Ophthalmology Times®
CUTTING-EDGE ADVANCEMENTS
March 15, 2014 VOL. 39, NO. 6
CLINICAL DIAGNOSIS | SURGERY | DRUG THERAPY

OphthalmologyTimes.com
FOLLOW US ONLINE:

Special Report

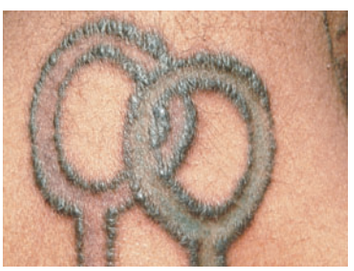
CXL OUTCOMES FAVORABLE OVER THE LONG TERM

ZURICH, SWITZERLAND :: **RESULTS FROM 5 YEARS** of follow-up support the efficacy and safety of corneal crosslinking (CXL) using the original Dresden protocol for the treatment of progressive keratectasia, said Theo Seiler, MD, PhD, who pioneered the procedure. Data show that CXL results in a significant keratometric flattening effect that is stable in most eyes, while causing minimal complications or significant best spectacle-corrected visual acuity loss, he explained.

*(See story on page 31 : **Crosslinking**)*

Clinical Diagnosis

BLACK INK MAY BE LINK IN TATTOO-RELATED UVEITIS



BALTIMORE :: **THOUGH TATTOO**-associated uveitis is rarely reported, the likelihood of its presence is more common than the literature would suggest, according to Trucian Ostheimer, MD. Only eight cases of patients with uveitis and associated changes in tattooed skin have been published in the English literature, noted Dr. Ostheimer, a second-year uveitis fellow, Wilmer Eye Institute, Johns Hopkins University, Baltimore. He has seen seven such patients since beginning his fellowship.

*(See story on page 18 : **Tattoo**)*

PEDIATRIC CATARACT takes individualized approach

Technique combines art with science to determine timing of IOL implantation, power selection

By Cheryl Guttman Krader;
Reviewed by M. Edward Wilson, MD

CHARLESTON, SC ::
"THE PRACTICE OF medicine is an art based on science," Sir William Osler once said.

"There is no place that is more true than in the refractive surgery we call pediatric cataract surgery," said M. Edward Wilson, MD, professor of ophthalmology and pediatrics, and the N. Edgar Miles Endowed Chair, Albert Florens Storm Eye Institute, Medical University of South Carolina, Charleston.

The modern era of pediatric cataract surgery began in 1976 when Marshall Parks, MD, began performing lensectomy and vitrectomy, according to Dr. Wilson.

Though the operation has stayed similar in many respects, it is now being approached as a refractive surgery. However, there is no nomogram for guiding the refractive management of the pediatric lens, he noted.

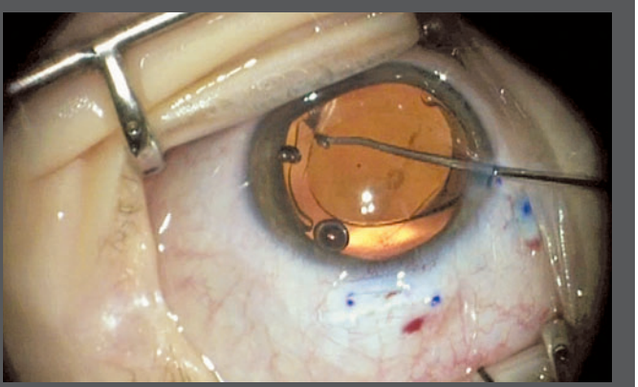
"We use a multifactorial approach to choose the timing of IOL implantation and power selection for each patient," Dr. Wilson said. "Then, we track axial eye growth, myopic shift, eye development, and IOP over the long term, and from the time of the initial surgery, we prepare the family for refractive surgeries with supplementary IOLs, IOL exchange, and laser vision correction procedures in the second and third decades."

Factors considered in the refractive management decision for the individual patient include age, visual acuity and prognosis, status of the other eye, interocular axial length difference (IALD), expected compliance with treatment (glasses, contact lenses, occlusion therapy), and what is thought would be an acceptable amount of late myopia for this patient.

Dr. Wilson noted that his institution has collected preoperative and serial postoperative data from more than 1,200 pediatric cataract and IOL surgeries and is mining this tremendous resource to understand factors influencing outcomes and ways to refine patient management. For example, IALD is considered as a factor for IOL power selection based on analyses that showed it both predicted and was modulated by visual acuity.[1,2]

*(Continues on page 24 : **Pediatric cataract**)*

CHILDHOOD PIGGYBACK IOLS



VIDEO A 10-month-old child undergoes implantation of a "permanent" single-piece acrylic IOL in the capsular bag followed by a "temporary" three-piece acrylic IOL in the ciliary sulcus. The aim is for emmetropia immediately after surgery. A planned explantation of the sulcus IOL will be done when the eye grows sufficiently to allow emmetropia with the capsular fixated IOL alone. This is predicted by serial biometry and retinoscopy.
To watch the video, go to **http://bit.ly/1eXVkU4.**
(Video courtesy of M. Edward Wilson, MD)

Smarter. Better. Faster.
LenSx® Laser. There's only one.

Delivering uncompromised precision and consistency, the LenSx® Laser has maintained its global leadership through continuous innovation in laser refractive cataract surgery. The LenSx® Laser leverages the power of The Cataract Refractive Suite by Alcon with tools designed to further streamline and improve the entire procedure. **LenSxLasers.com**

SMARTER
- Pre-population of patient and incision data
- Advanced pre-positioning of incisions and capsulotomy
- Platform design enables continued innovation and rapid enhancements

BETTER
- Customizable lens fragmentation for easy lens removal[2]
- SoftFit™ Patient Interface for easy docking, secure fixation and lower IOP[3]
- Compatible with the VERION™ Digital Marker for surgical planning and execution[1]

FASTER[2]
- Laser procedure efficiency with reduced programming and suction time
- Designed for maximum procedural flexibility and ease of patient flow and transfer
- Simpler, easier patient docking

1. Multicenter prospective clinical study. Alcon data on file.
2. Using current LenSx® Laser systems
3. Alcon data on file.

Alcon®
a Novartis company

For important safety information, please see adjacent page.

 10/13 LSX13286JAD

LenSx® LASER
Designed for Growth™
THE CATARACT REFRACTIVE SUITE BY ALCON

LenSx® LASER

Designed for Growth™

VERION™

IMAGE GUIDED SYSTEM

IMPORTANT SAFETY INFORMATION

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.

INDICATION: 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 multi-plane arc cuts/incisions in the cornea, each of which may be performed either individually or consecutively during the same procedure.

RESTRICTIONS:

- Patients must be able to lie flat and motionless in a supine position.
- Patient must be able to understand and give an informed consent.
- Patients must be able to tolerate local or topical anesthesia.
- Patients with elevated IOP should use topical steroids only under close medical supervision.

Contraindications:

- Corneal disease that precludes applanation of the cornea or transmission of laser light at 1030 nm wavelength
- Descemetocele with impending corneal rupture
- Presence of blood or other material in the anterior chamber
- Poorly dilating pupil, such that the iris is not peripheral to the intended diameter for the capsulotomy
- Conditions which would cause inadequate clearance between the intended capsulotomy depth and the endothelium (applicable to capsulotomy only)
- Previous corneal incisions that might provide a potential space into which the gas produced by the procedure can escape
- Corneal thickness requirements that are beyond the range of the system
- Corneal opacity that would interfere with the laser beam
- Hypotony or the presence of a corneal implant
- Residual, recurrent, active ocular or eyelid disease, including any corneal abnormality (for example, recurrent corneal erosion, severe basement membrane disease)
- History of lens or zonular instability
- Any contraindication to cataract or keratoplasty
- This device is not intended for use in pediatric surgery.

WARNINGS: The LenSx® Laser System should only be operated by a physician trained in its use.
The LenSx® Laser delivery system employs one sterile disposable LenSx® Laser Patient Interface consisting of an applanation lens and suction ring. The Patient Interface is intended for single use only. The disposables used in conjunction with ALCON® instrument products constitute a complete surgical system. Use of disposables other than those manufactured by Alcon may affect system performance and create potential hazards.
The physician should base patient selection criteria on professional experience, published literature, and educational courses. Adult patients should be scheduled to undergo cataract extraction.

PRECAUTIONS:

- Do not use cell phones or pagers of any kind in the same room as the LenSx® Laser.
- Discard used Patient Interfaces as medical waste.

AES/COMPLICATIONS:

- Capsulotomy, phacofragmentation, or cut or incision decentration
- Incomplete or interrupted capsulotomy, fragmentation, or corneal incision procedure
- Capsular tear
- Corneal abrasion or defect
- Pain
- Infection
- Bleeding
- Damage to intraocular structures
- Anterior chamber fluid leakage, anterior chamber collapse
- Elevated pressure to the eye

ATTENTION: Refer to the LenSx® Laser Operator's Manual for a complete listing of indications, warnings and precautions.

IMPORTANT SAFETY INFORMATION FOR THE VERION™ REFERENCE UNIT AND VERION™ DIGITAL MARKER

CAUTION: Federal (USA) law restricts this device to sale by, or on the order of, a physician.

INTENDED USES: The VERION™ Reference Unit is a preoperative measurement device that captures and utilizes a high-resolution reference image of a patient's eye in order to determine the radii and corneal curvature of steep and flat axes, limbal position and diameter, pupil position and diameter, and corneal reflex position. In addition, the VERION™ Reference Unit provides preoperative surgical planning functions that utilize the reference image and preoperative measurements to assist with planning cataract surgical procedures, including the number and location of incisions and the appropriate intraocular lens using existing formulas. The VERION™ Reference Unit also supports the export of the high-resolution reference image, preoperative measurement data, and surgical plans for use with the VERION™ Digital Marker and other compatible devices through the use of a USB memory stick.

The VERION™ Digital Marker links to compatible surgical microscopes to display concurrently the reference and microscope images, allowing the surgeon to account for lateral and rotational eye movements. In addition, the planned capsulorhexis position and radius, IOL positioning, and implantation axis from the VERION™ Reference Unit surgical plan can be overlaid on a computer screen or the physician's microscope view.

CONTRAINDICATIONS: The following conditions may affect the accuracy of surgical plans prepared with the VERION™ Reference Unit: a pseudophakic eye, eye fixation problems, a non-intact cornea, or an irregular cornea. In addition, patients should refrain from wearing contact lenses during the reference measurement as this may interfere with the accuracy of the measurements.

Only trained personnel familiar with the process of IOL power calculation and astigmatism correction planning should use the VERION™ Reference Unit. Poor quality or inadequate biometer measurements will affect the accuracy of surgical plans prepared with the VERION™ Reference Unit.

The following contraindications may affect the proper functioning of the VERION™ Digital Marker: changes in a patient's eye between preoperative measurement and surgery, an irregular elliptic limbus (e.g., due to eye fixation during surgery, and bleeding or bloated conjunctiva due to anesthesia). In addition, the use of eye drops that constrict sclera vessels before or during surgery should be avoided.

WARNINGS: Only properly trained personnel should operate the VERION™ Reference Unit and VERION™ Digital Marker.

Only use the provided medical power supplies and data communication cable. The power supplies for the VERION™ Reference Unit and the VERION™ Digital Marker must be uninterruptible. Do not use these devices in combination with an extension cord. Do not cover any of the component devices while turned on.

Only use a VERION™ USB stick to transfer data. The VERION™ USB stick should only be connected to the VERION™ Reference Unit, the VERION™ Digital Marker, and other compatible devices. Do not disconnect the VERION™ USB stick from the VERION™ Reference Unit during shutdown of the system.

The VERION™ Reference Unit uses infrared light. Unless necessary, medical personnel and patients should avoid direct eye exposure to the emitted or reflected beam.

PRECAUTIONS: To ensure the accuracy of VERION™ Reference Unit measurements, device calibration and the reference measurement should be conducted in dimmed ambient light conditions. Only use the VERION™ Digital Marker in conjunction with compatible surgical microscopes.

ATTENTION: Refer to the user manuals for the VERION™ Reference Unit and the VERION™ Digital Marker for a complete description of proper use and maintenance of these devices, as well as a complete list of contraindications, warnings and precautions.

Alcon®

a Novartis company

Not to wax poetic . . .

What this year's winter and health-care reform have in common

By Peter J. McDonnell, MD

director of the Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore, and chief medical editor of *Ophthalmology Times*.

He can be reached at 727 Maumenee Building
600 N. Wolfe St. Baltimore, MD 21287-9278
Phone: 443/287-1511 Fax: 443/287-1514
E-mail: pmcdonn1@jhmi.edu

"Thus having prepared their buds
against a sure winter
the wise trees
stand sleeping in the cold."
—William Carlos Williams

THANKS TO THE POLAR vortex, this has been a harsh—some might say cruel—winter in my little town that sits along the border between North and South.

Thankfully, we have the poetry of William Carlos Williams to help get us through these frigid days—reminding us that winter is a time of peace, and that the wise trees of Baltimore have prepared their buds and will soon bring forth a beautiful and fragrant springtime.

Williams was a physician who practiced in Paterson, NJ. Although he was only a part-time poet, he won the first National Book Award for Poetry in 1950, was posthumously awarded the Pulitzer Prize in 1963, and—like all the true greats—was inducted into the New Jersey Hall of Fame in 2009.

Although many of us physicians might view his two careers as not an obvious fit—with most medical students these days having been science majors in school—Williams considered the pairing to be a natural one.

He said: "When they ask me, as of late they frequently do, how I have for so many years continued an equal interest in medicine and the poem, I reply that they amount for me to nearly the same thing."

This feeling that medicine and the poem are the same is reflected in these lines by Williams, in which we can imagine that he is reflecting equally on the effect of winter's arrival on the leaves and on the effect of advancing age on an elderly patient who is encountering the frailty that comes in the winter of life:

"Some leaves hang late, some fall
before the first frost—so goes
the tale of winter branches and old bones."

A READER'S SUGGESTION

My alleged friend in California, a loyal *Ophthalmology Times* reader, e-mailed me recently, clearly expressing her *Schadenfreude* upon the latest snowstorm to blanket my part of the country.

Her message asked me to perform a certain task:

"I hope (if you haven't done so yet) you provide a provocative editorial comparing the polar vortex akin to health-care reform—or something along that line. . . . :-)"

Normally I don't take such suggestions seriously. Plus, at the time this is written we are still in winter, a time of peace and rest, and not the time to provoke my dear readers. But it is heartless to ignore e-mails that end with an emoticon.

So, I asked another friend for some insights about our vigorous winter and health-care reform.

"What is the difference between our winter weather and health-care reform?" I asked.

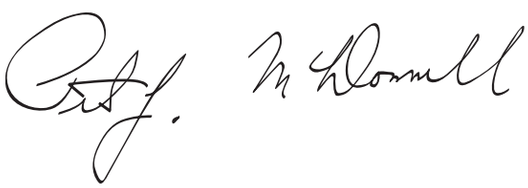
"That's easy," she replied. "Some people can actually predict what will happen with the weather."

"I think you are joking," I said. "What I want to know is, what distinguishes the polar vortex from 'ObamaCare'?"

"That's easy. One is making people miserable and confused, from Chicago to Atlanta, and according to economists, is hurting the economy and our industries. The other is cold weather."

"No, I mean the *storms*!" I said.

"Well," responded my friend, "William Carlos Williams wrote that 'Time is a storm in which we are all lost. Only inside the convolutions of the storm itself shall we find our directions.'" ■



Ophthalmology Times
MARCH 15, 2014 ■ VOL. 39, NO. 6

Official publication sponsor of INTERNATIONAL VISION EXPO & CONFERENCE NEW YORK INTERNATIONAL VISION EXPO & CONFERENCE LAS VEGAS

How to Contact Ophthalmology Times

Editorial
24950 Country Club Blvd.,
Suite 200
North Olmsted, OH 44070-5351
440/243-8100
FAX: 440/756-5227

Subscription Services
Toll-Free: 888/527-7008 or
218/740-6477
FAX: 218/740-6417

Advertising
485 Route 1 South
Building F, Suite 210,
Iselin, NJ 08830-3009
732/596-0276
FAX: 732/596-0003

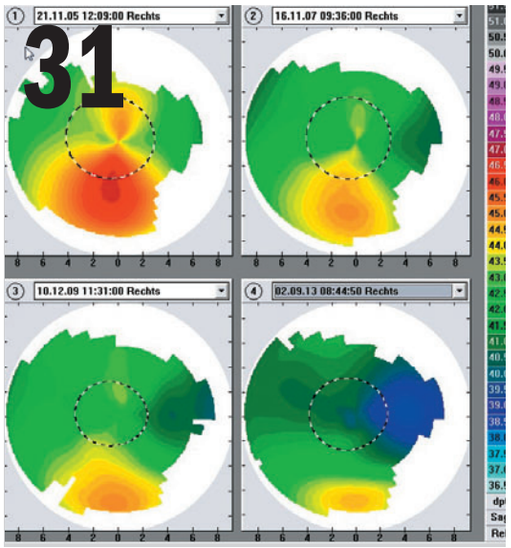
Production
131 W. First St.
Duluth, MN 55802-2065
800/346-0085
FAX: 218/740-7223,
218/740-6576

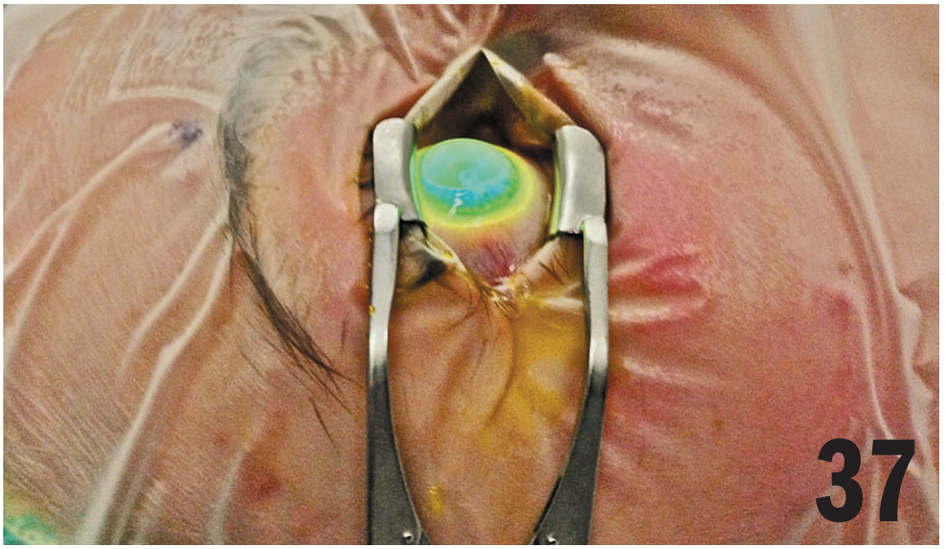
Ophthalmology Times *Mission Statement*

Ophthalmology Times is a physician-driven media brand that presents cutting-edge advancements and analysis from around the world in surgery, drug therapy, technology, and clinical diagnosis to elevate the delivery of progressive eye health from physician to patient.

Ophthalmology Times' vision is to be the leading content resource for ophthalmologists.

Through its multifaceted content channels, *Ophthalmology Times* will assist physicians with the tools and knowledge necessary to provide advanced quality patient care in the global world of medicine.





Special Report on page 31

ADVANCEMENTS IN SURGICAL & CLINICAL SOLUTIONS FOR

CORNEAL DISEASE

Surgery

8 ORTHOPTISTS PLAY ROLE IN CRANIOFACIAL SYNDROME THERAPY
Skills valuable with diagnosis

11 ACHIEVING SUCCESS IN YOUTHS WITH HIGH AC/A
Methods include varying surgical strategy

12 FLAP CREATION EVOLVES WITH TECHNOLOGY
Safety, efficacy, patient preference data all favor femtosecond laser

16 TECHNIQUES, TIPS FOR CORTEX REMOVAL
Plays role in pediatric cataract surgery

Clinical Diagnosis

18 BLACK INK MAY BE CULPRIT IN TATTOO-RELATED UVEITIS
Findings may represent a forme fruste of sarcoidosis

21 NUTRITIONAL THERAPY MAY FUEL AMD OUTCOMES
AREDS supplementation beneficial, genetic risk can help with best approach

27 GLP-1 TARGETED THERAPY AND TYPE 2 DIABETES
Exenatide important adjunctive therapy to prevent cardiovascular side effects

28 TRACING OCULAR MANIFESTATION OF MUMPS
History shows virus can affect lacrimal gland, cause dacryoadenitis

InDispensable

41 FRAME BOARD MANAGEMENT STRATEGIES
Careful planning is the key to a strong dispensary business

44 OPENING DISPENSARY SALE
What opticians say or do not say can hurt business

Practice Management

46 SECURITY RISK ANALYSIS
How to protect patient records and remain HIPAA compliant

49 SETTING SALARIES, DEALING WITH RAISE REQUESTS
A look into how to handle personnel matters

In Every Issue

4 EDITORIAL
51 MARKETPLACE

Knowing the osmolarity of your patient's tears is essential

Visit us at ASCRS Booth 371 to learn more about
using TearLab to diagnose and manage Dry Eye Disease.

TearLab™

www.tearlab.com

CLIA WAIVED - Reimbursed at $45.08/patient

by Medicare under the Laboratory Fee Schedule - CPT 83861 QW*

CE | FDA 510(k) Cleared (k083184) | CPT is a copyright and registered trademark of the American Medical Association (AMA). *Please consult Medicare payment rules for your area; this is not an official guide on all matters pertaining to reimbursement. | 920132 REV C

How orthoptists play a key role in craniofacial syndrome therapy

Skills valuable with diagnosis, management of patients who have amblyopia, strabismus

By Lynda Charters; *Reviewed by Bonita Schweinler, CO, COMT*

TAKE-HOME

- ***Orthoptists' skills can be extremely helpful in the management of patients with craniofacial syndromes, since large percentages of patients afflicted by various syndromes have amblyopia or strabismus.***

BOISE, ID ::

Orthoptists can be extremely helpful in the management of children with craniofacial syndromes. Large percentages of patients who are afflicted by various syndromes have amblyopia or strabismus and it is for these patients that orthoptists' skills are so valuable.

Bonita Schweinler, CO, COMT—an orthoptist at St. Luke's Children's Hospital, Boise, ID—described the most frequently seen craniofacial syndromes and their manifestations (See sidebar "Craniofacial syndromes").

THE ROLE OF ORTHOPTISTS

"In children with these syndromes, the common causes of visual problems are corneal abnormalities, ocular adnexa abnormalities, amblyopia, strabismus, and optic neuropathy," Schweinler said.


Schweinler

Corneal abnormalities include corneal exposure resulting from neurotrophic keratitis, eyelid malposition, and eyelid retraction.

Ocular adnexa abnormalities are hypertelorism, telecanthus, ptosis, proptosis, corneal exposure, and epiphora. Optic neuropathy can occur with papilledema and optic nerve atrophy.

By far, the most common disorders are amblyopia and strabismus, she noted.

Amblyopia affects a high percentage of patients. A study by Khan and associates (*Br J Ophthalmol.* 2003;87:999-1003) of 141 patients found that 52% of eyes had a Snellen visual acuity of 20/40 or worse.

About 40% of patients had a visual acuity of 20/40 or worse in the better eye and 64.6% had 20/40 or worse in at least on eye.

"This study indicated that there is a huge chance for decreased vision in this population," Schweinler said.

The same study also found that about 40% of patients had 1 D or more of astigmatism in either eye, and 64% of them had oblique astigmatism.

Anisometropia is a factor in a substantial number of patients: 58% of those with Crouzon syndrome and 33% of Apert syndrome, she explained

Deprivational amblyopia can result from corneal scarring and ptosis.

Strabismus develops in a large number of these patients—i.e., in 94% of those with Apert syndrome, 82% in Crouzon syndrome, 56% of patients with craniosynostosis, and 29% with Goldenhar syndrome.

Khan et al. also reported that the strabismus was exotropic in 38% of patients, esotropic in 32%, straight in 24%, and vertical only in 6%, the last of which could have been higher except for the lack of patient cooperation, according to Schweinler.

In patients with amblyopia and strabismus, orthoptists can play a big role in managing these patients, Schweinler said.

UNIQUE SKILLS

During the visual examination, orthoptists have special skills to examine patients with a variety of disabilities.

"Orthoptists are taught unique skills for diagnostic testing and are trained to evaluate and diagnose disorders of binocular vision and ocular motility," she said.

Orthoptists follow patients with amblyopia closely in clinic and use patching and atropine to manage the patients.

