be a factor in the rates of disease: In parts of the United Kingdom where AK incidence is 15 times that of the United States, infrequently flushed-out rooftop tanks serve as holding tanks for public water supplies.[18] Most U.S. public water systems use disinfectants such as chlorine that effectively destroy the free trophozoites and inhibit protozoan growth and reproduction.[8,9]

The CDC formalized its investigation with the formation of the AK investigation team (AKIT) in March 2011.[19] This program is designed to follow up with AK patients and eye-care providers using a standardized interview focused on their eye-care practices before and around the time of diagnosis. At the same time, CDC will collect similar data from control patients matched to the AK group for age, geographic area and contact lens use. The emphasis on standardized interviews and careful data collection on controls should ensure that this study will provide an unbiased assessment of health risks associated with AK, as well as valuable information on how to combat future outbreaks. In the CDC report regarding the 2006 outbreak in Chicago, the authors pointed out that unavoidable bias was introduced because of the post-hoc nature of the investigation, and the AKIT study is designed to avoid that pitfall. While the final report is not scheduled for release until later this year, "preliminary analysis identified an association with contact lens use ... but did not reveal the need to recall any particular contact-lens associated product."[19] This underscores the principal message from all recent studies: The best way to avoid AK is for patients to be conscientious in following the hygiene guidelines for their specific lens products.

Diagnosis and Treatment

The first step in what researchers refer to as the "pathogenic cascade"[4] associated with AK is the binding of an *Acanthamoeba* surface protein to mannose-glycoproteins on the ocular epithelial surface. Expression of these glycoproteins is variable, and may explain the disconnect between high levels of *Acanthamoeba* in the environment and the relatively low rates of infection. Two other factors point to these glycoproteins as players in AK: Their expression is upregulated at sites of corneal trauma and in contact lens wearers.[4] Once bound to the ocular surface, the pathogen produces cytotoxic proteases and additional factors which lead to the destruction of corneal tissue.

One consequence of the increased incidence of AK is an improvement of diagnostic and therapeutic techniques for identifying and treating the disease. The first sign of trouble can be any of those commonly associated with keratitis, but most often patients report foreign body sensation, photophobia and

mild to severe pain.[20,21] Pain may be accompanied by a radial kerato-neuritis, while other cases of AK present with ring-like stromal infiltrates, believed to be composed of inflammatory cells. Early diagnosis is essential, as it's the best means to prevent stromal infiltration where permanent tissue damage becomes more likely. Inappropriate therapy with antivirals, antibiotics or steroids may delay appropriate treatments and exacerbate the keratitis.

A careful slit-lamp exam can reveal evidence of *Acanthamoeba*, either directly or by the presence of inflammation. It's essential that AK be differentiated from the more common viral keratitis. The lack of bulbous dendrites can be diagnostic of AK, as they are typical of herpes infections. Corneal scrapings can be stained for the presence of either trophozoites or cysts, and these samples can also be cultured for diagnostic confirmation of viable *Acanthamoeba*. However, while they represent the gold standard, protozoan cultures can take days to give results.

Recently, advances in corneal confocal imaging have allowed its use in many practices, where it can be an invaluable tool in timely, accurate identification of *Acanthamoeba*. In a recent survey of ophthalmologists,[21] 77 percent reported using both examination and culturing in diagnosis of AK, and 44 percent reported using confocal microscopy. A majority of this last group were in university-based practices, so instrument availability still plays a role. In comparative studies, confocal microscopy showed high sensitivity and specificity as a diagnostic tool.[22] Despite this, most practitioners do not have access to these instruments, so traditional methods will likely remain essential for proper AK diagnosis. When these methods fail to produce a diagnosis, corneal biopsy may become necessary.

Therapies haven't advanced to the extent that diagnostics have, but the goal of prompt, aggressive treatment is well-established. Most practitioners employ a cationic antiseptic such as polyhexamethylene biguanide 0.02% or chlorhexidine 0.02%, in combination with a diamidine such as Brolene.[20,23] This combination of agents with complementary mechanisms of action is usually effective, and with time can eradicate both active amoebae and cysts. Use of either agent alone can also be effective, but combination therapy was favored by greater than 90 percent of surveyed ophthalmologists.[21] A similar proportion focus on medical therapy before considering surgical options, and most employ steroids after about a month of antimicrobial therapy.

Acanthamoeba infection requires a long duration of therapy. A recent study examining clearance of detectable *Acanthamoeba* in the course of a long-term combination therapy reported a median clearance time of just over six weeks in the 37 patients surveyed.[24] The study also showed that either early use of steroids or stromal involvement was associated with clearance times twice that of the median.

Acanthamoeba keratitis is a rare but serious disease that, if undetected, can cause permanent corneal damage and result in blindness or significant loss in visual acuity. The ephemeral nature of AK outbreaks has reinforced the misconception that the disease is primarily the result of contaminated or otherwise faulty contact lens solutions. The reality is that the organism is common, and contact lens wearers must use good hygiene to minimize their risk. Patients need to understand that showering or swimming without removing their contacts may cost them their eyesight. Also, the upcoming report from the CDC should provide guidance in terms of the role public health officials can play. Ultimately, our response to AK outbreaks should focus on proper contact lens habits, and when needed, prompt diagnosis and treatment. REVIEW

Dr. Abelson, a clinical professor of ophthalmology at Harvard Medical School and Senior Clinical Scientist at the Schepens Eye Research Institute, consults in ophthalmic pharmaceuticals. Dr. Udell is professor and chairman of the department of ophthalmology, Hofstra-North Shore Long Island Jewish School of Medicine. Dr. McLaughlin is a medical writer at Ora, Inc.