Their refractometry skills become very useful by conducting the ocular motility examination and diagnosing exotropia, esotropia, inferior oblique overaction, superior oblique underaction, and identify V patterns in patients with exotropia, Schweinler added.

The primary message is that orthoptists can be extremely helpful with patients with craniofacial syndromes.

"Orthoptists can help by being creative, by being patient, and by being ready to perform a great examination to gain the maximal ophthalmic information and optimize the treatment to achieve better vision and straight eyes," Schweinler concluded. ■

Craniofacial syndromes

Craniosynostosis—premature closure of one or more cranial sutures—is the most common human congenital skull defect.

Apert syndrome is characterized by a high full forehead, small nose, flat faces, shallow orbits, hypopituitarism, strabismus, down-slanting palpebral fissures, varying degrees of syndactyly, and dental anomalies.

Crouzon syndrome is often characterized by ocular proptosis due to shallow orbits, exposure keratitis, optic atrophy, keratoconus, iris colobomas, and strabismus.

Patients with Pfeiffer syndrome have brachycephaly, a high forehead, hyperpituitarism, small nose with a low nasal bridge, syndactyly, and normal to near-normal intelligence.

Saethre-Chotzen syndrome features brachycephaly, a high flat forehead, facial asymmetry, deviated septum, shallow orbits, ptosis, lacrimal duct abnormalities, and strabismus.

Treacher-Collins syndrome is characterized by mandibulofacial dystosis, micromasia, absent cheekbone, eyelid colobomas, hearing loss, and down-slanting palpebral fissures.

Goldenhar syndrome shows limbal dermoids, Duane's syndrome, preauricular skin tag, strabismus, and cleft palate and lip. ■

BONITA SCHWEINLER, CO, COMT
E: *schweinb@slhs.org*
Schweinler has no financial interest in any aspect of this report.

ThromboGenics®

JETREA™
(ocriplasmin)
Intravitreal Injection, 2.5 mg/mL

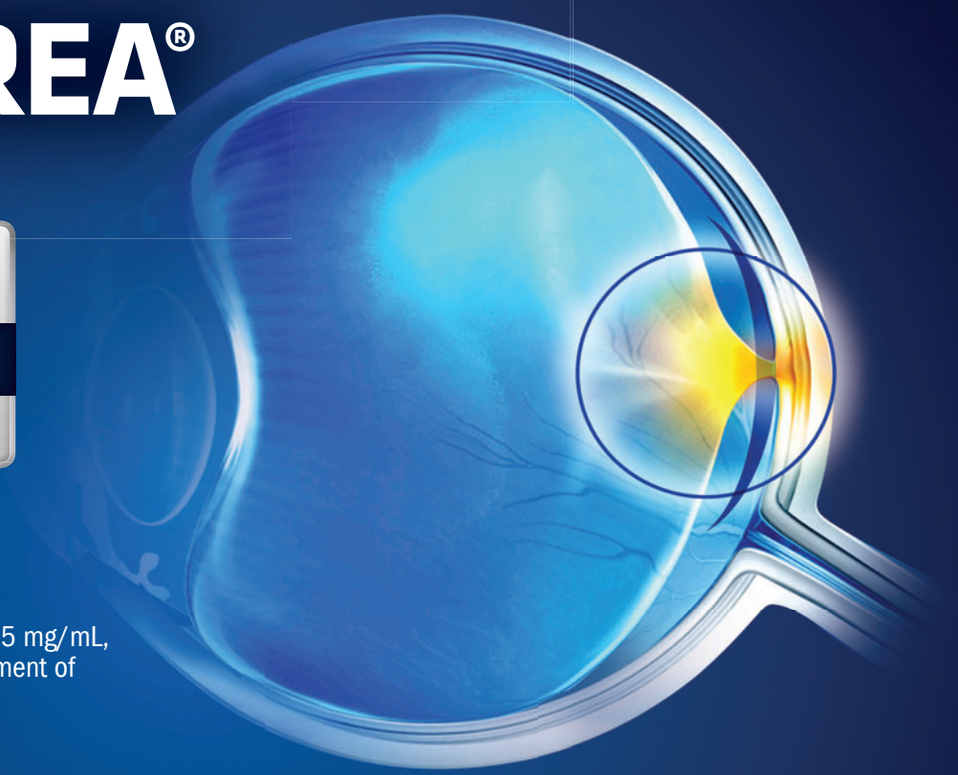
The FIRST AND ONLY pharmacologic treatment for symptomatic VMA

TAKE IMMEDIATE ACTION WITH JETREA®

Permanent J-Code for JETREA®
NOW AVAILABLE

J7316

Effective January 1, 2014



Indication

JETREA® (ocriplasmin) Intravitreal Injection, 2.5 mg/mL, is a proteolytic enzyme indicated for the treatment of symptomatic vitreomacular adhesion (VMA).

IMPORTANT SAFETY INFORMATION

Warnings and Precautions

- A decrease of ≥3 lines of best-corrected visual acuity (BCVA) was experienced by 5.6% of patients treated with JETREA® and 3.2% of patients treated with vehicle in the controlled trials. The majority of these decreases in vision were due to progression of the condition with traction and many required surgical intervention. Patients should be monitored appropriately.
- Intravitreal injections are associated with intraocular inflammation/infection, intraocular hemorrhage, and increased intraocular pressure (IOP). Patients should be monitored and instructed to report any symptoms without delay. In the controlled trials, intraocular inflammation occurred in 7.1% of patients injected with JETREA® vs 3.7% of patients injected with vehicle. Most of the post-injection intraocular inflammation events were mild and transient. If the contralateral eye requires treatment with JETREA®, it is not recommended within 7 days of the initial injection in order to monitor the post-injection course in the injected eye.
- Potential for lens subluxation.
- In the controlled trials, the incidence of retinal detachment was 0.9% in the JETREA® group and 1.6% in the vehicle group, while the incidence of retinal tear (without detachment) was 1.1% in the JETREA® group and 2.7% in the vehicle group. Most of these events occurred during or after vitrectomy in both groups.
- Dyschromatopsia (generally described as yellowish vision) was reported in 2% of all patients injected with JETREA®. In approximately half of these dyschromatopsia cases, there were also electroretinographic (ERG) changes reported (a- and b-wave amplitude decrease).

Adverse Reactions

- The most commonly reported reactions (≥5%) in patients treated with JETREA® were vitreous floaters, conjunctival hemorrhage, eye pain, photopsia, blurred vision, macular hole, reduced visual acuity, visual impairment, and retinal edema.

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

VISIT JETREACARE.COM OR SCAN QR CODE FOR REIMBURSEMENT AND ORDERING INFORMATION

01/14 OCRVMA0133 R1

JETREA.COM

JETREA™
(ocriplasmin)
Intravitreal Injection, 2.5 mg/mL

BRIEF SUMMARY OF FULL PRESCRIBING INFORMATION

Please see the JETREA® package insert for full Prescribing Information.

1 INDICATIONS AND USAGE
JETREA is a proteolytic enzyme indicated for the treatment of symptomatic vitreomacular adhesion.

2 DOSAGE AND ADMINISTRATION
2.1 General Dosing Information
Must be diluted before use. For single-use ophthalmic intravitreal injection only. JETREA must only be administered by a qualified physician.

2.2 Dosing
The recommended dose is 0.125 mg (0.1 mL of the diluted solution) administered by intravitreal injection to the affected eye once as a single dose.

2.3 Preparation for Administration
Remove the vial (2.5 mg/mL corresponding to 0.5 mg ocriplasmin) from the freezer and allow to thaw at room temperature (within a few minutes). Once completely thawed, remove the protective polypropylene flip-off cap from the vial. The top of the vial should be disinfected with an alcohol wipe. Using aseptic technique, add 0.2 mL of 0.9% w/v Sodium Chloride Injection, USP (sterile, preservative-free) into the JETREA vial and gently swirl the vial until the solutions are mixed.

Visually inspect the vial for particulate matter. Only a clear, colorless solution without visible particles should be used. Using aseptic technique, withdraw all of the diluted solution using a sterile #19 gauge needle (slightly tilt the vial to ease withdrawal) and discard the needle after withdrawal of the vial contents. Do not use this needle for the intravitreal injection.

Replace the needle with a sterile #30 gauge needle, carefully expel the air bubbles and excess drug from the syringe and adjust the dose to the 0.1 mL mark on the syringe (corresponding to 0.125 mg ocriplasmin). THE SOLUTION SHOULD BE USED IMMEDIATELY AS IT CONTAINS NO PRESERVATIVES. Discard the vial and any unused portion of the diluted solution after single use.

2.4 Administration and Monitoring
The intravitreal injection procedure should be carried out under controlled aseptic conditions, which include the use of sterile gloves, a sterile drape and a sterile eyelid speculum (or equivalent). Adequate anesthesia and a broad spectrum microbiocide should be administered according to standard medical practice.

The injection needle should be inserted 3.5 - 4.0 mm posterior to the limbus aiming towards the center of the vitreous cavity, avoiding the horizontal meridian. The injection volume of 0.1 mL is then delivered into the mid-vitreous.

Immediately following the intravitreal injection, patients should be monitored for elevation in intraocular pressure. Appropriate monitoring may consist of a check for perfusion of the optic nerve head or tonometry. If required, a sterile paracentesis needle should be available.

Following intravitreal injection, patients should be instructed to report any symptoms suggestive of endophthalmitis or retinal detachment (e.g., eye pain, redness of the eye, photophobia, blurred or decreased vision) without delay *[see Patient Counseling Information]*.

Each vial should only be used to provide a single injection for the treatment of a single eye. If the contralateral eye requires treatment, a new vial should be used and the sterile field, syringe, gloves, drapes, eyelid speculum, and injection needles should be changed before JETREA is administered to the other eye, however, treatment with JETREA in the other eye is not recommended within 7 days of the initial injection in order to monitor the post-injection course including the potential for decreased vision in the injected eye.

Repeated administration of JETREA in the same eye is not recommended *[see Nonclinical Toxicology]*.

After injection, any unused product must be discarded.

No special dosage modification is required for any of the populations that have been studied (e.g. gender, elderly).

3 DOSAGE FORMS AND STRENGTHS
Single-use glass vial containing JETREA 0.5 mg in 0.2 mL solution for intravitreal injection (2.5 mg/mL).

4 CONTRAINDICATIONS
None

5 WARNINGS AND PRECAUTIONS
5.1 Decreased Vision
A decrease of ≥ 3 line of best corrected visual acuity (BCVA) was experienced by 5.6% of patients treated with JETREA and 3.2% of patients treated with vehicle in the controlled trials *[see Clinical Studies]*.

The majority of these decreases in vision were due to progression of the condition with traction and many required surgical intervention. Patients should be monitored appropriately *[see Dosage and Administration]*.

5.2 Intravitreal Injection Procedure Associated Effects
Intravitreal injections are associated with intraocular inflammation / infection, intraocular hemorrhage and increased intraocular pressure (IOP). In the controlled trials, intraocular inflammation occurred in 7.1% of patients injected with JETREA vs. 3.7% of patients injected with vehicle. Most of the post-injection intraocular inflammation events were mild and transient. Intraocular hemorrhage occurred in 2.4% vs. 3.7% of patients injected with JETREA vs. vehicle, respectively. Increased intraocular pressure occurred in 4.1% vs. 5.3% of patients injected with JETREA vs. vehicle, respectively.

5.3 Potential for Lens Subluxation
One case of lens subluxation was reported in a patient who received an intravitreal injection of 0.175 mg (1.4 times higher than the recommended dose). Lens subluxation was observed in three animal species (monkey, rabbit, minipig) following a single intravitreal injection that achieved vitreous concentrations of ocriplasmin 1.4 times higher than achieved with the recommended treatment dose. Administration of a second intravitreal dose in monkeys, 28 days apart, produced lens subluxation in 100% of the treated eyes *[see Nonclinical Toxicology]*.

5.4 Retinal Breaks
In the controlled trials, the incidence of retinal detachment was 0.9% in the JETREA group and 1.6% in the vehicle group, while the incidence of retinal tear (without detachment) was 1.1% in the JETREA group and 2.7% in the vehicle group. Most of these events occurred during or after vitrectomy in both groups. The incidence of retinal detachment that occurred pre-vitrectomy was 0.4% in the JETREA group and none in the vehicle group, while the incidence of retinal tear (without detachment) that occurred pre-vitrectomy was none in the JETREA group and 0.5% in the vehicle group.

5.5 Dyschromatopsia
Dyschromatopsia (generally described as yellowish vision) was reported in 2% of all patients injected with JETREA. In approximately half of these dyschromatopsia cases there were also electroretinographic (ERG) changes reported (a- and b-wave amplitude decrease).

6 ADVERSE REACTIONS
The following adverse reactions are described below and elsewhere in the labeling:

- Decreased Vision *[see Warnings and Precautions]*
- Intravitreal Injection Procedure Associated Effects *[see Warnings and Precautions and Dosage and Administration]*
- Potential for Lens Subluxation *[see Warnings and Precautions]*
- Retinal Breaks *[see Warnings and Precautions and Dosage and Administration]*

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

Approximately 800 patients have been treated with an intravitreal injection of JETREA. Of these, 465 patients received an intravitreal injection of ocriplasmin 0.125 mg (187 patients received vehicle) in the 2 vehicle-controlled studies (Study 1 and Study 2).

The most common adverse reactions (incidence 5% - 20% listed in descending order of frequency) in the vehicle-controlled clinical studies were: vitreous floaters, conjunctival hemorrhage, eye pain, photopsia, blurred vision, macular hole, reduced visual acuity, visual impairment, and retinal edema.

Less common adverse reactions observed in the studies at a frequency of 2% - < 5% in patients treated with JETREA included macular edema, increased intraocular pressure, anterior chamber cell, photophobia, vitreous detachment, ocular discomfort, iritis, cataract, dry eye, metamorphopsia, conjunctival hyperemia, and retinal degeneration.

Dyschromatopsia was reported in 2% of patients injected with JETREA, with the majority of cases reported from two uncontrolled clinical studies. In approximately half of these dyschromatopsia cases there were also electroretinographic (ERG) changes reported (a- and b-wave amplitude decrease).

6.2 Immunogenicity
As with all therapeutic proteins, there is potential for immunogenicity. Immunogenicity for this product has not been evaluated.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy: Teratogenic Effects
Pregnancy Category C. Animal reproduction studies have not been conducted with ocriplasmin. There are no adequate and well-controlled studies of ocriplasmin in pregnant women. It is not known whether ocriplasmin can cause fetal harm when administered to a pregnant woman or can affect reproduction capacity. The systemic exposure to ocriplasmin is expected to be low after intravitreal injection of a single 0.125 mg dose. Assuming 100% systemic absorption (and a plasma volume of 2700 mL), the estimated plasma concentration is 46 ng/mL. JETREA should be given to a pregnant woman only if clearly needed.

8.3 Nursing Mothers
It is not known whether ocriplasmin is excreted in human milk. Because many drugs are excreted in human milk, and because the potential for absorption and harm to infant growth and development exists, caution should be exercised when JETREA is administered to a nursing woman.

8.4 Pediatric Use
Safety and effectiveness in pediatric patients have not been established.

8.5 Geriatric Use
In the clinical studies, 384 and 145 patients were ≥ 65 years and of these 192 and 73 patients were ≥ 75 years in the JETREA and vehicle groups respectively. No significant differences in efficacy or safety were seen with increasing age in these studies.

10 OVERDOSAGE
The clinical data on the effects of JETREA overdose are limited. One case of accidental overdose of 0.250 mg ocriplasmin (twice the recommended dose) was reported to be associated with inflammation and a decrease in visual acuity.

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility
No carcinogenicity, mutagenicity or reproductive and developmental toxicity studies were conducted with ocriplasmin.

13.2 Animal Toxicology and/or Pharmacology
The ocular toxicity of ocriplasmin after a single intravitreal dose has been evaluated in rabbits, monkeys and minipigs. Ocriplasmin induced an inflammatory response and transient ERG changes in rabbits and monkeys, which tended to resolve over time. Lens subluxation was observed in the 3 species at ocriplasmin concentrations in the vitreous at or above 41 mcg/mL, a concentration 1.4-fold above the intended clinical concentration in the vitreous of 29 mcg/mL. Intraocular hemorrhage was observed in rabbits and monkeys.

A second intravitreal administration of ocriplasmin (28 days apart) in monkeys at doses of 75 mcg/eye (41 mcg/mL vitreous) or 125 mcg/eye (68 mcg/mL vitreous) was associated with lens subluxation in all ocriplasmin treated eyes. Sustained increases in IOP occurred in two animals with lens subluxation. Microscopic findings in the eye included vitreous liquefaction, degeneration/disruption of the hyaloideo-capsular ligament (with loss of ciliary zonular fibers), lens degeneration, mononuclear cell infiltration of the vitreous, and vacuolation of the retinal inner nuclear cell layer. These doses are 1.4-fold and 2.3-fold the intended clinical concentration in the vitreous of 29 mcg/mL, respectively.

14 CLINICAL STUDIES
The efficacy and safety of JETREA was demonstrated in two multicenter, randomized, double masked, vehicle-controlled, 6 month studies in patients with symptomatic vitreomacular adhesion (VMA). A total of 652 patients (JETREA 464, vehicle 188) were randomized in these 2 studies. Randomization was 2:1 (JETREA:vehicle) in Study 1 and 3:1 in Study 2.

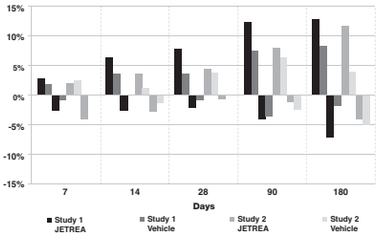
Patients were treated with a single injection of JETREA or vehicle. In both of the studies, the proportion of patients who achieved VMA resolution at Day 28 (i.e., achieved success on the primary endpoint) was significantly higher in the ocriplasmin group compared with the vehicle group through Month 6.

The number of patients with at least 3 lines increase in visual acuity was numerically higher in the ocriplasmin group compared to vehicle in both trials, however, the number of patients with at least a 3 lines decrease in visual acuity was also higher in the ocriplasmin group in one of the studies (Table 1 and Figure 1).

Table 1: Categorical Change from Baseline in BCVA at Month 6, Irrespective of Vitrectomy (Study 1 and Study 2)

Study 1			
	JETREA	Vehicle	Difference
	N=219	N=107	(95% CI)
≥ 3 line Improvement in BCVA			
Month 6	28 (12.8%)	9 (8.4%)	4.4 (-2.5, 11.2)
> 3 line Worsening in BCVA			
Month 6	16 (7.3%)	2 (1.9%)	5.4 (1.1, 9.7)
Study 2			
	JETREA	Vehicle	Difference
	N=245	N=81	(95% CI)
≥ 3 line Improvement in BCVA			
Month 6	29 (11.8%)	3 (3.8%)	8.1 (2.3, 13.9)
> 3 line Worsening in BCVA			
Month 6	10 (4.1%)	4 (5.0%)	-0.9 (-6.3,4.5)

Figure 1: Percentage of Patients with Gain or Loss of ≥ 3 Lines of BCVA at Protocol-Specified Visits



16 HOW SUPPLIED/STORAGE AND HANDLING
Each vial of JETREA contains 0.5 mg ocriplasmin in 0.2 mL citric-buffered solution (2.5 mg/mL). JETREA is supplied in a 2 mL glass vial with a latex free rubber stopper. Vials are for single use only.

Storage
Store frozen at or below -4°F (-20°C). Protect the vials from light by storing in the original package until time of use.

17 PATIENT COUNSELING INFORMATION
In the days following JETREA administration, patients are at risk of developing intraocular inflammation/ infection. Advise patients to seek immediate care from an ophthalmologist if the eye becomes red, sensitive to light, painful, or develops a change in vision *[see Warnings and Precautions]*.

Patients may experience temporary visual impairment after receiving an intravitreal injection of JETREA *[see Warnings and Precautions]*. Advise patients to not drive or operate heavy machinery until this visual impairment has resolved. If visual impairment persists or decreases further, advise patients to seek care from an ophthalmologist.

Manufactured for:
ThromboGenics, Inc.
101 Wood Avenue South, 6th Floor
Iselin, NJ 08830

U.S. License Number: 1866

Version 1.0
Initial U.S. Approval: 2012
ThromboGenics U.S. patents: 7,445,775; 7,547,435; 7,914,783 and other pending patents.

05/13 OCRVMA0072 PI G

Varying surgical strategy achieves success in youths with high AC/A ratios

For patients who remained aligned at distance, 99% outgrew need for bifocals by age 18

By Lynda Charters; *Reviewed by Burton J. Kushner, MD*

TAKE-HOME

- ***Alignment at distance and patient age are factors contributing to treatment approaches for juvenile patients with high accommodative convergence-to-accommodation ratios.***

MADISON, WI ::

ADOLESCENTS WITH HIGH accommodative convergence-to-accommodation (AC/A) ratios should be treated differently based on whether the patient is aligned at distance and depending on patient age.

"If the patient is aligned in the distance, my experience influences my recommendations," explained Burton J. Kushner, MD. He is the John W. and Helen Doolittle Professor, Department of Ophthalmology and Visual Science, University of Wisconsin School of Medicine and Public Health, Madison, where he is the director of the Pediatric Ophthalmology and Adult Strabismus Clinic.

Dr. Kushner

A review of 374 patients with high AC/A ratio esotropia by Dr. Kushner revealed that 99% of patients who maintained good distance alignment outgrew the need for bifocals by age 18.

A high AC/A ratio is one in which the near esotropia exceeds the distance esotropia by 10 prism diopters (PD) or more and is approximately equal to the distance esotropia with added plus lenses at near.

Dr. Kushner dichotomizes his treatments based on two different parameters. He uses a different approach if optical correction achieves satisfactory alignment at distance than if the distance alignment is unsatisfactory.

For his purposes, he defined satisfactory alignment as being within 8 PD of straight. He also adjusts his treatment depending on the patient age—i.e., a young teenager at age 13 versus an older teenager at age 18.

PATIENTS NOT ALIGNED AT DISTANCE

In this patient group, most surgeons agree that surgery is a necessary option, Dr. Kushner explained.

Common treatment options are:

- **Recessions of the medial rectus (MR) muscle for the near angle with or without prism adaptation.**
- **MR recession with posterior fixation.**
- **MR recession for the accommodative component, e.g., the angle without glasses.**
- **MR recession for the distance deviation with 1 mm added to both of the MR recessions as was advocated by Marshall Parks, MD.**

WHEN MR RECESSION IS RECOMMENDED

MR recession with posterior fixation works, however, the procedure is less predictable and less reversible compared with other approaches, according to Dr. Kushner.

"Importantly, it is not predictable and easily reversible and its mechanism of action is unclear," he said.

Dr. Kushner said he also does not recommend MR recession for the angle without glasses, because this approach is not physiologic, and no long-term studies have proven the efficacy and stability of the procedure. Regarding MR recession for distance deviation with 1 mm added, he reported a substantial number of undercorrections in his experience and many patients remained in bifocals.

He said he prefers to perform MR recessions that target the near angle when patients are wearing their full cyclolegic distance correction. In 22 patients in whom Dr. Kushner used this approach, he found that after 15 years of follow-up, the results were good and the patients were stable.

Dr. Kushner's total experience includes 234 patients, 53 of whom were teenagers; 86% were aligned within 10 PD of esotropia. He reported that 42% required glasses for visual purposes; 31% needed single-vision glasses for control.

"Only 4% needed to continue using bifocals over the long term," he said. "Only 2 patients had an exotropia at distance, yet were aligned at near. The results were similar for the teenage subset. No patients underwent prism adaptation."

He recounted his findings with 374 patients with high AC/A esotropia. Of these, 67% were initially aligned; the remainder was not and underwent surgery. Slightly more than half of those who were aligned initially remained so, whereas 44% had a decompensated distance angle and underwent surgery. Among the patients who remained aligned at distance, 99% outgrew the need for bifocals by age 18; 2 patients did not and underwent MR recession for the near angle at age 18 and did well.

THE IMPORTANCE OF AGE

Of the patients who outgrew the need for bifocals, 23% still needed a bifocal by age 13, and 94% of those subsequently outgrew that need by age 18, according to Dr. Kushner.

"Only two patients still needed bifocals, despite . . . a large number of these patients (needing) bifocals when they were younger," he said. "This is why I am surgically conservative when operating just for the purpose of eliminating the need of a bifocal for near alignment.

"In teenagers with esotropia at distance that is greater than 10 PD while wearing full plus correction, recess the MR muscles bilaterally operating for the near angle in the full distance optical correction," Dr. Kushner advised.

If younger teenagers are aligned at distance but need a bifocal for near alignment, continue to treat them optically as most will outgrow the need of the bifocal, he continued.

"If the patient is close to 18 years, you can safely operate for the near angle in the full distance-plus without using prism adaptation," Dr. Kushner concluded. ■

BURTON J. KUSHNER, MD

E: *bkushner@wisc.edu*

Dr. Kushner has no financial interest in any aspect of this report.

Flap creation evolves with technology

Efficacy, safety, and patient preference data all favor the femtosecond laser for LASIK

By Cheryl Guttman Krader; *Reviewed by Steven C. Schallhorn, MD*

TAKE-HOME

- ***Data from analyses of large, retrospective case series show better safety and efficacy when LASIK is performed using a femtosecond laser for flap creation.***

REFRACTIVE SURGEONS CAN now choose from among many excellent femtosecond lasers for LASIK flap creation. In addition, there are many solid reasons for using this technology rather than a mechanical microkeratome, said Steven C. Schallhorn, MD.

"The femtosecond laser has revolutionized LASIK and is preferred by surgeons and patients," said Dr. Schallhorn, professor of ophthalmology, University of San Francisco; private practice, San Diego; and chief medical director, Optical Express.


Dr. Schallhorn

"Using a femtosecond laser instead of a mechanical microkeratome, flap creation is more consistent and more precise," he said. "In addition, use of the femtosecond laser is associated with fewer intraoperative and postoperative flap-related complications and better safety and efficacy outcomes for LASIK."

To support his statements, Dr. Schallhorn presented the findings from analyses of data from large cohorts of eyes that underwent LASIK.

Distance uncorrected visual acuity (UCVA) and best-corrected visual acuity (BCVA) outcomes after wavefront-guided LASIK with a femtosecond laser or mechanical microkeratome for flap creation were evaluated in matched groups of 3,000 eyes each.

Results from follow-up visits at 1 day, 1 week, 1 month, and 3 months showed that the percentage of eyes achieving 20/16 or better distance UCVA was higher in the femtosecond laser group at all intervals, and the difference between groups favoring the femtosecond laser was consistently statistically significant due to the large size of the population studied.

In addition, the rate of BCVA loss of 2 or more lines from baseline was consistently significantly lower in the femtosecond laser group than in eyes that had a mechanical microkeratome-created flap.

LOWER RATE OF COMPLICATIONS

Another analysis of data from consecutive series comprising tens of thousands of eyes showed rates of intraoperative and postoperative complications were also significantly lower using a femtosecond laser instead of a mechanical microkeratome for flap creation.

Flap creation complications occurred in about 1 in 700 cases using a mechanical microkeratome compared with 1 in 900 eyes that had a femtosecond laser-created flap.

"Furthermore, the complications with the microkeratome tended to be 'showstopping' events causing LASIK to be aborted," Dr. Schallhorn said. "However, about half of the flap creation complications with the femtosecond laser involved suction loss, and when that occurs, suction can be reapplied immediately and the flap recut without difficulty."

EPITHELIAL INGROWTH

The rate of primary epithelial ingrowth was also significantly lower in eyes having a femtosecond laser-created flap than in the mechanical microkeratome group—0.01% versus 0.02%—and flap displacement during the first year after surgery was significantly less common as well with use of the femtosecond laser than a mechanical microkeratome, 0.03% versus 0.14%, respectively.

"Differences in flap edge geometry between femtosecond laser and mechanical microkeratome flaps likely explain these differences in postoperative flap complication rates," Dr. Schallhorn said. "A femtosecond laser-created flap with a beveled-in sidecut enables better positioning to reduce epithelial ingrowth risk and results in greater adhesion strength for increased resistance to traumatic dislocation."

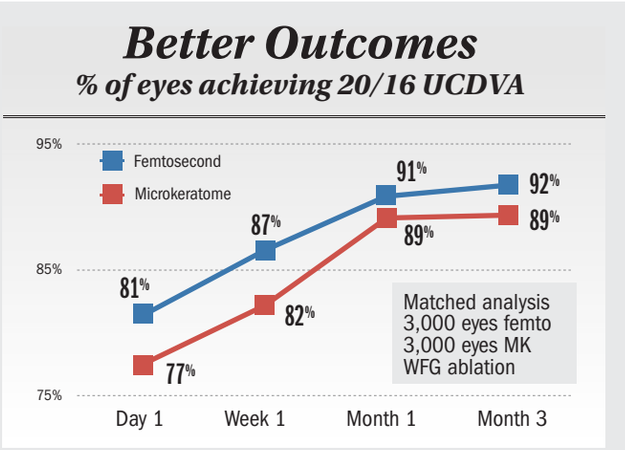
An analysis including data from almost 380,000 consecutive eyes undergoing LASIK, of which about two-thirds had a femtosecond laser-created flap, showed the risk of postLASIK microbial keratitis was also significantly lower in eyes with a femtosecond laser-created flap than in those where a mechanical microkeratome was used, 0.01% versus 0.02%.

The rate of microbial keratitis was significantly lower after LASIK than in a group of 40,000 eyes that underwent PRK, 0.01% versus 0.03%.

"There is a tendency to think PRK is safer than LASIK because PRK does not involve a flap," Dr. Schallhorn said. "However, the epithelium is removed with PRK, and so it makes sense that the surface ablation procedure is associated with a higher corneal infection risk."

Data from more than 40,000 LASIK patients also show a clear preference for an all-laser procedure. Even though use of a femtosecond laser for flap creation added $1,200 to the procedure fee per patient, 70% of patients chose to undergo LASIK with a femtosecond laser-created flap.

"Not only is there a clear preference for the femtosecond laser, but patients are willing to pay a substantial fee for that preference," Dr. Schallhorn said. ■



Eyes achieving 20/16 or better uncorrected distance visual acuity was higher in the femtosecond laser group at all intervals.

(Figure courtesy of Steven C. Schallhorn, MD)

STEVEN C. SCHALLHORN, MD

E: *scschallhorn@yahoo.com*

Dr. Schallhorn is a consultant to Abbott Medical Optics.

For the reduction of IOP in patients with POAG or OHTN

When it's important to consider ocular and systemic side effects...

An alternate route to IOP reduction

- Effective at lowering IOP throughout the day and over the long term[1-3]
- Excellent systemic safety profile including no deleterious effects on CV or pulmonary function in clinical studies[1]
- Established ocular side effects profile: In clinical trials comparing RESCULA and timolol,* both were generally well tolerated regarding ocular adverse events, with similar incidence of hyperemia and similar changes to eyelash length and density[1,4,5]
  - The only events seen significantly more often with RESCULA than with timolol were burning and stinging and burning/stinging upon instillation; these events were generally mild and transient[2,4]
- No labeled drug-drug interactions[1,4]

Indication

RESCULA (unoprostone isopropyl ophthalmic solution) 0.15% is indicated for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

Important Safety Information

RESCULA is contraindicated in patients with hypersensitivity to unoprostone isopropyl or any other ingredient in this product.

RESCULA has been reported to increase pigmentation of the iris, periorbital tissues, and eyelashes. Patients should be advised about the potential for increased brown iris pigmentation which is likely to be permanent.

RESCULA should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Macular edema, including cystoid macular edema, has been reported. RESCULA 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.

*In pooled safety analyses of pivotal trials comparing RESCULA with timolol maleate 0.5%.[4]

Please see Brief Summary on reverse and full Prescribing Information, available from your Sucampo representative.

Rescula®
(Unoprostone isopropyl
ophthalmic solution) 0.15%

Brief Summary of Prescribing Information for RESCULA.

INDICATIONS AND USAGE
Rescula (unoprostone isopropyl ophthalmic solution) 0.15% is indicated for the lowering of intraocular pressure in patients with open-angle glaucoma or ocular hypertension.

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

Rescula may be used concomitantly with other topical ophthalmic drug products to lower intraocular pressure. If two drugs are used, they should be administered at least five (5) minutes apart.

CONTRAINDICATIONS
Rescula is contraindicated in patients with hypersensitivity to unoprostone isopropyl or any other ingredient in this product.

WARNINGS AND PRECAUTIONS
Iris Pigmentation
Unoprostone isopropyl ophthalmic solution may gradually increase the pigmentation of the iris. The pigmentation change is believed to be due to increased melanin content in the melanocytes rather than to an increase in the number of melanocytes. The long term effects of increased pigmentation are not known. Iris color changes seen with administration of unoprostone isopropyl ophthalmic solution 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. Treatment with Rescula solution can be continued in patients who develop noticeably increased iris pigmentation. Patients who receive treatment with Rescula should be informed of the possibility of increased pigmentation.

Lid Pigmentation
Unoprostone isopropyl has been reported to cause pigment changes (darkening) to periorbital pigmented tissues and eyelashes. The pigmentation is expected to increase as long as unoprostone isopropyl is administered, but has been reported to be reversible upon discontinuation of unoprostone isopropyl ophthalmic solution in most patients.

Intraocular Inflammation
Rescula should be used with caution in patients with active intraocular inflammation (e.g., uveitis) because the inflammation may be exacerbated.

Macular Edema
Macular edema, including cystoid macular edema, has been reported. Rescula 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.

Contamination of Tip and Solution
To minimize 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 bottle tightly closed when not in use. There have been reports of bacterial keratitis associated with the use of multiple-dose containers of topical ophthalmic products.

Use with Contact Lenses
Rescula contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to application of solution 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, the most common ocular adverse reactions with use of Rescula were burning/stinging, burning/stinging upon drug instillation, dry eyes, itching, increased length of eyelashes, and injection. These were reported in approximately 10–25% of patients. Approximately 10–14% of patients were observed to have an increase in the length of eyelashes (≥ 1 mm) at 12 months, while 7% of patients were observed to have a decrease in the length of eyelashes.

Ocular adverse reactions occurring in approximately 5–10% of patients were abnormal vision, eyelid disorder, foreign body sensation, and lacrimation disorder.

Ocular adverse reactions occurring in approximately 1–5% of patients were blepharitis, cataract, conjunctivitis, corneal lesion, discharge from the eye, eye hemorrhage, eye pain, keratitis, irritation, photophobia, and vitreous disorder.

The most frequently reported nonocular adverse reaction associated with the use of Rescula in the clinical trials was flu-like syndrome that was observed in approximately 6% of patients. Nonocular adverse reactions reported in the 1–5% of patients were accidental injury, allergic reaction, back pain, bronchitis, increased cough, diabetes mellitus, dizziness, headache, hypertension, insomnia, pharyngitis, pain, rhinitis, and sinusitis.

Postmarketing Experience
The following adverse reactions have been identified during post-approval use of Rescula. Because these reactions are reported voluntarily from a population of uncertain size, it is not always possible to reliably estimate their frequency or establish causal relationship to drug exposure.

Voluntary reports of adverse reactions occurring with the use of Rescula include corneal erosion.

There have been rare spontaneous reports with a different formulation of unoprostone isopropyl (0.12%) of chemosis, dry mouth, nausea, vomiting and palpitations.

USE IN SPECIFIC POPULATIONS
Pregnancy Category C - There are no adequate and well-controlled studies in pregnant women. Because animal studies are not always predictive of human response, RESCULA should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Pediatric Use - the safety and efficacy of RESCULA in pediatric patients have not been established.

It is not known whether RESCULA is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when RESCULA is administered to a nursing woman.

No overall differences in safety or effectiveness of RESCULA have been observed between elderly and other adult populations.

CLINICAL PHARMACOLOGY
Mechanism of Action
Rescula is believed to reduce elevated intraocular pressure (IOP) by increasing the outflow of aqueous humor through the trabecular meshwork. Unoprostone isopropyl (UI) may have a local effect on BK (Big Potassium) channels and ClC-2 chloride channels, but the exact mechanism is unknown at this time.

STORAGE AND HANDLING
Store between 2°–25°C (36°–77°F).

For more detailed information please read the Prescribing Information.

Marketed by:

Sucampo Pharma Americas, LLC
Bethesda, MD 20814

Revised 01/2013

References: **1.** RESCULA [package insert]. Bethesda, MD: Sucampo Pharmaceuticals, Inc; 2012. **2.** Data on file. CSR C97-UIOS-004. Sucampo Pharmaceuticals, Inc. **3.** Data on file. CSR C97-UIOS-005. Sucampo Pharmaceuticals, Inc. **4.** Data on file. Integrated summary of clinical safety. Sucampo Pharmaceuticals, Inc. **5.** McCarey BE, Kapik BM, Kane FE; Unoprostone Monotherapy Study Group. Low incidence of iris pigmentation and eyelash changes in 2 randomized clinical trials with unoprostone isopropyl 0.15%. *Ophthalmology*. 2004;111(8):1480-1488.

SUCAMPO
PHARMA AMERICAS, LLC.

UNO-1091 Printed in USA 02/2013

Long-term outcomes favorable for femtosecond lenticule extraction

Study found technique produced good safety and extended stability for myopia treatment

By Cheryl Guttman Krader; *Reviewed by Ernest W. Kornmehl, MD, FACS*

TAKE-HOME

- ***Data from a series of 56 eyes examined at 5 years after femtosecond lenticule extraction (FLEx, Carl Zeiss Meditec) show good safety and long-term stability of the refractive and functional results.***

MUMBAI, INDIA ::

DATA FROM EYES EXAMINED at 5 years of follow-up support the conclusion that femtosecond lenticule extraction (FLEx, Carl Zeiss Meditec)—performed using a proprietary femtosecond laser (VisuMax, Carl Zeiss Meditec)—is a safe, effective, and predictable treatment for myopia and myopic astigmatism with good long-term stability, according to Rupal S. Shah, MD.

Dr. Shah said she first began performing the all-femtosecond laser procedure in August 2008, and had reported 1-month results for the first 85 eyes she treated.

The long-term analysis she presented included data for two-thirds (56 eyes) of the eyes in her initial cohort.

A comparison of the outcomes achieved after 1 month and at 5 years showed that the long-term changes were in a positive direction toward higher efficacy and predictability.

"This study is a work in progress, but I believe that femtosecond lenticule extraction will truly lead to a paradigm shift in refractive surgery," said Dr. Shah, clinical director, New Vision Laser Centers-Centre for Sight, Mumbai, India.

EXPLORING THE STUDY

Baseline data for the first 85 eyes showed they had a mean spherical equivalent of –3.90 D, with a mean sphere of –3.56 D (range –0.50 to –9) and mean cylinder of 0.69 D (range 0 to 3 D). The eyes that were available for follow-up at 5 years represented a slightly narrower range of correction with baseline sphere of up to –8 D and cylinder up to 2.25 D.

In all eyes, the extracted lenticule measured 6 mm in diameter, the overlying flap was 100- to 120-µm thick, and the residual stromal bed was >250 µm.

The target refraction was plano in all cases.

Findings from the original analyses showed that patients experienced a delay in visual recovery after the procedure.

At 1 week, 47% of eyes had lost 2 or more lines from baseline best spectacle-corrected visual acuity (BSCVA).

Outcomes were better at 1 month when no eyes had lost more than 2 lines of BSCVA and BSCVA was unchanged or improved from baseline in 71% of eyes.

At 5 years, no eyes had lost 1 or more lines from their baseline BSCVA. Mean spherical equivalent at 1 year was about 0.05 D and showed remarkable stability over time.

"In fact, our data show continued improvement in refractive outcomes," Dr. Shan said. "At 5 years, 100% of eyes were within 0.5 D of their plano target and all had uncorrected visual acuity of 20/25 or better."

COMPARING PROCEDURES

FLEx is one of two versions of the all-femtosecond laser refractive procedures known as Refractive Lenticule Extraction (ReLEx, Carl Zeiss Meditec).

The laser is used to prepare both a corneal flap and the refractive lenticule.

A newer version of ReLEx—known as Small Incision Lenticule Extraction (SMILE)—is a flapless procedure in which the lenticule is removed through a small, 2-3 mm corneal incision.

"Compared with LASIK, SMILE has advantages for the patient and the surgeon," Dr. Shah explained. "SMILE can be performed with only one laser, and it induces less dry eye, avoids concerns about flap displacement, and has the potential for better corneal biomechanical stability."

Dr. Shah noted that it takes about 25 seconds for the femtosecond laser to complete the two passes that are needed to dissect the lenticule with the SMILE procedure.

She added that the VisuMax laser has a curved corneal interface that does not cause a significant increase in IOP. Therefore, patients are able to maintain fixation on the laser's green blinking light during the entire procedure.

After the incision is opened, the anterior and posterior surfaces of the lenticule are easily separated from the overlying and underlying stroma using a blunt instrument.

The surgical microscope that is integrated within the femtosecond laser facilitates identification of the lenticule surfaces.

However, a slit lamp attachment is also available for use if needed.

Over the past 5 years, almost 4,000 eyes have undergone a ReLEx procedure at a New Vision Laser Center, Dr. Shah said.

"ReLEx has definitely become the most premium refractive procedure in our practice," she said.■

'At 5 years,

100%

of eyes were within

0.5 D

of their plano target and all had uncorrected visual acuity of

20/25

or better.'

—Rupal S. Shah, MD

RUPAL S. SHAH, MD

E: *rupal@newvisionindia.com*

Dr. Shah is a consultant to Carl Zeiss Meditec and receives fees for research and travel support.

Tactics for tackling cortex removal

How instrument selection and host of maneuvers play role in pediatric cataract surgery

By Cheryl Guttman Krader; *Reviewed by M. Edward Wilson, MD*

TAKE-HOME

- ***Complete removal of lens substance is critical in pediatric cataract surgery. M. Edward Wilson, MD, offers helpful strategies.***

CHARLESTON, SC ::

USE OF A BIMANUAL approach and a sequence that removes subincisional cortex first and the entire peripheral cortex before aspirating the central nucleus will enable safe and thorough removal of the cortex in pediatric cataract surgery, said M. Edward Wilson, MD.

Dr. Wilson discussed instrument selection as well as a variety of standard and advanced maneuvers that may be used for successfully removing difficult cortex.

Dr. Wilson

"I consider using a bimanual technique a big advantage, because it allows the surgeon to switch hands as needed to better reach cortex while maintaining chamber stability," said Dr. Wilson, professor of ophthalmology and pediatrics, and the N. Edgar Miles Endowed Chair, Albert Florens Storm Eye Institute, Medical University of South Carolina, Charleston.

"Removing the peripheral cortex before the nucleus is the reverse of what is done in adult eyes, but is helpful in pediatric cataract surgery for preventing a convex posterior capsulethat can occur because of posterior vitreous pressure," Dr. Wilson said.

This is a uniquely pediatric phenomenon, he explained.

INSTRUMENT CHOICE AND ENTRY

Use of tapered and curved bimanual irrigation and aspiration handpieces is another consideration for optimizing full accessibility to cortex. Placing the instruments through peripheral corneal tunneled paracentesis openings created with a matching gauge microvitreoretinal blade optimizes safety, as well as maneuverability.

"There can be a lot of chamber bounce and collapse in pediatric eyes during cataract surgery," Dr. Wilson said.

Therefore, surgeons want the instruments to fit tightly through their entry sites to maintain the chamber stability needed to get the often "gummy" cortex out, he said.

He added that avoiding an excessively long tunnel is important when creating the paracenteses as that architecture will lead to oar-locking with restricted instrument movement. Distancing the paracenteses farther apart from each other is also helpful for enabling instrument maneuverability.

Cortex can also be removed using a vitrector handpiece, but it is a less efficient choice because the vitrector handpiece is not tapered and has a larger aspiration port opening, he noted.

If a vitrector is used, Dr. Wilson recommended applying short bursts of cutting to move thick cortex into the aspiration port while remaining vigilant not to inadvertently cut iris or capsule.

STANDARD AND ADVANCED MANEUVERS

In using the aspiration handpiece for cortex removal, Dr. Wilson advised placing the instrument just under the edge of the capsulorhexis with the aspiration port turned toward the capsular equator.

Then, the surgeon should build suction and wait for cortex to come to the instrument opening.

He noted a Venturi-pump machine is preferred for this maneuver.

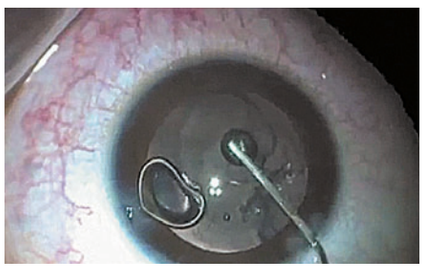
"In pediatric eyes we try to avoid early stripping and tearing of the cortex," Dr. Wilson said.

While that technique is used in adults, in pediatric eyes it tends to leave small pieces of residual cortex in the equator that will be difficult to remove, he explained.

"Keeping the instrument under the edge of the capsulorhexis promotes full evacuation of equatorial cortex," he said.

To enhance efficiency and safety, the irrigation cannula can be used to hold the iris back and to feed cortex into the aspiration opening.

POSTERIOR CAPSULE RUPTURE

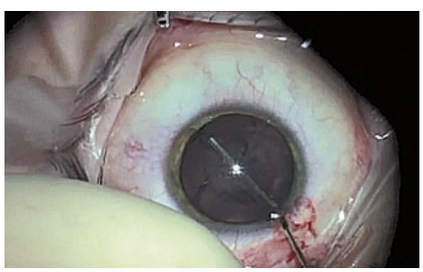


VIDEO This video demonstrates cortex removal after inadvertent posterior capsule rupture during bimanual irrigation and aspiration. OVD is used followed by a manual posterior capsulorhexis. Only then is the residual cortex removed using dry aspiration.

To watch the video, go to **http://bit.ly/1izU091**.

(Videos courtesy of M. Edward Wilson, MD)

BIMANUAL IRRIGATION/ASPIRATION



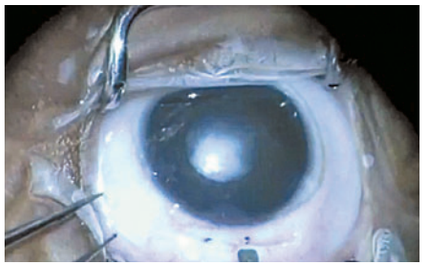
VIDEO Childhood cataract surgery using bimanual irrigation and aspiration. Hydrodissection is used and right-handed aspiration is followed by left-handed aspiration to complete the cortex removal. Having two matching-gauge irrigation and aspiration instruments facilitates a tight-fit wound for a stable anterior chamber—even when switching hands to retrieve hard-to-reach cortex.

To watch the video, go to **http://bit.ly/1dQaOZm**.

"Using the irrigation handpiece to loosen cortex and bring it out of the capsular equator represents a form of precise and safe hydro-dissection," Dr. Wilson said.

Conventional hydro-dissection and hydro-delineation have a more limited role in pediatric procedures than in adult eyes, due

POORLY DILATING PUPILS



VIDEO Infant cataracts can be a challenge to remove completely without leaving residual lens cortex. This video shows two different infants with poorly dilating pupils. In one infant, a Malyugin ring was used and in the other, iris hooks were used to facilitate visualization of peripheral lens cortex. These devices are underutilized in pediatric cataract cases, but they can help assure that all of the lens cortex is removed.

To watch the video, go to **http://bit.ly/1cQujD4**.

to the absence of a firm solid nucleus and the frequency of posterior capsule pathology,

"Many times in pediatric cases we are dealing with posterior polar cataracts, lentiglobus, or fetal nuclear cataract with posterior capsule plaques where the posterior capsule is adherent to cortex and often is incompetent," Dr. Wilson said.

Hydro-dissection or hydro-delineation in eyes with these types of cataract may cause posterior capsule tears, and the payoff achieved by performing these maneuvers in an effort to speed cortex removal is relatively modest in pediatric cataract cases in general compared to adults, he noted.

"Therefore, it may not be worth the risk," Dr. Wilson said.

OTHER SURGICAL AIDS FOR CORTEX REMOVAL

Dr. Wilson advocated expanding the pupil as needed with iris hooks or rings to improve visualization and therefore the ability to remove difficult cortex safely.

Getting the cortex out completely without traumatizing the iris can be a struggle if the pupil is not opened widely.

"I believe devices for enlarging the pupil are underutilized in pediatric cataract surgery," he said.

Surgeons may also find it helpful to use an ophthalmic viscosurgical device (OVD) to viscodissect residual cortex into the center of the capsular space where it can be removed "dry" with a cannula or the aspiration handpiece.

"Sometimes, however, difficult cortex is best brought out with viscodissection at the end of the procedure," Dr. Wilson said. "After IOL insertion, the viscodissected material can be removed along with the OVD using the bimanual handpieces."■

M. EDWARD WILSON, MD

E: *wilsonme@musc.edu*

Dr. Wilson has no relevant financial interests to disclose.