1. Moore MB, McCulley JP, Luckenbach M, et al. Acanthamoeba keratitis associated with soft contact lenses. Am J Ophthalmol. 1985;100:396-403.
2. Schuster FI, Visvesvara GS. Free-living amoebae as opportunistic and non-opportunistic pathogens of humans and animals. Int J Parasitology 2004;34:1001-27.
3. Marciano-Cabral F, Cabral G. Acanthamoeba spp. as agents of disease in humans. Clin Microbiol Rev 2003;16:273-307.
4. Clarke DW, Niederkorn JY. The pathophysiology of Acanthamoeba keratitis. Trends in Parasitology 2006;22:175.
5. Hiti K, Walochnik J, Haller-Schober EM, Faschinger C, Aspöck H. Viability of Acanthamoeba after exposure to a multipurpose disinfecting contact lens solution and two hydrogen peroxide systems. Br J Ophthalmol. 2002; 86:144-6.
6. Visvesvara GS, Moura H, Schuster FL. Pathogenic and opportunistic free-living amoebae. FEMS Immunol Med Microbiol. 2007;50:1-26.
7. Meier PA, Mathers WD, Sutphin JE, Folberg R, Hwang T, Wenzel RP. An epidemic of presumed Acanthamoeba keratitis that followed regional flooding. Arch Ophthalmol 1998;116:10904.
8. Joslin CE, Tu EY, McMahon RR, Passaro OJ, Stayner LT, Sugar J. Epidemiological characteristics of a Chicago-area Acanthamoeba keratitis outbreak. Am J Ophthalmol 2006; 142:212-217.
9. Verani JR, Lorick SA, Yoder JS, et al, The Acanthamoeba Keratitis Investigation Team. National outbreak of Acanthamoeba keratitis associated with use of a contact lens solution, United States. Emerg Infect Dis 2009;15:1236-42.
10. Butcko V, McMahon RR, Joslin CE, Jones L. Microbial keratitis and the role of rub and rinsing. Eye Contact Lens 2007;33:421-3.
11. Shoff ME, Joslin CE, Tu EY, Kubatko L, Fuerst PA. Efficacy of contact lens systems against recent clinical and tap water Acanthamoeba isolates. Cornea 2008; 27:713-9.
12. Steinemann TL. Micobiological testing for contact lens care products-public workshop: FDA white oak conference center, Silver Spring, Maryland. Eye Contact Lens. 2009; 35:115-6.
13. Lam OS, Houang E, Fan OS, Lyon D, Seal 0, Wong E; Hong Kong Microbial Keratitis Study Group. Incidence and risk factors for microbial keratitis in Hong Kong: Comparison with Europe and North America. Eye 2002;16:608-18.
14. Tu EY, Joslin CE. Recent outbreaks of atypical contact lens-related keratitis: What have we learned? Am J Ophthalmol. 2010;150:602-608.
15. Shoff ME, Rogerson A, Kessler K, Schatz S, Seal DV. Prevalence of Acanthamoeba and other naked amoebae in south Florida domestic water. J Water Health 2008;6:99-104.
16. Stockman LJ, Wright CJ, Visvesvara GS, Fields BS, Beach MJ. Prevalence of Acanthamoeba spp. and other free-living amoebae in household water, Ohio, USA—1990–1992. Parasitol Res. 2011;108:621–627.
17. Magliano ACM, Maia da Silva F, Teixeira MMG, Alfieri SC. Genotyping, physiological features and proteolytic activities of a potentially pathogenic Acanthamoeba isolated from tap water in Brazil. Experimental Parasitology 2009; 123: 231–235.
18. Kilvington S, Gray T, Dart J, Morlet N, Beeching JR, Frazer DG, et al. Acanthamoeba keratitis: the role of tap water contamination in the United Kingdom. Invest Ophthalmol Vis Sci.2004;45 :165–9.
19. http://www.cdc.gov/parasites/Acanthamoeba/outbreaks/2011/index.html accessed December 11, 2011.
20. Dart JKG, Saw VPJ, Kilvington S. Acanthamoeba Keratitis: Update 2009. Am J Ophthalmol 2009;148:487–499.
21. Oldenburg CE, Acharya NR, Tu EY, et al. Practice Patterns and opinions in the Treatment of Acanthamoeba Keratitis. Cornea 2011;30:1363–1368.
22. Tu EY, Joslin CE, Sugar J, et al. The relative value of confocal microscopy and superficial corneal scrapings in the diagnosis of Acanthamoeba keratitis. Cornea. 2008; 27:764-72.
23. Hammersmith KM. Diagnosis and management of Acanthamoeba keratitis. Curr Opin Ophthalmol 2006;17:327-331.
24. Oldenburg CE, Keenan JD, Cevallos V, et al. Microbiological cure times in Acanthamoeba keratitis. Eye 2011;25:1155–1160.

CPE
OPHTHALMOLOGY
Continuing • Professional • Education

SAVE THE DATE

2012 CALENDAR

CONTINUING & PROFESSIONAL EDUCATION

Dear Residency Directors,

We would like to invite you to review this Save the Date Calendar for third-year residency programs we are planning for 2012. Each program offers a unique educational opportunity for third-year residents by providing the chance to meet and exchange ideas with some of the most respected thought leaders in ophthalmology. The programs are designed to provide residents with a state-of-the-art didactic and wet lab experience. The programs also serve as an opportunity to network with residents from other programs. After reviewing the material, it is our hope that you will select and encourage your residents to attend these educational programs.