Black ink may be culprit in tattoo-related uveitis

Physical findings in these patients may represent a forme fruste of sarcoidosis

By Liz Meszaros; *Reviewed by Trucian Ostheimer, MD*

TAKE-HOME

- ***Physicians who treat uveitis should ask patients about any tattoo changes. Some component of black tattoo ink may act as an environmental trigger—leading to the development of simultaneous bilateral ocular inflammation and elevation of tattooed skin.***

BALTIMORE ::

Though tattoo-associated uveitis is rarely reported, the likelihood of its presence is more common than the literature would suggest, according to Trucian Ostheimer, MD.

Only eight cases of patients with uveitis and associated changes in tattooed skin have been published in the English literature, said Dr. Ostheimer, second-year uveitis fellow, Wilmer Eye Institute, Johns Hopkins University School of Medicine, Baltimore. Interestingly, he has seen seven such patients since beginning his fellowship with the Wilmer Ocular Immunology Service.

"All of these patients were young, aged 20 to 44 years, at the time of presentation," he said.

Portions of tattooed skin containing black pigment were affected and visibly raised. *(Photo courtesy of Trucian Ostheimer, MD)*

Five of seven patients had bilateral non-granulomatous anterior uveitis—four with chronic and one with recurrent disease. Two patients had bilateral chronic granulomatous panuveitis. Initial visual acuity varied widely.

Five of seven patients presented with potentially vision-threatening ocular complications, such as severe cystoid macular edema, neurosensory retinal detachment, and iris bombe.

WHAT THEY HAD IN COMMON

Most of the patients had extensive tattoos, and many of these were multicolored.

Interestingly, only portions of tattooed skin containing black pigment were affected and visibly raised, Dr. Ostheimer noted.

No abnormalities were noted in the portions of tattoo containing other types of pigment.

OCULAR MANIFESTATIONS

The pathologic hallmark of sarcoidosis is the non-caseating granuloma, but it remains a diagnosis of exclusion because of its lack of pathognomonic histopathology, imaging, or serologic studies.

Anywhere from 25% to 80% of those with sarcoidosis develop ocular or adnexal involvement. Anterior uveitis is the most common ocular manifestation, accounting for 65% of patients with ocular involvement. About 25% to 35% of those with sarcoidosis develop skin findings, Dr. Ostheimer said.

Various patterns of reactions occur in tattooed skin, and one of the more common findings is granulomatous inflammation.

"Histologically, this can be classified as a foreign body or sarcoid-type reaction, and the differentiation of these two types of granulomas may be challenging and open to controversy," Dr. Ostheimer said.

"It is purely speculative, but I think it is reasonable to conclude that there may be some component of black tattoo ink that acts as an environmental trigger—leading to the development of simultaneous bilateral ocular inflammation and elevation of tattooed skin," he said.

OphthalmologyTimes.com PODCAST

LISTEN TO Trucian Ostheimer, MD, present cases of tattoo-associated uveitis and his findings during the annual Current Concepts in Ophthalmology meeting at the Wilmer Eye Institute/Johns Hopkins University. Go to http://bit.ly/1njRw53

Altogether, the physical findings in these patients may represent a forme fruste of sarcoidosis, Dr. Ostheimer concluded.

A manuscript detailing his findings in currently under review. ■

Suggested reading

- Anolik R, Mandal R, Franks A. Sarcoidal tattoo granuloma. *Dermatology Online Journal. 2010;16:19.*
- Barbarasi Z, Kiss E, Balaton G, Vajo Z. Cutaneous granuloma and uveitis caused by a tattoo [in German]. *Wien Klin Wochenschr.* 2008;120:18.
- Bonfioli AA, Orefice F. Sarcoidosis. *Semin Ophthalmol.* 2005;20:177-182.
- Iannuzzi MC, Rybicki BA, Teirstein AS. Sarcoidosis. *N Engl J Med.* 2007;357:2153-2165.
- Lubeck G, Epstein E. Complications of tattooing. *Calif Med.* 1952;76:83-85.
- Morales-Callaghan AM, Aquilar-Bernier M, Martinez-Garcia G, Miranda-Romero A. Sarcoid granuloma on black tattoo. *J Am Acad Dermatol.* 2006;55(5 Suppl):S71-3. Epub 2006 Aug 28.
- Marcoval J, Mana J, Moreno A, et al. Foreign bodies in granulomatous cutaneous lesions of patients with systemic sarcoidosis. *Arch Dermatol.* 2001;137:427-430.
- Post J, Hull P. Tattoo reactions as a sign of sarcoidosis. *CMAJ.* 2012;184:432.
- Rorsman H, Brehmer-Andersson E, Dahlquist I, et al. Tattoo granuloma and uveitis. Lancet. 1969;294:27-28.
- Saliba N, Owen M E, Beare N. Tattoo-associated uveitis. *Eye.* 2010;24:1406.

TRUCIAN OSTHEIMER, MD

P: *410/955-2966* **E:** *tosthei1@jhmi.edu*

This article was based on Dr. Ostheimer's presentation at the annual Current Concepts in Ophthalmology meeting at Wilmer Eye Institute/Johns Hopkins University, Baltimore. He has no financial interest in the subject matter.

In the face of elevated IOP after monotherapy

RELEASE THE POWER

Most Covered Branded Combination

92% of Commercial and Part D member lives covered[1,a] As of December 2013.

Individual plans and out-of-pocket costs will vary.
Most covered based on lives vs *Cosopt®*, *Cosopt® PF*, and *Simbrinza™*.

POWER: Still a reason you choose COMBIGAN®

(brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5%

INDICATIONS AND USAGE: COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% is an alpha-adrenergic receptor agonist with a beta-adrenergic receptor inhibitor indicated for the reduction of elevated intraocular pressure (IOP) in patients with glaucoma or ocular hypertension who require adjunctive or replacement therapy due to inadequately controlled IOP; the IOP-lowering of COMBIGAN® dosed twice a day was slightly less than that seen with the concomitant administration of 0.5% timolol maleate ophthalmic solution dosed twice a day and 0.2% brimonidine tartrate ophthalmic solution dosed three times per day.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS: COMBIGAN® is contraindicated in patients with bronchial asthma; a history of bronchial asthma; severe chronic obstructive pulmonary disease; in patients with sinus bradycardia; second or third degree atrioventricular block; overt cardiac failure; cardiogenic shock; in neonates and infants (under the age of 2 years); in patients with a hypersensitivity reaction to any component of COMBIGAN® in the past.

WARNINGS AND PRECAUTIONS: COMBIGAN® contains timolol maleate; while administered topically, it can be absorbed systemically and systemic adverse reactions to beta-blockers may occur (eg, severe respiratory reactions including death due to bronchospasm in patients with asthma have been reported).

Sympathetic stimulation may be essential to support the circulation in patients with diminished myocardial contractility and its inhibition by beta-adrenergic receptor blockade may precipitate more severe failure. In patients with no history of cardiac failure, continued depression of the myocardium with beta-blocking agents over time can lead to cardiac failure. Discontinue COMBIGAN® at the first sign or symptom of cardiac failure.

Patients with chronic obstructive pulmonary disease (eg, chronic bronchitis, emphysema) of mild or moderate severity, bronchospastic disease, or a history of bronchospastic disease should not receive COMBIGAN®.

COMBIGAN® may potentiate syndromes associated with vascular insufficiency. Use caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangiitis obliterans.

IMPORTANT SAFETY INFORMATION (continued)

WARNINGS AND PRECAUTIONS: (continued)

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

Although rare, timolol can increase muscle weakness in some patients with myasthenia gravis or myasthenic symptoms.

Beta-blockers may mask the signs and symptoms of acute hypoglycemia and clinical signs (eg, tachycardia) of hyperthyroidism. Use caution in patients subject to spontaneous hypoglycemia or diabetics (especially those with labile diabetes) who are receiving insulin or oral hypoglycemic agents. Carefully manage patients who may develop thyrotoxicosis to avoid abrupt withdrawal of beta-blockers that might precipitate a thyroid storm.

Ocular hypersensitivity has occurred with brimonidine tartrate ophthalmic solutions 0.2% (eg, increase in IOP).

Some authorities recommend gradual withdrawal of beta-blockers due to impairment of beta-adrenergically mediated reflexes during surgery. If necessary during surgery, the effects of beta-blockers may be reversed by sufficient doses of adrenergic agonists.

ADVERSE REACTIONS: The most frequent reactions with COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% in about 5% to 15% of patients included: allergic conjunctivitis, conjunctival folliculosis, conjunctival hyperemia, eye pruritus, ocular burning, and stinging.

DRUG INTERACTIONS: Use caution in the co-administration of COMBIGAN® with: antihypertensives or cardiac glycosides; beta-blockers (concomitant use of two topical beta-blockers is not recommended); calcium antagonists (avoid co-administration in patients with impaired cardiac function); catecholamine-depleting drugs; CNS depressants /anesthetics; digitalis and calcium antagonists; CYP2D6 inhibitors; tricyclic antidepressants; and monoamine oxidase inhibitors.

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

[a]Includes preferred, approved, and tiers 1-4, with and without step-edits, and also includes prior authorization, based on 203,671,234 total lives.

1. Managed Markets Insight & Technology, LLC, database as of December 2013.

ALLERGAN

Combigan®
(brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5%

COMBIGAN®

(brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5%

BRIEF SUMMARY

Please see the **COMBIGAN®** package insert for full prescribing information.

INDICATIONS AND USAGE

COMBIGAN® (brimonidine tartrate/timolol maleate ophthalmic solution) 0.2%/0.5% is an alpha adrenergic receptor agonist with a beta adrenergic receptor inhibitor indicated for the reduction of elevated intraocular pressure (IOP) in patients with glaucoma or ocular hypertension who require adjunctive or replacement therapy due to inadequately controlled IOP; the IOP-lowering of **COMBIGAN®** dosed twice a day was slightly less than that seen with the concomitant administration of 0.5% timolol maleate ophthalmic solution dosed twice a day and 0.2% brimonidine tartrate ophthalmic solution dosed three times per day.

CONTRAINDICATIONS

Asthma, COPD: COMBIGAN® is contraindicated in patients with bronchial asthma; a history of bronchial asthma; severe chronic obstructive pulmonary disease.

Sinus bradycardia, AV block, Cardiac failure, Cardiogenic shock: COMBIGAN® is contraindicated in patients with sinus bradycardia; second or third degree atrioventricular block; overt cardiac failure; cardiogenic shock.

Neonates and Infants (Under the Age of 2 Years): COMBIGAN® is contraindicated in neonates and infants (under the age of 2 years).

Hypersensitivity reactions: Local hypersensitivity reactions have occurred following the use of different components of **COMBIGAN®**. **COMBIGAN®** is contraindicated in patients who have exhibited a hypersensitivity reaction to any component of this medication in the past.

WARNINGS AND PRECAUTIONS

Potentiation of respiratory reactions including asthma: COMBIGAN® contains timolol maleate; and although administered topically can be absorbed systemically. Therefore, the same types of adverse reactions found with systemic administration of beta-adrenergic blocking agents may occur with topical administration. For example, severe respiratory reactions including death due to bronchospasm in patients with asthma have been reported following systemic or ophthalmic administration of timolol maleate.

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, **COMBIGAN®** 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 **COMBIGAN®** is contraindicated] should, in general, not receive beta-blocking agents, including **COMBIGAN®**.

Potentiation of vascular insufficiency: COMBIGAN® may potentiate syndromes associated with vascular insufficiency. **COMBIGAN®** should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangiitis obliterans.

Increased reactivity to allergens: 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.

Potentiation of 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.

Masking of hypoglycemic symptoms in patients with 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.

Masking of 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.

Ocular Hypersensitivity: Ocular hypersensitivity reactions have been reported with brimonidine tartrate ophthalmic solutions 0.2%, with some reported to be associated with an increase in intraocular pressure.

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

Impairment of beta-adrenergically mediated reflexes during 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.

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. **COMBIGAN®:** In clinical trials of 12 months duration with **COMBIGAN®**, the most frequent reactions associated with its use occurring in approximately 5% to 15% of the patients included: allergic conjunctivitis, conjunctival folliculosis, conjunctival hyperemia, eye pruritus, ocular burning, and stinging. The following adverse reactions were reported in 1% to 5% of patients: asthenia, blepharitis, corneal erosion, depression, epiphora, eye discharge, eye dryness, eye irritation, eye pain, eyelid edema, eyelid erythema, eyelid pruritus, foreign body sensation, headache, hypertension, oral dryness, somnolence, superficial punctate keratitis, and visual disturbance.

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

Brimonidine Tartrate (0.1%-0.2%): Abnormal taste, allergic reaction, blepharoconjunctivitis, blurred vision, bronchitis, cataract, conjunctival edema, conjunctival hemorrhage, conjunctivitis, cough, dizziness, dyspepsia, dyspnea, fatigue, flu syndrome, follicular conjunctivitis, gastrointestinal disorder, hypercholesterolemia, hypotension, infection (primarily colds and respiratory infections), hordeolum, insomnia, keratitis, lid disorder, nasal dryness, ocular allergic reaction, pharyngitis, photophobia, rash, rhinitis, sinus infection, sinusitis, taste perversion, tearing, visual field defect, vitreous detachment, vitreous disorder, vitreous floaters, and worsened visual acuity. **Timolol (Ocular Administration):** *Body as a whole:* chest pain; *Cardiovascular:* Arrhythmia, bradycardia, cardiac arrest, cardiac failure, cerebral ischemia, cerebral vascular accident, claudication, cold hands and feet, edema, heart block, palpitation, pulmonary edema, Raynaud's phenomenon, syncope, and worsening of angina pectoris; *Digestive:* Anorexia, diarrhea, nausea; *Immunologic:* Systemic lupus erythematosus; *Nervous System/Psychiatric:* Increase in signs and symptoms of myasthenia gravis, insomnia, nightmares, paresthesia, behavioral changes and psychic disturbances including confusion, hallucinations, anxiety, disorientation, nervousness, and memory loss; *Skin:* Alopecia, psoriasiform rash or exacerbation of psoriasis; *Hypersensitivity:* Signs and symptoms of systemic allergic reactions, including anaphylaxis, angioedema, urticaria, and generalized and localized rash; *Respiratory:* Bronchospasm (predominantly in patients with pre-existing bronchospastic disease), dyspnea, nasal congestion, respiratory failure; *Endocrine:* Masked symptoms of hypoglycemia in diabetes patients; *Special Senses:* diplopia, choroidal detachment following filtration surgery, cystoid macular edema, decreased corneal sensitivity, pseudopemphigoid, ptosis, refractive changes, tinnitus; *Urogenital:* Decreased libido, impotence, Peyronie's disease, retroperitoneal fibrosis.

Postmarketing Experience: Brimonidine: The following reactions have been identified during post-marketing use of brimonidine tartrate ophthalmic solutions in clinical practice. Because they are reported voluntarily from a population of unknown size, estimates of frequency cannot be made. The reactions, which have been chosen for inclusion due to either their seriousness, frequency of reporting, possible causal connection to brimonidine tartrate ophthalmic solutions, or a combination of these factors, include: bradycardia, depression, iritis, keratoconjunctivitis sicca, miosis, nausea, skin reactions (including erythema, eyelid pruritus, rash, and vasodilation), and tachycardia. Apnea, bradycardia, hypotension, hypothermia, hypotonia, and somnolence have been reported in infants receiving brimonidine tartrate ophthalmic solutions. **Oral Timolol/Oral Beta-blockers:** The following additional adverse reactions 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:* Decreased exercise tolerance, extremity pain, weight loss; *Cardiovascular:* Vasodilatation, worsening of arterial insufficiency; *Digestive:* Gastrointestinal pain, hepatomegaly, ischemic colitis, mesenteric arterial thrombosis, vomiting; *Hematologic:* Agranulocytosis, nonthrombocytopenic purpura, thrombocytopenic purpura; *Endocrine:* Hyperglycemia, hypoglycemia; *Skin:* Increased pigmentation, pruritus, skin irritation, sweating; *Musculoskeletal:* Arthralgia; *Nervous System/Psychiatric:* An acute reversible syndrome characterized by disorientation for time and place, decreased performance on neuropsychometrics, diminished concentration, emotional lability, local weakness, reversible mental depression progressing to catatonia, slightly clouded sensorium, vertigo; *Respiratory:* Bronchial obstruction, rales; *Urogenital:* Urination difficulties.

DRUG INTERACTIONS

Antihypertensives/Cardiac Glycosides: Because **COMBIGAN®** may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with **COMBIGAN®** is advised. **Beta-adrenergic Blocking Agents:** Patients who are receiving a beta-adrenergic blocking agent orally and **COMBIGAN®** should be observed for potential additive effects of beta-blockade, 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 co-administration of beta-adrenergic blocking agents, such as **COMBIGAN®**, and oral or intravenous calcium antagonists because of possible atrioventricular conduction disturbances, left ventricular failure, and hypotension. In patients with impaired cardiac function, co-administration 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. **CNS Depressants:** Although specific drug interaction studies have not been conducted with **COMBIGAN®**, the possibility of an additive or potentiating effect with CNS depressants (alcohol, barbiturates, opiates, sedatives, or anesthetics) should be considered. **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. **Tricyclic Antidepressants:** Tricyclic antidepressants have been reported to blunt the hypotensive effect of systemic clonidine. It is not known whether the concurrent use of these agents with **COMBIGAN®** in humans can lead to resulting interference with the IOP-lowering effect. Caution, however, is advised in patients taking tricyclic antidepressants which can affect the metabolism and uptake of circulating amines. **Monoamine oxidase inhibitors:** Monoamine oxidase (MAO) inhibitors may theoretically interfere with the metabolism of brimonidine and potentially result in an increased systemic side-effect such as hypotension. Caution is advised in patients taking MAO inhibitors which can affect the metabolism and uptake of circulating amines.

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C: Teratogenicity studies have been performed in animals.

Brimonidine tartrate was not teratogenic when given orally during gestation days 6 through 15 in rats and days 6 through 18 in rabbits. The highest doses of brimonidine tartrate in rats (1.65 mg/kg/day) and rabbits (3.33 mg/kg/day) achieved AUC exposure values 580 and 37-fold higher, respectively, than similar values estimated in humans treated with **COMBIGAN®**, 1 drop in both eyes twice daily.

Teratogenicity studies with timolol in mice, rats, and rabbits at oral doses up to 50 mg/kg/day [4,200 times the maximum recommended human ocular dose of 0.012 mg/kg/day on a mg/kg basis (MRHOD)] 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 1,000 mg/kg/day (83,000 times the MRHOD) were maternotoxic in mice and resulted in an increased number of fetal resorptions. Increased fetal resorptions were also seen in rabbits at doses 8,300 times the MRHOD without apparent maternotoxicity.

There are no adequate and well-controlled studies in pregnant women; however, in animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent. Because animal reproduction studies are not always predictive of human response, **COMBIGAN®** should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Nursing Mothers: Timolol has been detected in human milk following oral and ophthalmic drug administration. It is not known whether brimonidine tartrate is excreted in human milk, although in animal studies, brimonidine tartrate has been shown to be excreted in breast milk. Because of the potential for serious adverse reactions from **COMBIGAN®** 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: COMBIGAN® is not recommended for use in children under the age of 2 years. During post-marketing surveillance, apnea, bradycardia, hypotension, hypothermia, hypotonia, and somnolence have been reported in infants receiving brimonidine. The safety and effectiveness of brimonidine tartrate and timolol maleate have not been studied in children below the age of two years.

The safety and effectiveness of **COMBIGAN®** have been established in the age group 2-16 years of age. Use of **COMBIGAN®** in this age group is supported by evidence from adequate and well-controlled studies of **COMBIGAN®** in adults with additional data from a study of the concomitant use of brimonidine tartrate ophthalmic solution 0.2% and timolol maleate ophthalmic solution in pediatric glaucoma patients (ages 2 to 7 years). In this study, brimonidine tartrate ophthalmic solution 0.2% was dosed three times a day as adjunctive therapy to beta-blockers. The most commonly observed adverse reactions were somnolence (50%-83% in patients 2 to 6 years) and decreased alertness. In pediatric patients 7 years of age or older (>20 kg), somnolence appears to occur less frequently (25%). Approximately 16% of patients on brimonidine tartrate ophthalmic solution discontinued from the study due to somnolence.

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

OVERDOSAGE

No information is available on overdosage with **COMBIGAN®** in humans. There have been reports of inadvertent overdosage with timolol ophthalmic solution resulting in systemic effects similar to those seen with systemic beta-adrenergic blocking agents such as dizziness, headache, shortness of breath, bradycardia, bronchospasm, and cardiac arrest. Treatment of an oral overdose includes supportive and symptomatic therapy; a patent airway should be maintained.

Rx Only

Irvine, CA 92612, U.S.A.

® marks owned by Allergan, Inc.

Based on package insert 72060US13 revised 10/2012.

Patented. See: www.allergan.com/products/patent_notices

APC33KM13

ALLERGAN

Why genotype-directed nutritional therapy may fuel AMD outcomes

AREDS supplementation beneficial; analysis of genetic risk could help determine best treatment

By Nancy Groves; *Reviewed by Carl C. Awh, MD*

TAKE-HOME

- ***An analysis of patient data and DNA from the Age-Related Eye Disease Study (AREDS) indicates that two genetic polymorphisms predict a differential response to antioxidants and zinc, the components of the AREDS formulation.***

NASHVILLE, TN

GENETIC TESTING MAY PLAY a role in targeting nutritional supplementation in patients with age-related macular degeneration (AMD).

Investigators found that genetic polymorphisms could explain widely differing responses to treatment with zinc and antioxidants, suggesting that genotype-directed nutritional therapy could result in improved outcomes for patients with moderate AMD.

Genotype-directed nutritional therapy could more than double the reduction in AMD progression compared with treatment of all patients with moderate AMD with the supplementation formula used in the Age-Related Eye Disease Study (AREDS), which consists of high levels of zinc and antioxidants, said Carl C. Awh, MD, an ophthalmologist in private practice in Nashville, TN.

Dr. Awh

"The benefit of AREDS supplements for the average patient with moderate AMD is undeniable," Dr. Awh said. "But we understand that this average benefit is driven by different individual responses, and we understand that these responses can be explained by differing genetic risk."

In a study analyzing AREDS data and DNA, Dr. Awh and his colleagues found that patients with high-risk complement factor H (CFH) genotypes may benefit more from antioxidants alone than from the complete AREDS formulation, due to a deleterious interaction between CFH and zinc.

Similarly, they found that some patients with high-risk age-related maculopathy sensitivity 2 (ARMS2) genotype may benefit more from a zinc supplement than from the complete AREDS formulation.

Moreover, these findings are consistent with prior research on the roles of CFH and ARMS2. CFH binds with zinc, which can neutralize its ability to inhibit component C3b, thus increasing inflammation associated with AMD, and ARMS2 localizes to mitochondria, potentially affecting the interaction of antioxidants and free radicals.

The results of their analysis were published in *Ophthalmology* in November 2013.[1] Noting that these findings are controversial, Dr. Awh said that further study—such as genetic subgroup analysis of the different zinc doses and antioxidant combinations used in AREDS2—may add insights to these findings.

The original AREDS randomly assigned patients into four groups assigned to take placebo, antioxidants, zinc, or antioxidants plus zinc. The Awh et al. analysis included 995 white AREDS patients with moderate AMD in at least one eye. The two-stage stratified statistical analysis was based on assigned AREDS treatment category. The placebo group had 235 patients; antioxidants, 256; zinc, 232; and antioxidants plus zinc, 272.

RISK FACTORS

In a forward stepwise Cox regression analysis to identify which genetic or non-genetic risk factors were significantly associated with progression within each treatment group, only two of 15 factors were statistically significant: CFH and ARMS2 in the placebo group; ARMS2 in the antioxidant group; CFH in the zinc group; and CFH and ARMS2 in the antioxidants plus zinc arm.

Next, investigators performed separate Cox proportional hazards regression analyses limited to each treatment group and the significant risk alleles. The results showed the additive impact of CFH and ARMS2 risk alleles on response to treatment.

The risk ratio for patients treated with antioxidants alone was 2.58 with one ARMS2 allele (95% CI 1.63-4.10, p = 5.749E-05) and 3.96 if two alleles were present (95% CI 2.24-7.01, p = 2.219E-06).

In patients treated with zinc only, the presence of one CFH risk allele was associated with a risk ratio of 2.18 (95% CI 1.03-4.63, p = 4.161E-02), increasing to 4.46 with two CFH alleles (95% CI 2.12-9.35, p = 7.722E-05).