Best regards,
Review of Ophthalmology

March 9-10, 2012 Fort Worth, TX	**August 3-4, 2012** Fort Worth, TX	**August 10-11, 2012** Fort Worth, TX	**September 14-15, 2012** Fort Worth, TX

For more information and to register, go to:
www.revophth.com/ResFellowEdu2012

Credit Designation Statement:
These activities have been approved for *AMA PRA Category1 Credit(s)™*.

Jointly Sponsored by:

REVIEW of Ophthalmology

ONRI

Partially supported by an independent medical educational grant from

Alcon

CME

One-year Outcomes in Ahmed/Baerveldt Study

One-year treatment outcomes were reported for the Ahmed versus Baerveldt Study

Patients aged 18 years or older with uncontrolled glaucoma refractory to medical, laser and surgical therapy were randomized to undergo implantation of an Ahmed-FP7 valve or a Baerveldt-350 implant, and followed for five years. The primary outcome measure was failure, defined as intraocular pressure out of target range (5 to 18 mmHg with ≥20 percent reduction from baseline) for two consecutive visits after three months; vision-threatening complications; additional glaucoma procedures; or loss of light perception.

The two groups' ocular and demographic characteristics were similar, with the exception of sex. Preoperatively, the study group had a mean IOP of 31.4 ±10.8 mmHg on a mean of 3.1 ±1.0 glaucoma medications with a median Snellen acuity of 20/100.

At one year, the cumulative probability of failure was 43 percent in the Ahmed group and 28 percent in the Baerveldt group (p=0.02). The Ahmed group's mean IOP was 16.5 ±5.3 mmHg; the Baerveldt group's was 13.6 ±4.8 mmHg (p<0.001). The mean number of glaucoma medications required was 1.6 ±1.3 in the Ahmed group and 1.2 ±1.3 in the Baerveldt group (p=0.03). Visual acuity was similar in both groups at all visits in the first year (p=0.66). A similar number of patients experienced postoperative complications in the two groups (45 percent Ahmed, 54 percent Baerveldt, p=0.19), but a greater number of patients in the Baerveldt group required interventions (26 percent Ahmed vs. 42 percent Baerveldt, p=0.009).

Ophthalmology 2011 Nov;118(11): 2180-9. Epub 2011 Sep 1.
Christakis PG, Kalenak JW, Zurakowski D, Tsai JC, et al.

Postop Antibiotics May Not Affect Endophthalmitis Rate

A group at the Medical College of Wisconsin, Milwaukee, reports that the use of postinjection antibiotics appears not to have a significant effect on the rate of endophthalmitis after intravitreal injections administered in a clinical practice setting when aseptic technique is used.

Current endophthalmitis rates after IV injection in the literature are based on studies where patients routinely received postinjection antibiotics. This retrospective chart review compared the rate of endophthalmitis over 12 months in a cohort of patients receiving postinjection antibiotics with that in a group that did not.

The rate of clinically suspected endophthalmitis in the patients receiving postinjection antibiotics after intravitreal injection and that in the cohort that did not was 0.22 percent and 0.20 percent, respectively. One culture-positive case was found overall. The difference between the two groups is not statistically significant (p= 0.75).

Retina 201131:2032-6.
Bhatt SS, Stepien KE, Joshi K.

Anti-VEGF Treatment Beneficial But at a High Financial Burden

A Duke University group used Medicare data to assess the increased financial burden of providing care for age-related macular degeneration patients since introduction of anti-VEGF intravitreal injections.

Beneficiaries with new diagnoses of neovascular AMD in 1994 (n=2,497), 2000 (n=3,927), and 2006 (n=6,041) were identified. The number of beneficiaries newly diagnosed with neovascular AMD more than doubled between the 1994 and 2006 cohorts. Overall yearly Part B payments per beneficiary increased significantly from $3,567 for the 1994 to $5,991 for the 2006 cohort (p<0.01) in constant 2008 dollars. Payments for eye care alone doubled from $1,504 for the 1994 cohort to $3,263 for the 2006 cohort (p<0.01). Most of the increase in payments for eye-care in 2006 reflected payments for anti-VEGF injections, which were $1,609 over one year. Mean annual numbers of visits and imaging studies also increased significantly between the 1994 and 2006 cohort.

Am J Ophthalmol 2011;152:1014-20.
Day S, Acquah K, Lee PP, Mruthyunjaya P, Sloan FA.

REVIEW Glaucoma Management

(continued from page 51)

imaging much more effectively in clinical practice than has been possible previously," he says. "That belief is also shared by the World Glaucoma Association, and the *Preferred Practice Patterns* of the American Academy of Ophthalmology, both of which recommend imaging as part of routine clinical care."

Dr. Weinreb notes that in the glaucoma community, the evolution of imaging technology has added fuel to the ongoing debate regarding whether structural or functional testing is more important for diagnosis and/or monitoring the progression of the disease. "If imaging technology is ready for clinical use in glaucoma management—and the clinical evidence suggests that it is—which approach should clinicians rely upon?" he asks. "My answer is that we need to take advantage of both structural and functional testing, rather than relying primarily on one or the other. The data they provide are complementary.

"Of course, because they monitor different aspects of the disease, one approach or the other may be more efficacious in a given situation, depending on factors such as how many tests you're doing and the stage of the patient's disease," he continues. "For example, structural testing is probably more sensitive early in the disease process; in late-stage disease, visual fields are probably better. The structure is so damaged at that point that it's hard to detect any increase in the damage.