For patients treated with both zinc and antioxidants, the presence of two CFH risk alleles resulted in a risk ratio of 1.83 (95% CI, 1.15-2.91, p = 1.026E-02), and two ARMS2 risk alleles had a risk ratio of 1.89 (95% CI, 1.30-2.74, p = 8.540E-04).

"We are able to use these risk ratios to calculate progression in each treatment group," Dr. Awh said. "We see that for patients with ARMS2 risk, we project that they are better treated with zinc without antioxidants, and that for patients with CFH risk alleles, they may fare better treated with high-dose antioxidants without high-dose zinc.

"If we look at our projected progression rates and the relative frequency of these genotype groups, we predict that the optimal treatment for 49% of study patients is something other than the AREDS formulation," he said. "Based on this, if all study patients were treated with

Continues on page 22 : ***AMD***

The reduction in 10-year progression to advanced AMD would be

33%

for the genotype-directed therapy versus

14%

for the AREDS formulation.

AMD

(Continued from page 21)

genotype-directed therapy, the reduction in 10-year progression to advanced AMD would be 33% for the genotype-directed therapy versus 14% for the AREDS formulation."

Genotype-directed therapy could more than double the reduction in AMD progression compared with treatment of all patients with the AREDS formulation, Dr. Awh noted.

These findings have generated considerable discussion, Dr. Awh said, and addressed several issues. He agreed that the results need to be independently validated and stated that he and his co-authors have actively sought independent validation. As proof of this, they chose to publish their findings in the peer-reviewed literature before they were presented in any public forum. To date, no one has identified any errors in their peer-reviewed statistical analysis.

Dr. Awh also commented on an alternate statistical analysis of 1,425 patients presented by Dr. Emily Chew of the National Eye Institute, saying it was underpowered.

"Unlike our two-step, stratified analysis, they combined all four treatment groups and eight genotype combinations into a single regression analysis, reporting only a single *p* value," he said. "Although this is a valid technique, this method requires more than 20,000 patients to have the power to detect the interaction we identified. As evidence of this, it fails to validate a peer-reviewed citation from their own abstract, an important paper by Dr. Klein.[2] The *p* value differences were 25-fold."

SUBGROUP ANALYSIS

Dr. Awh demonstrated that the statistical design of Dr. Chew's analysis rendered it unable to replicate or invalidate his findings. To illustrate this, he presented a subgroup analysis with a similar design to Dr. Chew's analysis, dividing AREDS study patients into nine separate genotype groups. Dr. Awh demonstrated that this method was statistically underpowered even to demonstrate that AREDS supplements were better than placebo.

Dr. Awh continued, "Does this mean that the AREDS formulation doesn't work? Of course not. It just means that this is a poorly designed analysis to answer that question. To prove or disprove something is challenging. To simply *not prove* something is easy."

He acknowledged that his study is a subgroup analysis and that some think the published treatment recommendations are not justified by the data. He explained that AREDS did not collect DNA from every patient and that he and his co-investigators used all available DNA from the AREDS DNA repository. DNA was available for almost 1,000 patients, and the analysis was based on this DNA and data obtained from the publicly available AREDS dataset. The widely referenced AREDS recommendations were also based on a subgroup analysis, he noted.

Dr. Awh concluded by acknowledging the benefit of AREDS supplements but emphasized that "we now understand that the overall benefit of AREDS supplements for patients with moderate AMD is the product of greatly differing individual responses and that these differences can largely be explained by measurable differences in genetic risk." ■

References

1. Awh CC, Lane AM, Hawken S, Zanke B, Kim IK. CFH and ARMS2 Genetic polymorphisms predict response to antioxidants and zinc in patients with age-related macular degeneration. *Ophthalmology.* 2013;120:2317-2323.
2. Klein ML, Francis PJ, Rosner B, Reynolds R, Hamon SC, Schultz DW, Ott J, Seddon JM. CFH and LOC387715/ARMS2 genotypes and treatment with antioxidants and zinc for age-related macular degeneration. *Ophthalmology.* 2008;115:1019-1025.

CARL C. AWH, MD
P: *615/983-6000*
E: *carlawh@gmail.com*
Dr. Awh is a consultant to and an equity owner in ArcticDx.

On Twitter

Follow *Ophthalmology Times* on Twitter for the latest news and advancements in ophthalmology **@OphthTimes**

@OphthTimes.@PBA_savingsight encourages workplace #eye wellness http://bit.ly/1dJ7z64

@OphthTimes Duke University ophthalmology chairman, Dr. David Epstein, dies http://bit.ly/1glqvVH

@OphthTimes The Smart System from M&S Technologies has been chosen as the #refraction system of choice in the part III tests by the NBEO

@OphthTimes John A. Moran Eye Center announces new research that will examine the role of erythropoietin (EPO) signaling in retinopathy of prematurity

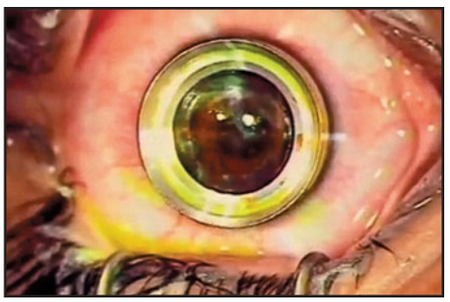
Digital App

Introducing the *Ophthalmology Times* app for iPad and iPhone. Download it for free today at *OphthalmologyTimes.com/OTapp.*

eReport

Sign up for *Ophthalmology Times*' weekly eReport at *http://bit.ly/XjksXX.*

Video



Lamellar-perforating keratoplasty (LPK) was developed by Cesar Carriazo, MD, as a modification to pachymetry-assisted lamellar keratoplasty (PALK).To watch a surgical case, go to *http://bit.ly/1fwkPa9*
(Videos courtesy of Cesar Carriazo, MD)

Facebook

Like *Ophthalmology Times* at **Facebook.com/OphthalmologyTimes.**

ellex

SLT
TECHNOLOGY

24 hours a day. 7 days a week.

SLT keeps IOP under control around the clock with 100% patient compliance.

Whether used as primary, adjunct, or replacement therapy, SLT lowers IOP as effectively as medication, has a consistent safety profile, and – best of all – works 24 hours a day, 7 days a week, putting you in control of the treatment.

Offering superior energy control, a sharp-edged aiming beam and the fastest firing rate at 3 shots per second, Ellex's proprietary SLT technology allows you to visualize the TM in greater detail and to perform procedures faster and with improved accuracy.

SLT technology from **Ellex** now available in the USA! Learn more at ellex.com.

ellex

slt-ellex.com | (855) 767-5784

PEDIATRIC CATARACT

(Continued from page 1)

The IOL power might be chosen to provide less residual hyperopia when the cataract eye is longer than the fellow eye, because it is likely to slow its future growth (and reduce the IALD) after surgery. IOL power might be chosen to result in more residual hyperopia in a shorter eye that would be expected to grow faster than normal (reducing IALD) after surgery.

A target of emmetropia might be chosen for an eye predicted to need intense patching for dense amblyopia if poor postoperative compliance with glasses is expected.

TAKE-HOME

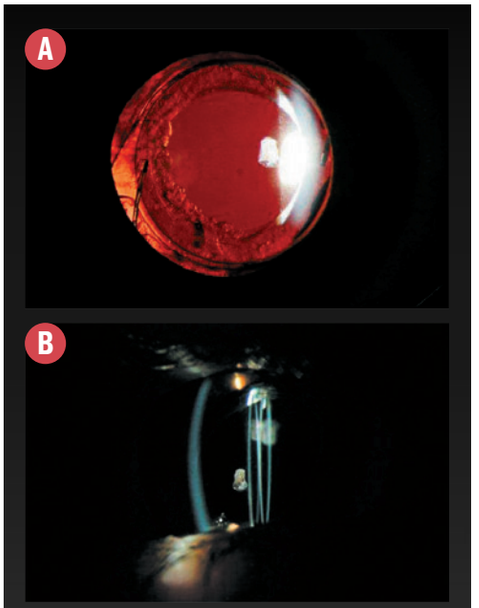
- ***Pediatric cataract surgery is now approached as a refractive procedure in which multiple factors are taken into account to determine the timing of IOL implantation and power selection.***

The latter approach would ease the burden on parents and would incorporate a plan for additional refractive procedures.

APHAKIA

Leaving the child aphakic—which was popularized by Dr. Parks and David Taylor, MD—remains the least traumatic surgery for infants and has multiple advantages, according to Dr. Wilson.

"Opacification of the visual axis is dramatically reduced by avoiding IOL implantation during the first 6 months of life," he said. "Aphakia also avoids multiple ins and outs of the eye, provides maximum flexibility to adjust for the rapidly changing refractive error of infancy, and gives a good image right away."



A Retroillumination shows permanent IOL in the capsular bag and temporary IOL in the ciliary sulcus.

B Slit lamp beam outlines the two IOL optics.

(Images courtesy of M. Edward Wilson, MD)

When choosing to leave a child aphakic, Dr. Wilson said he places a contact lens (SilSoft, Bausch + Lomb) on the eye at the end of the procedure and starts prednisolone acetate, antibiotic, and atropine drops immediately without using any patch or shield.

Contact lens power is chosen using the Holladay IOL formula, and a lens constant devised for the contact lens (111.9)[3]

Only two base curves need to be stocked—7.5 mm for use in infants up to age 18 to 24 months and 7.7 mm for those who are older.

Dr. Wilson

Aphakic spectacles, however, are sometimes the best option in the toddler age when contact lenses become more difficult, until a proper determination on IOL placement can be made, according to Dr. Wilson.

POLYPSEUDOPHAKIA

Polypseudophakia is an unproven—but reasonably safe—refractive option in pediatric cataract surgery patients, according to Dr. Wilson. Surgeons should consider this option when appropriate.

He advised against piggybacking both IOLs in the capsular bag, which leads to interlenticular opacification.

Rather, Dr. Wilson recommended placing a permanent lens in the bag and a temporary lens in the sulcus that can be easily removed without dislodging the capsule-fixated IOL.

With the latter piggybacking approach, the power of the permanent IOL is chosen as the power expected to be needed to provide emmetropia at age 20. The sulcus IOL power is chosen to provide a postoperative result of plano or mild hyperopia.

Children are followed with yearly biometry, and the temporary lens is removed when the biometry predicts that the refraction will be plano after removal of the temporary IOL.

Implantation of both IOLs in the ciliary sulcus can also be done.

Dr. Wilson said he chooses this piggybacking approach in a secondary IOL setting where the power need exceeds that available using a single IOL. ■

References

1. Gochnauer AC, et al. *J AAPOS*. 2010;14:20-24.
2. Trivedi RH, Wilson ME. *J AAPOS*. 2007;11:225-229.
3. Trivedi RH, Wilson ME. *Ophthalmology*. 2013;120:1973-1976.

M. EDWARD WILSON, MD

E: *wilsonme@musc.edu*

Dr. Wilson delivered the Marshall M. Parks Lecture at the 2013 meeting of the American Academy of Ophthalmology. He has no relevant financial interests to disclose.

Dr. Epstein, chairman at Duke University, dies

By Rose Schneider, *Content Specialist,* Ophthalmology Times

DURHAM, NC ::

DAVID L. EPSTEIN, MD, the Joseph A.C. Wadsworth Clinical Professor of Ophthalmology and chairman of the Department of Ophthalmology at Duke University School of Medicine, died March 4.

Dr. Epstein served as chairman for the past 22 years, and under his leadership, the department grew to include its current team of 73 faculty and more than 300 staff members.

Dr. Epstein also authored more than 230 scholarly papers and consulted in glaucoma clinical care, while maintaining an active glaucoma research program. He received many awards for his work, including the 2013 Mildred Weisenfeld Award for Excellence in Ophthalmology from the Association for Research in Vision and Ophthalmology (ARVO).

In 2012, he received the Duke University School of Medicine Medical Alumni Association's Distinguished Faculty Award.

From 1992 to 1993, he served as president of ARVO. He served as president of the Chandler-Grant Glaucoma Society from 2004 to 2005, and was president of the Association of University Professors of Ophthalmology in 2011.

Edward Buckley, MD, has been appointed acting chairman of the department. ■

Alphagan® P 0.1%
(brimonidine tartrate ophthalmic solution) 0.1%

EXTEND YOUR REACH...

All the Way From Prescription to Patient

Make certain your ALPHAGAN® P 0.1% Rx is filled the way you intended

INDICATIONS AND USAGE

ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% or 0.15% is an alpha-adrenergic receptor agonist indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

Neonates and Infants (under the age of 2 years): ALPHAGAN® P is contraindicated in neonates and infants (under the age of 2 years).

Hypersensitivity Reactions: ALPHAGAN® P is contraindicated in patients who have exhibited a hypersensitivity reaction to any component of this medication in the past.

WARNINGS AND PRECAUTIONS

Potentiation of Vascular Insufficiency: ALPHAGAN® P may potentiate syndromes associated with vascular insufficiency. ALPHAGAN® P should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangiitis obliterans.

Severe Cardiovascular Disease: Although brimonidine tartrate ophthalmic solution had minimal effect on the blood pressure of patients in clinical studies, caution should be exercised in treating patients with severe cardiovascular disease.

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

DRUG INTERACTIONS

Antihypertensives/Cardiac Glycosides: Because ALPHAGAN® P may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with ALPHAGAN® P is advised.

CNS Depressants: Although specific drug interaction studies have not been conducted with ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% or 0.15%, the possibility of an additive or potentiating effect with CNS depressants (alcohol, barbiturates, opiates, sedatives, or anesthetics) should be considered.

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

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

ADVERSE REACTIONS

Adverse reactions occurring in approximately 10% to 20% of the subjects receiving brimonidine ophthalmic solution (0.1% to 0.2%) included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritus. Adverse reactions occurring in approximately 5% to 9% included: burning sensation, conjunctival folliculosis, hypertension, ocular allergic reaction, oral dryness, and visual disturbance.

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

Write it RIGHT P 0.1%

Alphagan® P 0.1%
(brimonidine tartrate ophthalmic solution) 0.1%

ALPHAGAN® P

(brimonidine tartrate ophthalmic solution)
0.1% and 0.15%

BRIEF SUMMARY

Please see **ALPHAGAN® P** package insert for full prescribing information.

INDICATIONS AND USAGE

ALPHAGAN® P (brimonidine tartrate ophthalmic solution) 0.1% or 0.15% is an alpha adrenergic receptor agonist indicated for the reduction of elevated intraocular pressure (IOP) in patients with open-angle glaucoma or ocular hypertension.

CONTRAINDICATIONS

Neonates and Infants (under the age of 2 years)
ALPHAGAN® P is contraindicated in neonates and infants (under the age of 2 years).

Hypersensitivity Reactions

ALPHAGAN® P is contraindicated in patients who have exhibited a hypersensitivity reaction to any component of this medication in the past.

WARNINGS AND PRECAUTIONS

Potentiation of Vascular Insufficiency
ALPHAGAN® P may potentiate syndromes associated with vascular insufficiency.

ALPHAGAN® P should be used with caution in patients with depression, cerebral or coronary insufficiency, Raynaud's phenomenon, orthostatic hypotension, or thromboangiitis obliterans.

Severe Cardiovascular Disease
Although brimonidine tartrate ophthalmic solution had minimal effect on the blood pressure of patients in clinical studies, caution should be exercised in treating patients with severe cardiovascular disease.

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

ADVERSE REACTIONS

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

Adverse reactions occurring in approximately 10-20% of the subjects receiving brimonidine ophthalmic solution (0.1-0.2%) included: allergic conjunctivitis, conjunctival hyperemia, and eye pruritus. Adverse reactions occurring in approximately 5-9% included: burning sensation, conjunctival folliculosis, hypertension, ocular allergic reaction, oral dryness, and visual disturbance.

Adverse reactions occurring in approximately 1-4% of the subjects receiving brimonidine ophthalmic solution (0.1-0.2%) included: abnormal taste, allergic reaction, asthenia, blepharitis, blepharoconjunctivitis, blurred vision, bronchitis, cataract, conjunctival edema, conjunctival hemorrhage, conjunctivitis, cough, dizziness, dyspepsia, dyspnea, epiphora, eye discharge, eye dryness, eye irritation, eye pain, eyelid edema, eyelid erythema, fatigue, flu syndrome, follicular conjunctivitis, foreign body sensation, gastrointestinal disorder, headache, hypercholesterolemia, hypotension, infection (primarily colds and respiratory infections), insomnia, keratitis, lid disorder, pharyngitis, photophobia, rash, rhinitis, sinus infection, sinusitis, somnolence, stinging, superficial punctate keratopathy, tearing, visual field defect, vitreous detachment, vitreous disorder, vitreous floaters, and worsened visual acuity.

The following reactions were reported in less than 1% of subjects: corneal erosion, hordeolum, nasal dryness, and taste perversion.

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

DRUG INTERACTIONS

Antihypertensives/Cardiac Glycosides
Because **ALPHAGAN® P** may reduce blood pressure, caution in using drugs such as antihypertensives and/or cardiac glycosides with **ALPHAGAN® P** is advised.

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

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

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

USE IN SPECIFIC POPULATIONS

Pregnancy
Pregnancy Category B: Teratogenicity studies have been performed in animals.

Brimonidine tartrate was not teratogenic when given orally during gestation days 6 through 15 in rats and days 6 through 18 in rabbits. The highest doses of brimonidine tartrate in rats (2.5 mg /kg/day) and rabbits (5.0 mg/kg/day) achieved AUC exposure values 360- and 20-fold higher, or 260- and 15-fold higher, respectively, than similar values estimated in humans treated with **ALPHAGAN® P** 0.1% or 0.15%, 1 drop in both eyes three times daily.

There are no adequate and well-controlled studies in pregnant women; however, in animal studies, brimonidine crossed the placenta and entered into the fetal circulation to a limited extent. Because animal reproduction studies are not always predictive of human response, **ALPHAGAN® P** should be used during pregnancy only if the potential benefit to the mother justifies the potential risk to the fetus.

Nursing Mothers
It is not known whether brimonidine tartrate is excreted in human milk, although in animal studies, brimonidine tartrate has been shown to be excreted in breast milk. Because of the potential for serious adverse reactions from **ALPHAGAN® P** 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
ALPHAGAN® P is contraindicated in children under the age of 2 years (see **CONTRAINDICATIONS**). During postmarketing surveillance, apnea, bradycardia, coma, hypotension, hypothermia, hypotonia, lethargy, pallor, respiratory depression, and somnolence have been reported in infants receiving brimonidine. The safety and effectiveness of brimonidine tartrate have not been studied in children below the age of 2 years.

In a well-controlled clinical study conducted in pediatric glaucoma patients (ages 2 to 7 years) the most commonly observed adverse reactions with brimonidine tartrate ophthalmic solution 0.2% dosed three times daily were somnolence (50-83% in patients ages 2 to 6 years) and decreased alertness. In pediatric patients 7 years of age (>20 kg), somnolence appears to occur less frequently (25%). Approximately 16% of patients on brimonidine tartrate ophthalmic solution discontinued from the study due to somnolence.

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

Special Populations
ALPHAGAN® P has not been studied in patients with hepatic impairment.

ALPHAGAN® P has not been studied in patients with renal impairment. The effect of dialysis on brimonidine pharmacokinetics in patients with renal failure is not known.

OVERDOSAGE

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment of Fertility
No compound-related carcinogenic effects were observed in either mice or rats following a 21-month and 24-month study, respectively. In these studies, dietary administration of brimonidine tartrate at doses up to 2.5 mg/kg/day in mice and 1 mg/kg/day in rats achieved 150 and 120 times or 90 and 80 times, respectively, the plasma C_{max} drug concentration in humans treated with one drop of **ALPHAGAN® P** 0.1% or 0.15% into both eyes 3 times per day, the recommended daily human dose.

Brimonidine tartrate was not mutagenic or clastogenic in a series of in vitro and in vivo studies including the Ames bacterial reversion test, chromosomal aberration assay in Chinese Hamster Ovary (CHO) cells, and three in vivo studies in CD-1 mice: a host-mediated assay, cytogenetic study, and dominant lethal assay.

Reproduction and fertility studies in rats with brimonidine tartrate demonstrated no adverse effect on male or female fertility at doses which achieve up to approximately 125 and 90 times the systemic exposure following the maximum recommended human ophthalmic dose of **ALPHAGAN® P** 0.1% or 0.15%, respectively.

PATIENT COUNSELING INFORMATION

Patients should be instructed that ocular solutions, if handled improperly or if the tip of the dispensing container contacts the eye or surrounding structures, can become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions (see **WARNINGS AND PRECAUTIONS**). Always replace the cap after using. If solution changes color or becomes cloudy, do not use. Do not use the product after the expiration date marked on the bottle.

Patients also should be advised that if they have ocular surgery or develop an intercurrent ocular condition (e.g., trauma or infection), they should immediately seek their physician's advice concerning the continued use of the present multidose container.

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

As with other similar medications, **ALPHAGAN® P** may cause fatigue and/or drowsiness in some patients. Patients who engage in hazardous activities should be cautioned of the potential for a decrease in mental alertness.

Rx Only

Revised: 11/2011

Based on package insert 71816US15C

APC57BC13

Alphagan® P 0.1%
(brimonidine tartrate ophthalmic solution) 0.1%

How GLP-1 targeted therapy may help patients with type 2 diabetes

Exenatide an important adjunctive therapy to help prevent cardiovascular side effects

By Lynda Charters; *Reviewed by Susan M. Pepin, MD*

TAKE-HOME

- ***The role of ophthalmologists will become increasingly more vital in the management of type 2 diabetes as the numbers of patients with the disease is projected to double by 2030. Exenatide may prove to be an important adjunct to current oral anti-diabetes drugs.***

HANOVER, NH ::

GIVEN THAT THE NUMBERS of individuals with type 2 diabetes is nearly 300 million worldwide, and likely to double by 2030, ophthalmologists will play an even greater role in the management of the disease.

"Type 2 diabetes and cardiovascular disease are intimately linked," said Susan M. Pepin, MD, associate professor of surgery and pediatrics, Geisel School of Medicine, Dartmouth College, Hanover, NH,

A glucagon-like peptide-1 (GLP-1) agonist, exenatide (Byetta, Bydureon, Bristol-Myers Squibb), is proving to be an important adjunctive therapy to current oral anti-diabetes drugs by helping to prevent the cardiovascular side effects of type 2 diabetes.

Traditional oral anti-diabetic agents, according to Dr. Pepin, do not specifically address the severity of cardiovascular disease in patients with type 2 diabetes.

New therapeutic agents should be identified that involve GLP-1, a potent incretin. Also, the agents should be classified based on the GLP-1 effects to consider potential cardiovascular safety profiles, as well as potential increased risk of pancreatitis or cancer in patients undergoing treatment with these drugs.

Underscoring the importance of GLP-1, Dr. Pepin described the case of a 59-year-old obese (body mass index, 33) male with a 12-year history of diabetes and who presented with sudden-onset binocular horizontal diplopia.

The patient was treated with metformin 1,000 mg injected subcutaneously and atorvastatin (Lipitor, Pfizer) and denied having cardiovascular disease or diabetic retinopathy. The hemoglobin A1c was in the 8s, and blood pressure was 144/97 mm Hg. Clinical examination showed that the left eye did not adduct and the patient had a left sixth-nerve palsy.

Ophthalmologists are important in the care of such patients, she stressed, noting that cardiovascular disease is the leading cause of more than 60% of deaths in patients with diabetes. High glucose levels are believed to increase the risk of coronary artery disease and myocardial infarction, she noted.

"Most of the standard oral anti-diabetes drugs do not reduce the incidence rates of myocardial infarction, stroke, or cardiovascular death in patients with diabetes," Dr. Pepin added.

THE CASE FOR GLP-1

After a meal, L-cells in the gut release GLP-1, resulting in increased insulin secretion in the pancreas, glucose uptake in muscles, glucagon formation in the liver, improved satiety, and delayed gastric emptying, Dr. Pepin explained.

Inhibitors of the activity of dipeptidyl peptidase 4 (DDP-4)—a protein that rapidly degrades GLP-1—and GLP-1 receptor agonists—which resist the activity of DDP-4—are important potential therapeutic agents to augment the standard oral therapies, because in patients with type 2 diabetes, GLP-1 secretion is greatly reduced.

Currently, the DPP-4 inhibitors—sitagliptin (Januvia, Merck), saxagliptin (Onglyza, Bristol-Myers Squibb), and vildagliptin (Galvus, Novartis Pharmaceuticals)—are in clinical trials. GLP-1R agonists include exenatide, which received FDA approval in 2006, and liraglutide (Victoza, Novo-Nordisk), which is similar to exenatide.