"If your practice still relies primarily on basic examination and visual fields, this is a good time to consider investing in some of this technology, given all the outstanding instruments and software packages that are available," he concludes. "Just remember not to rely exclusively on imaging for final decisions about diagnosis or treatment. There's no substitute for good clinical judgment." REVIEW

1. Mansouri K, Leite MT, Medeiros FA, Leung CK, Weinreb RN. Assessment of rates of structural change in glaucoma using imaging technologies. Eye 2011;25:3:269-77.
2. Leung CK, Cheung CY, Weinreb RN, et al. Evaluation of retinal nerve fiber layer progression in glaucoma: A study on optical coherence tomography guided progression analysis. Invest Ophthalmol Vis Sci 2010;51:1:217-22.
3. Burgoyne CF, Mercante DE, Thompson HW. Change detection in regional and volumetric disc parameters using longitudinal confocal scanning laser tomography. Ophthalmology 2002;109:455-466.
4. Ervin JC, Lemij HG, et al. Clinician change detection viewing longitudinal stereophotographs compared to confocal scanning laser tomography in the LSU Experimental Glaucoma (LEG) Study. Ophthalmology 2002;109:467-481.
5. Chauhan BC, McCormick TA, et al. Optic disc and visual field changes in a prospective longitudinal study of patients with glaucoma: Comparison of scanning laser tomography with conventional perimetry and optic disc photography. Arch Ophthalmol 2001;119:1492-1499.
6. Kourkoutas D, Buys YM, Flanagan JG, Hatch WV, Balian C, Trope GE. Comparison of glaucoma progression evaluated with Heidelberg retina tomograph II versus optic nerve head stereophotographs. Can J Ophthalmol 2007;42:1:82-88.
7. Medeiros FA, Zangwill LM, Alencar LM, Bowd C, Sample PA, Susanna R Jr, Weinreb RN. Detection of glaucoma progression with stratus OCT retinal nerve fiber layer, optic nerve head, and macular thickness measurements. Invest Ophthalmol Vis Sci. 2009;50:12:5741-8.
8. Lee EJ, Kim TW, Weinreb RN, Park KH, Kim SH, Kim DM. Visualization of the lamina cribrosa using enhanced depth imaging spectral-domain optical coherence tomography. Am J Ophthalmol 2011;152:1:87-95.
9. Medeiros FA, Leite MT, Zangwill LM, Weinreb RN. Combining structural and functional measurements to improve detection of glaucoma progression using Bayesian hierarchical models. Invest Ophthalmol Vis Sci 2011;52:8:5794-803.

REVIEW Advertising Index

Equipment and Supplies

Equipment and Supplies

Products and Services

Practice For Sale

Lease Opportunity

Optometric Offices For Lease

Turnkey Optometric Offices Available For Lease. Exceptional Locations.

San Francisco • San Diego
Los Angeles • Chicago • Detroit
And Other Cities

Call Mark McEvoy
641-715-3900 ext. 221861

Void where prohibited by law

Seeking to Acquire

Seeking to Acquire Optical Stores

Investment Company Seeking to Acquire Successful Optical Stores And Dispensaries

Flexible investor. Favorable terms. Sell your optical retail store(s) today. Protect your valued employees. Exit immediately or transition over time.

For More Information Contact:
Sean Harty
641-715-3900 ext. 729987

Void where prohibited by law

Professional Services

Experienced Management Company Seeking To Establish And Manage Optical Dispensaries

Outsource Your Dispensary Operations

Increase profit and cash flow while maintaining absolute control of your optical dispensary. Elevate your brand and product assortment. Eliminate the distraction of managing a retail operation. Transition operations in 30 days or less.

For More Information Contact
Grace Kellogg
641-715-3900 ext. 169531

Void where prohibited by law

Equipment and Supplies

The leading reseller of Carl Zeiss Meditec pre-owned diagnostic instruments in the U.S.

EYE CARE ALLIANCE™

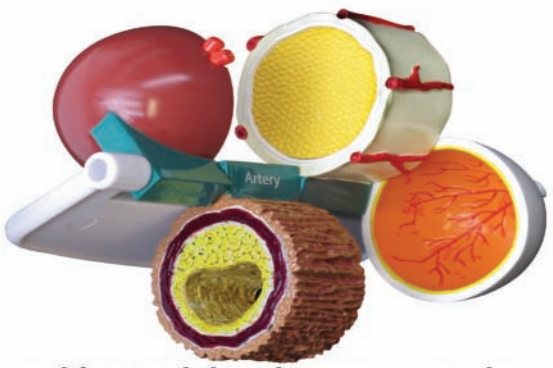
800-328-2020
www.eyecarealliance.com

HFA I series available!

We also buy used equipment
Call 1-800-328-2020 for a quote today!

Diabetes Education Model

NEW!



An excellent teaching tool that demonstrates the effects of diabetes on kidneys, arteries, nerves, and retina of the eye. Contact us for custom models.
website search "15252"

GuldenOphthalmics
time saving tools
800-659-2250 www.guldenophthalmics.com

For classified advertising
call 1-888-498-1460
or e-mail us at sales@kerhgroup.com

kerh group

Career Opportunities

JOHNS HOPKINS MEDICINE SCHOOL OF MEDICINE

The Wilmer Eye Institute, Johns Hopkins University School of Medicine (JHU-SOM) is expanding to Harford County, Bel Air, MD and is seeking a residency trained Comprehensive Ophthalmologist and a fellowship trained Cornea/Cataract/Anterior Segment ophthalmologist willing to relocate to Bel Air, MD or live in immediately adjacent areas.