CARDIOPROTECTIVE EFFECT

Exenatide affects the GLP-1 receptor and through a series of different mechanisms is thought to have a cardioprotective effect. Dr. Pepin cited a recent study by Mundil and associates (*Diabetes and Vascular Disease Research.* 2012;9:95-108) that combined data from six studies investigating treatment of hyperglycemia and the cardiovascular risk factors associated with GLP-1 receptor agonists in more than 2,000 patients.

"The study showed a substantial and significant reduction of hyperglycemia in these patients who were already receiving oral hyperglycemic agents and exenatide," Dr. Pepin explained.

Investigators found that GLP-1R agonists reduced body weight and systolic blood pressure and improved patients' lipid profiles. The proposed mechanisms by which these effects occurred were appetite suppression, reduced body fat stores, natriuresis and diuresis, and improved endothelial function.

The caveat associated with GLP-1 drugs is a potential risk for development of chronic pancreatitis as reported in cases submitted to the FDA.

However, this risk is questionable, Dr. Pepin noted, because patients who are obese and have type 2 diabetes already are at an increased risk of pancreatitis and pancreatic cancer. In a 3-year period from 2005 to 2007, more than 7 million exenatide prescriptions were written, but only 78 cases of kidney dysfunction were reported, she said.

"Because type 2 diabetes causes significant end-organ complications—primarily cardiovascular disease—anti-diabetic treatment should favor cardiovascular safety profiles and not result in weight gain," Dr. Pepin said. "Exogenous GLP-1 analogues are proving to be powerful adjunctive therapy for hyperglycemic control with these safety profiles." ■

SUSAN M. PEPIN, MD

E: *susan.m.pepin@dartmouth.edu*

Dr. Pepin has no financial interest in any aspect of this report.

Tracing the ocular manifestations of mumps throughout the ages

Historic perspective shows virus can affect lacrimal gland, cause acute dacryoadenitis

Our Ophthalmic Heritage **By Norman B. Medow, MD, FACS**

TAKE-HOME

- ***The treatment of mumps is unchanged since Hippocrates first prescribed supportive therapy, including rest, cool compressors, and pain medications.***

INFECTIONS OF THE EYE are not uncommon. Conjunctivitis caused by bacteria—such as *Streptococcus pneumoniae*—or viruses such as adenovirus—are well known to the ophthalmologist. But what about infections caused by a paramyxovirus? No, not the parainfluenza virus or the respiratory syncytial virus, but the paramyxovirus that causes mumps.

The term *mumps* most likely arose from British slang of the late 1500s. A mump described a person who mumbled or muttered. It was then used to describe people with this disorder whose facial swelling and sore throat led them to speak as a mump did. Hence, the term mumps was given to those with the condition.

This acute, highly contagious ribonucleic acid virus causes epidemic parotitis commonly called mumps, but it can affect the lacrimal gland and cause acute dacryoadenitis.

HISTORIC DESCRIPTION OF DISORDER

What is historically important about this condition is that Hippocrates first described it in the fifth century B.C.E. His description is very accurate. The preauricular region swells—mostly bilaterally—and most often occurs during the winter and spring. Fever is often an accompaniment, although bed rest was generally not required. None of these swellings suppurated. The area affected was enlarged without inflammation or pain and generally went away without problems.

Hippocrates commented on the causality of this disorder and how it occurred in people who congregated in groups, such as in gymnasiums or in highly crowded areas. Many people, he said, had dry coughs and became hoarse.

The disease affected mostly men or children. It seldom affected woman.

In some men, pain and swelling would affect the testicles, causing much suffering. In all other respects, the patient was free of disease requiring no medical assistance.

WHAT PHYSICIANS HAVE LEARNED

Physicians now know that the virus has a 2- to 3-week incubation period, and enters the patient via the respiratory tract.

From there it enters the salivary glands and local lymphatic glands and spreads to the other lymphatics of the body. This occurs in 7 to 10 days.

> The term *mumps* was given to those with this disorder whose facial swelling and sore throat led them to speak as a mump did.

At this time, a viremia occurs that lasts about 10 to 14 days. The virus can spread throughout the body to cause orchitis, oophoritis, pancreatitis, meningitis, deafness, arthritis, and myocarditis.

Epidemics of mumps were very common during the 18th and 19th centuries. Schools, ships at sea, and even entire armies were affected. The virus was isolated in 1934 by Johnson and Goodpasture.

In the late 1970s a live, attenuated vaccine was developed to immunize the public. The vaccine was called the MMR vaccine and immunized the recipient to measles, mumps, and rubella. In the late 1990s, it became compulsory in school children in the United States. Lifelong immunity occurs in about 85% of recipients.

The treatment of mumps is unchanged since Hippocrates first prescribed supportive therapy, including rest, cool compressors, and pain medications. History has shown us once again that centuries of knowledge often resist specific treatment of disease.

The more we learn, the more we stay the same. ■

References

1. Adams F. The genuine works of Hippocrates. New York: William Wood. 1849:1;293.
2. Johnson CD, Goodpasture EW. An investigation of the etiology of mumps. *J Exp Med.* 1934;59:1–19.

NORMAN B. MEDOW, MD, FACS, *is editor of the Our Ophthalmic Heritage column. He is director, pediatric ophthalmology and strabismus, Montefiore Hospital Medical Center, and professor of ophthalmology and pediatrics, Albert Einstein College of Medicine, Bronx, NY. He did not indicate a financial interest in the subject matter.*

Monotherapy Maintained.

Proven IOP reduction[1]

•

Established tolerability with
low discontinuation rate[2]

On Your Terms.

Broad preferred coverage[3]

•

Comprehensive patient support

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

Important Safety Information

Warnings and Precautions: LUMIGAN® 0.01% causes changes to pigmented tissues, mostly increased pigmentation of the iris, eyelid, and eyelashes as long as LUMIGAN® 0.01% is administered. Iris color change may not be noticeable for several months to years. After discontinuation of bimatoprost, iris pigmentation is likely to be permanent, while eyelid and eyelash changes have been reported to be reversible in some patients. Patients should be informed of the possibility of increased pigmentation. The long-term effects of increased pigmentation are not known.

LUMIGAN® 0.01% should be used with caution in patients with active intraocular inflammation (eg, uveitis) because the inflammation may be exacerbated. Macular edema, including cystoid macular edema, has been reported with LUMIGAN® 0.01%. LUMIGAN® 0.01% 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. LUMIGAN® 0.01% has not been studied to treat types of glaucoma other than open-angle glaucoma. Remove contact lenses prior to instillation of LUMIGAN® 0.01% and reinsert after 15 minutes.

Adverse Reactions: The most common (25%-45%) adverse event with LUMIGAN® 0.01% was conjunctival hyperemia. Approximately 0.5% to 3% of patients discontinued therapy due to conjunctival hyperemia. Other common events (> 10%) included growth of eyelashes and ocular pruritus.

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

1. LUMIGAN® Prescribing Information. **2.** Katz LJ, Cohen JS, Batoosingh AL, Felix C, Shu V, Schiffman RM. Twelve-month, randomized, controlled trial of bimatoprost 0.01%, 0.0125%, and 0.03% in patients with glaucoma or ocular hypertension. *Am J Ophthalmol.* 2010;149(4):661-671. **3.** Managed Markets Insight & Technology, LLC, database, as of November 2013.

LUMIGAN® 0.01%
(bimatoprost ophthalmic solution) 0.01%

Allergan at your service

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

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

INDICATIONS AND USAGE

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

CONTRAINDICATIONS

None

WARNINGS AND PRECAUTIONS

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

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

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

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

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

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

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

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

ADVERSE REACTIONS

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

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

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

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

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

USE IN SPECIFIC POPULATIONS

Pregnancy: Pregnancy Category C

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

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

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

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

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

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

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

OVERDOSAGE

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

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

NONCLINICAL TOXICOLOGY

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

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

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

PATIENT COUNSELING INFORMATION

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

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

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

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

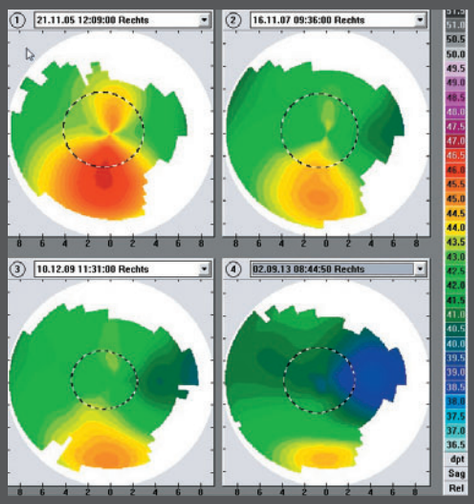
Use with Contact Lenses: Patients should be advised that **LUMIGAN®** 0.01% and 0.03% contains benzalkonium chloride, which may be absorbed by soft contact lenses. Contact lenses should be removed prior to instillation of **LUMIGAN®** and may be reinserted 15 minutes following its administration.

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

APC70EN12 based on 71807US13.

Rx only

ALLERGAN®



Cornea After CXL

These images track a case of a patient followed for 8 years after corneal crossslinking (CXL) in 2005. There is a constant change due to a remodeling of the cornea after CXL.

(Images courtesy of Theo Seiler, MD, PhD)

CORNEAL CROSSLINKING SHOWS FAVORABLE LONG-TERM OUTCOMES

Study examined CXL using Dresden protocol for the treatment of progressive keratectasia

By Cheryl Guttman Krader; *Reviewed by Theo Seiler, MD, PhD*

take-home

- **Studies with follow-up of 2 to 6 years show that corneal crosslinking for progressive keratectasia is safe and induces long-term structural changes.**

ZURICH, SWITZERLAND ::

Results from 5 years of follow-up support the efficacy and safety of corneal crosslinking (CXL) using the original Dresden protocol for the treatment of progressive keratectasia, said Theo Seiler, MD, PhD, who pioneered the procedure.

Data showed that CXL results in a significant keratometric flattening effect that is stable in most eyes, while causing minimal complications or significant best spectacle-corrected visual acuity (BSCVA) loss, said Dr. Seiler, professor of ophthalmology, University of Zurich, and chairman, IROC Zurich, Switzerland.


Dr. Seiler

"CXL induces structural changes in the cornea that may continue for many years," he said. "However, do not forget that the long-term results being published today are based on treatment with the Dresden protocol using an epithelium-off technique."

CXL SAFETY

In evaluating the safety of CXL, Dr. Seiler said he first used the criterion of a ≥2 line loss of Snellen BSCVA that is used by the FDA as a marker for complications. In a series of more than 100 eyes treated with CXL, the rate of BSCVA loss of 2 or more lines at 1 year was 1%, and risk factors for that outcome were age >35 years and better baseline vision (20/25 or better).

Failure of treatment to prevent disease progression is more difficult to identify, considering inherent keratometric measurement error.

Using a criterion of a Kmax increase ≥1 D—which represents >3 standard deviations of the measurement error—the 1-year failure rate in the same cohort of eyes was 3%. The only preoperative risk factor identified for failure was advanced keratoconus (Kmax >58 D), although there are many examples of eyes with severe keratoconus that benefit with significant flattening after CXL, he noted.

At 1 year postCXL, 35% of eyes treated with the standard irradiation protocol (3 mW/cm^2 for 30 minutes) using older UVA technology (UV-X 1000, IROC Innocross) achieved Kmax flattening >1 D, according to Dr. Seiler. However, success in achieving that outcome has been increased dramatically to 91% using a newer device that features an optimized beam profile (UV-X 2000, IROC Innocross).

LOOKING LONG TERM

Reviewing longer-term outcomes, Dr. Seiler cited a study from his original Dresden group that included data from 241 eyes with a mean follow-up of 27 months and reported a 2-year failure rate of 2% [*J Cataract Refract Surg*. 2008;34:796-801]. However, in a study by O'Brart et al. [*Br J Ophthalmol*. 2013;97:433-437] that included 40 eyes followed for 4 years, there were no cases with a Kmax increase ≥1 D.

"These are essentially very favorable long-term results and indicate CXL is a very effective procedure," Dr. Seiler said.

Data on long-term complication rates vary from 0% in the study by O'Brart et al. to 13.7% as reported by Hashemi et al. in a series of 40 eyes followed to 5 years [*Ophthalmology*. 2013;120:1515-1520].

"Likely, the true complication rate lies somewhere in between," Dr. Seiler said.

Data on keratometric flattening from the studies by O'Brart et al. and Hashemi et al. show the results are stable with some minor continued flattening over the long term. However, Dr. Seiler stressed that more dramatic progressive flattening might be observed in occasional patients. ■

THEO SEILER, MD, PHD

E: *claudia.kindler@iroc.ch*

Dr. Seiler is a scientific consultant to Alcon Laboratories/Wavelight.

Why prompt CXL treatment is vital with diagnosis of keratoconus

Early application in children and adolescents may prevent rapid progression

By Lynda Charters; *Reviewed by Farhad Hafezi, MD, PhD*

GENEVA, SWITZERLAND ::

OPHTHALMOLOGISTS HAVE STRUGGLED with decisions about whether to treat subpopulations of patients with keratoconus differently from the currently accepted approach.

The answer may be "yes," based on a study that found that the vast majority of children and adolescents aged 8 to 19 years have rapid keratoconic progression after the initial diagnosis is established. To avoid this, immediate treatment may be required.

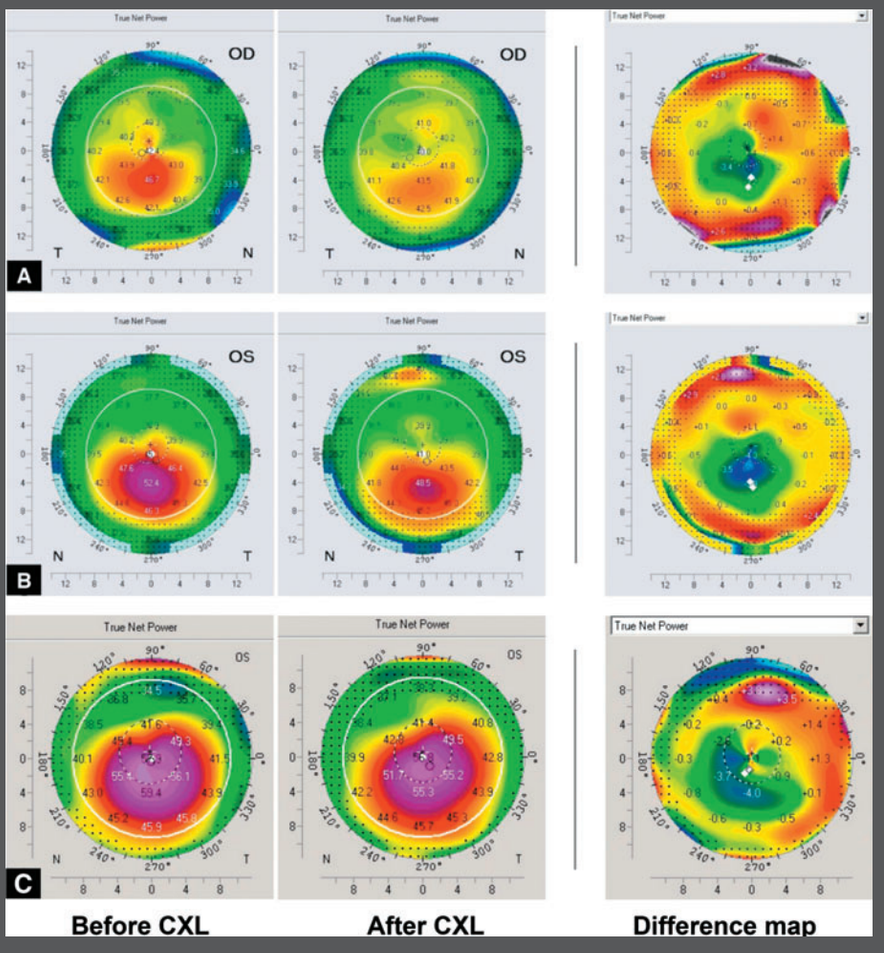
When corneal crosslinking (CXL) technology was first introduced, clinicians approached its use conservatively.

"When CXL initially began to be used, we always determined that the patient was progressing before CXL was applied to be sure that an emerging technology was used carefully to avoid unnecessary complications," said Farhad Hafezi, MD, PhD, who was part of the Swiss team that developed the first CXL device.

"However, it is now time to re-visit this strategy considering that CXL is used clinically in more than 100 countries worldwide," said Dr. Hafezi, professor and chairman, Department of Ophthalmology, Geneva University Hospital, Geneva, Switzerland, and clinical professor of ophthalmology, Doheny Eye Institute, University of Southern California, Los Angeles.

take-home

- **Children and adolescents with keratoconus may have rapid progression between the ages of 8 and 19 years and immediate treatment with corneal crosslinking may stop that progression.**



Flattening effect of corneal collagen crosslinking (CXL) in adolescent patients. Preoperative Scheimpflug imaging is depicted on the left side and the postoperative examination is depicted in the middle. The image to the right demonstrates the difference map. A 18-year-old male patient before and 12 months after CXL. B 17-year-old female patient before and 12 months after CXL. C 13-year-old male patient before and 12 months after CXL.

(Figure reproduced with permission of SLACK Inc.; J Refract Surg. 2012;28:753-758. doi:10.3928/1081597X-20121011-01)

STRATEGIES FOR PROGRESSION

Progression was defined as an increase of more than 1 D of Kmax of the anterior corneal curvature within a 12-month period.

Keratoconus can progress extremely rapidly in young patients and he reported a 4-D progression in a 15-year-old boy over 12 weeks.

"If we wait for progression over a very short interval, it might still be too long to wait," Dr. Hafezi emphasized.

Dr. Hafezi noted that he re-examines young patients after only 4 weeks to avoid missing any immediate progression.

To address the question about adjusting treatment strategies for these children, Dr. Hafezi and his colleagues conducted a retrospective interventional cohort study of 42 patients, 36 boys and 16 girls (average age, 16.6 years; range,

Continues on page 34 : ***Keratoconus***

WELCOME TO THE ERA OF CENTURION®

Optimize every moment of your cataract removal procedure with the NEW CENTURION® Vision System.

Active Fluidics™

Automatically optimizes chamber stability by allowing surgeons to customize and control IOP throughout the procedure.

Balanced Energy™

Enhances cataract emulsification efficiency using OZil® Intelligent Phaco and the new INTREPID® Balanced Tip design.

Applied Integration™

Designed to work seamlessly with other Alcon technologies for an integrated cataract procedure experience.

Learn more about the new era of cataract procedures. Visit MyAlcon.com.

Alcon®
a Novartis company

CENTURION®
VISION SYSTEM

For important safety information, please see adjacent page.

KERATOCONUS

(*Continued from page 32*)

9 to 19 years). Of 59 eyes examined, 52 eyes showed keratoconus progression and were included.

Informed consent from parents was received. Forty-six eyes underwent treatment after the patients provided informed consent. The patients had been followed for up to 3 years (mean, 26.3 months; range, 3 to 36 months).

"Interestingly, we found that when we looked at the arrested progression and the flattening effect of treatment, the children and adolescents behaved similarly to what we expect to see in adults," Dr. Hafezi said.

"In some cases, the children and adolescents reacted faster and we observed arrested progression in as soon as 3 months after treatment compared to at least 6 months in adults," he said.

TWO DIFFERENT FINDINGS

Two other findings in this study differed from those in adults, Dr. Hafezi noted.

During the first 2 years of follow-up, Dr. Hafezi and colleagues found that children and adolescents behaved like adults, with more than 1-D flattening of the Kmax readings. However, during the third year of follow-up, there was no additional flattening and the eyes stabilized.

When these results were compared with two other studies on the same topic, one study by Paolo Vinciguerra, MD, et al. (*Am J Ophthalmol.* 2012;154:520-526) showed the same results for the first 2 years of follow-up (no data were provided on the third year of follow-up) in a larger number of patients.

However, a second study by Aldo Caporossi, MD, et al. (*Cornea.* 2012;35:233-235) found that there was significant flattening during the first 2 years and additional flattening during the third year.

"The results of these studies indicated that we must pay particular attention to children with keratoconus after year 2," Dr. Hafezi said. "It seems sensible that during a period in their lives when they are susceptible to aggressive progression, cross-linking might not be the cure forever, but might be effective for a time, that is, perhaps limited to 2, 3, or 4 years. This requires closer study."

The second result that he found interesting involved the number of eyes of patients who initially presented with keratoconus between the ages of 8 and 19 years and showed keratoconic progression.

"Of the 59 eye that were diagnosed with keratoconus at the initial visit, 52 (88%) showed progression," he said. "About nine of 10 children will progress between ages 8 and 19 once keratoconus has been diagnosed."

CXL seems to be efficient in pediatric and adolescent patients, Dr. Hafezi said.

However, the long-lasting effect of the flattening is controversial and particular attention must be paid to year 3 after treatment. If almost 90% of children and adolescents have progression of keratoconus, treatment should be addressed immediately when the diagnosis is made.

"Once the diagnosis is made, this age group should be treated without waiting for progression," said Dr. Hafezi, noting this attitude was adopted as a general recommendation at the 9th International CXL Congress in Dublin, Ireland, in December 2013. ■

FARHAD HAFEZI, MD, PHD

E: FARHAD@HAFEZI.CH

Dr. Hafezi has no financial interest in the subject matter.

Corneal layer may have glaucoma link

By Rose Schneider, *Content Specialist,* Ophthalmology Times

NOTTINGHAM, ENGLAND :: **A NEW LAYER IN THE** human cornea—discovered by researchers at the University of Nottingham last year—has been found to play a vital role in the structure of the tissue that controls the flow of fluid from the eye.

The findings, published in the *British Journal of Ophthalmology*, could shed new light on glaucoma.

The latest research shows that the new layer—dubbed Dua's Layer after Harminder S. Dua, MD, PhD, who discovered it—makes an important contribution to the trabecular meshwork (TM) in the periphery of the cornea. Defective drainage through the TM is an important cause of glaucoma.

"Many surgeons who perform lamellar corneal transplant recognize this layer as an important part of the surgical anatomy of the cornea," said Dr. Dua, professor of ophthalmology and visual sciences, University of Nottingham, Queens Medical Centre, Nottingham, England. "This new finding . . . could have significance beyond corneal surgery."

By examining human donor eyes using electron microscopy, the researchers were able to look at the new layer beyond the central part of the cornea to shed more light on its features at the extreme periphery of the cornea. They discovered that the collagen fibers of the new layer also branch out to form a meshwork and that the core of TM is in fact an extension of Dua's Layer.

It is hoped the discovery will offer new clues on why the drainage system malfunctions in the eyes of some people, leading to high pressure. ■

Corneal confocal microscopy after CXL for keratoconus

CCM aids in comparing various protocols as well as during treatment and follow-up

By Nancy Groves; *Reviewed by David Touboul, MD*

BORDEAUX, FRANCE ::

CONVENTIONAL CORNEAL COLLAGEN crosslinking (C-CXL) has become the gold standard to halt keratoconus. Several new CXL procedures, however, have been developed.

Corneal confocal microscopy (CCM) appears to be a useful tool for noninvasive CXL titration and follow-up in patients with keratoconus treated with these protocols, according to David Touboul, MD, of the French National Reference Center for Keratoconus, Bordeaux, France.

Dr. Touboul

Based on a study Dr. Touboul and colleagues performed at the center, he concluded that keratocyte loss is probably a relevant parameter to make comparisons between different CXL protocols.

He also suggested that incorporation of data from biomechanics and topography could lead to better optimization of the compromise between safety and efficacy in CXL.

TRENDING NOW

New trends in CXL include improving safety with transepithelial protocols (T-CXL) and decreasing operating time with accelerated protocols (A-CXL), Dr. Touboul said.

T-CXL is similar to C-CXL, but in the newer protocol the epithelium is not removed and 0.1 tromethamine is used to enhance riboflavin uptake in the cornea, while dextran is not used.

The main differences between the accelerated protocol and the others are the times and fluency. In A-CXL, riboflavin is administered for 10 minutes instead of 30, and UVA time is only 3 minutes versus 30, reducing the overall time of the procedure to less than one-quarter of that required for the conventional protocol, 13 minutes versus 60. The fluency in A-CXL is 30 mW/cm^2 compared with 3 mW/cm^2 in C-CXL and T-CXL.

COMPARING THE PROTOCOLS

The study used CCM to compare conventional CXL with the two newer protocols.

Dr. Touboul and colleagues evaluated 24 eyes of 24 patients with progressive keratoconus and corneal thickness >400 µm. They were divided into three groups of eight each: Group 1, C-CXL; Group 2, A-CXL; group 3, T-CXL.

In vivo CCM was performed on each patient preoperatively and at 1, 3, and 6 months postoperatively.

"The main confocal findings after C-CXL were nerve plexus loss, keratocyte loss with a decrease of keratocyte density and decrease of nuclear reflectivity, and also a stromal honeycomb-like pattern," he said. "All of these signs decreased with stromal depth and with time."

At 1 month, the control eyes (no CXL) and the T-CXL eyes were similar, while there was a huge loss of keratocytes in the stroma in the C-CXL and A-CXL eyes. In eyes treated with A-CXL, the loss of keratocytes in the anterior stroma was even more pronounced than in the eyes treated with conventional CXL.

At month 3, there were signs of regression of the keratocyte loss, and at month 6 the trend was confirmed

Continues on page 36 : ***CXL protocols***

take-home

- **Corneal confocal microscopy may be a useful tool for physicians performing corneal collagen crosslinking.**

CXL PROTOCOLS

(*Continued from page 35*)

with minimal loss of keratocytes in the entire population.

There was no significant endothelial cell loss in any of the CXL protocols at any point during the follow-up ($p > 0.05$) The preoperative and 6-month counts were, respectively: C-CXL, 2995 ± 367 and 3013 ± 366; T-CXL, 3445 ± 250 and 3594 ± 260; A-CXL, 3591 ± 483 and 3577 ± 516.

Investigators found that epi-off CXL protocols exhibited long-term anterior nerve plexus loss.

"For the same amount of photons, based on confocal findings, there were very different reactions to crosslinking in the stroma," he said.

Dr. Touboul hypothesized that T-CXL did not exhibit changes with CCM. One theory to explain this is that the epithelium was soaked with riboflavin—preventing stomal crosslinking by acting as a UVA light shield—but this is probably wrong because riboflavin cannot enter the epithelial cells and natural UVA epithelial absorption is very low.

The more plausible option to explain the lack of visible changes on CCM is that there was insufficient riboflavin in the stroma at the end of the soaking time. With no riboflavin, there is no effect, Dr. Touboul added.

QUESTIONS RAISED

Another question is why A-CXL was located more anteriorly. Among several possibilities, the most likely is that the shorter soaking and UVA time caused the difference. The less likely choices are that higher fluency was used (30 versus 3 mW/cm^2), which is unlikely because at the end, the same dose of photons was used in this study as in others, or that the riboflavin was somehow different.

The study also raised questions about the relationship between keratocyte loss, corneal stiffening, and CXL efficacy, Dr. Touboul said.

Two key issues are whether collagen bonding remains possible and effective without killing keratocytes and whether the keratocyte, epithelium, and nerve plexus renewal play a role in keratoconus stabilization.

"Today, nobody knows," he concluded.

The study was published in the *Journal of Refractive Surgery* (2012;28:769-776). ■

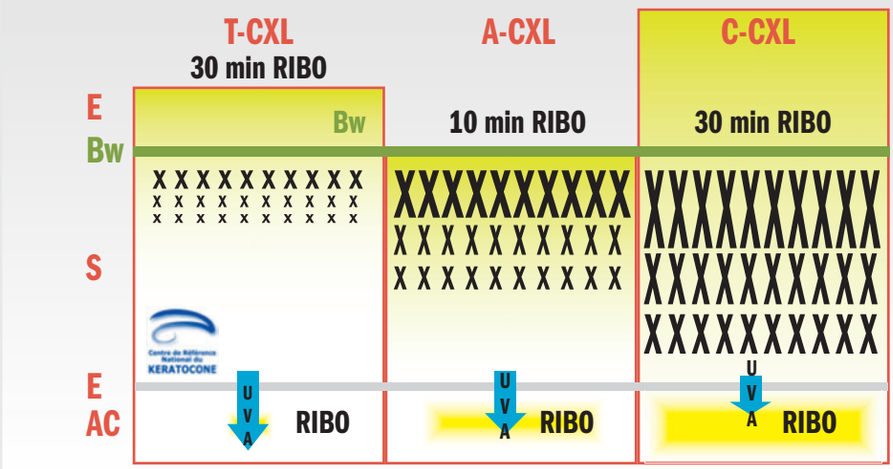
DAVID TOUBOUL, MD

E: *david.touboul@chu-bordeaux.fr*

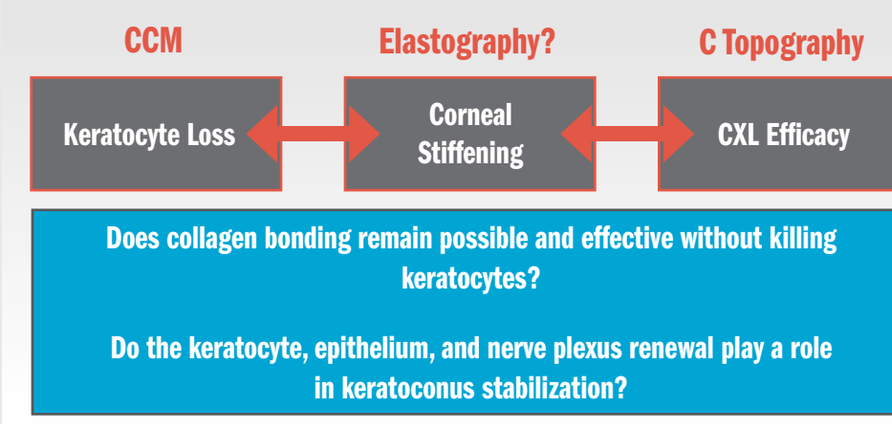
Dr. Touboul did not report any disclosures.

Comparison of CXL Protocols

CXL FEATURING	C-CXL	A-CXL	T-CXL
Epithelium	OFF	OFF	ON
Riboflavin % Dextran Name	0.1 Dextran 20% Ricrolin	0.1 Dextran 20% Vibex	0.1 +Tromethamine No Dextran Ricrolin TE
Riboflavin Soaking Time (min)	30	10	30
Fluency (mW/cm^2) UVA time (min) Laser type	3 30 Vega x-linker Sooft 	30 3 KXL Avedro 	3 30 Vega X-linker Sooft 
UV-A Dose (J/cm^2)	5.4	5.4	5.4



For the same amount of photons CXL interaction was very different due to different riboflavin kinetics.



The study also raised questions about the relationship between keratocyte loss, corneal stiffening, and CXL efficacy. *(Figures courtesy of David Touboul, MD)*

Study: Ionotophoresis efficient, effective for riboflavin delivery

Data show CXL performed after imbibition associated with good results in early follow-up

By Cheryl Guttman Krader; *Reviewed by Paolo Vinciguerra, MD*

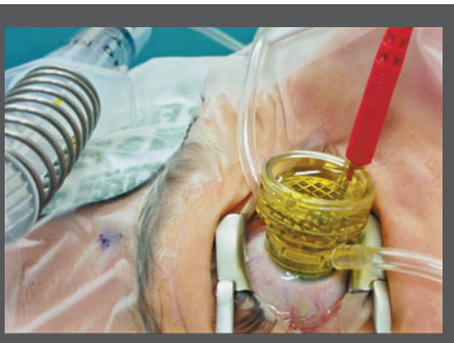
MILAN ::

EARLY EXPERIENCE WITH corneal crosslinking (CXL) using iontophoresis-assisted riboflavin imbibition shows it is a promising technique for treating eyes with progressive keratoconus, said Paolo Vinciguerra, MD.

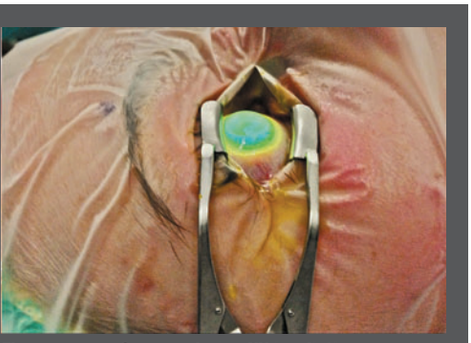
"Reliable delivery of riboflavin into the cornea is critical to the safety and success of CXL," said Dr. Vinciguerra, professor of ophthalmology, Humanitas University of Milan. "We have found that the iontophoresis-assisted method results in immediate strong corneal fluorescence after ultraviolet A (UVA) irradiation comparable to that achieved with the standard epi-off technique, and in vivo optical coherence tomography imaging shows a visible demarcation line representing riboflavin penetration depth at 200 to 250 µm."

Patient follow-up demonstrates the technique results in keratometric flattening by 3 months post-CXL—sooner than what is seen using other CXL techniques, Dr. Vinciguerra noted.

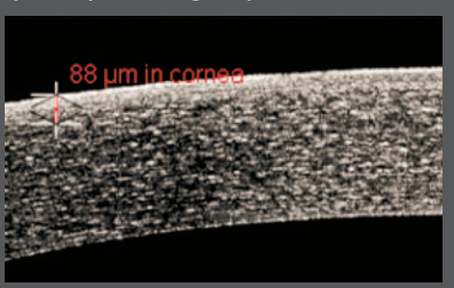
"In addition, we have documented improvements in corneal biomechanical properties," he said. "These are only preliminary results from a limited number of eyes with short follow-up. However, they are very promising."



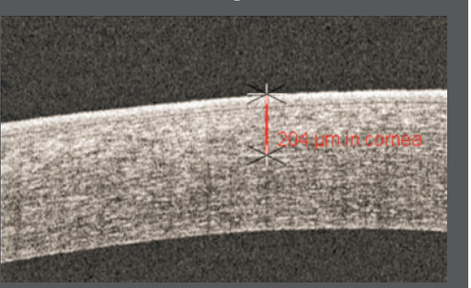
Eye of the patient during iontophoresis.



Fluorescence of cornea during UV irradiation.



High-definition optical coherence tomography (HD-OCT) after impregnation.



HD-OCT after irradiation.

(Images courtesy of Paolo Vinciguerra, MD)

HOW THE NON-INVASIVE PROCEDURE WORKS

Iontophoresis is a non-invasive approach that uses electrical current to enhance tissue penetration by an ionized compound. Riboflavin is well suited for use in iontophoresis, because it is negatively charged at physiological pH, has high aqueous solubility, and has a relatively low molecular weight that enables its transport into the cornea, Dr. Vinciguerra explained.

The procedure involves placement of the 8-mm ionotophoresis device onto the cornea using a 9-mm annular suction ring. The suction ring is fixed onto the cornea with low suction and is connected to a battery-powered DC generator emitting a current of 1 mA (I-ON XL, Sooft Italia). A second grounding electrode is placed on the patient's forehead, and the suction ring is filled with 0.5 ml of a hypotonic 0.1% riboflavin solution (Ricrolin +, Sooft Italia).

After just 5 minutes of iontophoresis, the concentration of riboflavin in the cornea is close to two-thirds that achieved following the standard 30-minute protocol of topical administration to a debrided cornea. UVA irradiation is then performed using 10 mW/cm^2 for 9 minutes.

Dr. Vinciguerra—along with colleagues in collaboration with Eberhard Spoerl, PhD, University of Dresden, Germany—obtained proof of principle for iontophoresis-assisted riboflavin delivery in preclinical studies using human cadaver eyes.

An initial investigation compared biomechanical changes (increase in Young's modulus) with different methods of riboflavin impregnation and UVA irradiation protocols.

Results showed the best outcome was achieved in the iontophoresis group, which was only 1 of 5 experimental groups, and they were confirmed in a second experiment.

take-home

Results from preclinical studies and early clinical experience show that iontophoresis is an efficient and effective method for delivering riboflavin into the cornea. Crosslinking performed after the procedure is associated with good results in early follow-up.

Based on this experience, a clinical trial was initiated enrolling patients aged 18 to 45 years with progressive keratoconus and no previous ocular surgery. In addition to showing keratometric flattening, data collected in the study indicated that patients experience less pain with the ionotophoresis riboflavin delivery versus with the standard technique, although some patients did develop an epithelial defect.

Follow-up showed good recovery of BCVA with improvements in higher order aberrations. There is no evidence of endothelial toxicity. ■

PAOLO VINCIGUERRA, MD

E: *paolo.vinciguerra@humanitas.it*

Dr. Vinciguerra has no relevant financial interests to disclose.

Corneal inlay scores 'impressive' in 24-month data from visual tasks

Procedure may increase near and intermediation vision without compromising stereopsis

By Nancy Groves; *Reviewed by Jay S. Pepose, MD, PhD*

ST. LOUIS ::

FINDINGS FROM SEVERAL studies of the small-aperture corneal inlay (Kamra, AcuFocus)—an investigational device in the United States—suggest that it is an effective alternative to other treatments for presbyopia, according to Jay S. Pepose, MD, PhD.

Recent studies found that binocular and monocular mesopic and photopic contrast scores showed a reduction—although results remained well within normal limits—and that stereopsis scores are unaffected by the presence of the inlay, said Dr. Pepose, founder and medical director of the Pepose Vision Institute, St. Louis.

Patients also reported that they could easily perform near, intermediate, and distance tasks without glasses in different lighting conditions and had a low incidence of visual symptoms 24 months after implantation, added Dr. Pepose, who also serves as professor of clinical ophthalmology at Washington University School of Medince and Barnes-Jewish Hospital, St. Louis.

The inlay is designed to improve functional near and intermediate vision, as well as reducing dependence on reading glasses while maintaining distance vision. It is 3.8 mm in diameter and works by blocking unfocused light and expanding depth of field through its fixed 1.6-mm central aperture.

Made of polyvinylidene fluoride—a biocompatible material commonly used in intraocular lens haptics—the inlay is 5 µm thick. It received CE Mark approval for use in Europe in 2005, and a pre-market approval application was submitted to the FDA in December 2012.

take-home

- **An investigational small-aperture corneal inlay (Karma, AcuFocus) may improve near and intermediation vision in patients with presbyopia without compromising stereopsis, like other current treatment options, such as LASIK monovision or contact lens monovision.**

EXAMINING THE STUDY

Dr. Pepose said the objective and subjective results were from a prospective, non-randomized clinical trial that was conducted at 24 sites in the United States, Europe, and the Asia-Pacific region. The study enrolled 507 subjects who were naturally occurring presbyopic emmetropes aged 45 to 60 years old with a spherical equivalent between +0.50 and –0.75D for implantation. Uncorrected near visual acuity was worse than 20/40 and better than 20/100 preoperatively.

Binocular photopic contrast sensitivity remained within normal limits at 24 months postoperatively, although there was a statistically significant decrease from preoperative levels ($p < 0.001$) at certain spatial frequencies.

Similarly, monocular and binocular mesopic contrast sensitivity were also within the normal range at 24 months.

Stereopsis was evaluated preoperatively and at 6 months postoperatively in a substudy of 60 patients treated by Phillip C. Hoopes, MD, in Salt Lake City.

The difference in mean preoperative and postoperative distance stereoacuity was not statistically significant (36.1 ± 31.3 versus 35.5 ± 34.7 arc sec).

Dr. Pepose compared treatment with the inlay to alternative procedures for presbyopic vision correction.

FURTHER INVESTIGATIONS

Monovision with LASIK resulted in a 2.75-fold increase in arc seconds ($p < 0.05$) between preoperative and postoperative examinations (165.55 ± 138.25 versus 451.74 ± 286.97) in a study of 25 patients. These findings were reported by Alarcon et al. (*J Cataract Refract Surg.* 2011;37:1629-1635).

In a study of increasing amounts of contact lens monovision, statistically significant changes from baseline (32 ± 33 arc sec) occurred at all levels (+0.75 D: 44 ± 38, 1.38-fold increase; +1.5 D, 77 ± 76, 2.41-fold increase; +2.5 D, 182 ± 142, 5.7-fold increase. $p < 0.01$).

This prospective study was performed by Durrie (*Trans Am Ophthalmol Soc.* 2006:104:366-401).

"The inlay is in marked contrast to the findings of monovision's loss of stereopsis after pseudophakic LASIK and contact lens monovision," Dr. Pepose said.

He also reported the results for near vision tasks, as data was obtained from a questionnaire in which patients were asked how easy it was to perform a series of near vision tasks with both eyes without their glasses.

The scale ranged from 1, "not easy at all," to 7, "very easy." At 24 months, statistically significant improvement was seen in mean scores for performing near tasks in both dim and bright light conditions ($p < 0.001$). These included intermediate vision tasks (such as viewing a computer) and near tasks (such as reading a book or newspaper).

Mean scores for viewing a computer improved significantly from 2.74 ± 1.42 preoperatively to 5.09 ± 1.72 at 24 months, and mean scores for reading a book improved significantly from 1.73 ± 1.04 to 4.66 ± 1.76 over the same period.

"This is impressive, especially given that the mean manifest refraction spherical equivalent in the inlay-implanted eye was +0.18 D ± 0.79, and we have learned commercially that having a small amount of myopia further enhances near and intermediate vision," Dr. Pepose said. "We shouldn't minimize the need of good intermediate vision for our patients who now are using many handheld devices."

The ease of distance task performance remained stable at 24 months postoperatively, and there was little or no change in patients' ranking of the ease of performing the tasks ($p = 0.016$).

Patients reported a very low incidence of visual symptoms postoperatively, such as glare, halo, and night vision problems. All mean symptom scores were reported between 0.2 and 1.6 on a scale of 1 to 7 at 24 months. There was no indication of the photopsia sometimes associated with multifocal lens implants. ■

JAY S. PEPOSE, MD, PHD
E: *jpepose@peposevision.com*
Dr. Pepose is a consultant for AcuFocus.

CXL use with primary LASIK at crossroads

Evidence insufficient to support combined procedure to reduce ectasia risk

By Cheryl Guttman Krader; *Reviewed by Perry S. Binder, MS, MD*

IRVINE, CA ::
AN ASSESSMENT OF CURRENT knowledge on the potential risks and benefits of performing corneal crosslinking (CXL) at the time of primary LASIK indicates there is no current justification for routine application of the combined procedure, according to Perry S. Binder, MS, MD.

"The idea of performing CXL on every LASIK case is based on the hope of preventing ectasia," said Dr. Binder, clinical professor of ophthalmology, Gavin Herbert Eye Institute, University of California, Irvine. "However, peer-reviewed studies of CXL at the time of primary LASIK are very limited, and there are alternatives to LASIK that can be used successfully in cases deemed at risk for ectasia.

"In addition, I don't believe we can defend the increased cost of CXL to patients in lieu of what we know about the current risk/incidence of ectasia," he added. "Therefore, my recommendation is that CXL should not be performed at the time of LASIK until research is published or presented that tips the risk:benefit ratio in favor of the combined procedure."

Editor's Note: See related article (at right) in which A. John Kanellopoulos, MD, presents outcomes from studies comparing LASIK with and without simultaneous CXL.

UNDERLYING FACTORS

Outlining his arguments against performing primary CXL to prevent postLASIK ectasia, Dr. Binder highlighted the current low risk for that complication and explained underlying factors.

Surgeons have better methods for screening, more reliable technology for achieving predictable flap thickness, and more ways to measure postoperative flap and residual stromal bed thickness, according to Dr. Binder.

Performing CXL routinely can add risks—particularly corneal ulcers, corneal infiltrates, risks associated with epithelial removal, and corneal endothelial damage, he noted.

In addition, there are a variety of unknowns accompanying simultaneous CXL-LASIK.

One of the most basic questions that must be answered is whether CXL at the time of primary LASIK is effective in preventing ectasia.

With all of the clinical variables that would need to be accounted for in stratifying treatment groups, a study would need to enroll a minimum of 300 to 400 eyes to detect a benefit of CXL for reducing the risk of ectasia after primary LASIK, Dr. Binder noted.

Considering the multiple differences between CXL performed with LASIK—versus the standard Dresden protocol used to treat keratoconus—provides reason to question the safety and efficacy of combining CXL with LASIK.

"We don't know how riboflavin or UVA penetration into the cornea is affected by a healthy LASIK epithelium or how riboflavin diffuses from the LASIK interface in either direction," Dr. Binder said. "In addition, it is not known how CXL might affect primary and enhancement excimer laser ablation rates or the stability of refraction postLASIK.

"How would one determine the contribution of CXL versus routine wound healing to the outcomes, and knowing that the effects of CXL can continue for many years, when would it be appropriate to perform an enhancement procedure?" he asked.

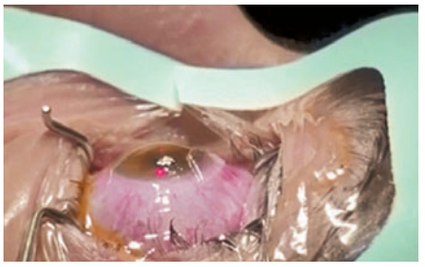
Other questions remaining to be answered include whether the CXL procedure might affect LASIK flap adhesion, have long-term adverse effects on the crystalline lens, or affect calculations for subsequent pseudophakic IOL implantation.

In addition to the need for studies addressing these many issues to understand the risks and benefits of the combination procedure, Dr. Binder called for research toward improving the predictability, efficacy, and safety of CXL. A variety of CXL protocols are being used without any laboratory data or clinical studies to support their efficacy or safety.

More information is needed to establish the best method for riboflavin delivery, and investigations of other photosensitizers would also be worthwhile. There is also a need to develop systems for delivering focal irradiation to the affected cornea and for more accurately determining the depth of treatment and its effects on corneal biomechanics. ■

PERRY S. BINDER, MS, MD
E: *garrett23@aol.com*
Dr. Binder has no relevant financial interests to disclose.

LASIK-XTRA TECHNIQUE



VIDEO To watch a hyperopic LASIK-Xtra surgical technique, go to **http://bit.ly/1iubbgt**. *(Video courtesy of A. John Kanellopoulos, MD)*

LASIK-Xtra reinforces cornea stability

Stabilization with concurrent CXL helps maintain LASIK treatment effects

By Cheryl Guttman Krader;
Reviewed by A. John Kanellopoulos, MD

ATHENS, GREECE ::
ABOUT 1 IN 40 patients who present for laser vision correction of myopia to the private surgery center of A. John Kanellopoulos, MD, in Athens, Greece, have topographic evidence of keratoconus.

Considering the endemic nature of this disease in his patient population—together with evidence demonstrating the occurrence of long-term refractive regression after LASIK for hyperopia and high myopia—in 2007 Dr. Kanellopoulos introduced performing collagen crosslinking (CXL) concurrently with primary LASIK in all patients with hyperopia and myopia considered at risk for ectasia or regression.

He theorized that the addition of CXL would stabilize the cornea, and results from subsequent comparative studies demonstrate the combined procedure (known as LASIK-Xtra) is effective for increasing refractive and keratometric stability.

"Although not universally considered mainstay, LASIK-Xtra requires just 2.5 minutes of additional time following routine LASIK, and may provide reinforcement to the known inadvertent biomechanical change associated with standard LASIK," said Dr. Kanellopoulos, medical director, Laservision.gr Eye Institute, Athens, and clinical professor of ophthalmology, New York University Medical College, New York.

Currently, he performs LASIK-Xtra in pa-

Continues on page 40 : ***Stability***

STABILITY

(Continued from page 39)

tients with myopia exhibiting any of the following characteristics:

- Spherical error ≥–6 D.
- Age <30 years.
- Astigmatism >1.5 D.
- Intereye astigmatism difference ≥1 D.

The CXL procedure is performed following the excimer laser ablation. Being careful to protect the flap and hinge from riboflavin exposure, 0.10% saline-diluted riboflavin solution is applied directly onto the stromal bed, he said.

After a 60-second soak time, the flap is replaced and residual riboflavin removed by irrigation. Once the flap position is secured, the cornea is irradiated with the UVA light source using a fluence of 30 mW/cm^2.

Dr. Kanellopoulos is currently using an exposure time of 80 seconds.

"In contrast to epi-on CXL, a key concept here is to have minimal riboflavin present in the epithelium and flap stroma," Dr. Kanellopoulos said. "Therefore, the UV light can penetrate through freely and interact with the underlying stroma soaked with riboflavin."