The successful candidate will provide medical, ophthalmologic consultation and treatment at this location and will perform surgery at the on-site ASC or Johns Hopkins Hospital (JHH). The faculty member will be expected to contribute to the JHU-SOM missions of teaching, research, and patient care. Full time faculty (JHU) and active staff (JHHI) appointments will be at the academic ranking commensurate with experience and background. Candidates must be Board Certified or Eligible in Ophthalmology, eligible for a Maryland medical license and pass a criminal background check.

Curriculum vitae, bibliography and 3 professional references should be directed to:

Wilmer Eye Institute Search Committee-Bel Air: lyoung21@jhmi.edu

Johns Hopkins University is an affirmative action/equal opportunity employer and is especially interested in identifying female and minority candidates.

www.hopkinsmedicine.org/wilmer

EEO/MFDV, Smoking Drug Free

Equipment and Supplies

Ophthalmic Equipment Resources
www.oersales.com

Ophthalmic Sales & Service
- Quality Refurbished Equipment
- Traditional Lane Equipment
- Pre-Test Equipment
- **New & Pre-Owned** Digital Retinal Camera Systems

We purchase used equipment.

We stand behind our product after delivery.

Call toll free: 888-894-2040
O: 770-207-1133 • F: 770-207-9225
549 Camp Lake Rd., Suite 1
Monroe, GA 30655

Ophthalmic Equipment Resources, LLC

REVIEW of Ophthalmology

Targeting Ophthalmologists?

CLASSIFIED ADVERTISING WORKS

- JOB OPENINGS
- CME PROGRAMS
- PRODUCTS & SERVICES
- AND MORE...

Contact us today for classified advertising:
Toll free: **888-498-1460**
E-mail: **sales@kerhgroup.com**

kerh group

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

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 (eg, 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 event 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 events (> 10%) included growth of eyelashes and ocular pruritus.

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

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 that 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/m^2 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: If more than one topical ophthalmic drug is being used, the drugs should be administered at least five (5) minutes between applications.

APC81RP11 based on 71807US12B.

Rx only

ALLERGAN®

Before reading on, please see p. 66 for presenting complaint, history and examination.

Diagnosis, Workup and Treatment

Considering this patient's significant optic disc edema, uveitis and social risk factors, the differential diagnosis encompassed inflammatory etiologies, including sarcoid, systemic lupus erythematosus, and Vogt-Koyanagi-Harada syndrome; infectious etiologies, such as syphilis, tuberculosis and bartonella henselae; and lymphoproliferative malignancies. The patient was admitted and underwent a non-contrast head CT and a brain MRI with gadolinium and fat suppression. Both were normal. Blood-work included human immunodeficiency virus (HIV) testing, fluorescent treponemal antibody-absorption (FTA-Abs), rapid plasma reagin (RPR), hepatitis B and C antibodies, HLA B-27, angiotensin converting enzyme (ACE), Lyme antibody, ANA panel and rheumatoid factor. A lumbar puncture was performed and the cerebral spinal fluid (CSF) was tested for cell count, protein, glucose, venereal disease research laboratory (VDRL), Lyme and ACE levels.

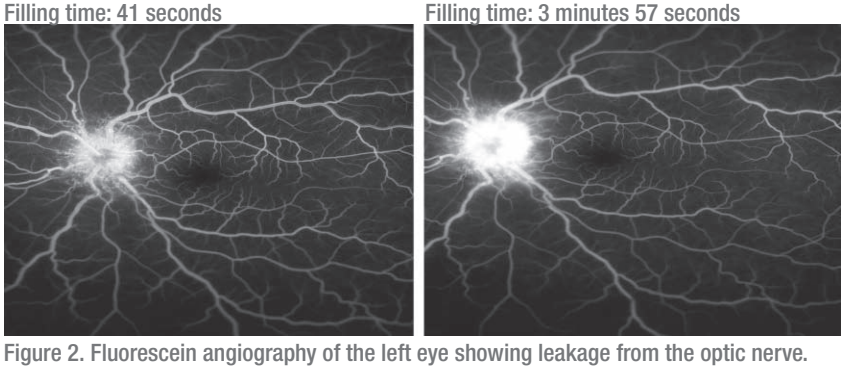


Figure 2. Fluorescein angiography of the left eye showing leakage from the optic nerve. The right eye showed similar findings

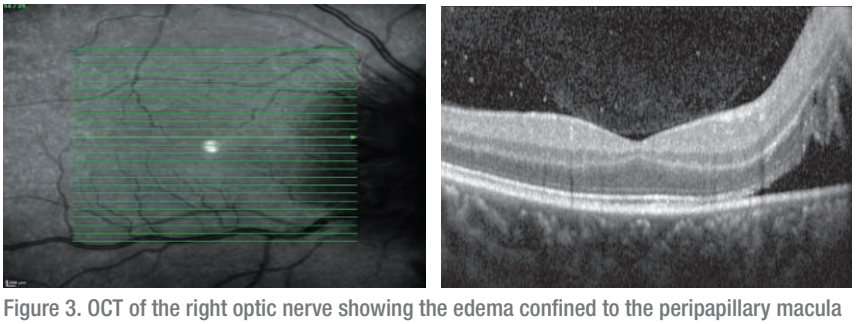


Figure 3. OCT of the right optic nerve showing the edema confined to the peripapillary macula sparing the fovea. The left eye showed similar findings.

In the interim the patient underwent an intravenous fluorescein angiography, which confirmed optic disc edema; however, it did not reveal significant vasculitis *(See Figure 2)*. An optical coherence tomography of both optic nerves was obtained, which showed edema localized to both optic discs and nasal macula, sparing the fovea *(See Figure 3)*.

The systemic workup revealed HIV positivity (CD4 240) as well as a reactive FTA-Abs and highly reactive RPR (titer >1:1,024). The CSF was significant for an elevated protein of 108 and positive VDRL reactivity. The patient was newly diagnosed with HIV and neurosyphilis. He was treated with intravenous penicillin and discharged home to complete a 14-day infusion course. Three-month follow-up revealed resolution of the bilateral optic disc swelling and intraocular inflammation.

Discussion

Syphilis is a bacterial infection caused by the spirochete, *Treponema pallidum*, which is primarily sexually transmitted, but may be vertically transmitted, leading to congenital syphilis. The incidence of syphilis in the United States has been on the rise for the past decade. An August 2011 report, funded by the Centers for Disease Control and Prevention, identified young black men who have sex with men as the demographic group disproportionately affected by the rising incidence of syphilis. Mirroring this trend is the rising incidence of HIV infection over the past 10 years in the same demographic, as the two infections are often seen in tandem.

Syphilis is typically characterized as presenting in one of four different stages: primary; secondary; latent; or tertiary. This conventional staging system contributes very little towards the understanding and classification

of ocular syphilis. Ocular syphilis is by definition neurosyphilis, and it can occur in any of the four stages. Neurosyphilis seen in the tertiary phase refers to the general paresis, tabes dorsalis, and meningitis or meningiovascular complications that can be seen with prolonged untreated infection. Ocular syphilis is considered to be the most common form of neurosyphilis encountered. Syphilis, often referred to as the "great imitator," can have innumerable manifestations throughout the body. The more common presentations of ocular syphilis include interstitial keratitis; anterior, intermediate and posterior uveitis; chorioretinitis; retinitis; retinal vasculitis; and cranial neuritis, including optic neuritis. This wide variability warrants a consideration of syphilis for many ophthalmic pathologies, particularly in the demographic groups most at risk.

A diagnosis of syphilis is confirmed by serology or dark field microscopy of tissue; however, in clinical practice the latter is rarely used. The initial screening tests with high sensitivity are the nontreponemal serologies that include VDRL and RPR tests. The more specific confirmatory test uses treponemal serologies, including FTA-Abs and *Treponemal pallidum* particle agglutination (TPHA) tests. Given the high co-infection rate with HIV, standard of care should include HIV serologies when considering a new diagnosis of syphilis. In a 2011 systematic review of the literature, Joseph D. Tucker, MD, and colleagues found that in 101 cases of ocular syphilis and HIV, ocular syphilis led to the diagnosis of HIV in 62 percent of the cases.

Lumbar puncture is not routine in the diagnostic workup for all stages of syphilis; however, it is indicated in the setting of neurosyphilis, patients with concerning neurologic findings in the setting of positive serologies, co-infection with HIV, and any patient with serological evidence of treatment failure despite standard-of-care treatment. Posterior segment manifestations of ocular syphilis often warrant further diagnostic testing including OCT and IVFA to further classify posterior syphilitic involvement as well as to evaluate response to treatment.

Treatment of ocular syphilis is the same as the treatment for neurosyphilis. The CDC recommends two regimens dictated by patient reliability. The standard regimen is IV penicillin G given for 10 to 14 days. A highly compliant patient may also be treated with daily intramuscular procaine penicillin and oral probenecid four times a day for 10 to 14 days.

The rising incidence of ocular syphilis and co-infection with HIV exists in contrast to the declining incidence of other HIV-related infections in the post-HAART era, particularly CMV-retinitis. This has prompted recent studies and literature reviews to investigate differences in presentation, clinical course and overall outcome in these patients. Dr. Tucker's group found that posterior segment manifestations were the most common initial presentation in the HIV-positive group with ocular syphilis, particularly posterior uveitis and optic neuritis. The group also found a statistically significant association between the increased incidence of posterior uveitis and a CD4 count of less than 200. Both Dr. Tucker's group and David J. Browning MD, PhD, and colleagues did not find that HIV negatively affected response to treatment for neurosyphilis; however, there have been reports of delay in resolution of symptoms for up to a year in HIV-positive cohorts.

Given the high co-infection rate with HIV, standard of care should include HIV serologies when considering a new diagnosis of syphilis.

CSF analysis may show pleocytosis as well as higher VDRL reactivity in the HIV-infected patient versus the non-HIV-infected patient. Post-treatment surveillance lumbar punctures are indicated when highly abnormal parameters are initially present in the CSF. HIV infection can slow the resolution of these parameters. Current CDC recommendations in the HIV-positive population dictate a consideration of retreatment if the CSF cell count has not decreased six months after initiating treatment, or if the CSF continues to show abnormalities two years after initiation of treatment. REVIEW

The author would like to thank James Vander, MD, of the Wills Eye Retina Service for his assistance with this case.

1. Browning, DJ. Posterior segment manifestations of active ocular syphilis, their response to a neurosyphilis regimen of penicillin therapy and the incidence of human immunodeficiency virus status on response. Ophthalmol 2000;107:2015-2023.
2. Centers for Disease Control and Prevention. "Sexually Transmitted Diseases Treatment Guideline, 2010." Centers for Disease Control and Prevention Sexually Transmitted Diseases. Centers for Disease Control and Prevention. Web. 28 January 2011< http://www.cdc.gov/std/treatment/2010/genital-ulcers.htm#neuro.>
3. Danesh-Meyer H, Kubis KC, Sergott RC. Not so slowly progressive visual loss. Surv Ophthalmol 1999;44:247-252.
4. Ghanem KG, Moore RD, Rompalo AM. Neurosyphilis in a clinical cohort of HIV-1-infected patients. AIDS 2008;22:1145-51.
5. Gonzalez-Lopez JJ, Fernandez Guerrero ML, Lujan R, et al. Factors determining serologic response to treatment in patients with syphilis. Clin Infec Dis 2009;49:1505-1511.
6. Katz DA, Berger JR, Duncan RC. Neurosyphilis: A comparative study of the effect of infection with human immunodeficiency virus. Arch Neurol 1993;50:243-9.
7. Kiss S, Damico FM,Young LH. Ocular manifestations and treatment of syphilis. Semin Ophthalmol 2005;20:161-7.
8. Lukehart SA, Hook EW 3rd, Baker-Zander SA, et al. Invasion of the central nervous system by treponema pallidum: Implications for diagnosis and treatment. Ann Intern Med 1988;109:855-62.
9. Musher DM, Hamill RJ, Baughn RE. Effect of human immunodeficiency virus (HIV) infection on the course of syphilis and on the response to treatment. Ann Intern Med 1990:113:872-81.
10. Su JR, Beltrami JF, Zaidi AA, et al. Primary and secondary syphilis among black and Hispanic men who have sex with men: Case report data from 27 states. Ann Intern Med 2011;155:145-51.
11. Tucker JD, Li JZ, Robbins GK et al. Ocular syphilis among HIV-infected patients: A systematic analysis of the literature. Sex Transm Infect 2011;87:4-8.

A young man with a recent complaint of blurry spots and smudges in his peripheral vision presents to the Wills ER.

Sarah J. Driscoll, MD

Presentation

A 27-year-old African-American male presented to the Wills Eye Emergency Room with the chief concern of blurry vision in both eyes. He had been in a motor vehicle accident two weeks prior and since then had been experiencing visual symptoms. He initially noticed flashes of light and floaters with a "blurry smudge" in the periphery of his right eye. For the past three days he felt his left eye was developing "blurry spots." There was no associated ocular pain, irritation or photosensitivity. The patient denied headache or neck pain.

Medical History

The patient was diagnosed with bilateral keratitis by his optometrist one month prior to presentation. He was treated with polymixin B, which was discontinued prior to his visit to the emergency room. His past medical history was also significant for chronic sinusitis. He was not taking any chronic medications.

His family history was significant for diabetes and cerebrovascular disease. The patient self-identified as a sexually active homosexual who did not consistently use protection. He worked as a nurse and was up-to-date on vaccinations. He smoked tobacco, but denied alcohol and intravenous drug use.

His review of systems was positive for a non-tender, non-pruritic red rash on his chest and abdomen that had been present for "a few weeks." He also noted right wrist and ankle pain as well as fatigue. He denied fever, chills, night sweats, weight loss, nausea and vomiting.

Examination

The patient's ocular examination revealed a corrected visual acuity of 20/25 in each eye. Color plates were 10 out of 10 briskly in each eye. Gross exam showed no mass or proptosis. Pupils were briskly reactive without an afferent pupillary defect. The patient had full motility with normal ductions and versions. Visual fields were full by confrontational field testing. Intraocular pressure was 16 mmHg in both eyes.

The anterior slit lamp exam revealed clear corneas with four white blood cells per high-power field in the anterior chamber of both eyes without evidence of flare. Additionally, the anterior vitreous was positive for cell in both eyes.

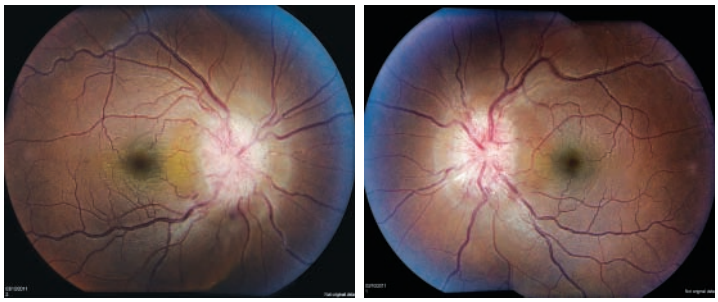
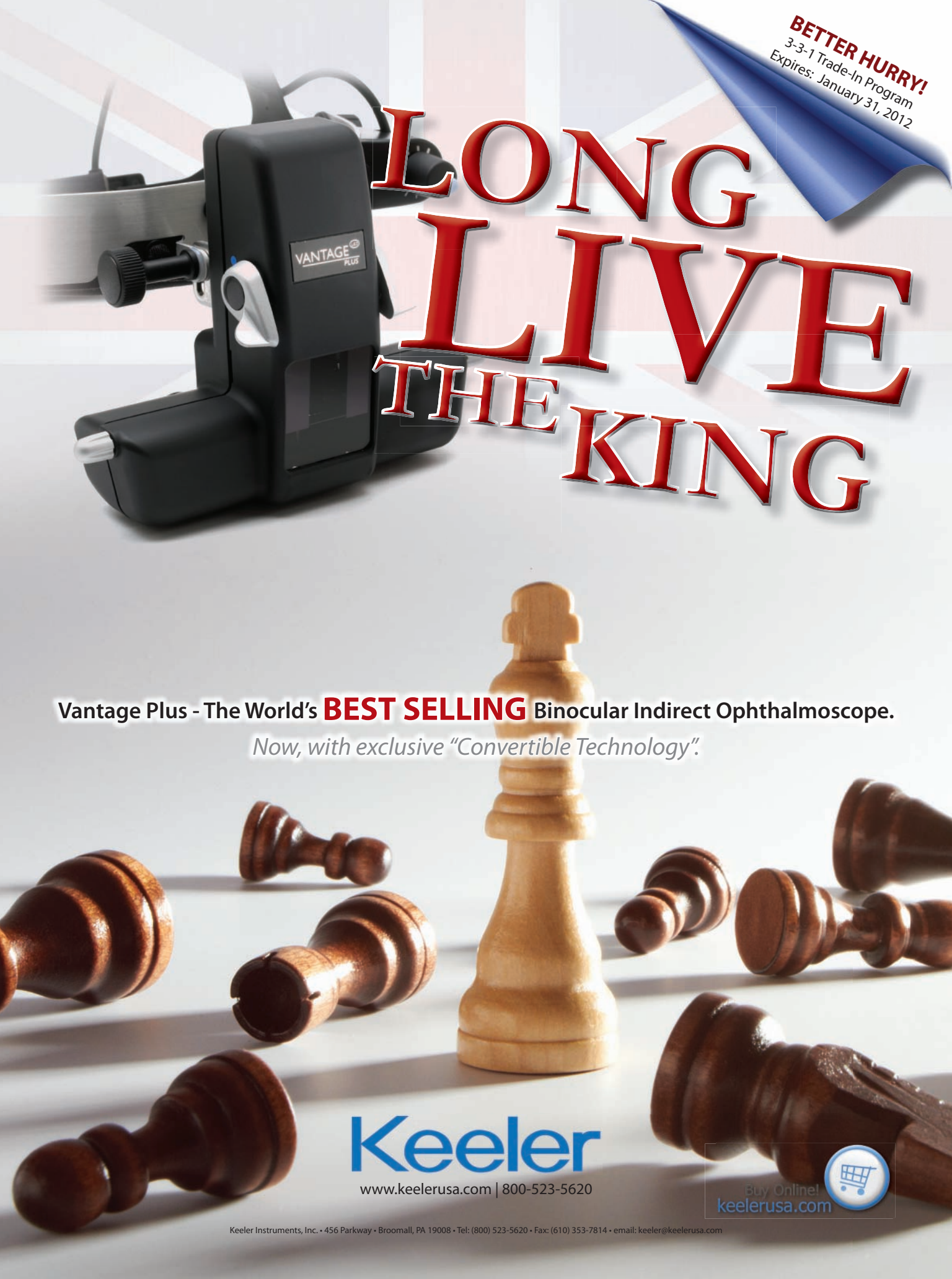


Figure 1. Fundus photo showing significant optic disc swelling bilaterally.

The dilated fundoscopic exam revealed vitreous snowballs in both eyes. There was significant disc edema bilaterally with small, peripapillary cotton wool spots in the left eye *(See Figure 1)*. The periphery was significant for inferior snow-banking and vascular sheathing in both eyes. Further physical examination revealed an erythematous maculopapular rash on the chest and abdomen.

What is your differential diagnosis? What further workup would you pursue? Please turn to p. 64


BETTER HURRY!
3-3-1 Trade-In Program
Expires: January 31, 2012
LONG LIVE THE KING
VANTAGE PLUS
Vantage Plus - The World's BEST SELLING Binocular Indirect Ophthalmoscope.
Now, with exclusive "Convertible Technology".
Keeler
www.keelerusa.com | 800-523-5620
Buy Online!
keelerusa.com
Keeler Instruments, Inc. • 456 Parkway • Broomall, PA 19008 • Tel: (800) 523-5620 • Fax: (610) 353-7814 • email: keeler@keelerusa.com

For patients starting or changing PGA therapy, consider…

91%
Commercial and Part D member lives covered as of 03/29/11[1]

A drop with low dropout

Prescribe LUMIGAN® 0.01% efficacy with low discontinuation[2]

Indication: 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.

Important Safety Information

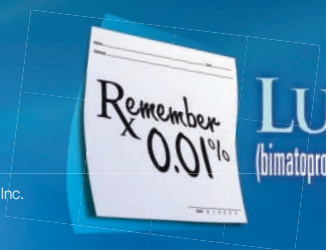
Warnings and Precautions: Pigmentation: Bimatoprost ophthalmic solution has been reported to cause changes to pigmented tissues: most frequently, increased pigmentation of the iris, eyelid, and eyelashes. Increases are expected as long as bimatoprost is administered. Iris color change may not be noticeable 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.

Intraocular Inflammation: LUMIGAN® 0.01% and 0.03% should be used with caution in patients with active intraocular inflammation (eg, 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.

Adverse Reactions: In clinical studies with bimatoprost ophthalmic solutions (0.01% or 0.03%), the most common adverse event 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 events (> 10%) included growth of eyelashes and ocular pruritus.

Please see brief prescribing information on adjacent page.



FIRST-LINE
LUMIGAN® 0.01%
(bimatoprost ophthalmic solution) 0.01%

1. Medimedia Formulary Compass. March 2011.
2. LUMIGAN® 0.01% and 0.03% Prescribing Information.

Visit us at www.lumigan.com