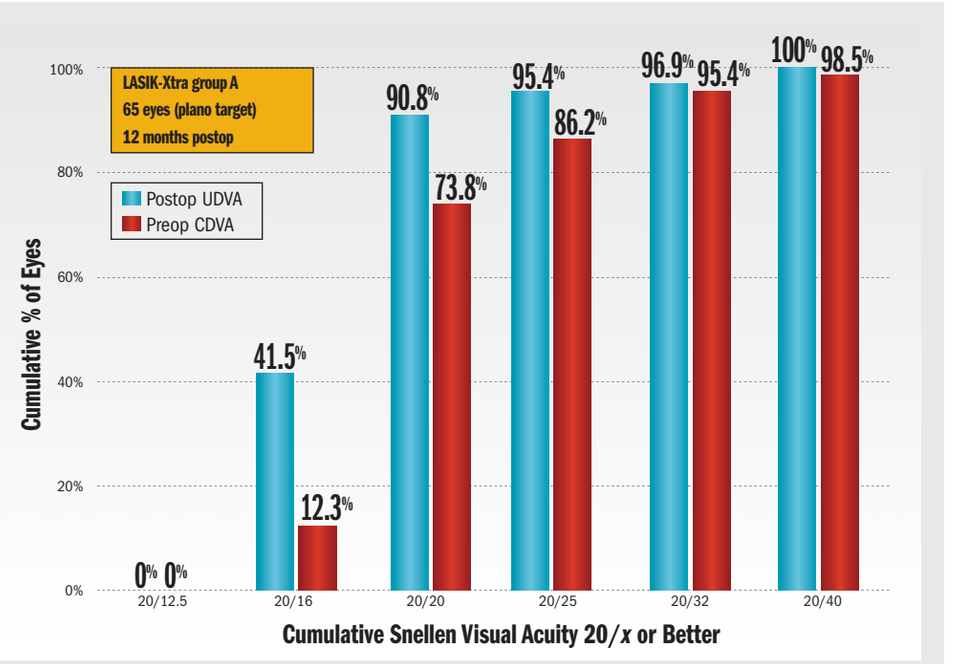
COMPARING OUTCOMES

In a paper in press in *Cornea*, Dr. Kanellopoulos and colleagues report a comparison of outcomes in a consecutive cohort of 140 patients who underwent myopic femtosecond-LASIK with or without concurrent high-fluence CXL. Baseline data showed that compared with the controls having LASIK alone, the LASIK-Xtra eyes had higher cylinder (–1.35 versus –0.85 D), MRSE (–6.75 versus –5.33 D), and keratometry values (flat: 43.92 versus 43.15 D; steep: 45.15 versus 44.03 D).

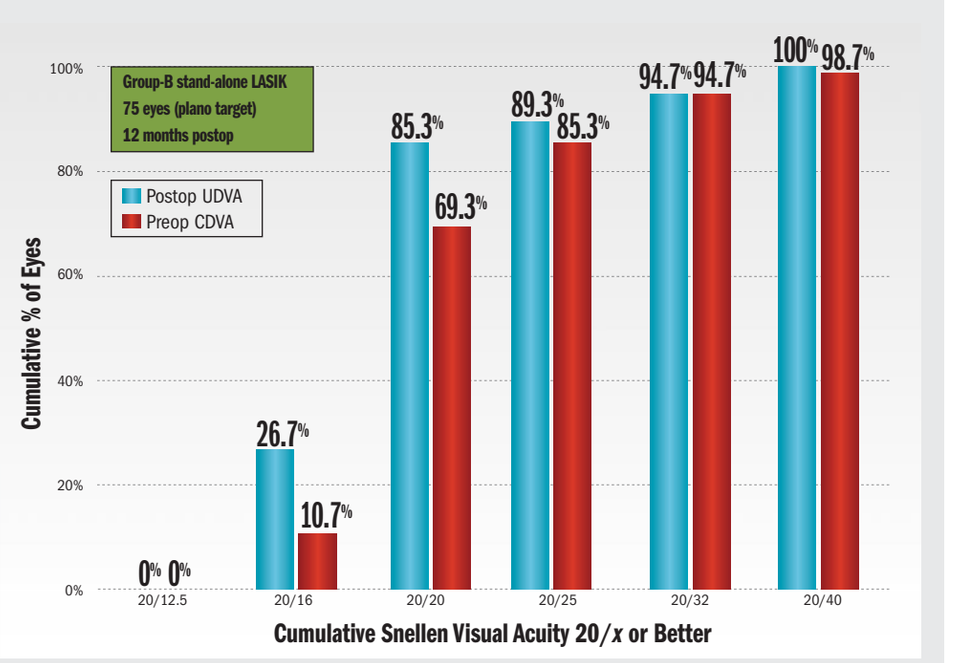
However, the groups were otherwise well matched, as they were all operated on by Dr. Kanellopoulos using the same ablation zone, laser systems (topography-guided with the Alcon Refractive Suite), flap dimensions, and postoperative care regimen.

Data from long-term serial follow-up visits through 24 months demonstrated better refractive and keratometric stability in the combined procedure group. Between postoperative months 1 and 12, mean MRSE showed a slightly greater myopic shift in the LASIK only group compared with the LASIK-Xtra eyes (–0.27 versus –0.24 D). Mean keratometry in the flat and steep meridians increased by +0.57 D and +0.54 D in the LASIK only eyes but by only +0.03 D and +0.05 D in the LASIK-Xtra group. At 1 year, uncorrected visual acuity outcomes were also significantly better in the LASIK-Xtra group.

Findings from a randomized trial using a contralateral eye-controlled design demonstrated the benefit of simultaneous CXL for improving long-term refractive and keratometric stability after hyperopic LASIK [*J Refract Surg*. 2012.28(11 Suppl):S837-40]. Baseline mean MRSE and cylinder values were +3.15 and 1.20 D in the LASIK-Xtra group and +3.40 D and 1.40 D in eyes having LASIK alone. After a mean follow-up of 23 months, mean MRSE regression was significantly less in eyes treated with the combined procedure than in those receiving LASIK alone, +0.22 D versus +0.72 D, respectively. ■



Snellen visual acuity measurement for patients in the LASIK-Xtra group.



Snellen visual acuity measurement for patients in the stand-alone LASIK group.

(Figures courtesy of A. John Kanellopoulos, MD)

A. JOHN KANELLOPOULOS, MD

E: *ajkmd@mac.com*

Dr. Kanellopoulos is a consultant to Avedro and Alcon Laboratories.

Turning frame inventory four times a year is a good goal, but a good selection of inventory still must be offered to remain competitive.

(Photo courtesy of Shauns California)

Simple *strategies for* frame *board* management

Careful planning is the key to a strong dispensary business

By Lisa Frye, ABOC

At the heart of every optical dispensary lies the important job of managing the frame board inventory. This task can appear to be challenging at times, but by following some simple strategies, it will lead to success. As with any investment, your view should be from the perspective of keeping a balanced budget with growth and profit in mind.

Most practices start out with a goal of how many frames they plan to display and make an initial investment. After the initial investment, it becomes relatively easy to produce reports to track patterns that will show you exactly what your needs are in specific areas. A smaller dispensary may carry only 500 to 600 frames, while others, particularly if in a higher income demographic, may need as many as 1,000 frames in order to offer a great selection.

To determine the ideal number of frames your dispensary should carry, you must understand that setting this number is directly related to sales volume and inventory turn ratio.

CRUNCHING THE NUMBERS

Profit for your practice is maximized when you can turn the inventory quickly. If you have more frames than you need in inventory, you have tied up working capital dollars that could be best served elsewhere in your practice. The average practice turns inventory two to three times a year, but a goal of at least four times would be more profitable.

There is a simple formula to determine your turn ratio: take the annual cost of frame goods sold, divide it by the average monthly inventory, and you will get the number of inventory turns or your turn ratio. Here are some examples to simplify understanding:

Continues on page 42 : ***Inventory***

In Brief

FROM STAFF REPORTS

Optical frames collection

SHAUNS CALIFORNIA LINE MAKES MARCH DEBUT

NEW YORK :: **SHAUNS CALIFORNIA UNVEILS** the newest addition to its eyewear offerings, a debut collection of optical frames set to hit stores nationwide this month.

The collection consists of eight optical styles. Four of the new shapes are 100% premium acetate, whereas the remaining four continue the brand's exploration of combining acetate with stainless steel and colorful enamel.

A balance of rounds, rectangles, and cat-eye shapes of varying sizes are offered in the debut optical collection, as well as the unique retro racer shape in the crossover sun frame, the "Dee" (inspired by early 1970s sports cars, particularly the Porsche 911). The "Tiree," on the other hand, offers a new, refined take on the popular cat-eye shape with a combination acetate and stainless steel front.

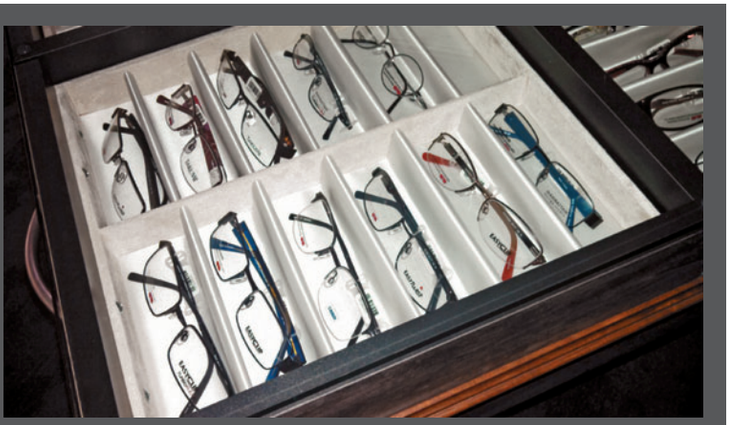
Language resource

BILINGUAL POCKET CARD OUTLINES EYEWEAR OPTIONS

PINELLAS PARK, FL :: **TRANSITIONS OPTICAL** introduces a bilingual pocket card to overview the benefits and features of the latest option in everyday adaptive eyewear (Transitions Signature lenses). The 5.5- × 7.5-inch card lets English-speaking eye-care professionals (ECPs) easily explain the new adaptive lens technology to Spanish-speaking customers.

"We designed this tool to help eliminate confusion by allowing ECPs to simply point to their recommendations—or patients to point out their preferences—to make communication easier," said Manuel Solis, marketing manager, labs and strategic partnerships, Transitions Optical. ■

By limiting the number of frame vendors, eye-care professionals can better manage time with representatives, offer a larger selection within a line, and ease the billing process as well.



The average frame sale is the midpoint between the highest-end and lowest-end frame retail. *(Photos courtesy of Lisa Frye, ABOC)*

INVENTORY

(Continued from page 41)

- ***EXAMPLE 1:*** **Annual frame cost of goods $50,000/Average monthly frame inventory $30,000=turn ratio of 1.6 turns. (Not ideal)**
- ***EXAMPLE 2:*** **Annual frame cost of goods $100,000/ Average monthly frame inventory $40,000=turn ratio of 2.5 turns. (Average)**
- ***EXAMPLE 3:*** **Annual frame cost of good $80,000/ Average monthly frame inventory $20,000 turn ratio of 4 turns. (Excellent)**

Although turning your inventory four times is a noble goal, in these competitive times, you still have to offer an adequate selection of inventory. By understanding sales volume and turns, you can better decide inventory needs.

Budget wise, one could look at the previous year and see the total monthly dollars spent on frame inventory in each particular month or calculate how many frames were sold that month to set a monthly budget allowance. If you go over that budget, offset it the next month.

By adding the total dollar amount of your frame vendor statements each month and comparing it to the report of the wholesale dollar amount of frames sold for that month, you can easily identify whether you maintained the desired budget or were under or over budget.

Examples of tracking your monthly budget:

- ***FRAMES SOLD IN JANUARY: $10,000;*** **purchases made in January $12,000; over budget $2,000.**
- ***FRAMES SOLD IN FEBRUARY: $8,000;*** **purchases $6,000; under budget $2,000.**

IDENTIFY YOUR MARKET

You can confirm the particulars of gender, vendor, and price point that identify your market. Once you get a feel for your market, begin to set up your dispensary to reach that market. Divide your categories and set numbers for each category and each vendor. Invest in the areas in which you would like growth. Sunglasses would be a good example in spring and summer. Track your trends with frame sales reports.

Most often, the average frame sale is the midpoint between your highest-end and lowest-end frame retail. You can control your average sale by planning accordingly.

If one vendor sells exceedingly well, increase that line or vendor and offset the increase by decreasing or replacing a line that is slow moving. Although you track and adjust your core lines, those areas that do not turn as quickly, such as high-end, children's frames, readers, sports frames, etc., should still have adequate representation and selection.

If you become in-network for local accounts, often you will be provided, free of charge, safety frame kits or consignments, which offset the cost of inventory investments. This is still a viable option in a lot of markets. If available, certainly take advantage when offered. Deal with current merchandise and avoid closeouts unless that is your market.

By limiting the number of vendors in your practice, you can invest better in time management with frame sales representatives, offer a larger selection of a particular line in order to capture the "presence" of the line, and ease the monthly statement and billing process, as well.

A good representation covers your core product, allowing you to have your niche areas or higher-end selections, and to reserve an area for new merchandise, also. After all, a department store does offer the core, but we always expect to see something new and exciting that represents changing fashion and current trends.

By planning and reordering your inventory, you can easily manage costs and numbers. You keep track of what was sold. Decide whether to reorder a particular frame, wait until you have enough pieces to make shipping costs reasonable, and reorder weekly or bi-weekly for each vendor. You should keep under-stock of best sellers, but a good rule of thumb is to limit under-stock to 10% or less of your total inventory numbers.

Merchandising can make less appear more, and rearranging your dispensary can make old look new. Most sell the frame displayed and order what was sold, maintaining representation of the line, but update styles as they become available.

Each practice is unique, but by looking at your frame sales history, you can set guidelines, adjust in areas as the need arises, and by following these strategies, the process can become quite simple.

Stay within your budget, adjust with the trends, keep inventory fresh, work your frame boards with merchandising, make them appealing, cater to your market, and you will be successful with growth and profit.

Involve your staff in creating excitement and allow them to be a part of the process, take control of your frame boards, and take your practice in the direction you wish to go. ■

TAKE-HOME

- ***To make the most of your dispensary business, it is important to manage your inventory, keep a budget, and identify your market in order to maximize profits. An ideal goal would be an inventory turn rate of four times per year, while maintaining an adequate selection that will best serve the needs of your customers.***

LISA FRYE, ABOC, *is a longstanding Fellow of the National Academy of Opticians. She has more than 30 years of experience in optometric management. Reach her at fryegang@yahoo.com.*

A NEW NAME. A LEGACY OF INGENUITY.
THE METHODIST HOSPITAL IS NOW HOUSTON METHODIST HOSPITAL.

We've changed our name. The Methodist Hospital is now Houston Methodist Hospital. We're moving forward, and bringing tomorrow's advances in ophthalmology to our patients today. The finest researchers and clinicians from around the world are joining us in Houston, to build on our legacy of ingenuity, and accelerate the discovery and delivery of better care and better cures. That's the difference between practicing medicine and leading it.

See all the ways we're leading at **hmleadingmedicine.com.**

HOUSTON Methodist℠
LEADING MEDICINE

Opening the dispensary sale

What opticians say or do not say can hurt business

Dispensing Solutions By Arthur De Gennaro

TAKE-HOME

- ***An effective opening in the selling process between an optician and an optical customer will increase the likelihood for increased closing rates and improved sales.***

THOSE OPTICIANS WHO have studied the retail-selling process know there are specific parts to a retail sales presentation (See "7 Steps of a Retail Sale" on page 45). Each part or step is important for a different reason.

If all the parts are accomplished and executed well, the likelihood a customer will purchase increases dramatically.

The reverse is also true—leaving steps out or delivering some steps poorly in the process decreases the likelihood of making a sale.

The first step in the selling process is known as the *opening*, which is important because it accomplishes several things:

STARTS THE SELLING PROCESS.

If an optician cannot get a customer to speak with him or her, the selling process cannot begin—the sale ends before it starts. In this instance, the customer browses the dispensary without assistance. This allows the customer to make assumptions about the dispensary's merchandise, prices, and level of service. Those assumptions, unfortunately, are often wrong. Regardless, many customers will leave without hearing the dispensary's value propositions.

OVERCOMES RESISTANCE.

Every person I remember asking has been able to relate a story of a time when he or she had a bad experience with a salesperson. Common threads are salespeople who were "pushy"; who did not listen to the customer's needs or wants; who tried to sell the customer something for which he or she did not ask, need, or want; or who were rude, arrogant, or (worst of all) apathetic. The list goes on. When approaching a customer, a salesperson must be aware that because of prior bad experiences customers are distrustful of salespeople.

BEGINS A RELATIONSHIP.

I like to say that "People do business with people they know and like, not people they don't know or don't like." Opening a sale is where that "getting to know you" relationship begins. The best sellers I know have learned that the first thing they say to a customer can be the difference between making and losing a sale.

Opening seems like it would be a pretty straightforward thing to do.

Simply approach the customer, smile, greet him or her and then ask: "How may I help you?"

> 'People do business with people they know and like, not people they don't know or don't like.'
>
> — Arthur De Gennaro

Unfortunately, in 90% of the cases, such a direct approach will result in the customer saying: "I'm just looking."

The obvious question is: If you know a customer is likely to respond with "I'm just looking" why would you ask that or a similar question? For this reason, whatever opening technique the optician uses must be capable of winning the customer's trust, at least initially, enough to continue the selling process.

All of the sales trainers I know advise against the "How-may-I-help-you?" approach, pretty much for the reason stated above. Instead they suggest some different ways of accomplishing this task. Let's look at why.

7 Steps of a Retail Sale

1. OPENING. Overcomes resistance to being served. Establishes a person-to-person relationship or trust and confidence. Characterizes the salesperson as caring, attentive, and human.

2. INTERVIEW. By asking a series of targeted questions, the optician learns about the specific set of needs and wants of the customer. The goal is to learn how, when, where, and why the customer uses his or her eyes each day.

3. DEMONSTRATION. The optician recommends and demonstrates eyewear products that will enhance the customer's visual lifestyle and appearance. The customer is educated and has the opportunity, whenever possible, of experiencing the recommended product.

4. TRIAL CLOSE. The optician asks the customer to make the purchase.

5. OVERCOMING OBJECTIONS. This step provides the optician with a method to determine the reason why the customer decided not to purchase. The goal is to be able to answer successfully any concern or question the customer has.

6. CLOSING. The optician uses one of any number of closing techniques. The customer agrees to make the purchase.

7. MAINTAINING AN ONGOING RELATIONSHIP. After the sale is completed the optician maintains an ongoing relationship in ways the customer views as beneficial. This includes invitations to special events, sales, and providing information about products or articles in which the customer may be interested. ■

APPROACHING THE CUSTOMER

Imagine you are invited to a party and are introduced to a celebrity you have always wanted to meet (a recording artist or actor, for example).

Your dream is to get an autograph and perhaps a photo with this person. You know that the celebrity's time is precious, but that if he or she finds the interaction interesting your time together could go longer, giving you more time to get acquainted.

What is the first thing you would say? "May I have your autograph?" "Would you take a picture with me?"

I doubt it. You would probably tell the celebrity how much you admire his or her work and ask some questions about his or her life and work. I suspect you would pay close attention to every word the celebrity says and carefully watch his or her body language to see if the questions you ask are being received well or not.

GETTING COMFORTABLE

Eventually, when you feel comfortable that it will not be an inconvenience or offensive, you would ask the celebrity for an autograph and to pose for a picture.

Similarly, the most successful salespeople I know say that approaching a customer with non-business related questions is the best way to deflect resistance and get the customer into an attitude where he or she will be willing to open up.

For example, if you travel, you know that people who work in hotel shops are trained to ask customers where they are from. Regardless of where the customer is from, the salesperson will follow up with questions or comments about that place.

Based on how the customer replies, the salesperson may take the conversation in other directions, but all of them will be non-business related. Only after a minute or two of such conversation will the salesperson ask what the customer is shopping for.

The concept to keep in mind is that a customer is more likely to continue with a transaction when he or she has begun to feel comfortable with a salesperson.

One could say the customer is beginning to develop trust. A salesperson who presents as interested, interesting, customer centric, and caring is more likely to be trusted than someone who pounces on customers as soon as one enters the dispensary.

This type of opening is not an easy thing to learn. It requires sensitivity, empathy, a caring attitude, respect, and a willingness to serve.

The more open-hearted a salesperson, the more he or she will be successful at gaining the customer's initial trust and moving on to the next step in the selling process.

The result will be an increased closing rate and improved sales. ■

ARTHUR DE GENNARO *is president of Arthur De Gennaro & Associates LLC, an ophthalmic practice management firm that specializes in optical dispensary issues. De Gennaro is the author of the book The Dispensing Ophthalmologist. He can be reached at 803/359-7887, arthur@adegennaro.com, or through the company's Web site, www.adegennaro.com. He maintains a blog at www.adgablog.wordpress.com.*

How to protect patient records and remain HIPAA compliant

Conduct security risk analysis to identify threats, vulnerabilities to protected health records

By Mark Norris

TAKE-HOME

- ***Managing risk to protected health information is an ongoing process that includes physical, administrative, technical, policy, and organizational solutions.***

Probably the least understood and greatest exposure and risk for practices attesting to Meaningful Use (MU) is the need to complete a security risk analysis. When it comes to the technical concepts like firewalls, routers, and security protocols, most offices just do not know where to begin.

You trust your vendors and business associates to keep you compliant, but what if they do not?

The use of health information technology continues to expand in health care. Although these new technologies provide many opportunities and benefits for consumers, they also pose new risks to consumer privacy.

INCREASED RISKS

Because of these increased risks, the Health Insurance Portability and Accountability Act (HIPAA) and the Health Information Technology for Economic and Clinical Health Act (HITECH) include national standards for the privacy of protected health information, the security of electronic protected health information, and for breach notification to consumers. HITECH also requires Health and Human Services (HHS) to perform periodic audits of covered entity and business associate compliance with the HIPAA Privacy, Security, and Breach Notification Rules.

Many of the MU measures are already familiar to practices. Physicians can perform actions—such as gathering vitals, demographic documentation, and medication histories—in their sleep. While learning the interface of their new electronic health record (EHR) system is a very real obstacle, in time, staff learn what button to push and box to click to be compliant.

But the technical issues can be much trickier for physicians, who aren't necessarily IT experts.

An example: In a recent visit at a rural practice, a national telecommunications provider had been onsite to upgrade the practice's broadband connection.

In the process, they disconnected the firewall because they could not configure it correctly, and left it unplugged. They did not notify the practice of their actions and left after

Continues on page 48 : ***Patient records***

5 Security Components for Risk Management

SECURITY COMPONENTS	EXAMPLES	EXAMPLES OF SECURITY MEASURES
Physical Safeguards	Your facility and other places where patient data is accessed Computer equipment Portable devices	Building alarm systems Locked offices Screens shielded from secondary viewers
Administrative Safeguards	Designated security officer Workforce training and oversight Controlling information access Periodic security reassessment	Staff trainging Monthly review of user activities Policy enforcement
Technical Safeguards	Controls on access to EHR Use of audit logs to monitor users and other EHR activities Measures that keep electronic patient data from improper changes Secure, authorized electronic exchanges of patient information	Secure passwords Backing-up data Virus checks Data encryption
Policies and Procedures	Written policies and procedures to assure HIPAA security compliance Documentation of security measures	Written protocols on authorizing users Record retention
Organizational Requirements	Breach notification and associated policies Business associate agrements	Agreement review and updates

Source: The Office of the National Coordinator for Health Information Technology

Mitigate security risks to your medical practice

The security infrastructure of a medical practice should have five components, according to the Health Insurance Portability and Accountability Act (HIPAA) security rule. Above, the table briefly outlines each component and provides examples.

Incorporating New Knowledge Into Daily Glaucoma Management To Improve Overall Outcomes

Watch on demand NOW!

Featuring Steven T. Simmons, MD

- Better understand recent study results and how they require changing routine glaucoma care
- Better utilize target pressures in your patients and incorporate IOP fluctuation into the setting of these targets
- Better utilize present glaucoma therapies, both medical and surgical, to improve the overall glaucoma outcomes in your practice

Watch On Demand

Visit: https://engage.vevent.com/rt/advanstar_events?code=print

Ophthalmology Times®
CUTTING-EDGE ADVANCEMENTS

Sponsored by
ALLERGAN

APC26CS13

PATIENT RECORDS

(Continued from page 46)

assuming completion of the job. It was not until a week later, when the practice network went down and they called in their local hardware vendor, that they discovered the potential breach situation.

The practice, through no fault of its own, was completely exposed.

In a follow-up call to the vendor, they responded, "We don't know what you are talking about."

Really? This time everyone got lucky.

Here is what medical practices attesting to meaningful use stage 1 need to know about completing a security risk analysis.

RISK ANALYSIS EXPLAINED

The Centers for Medicare and Medicaid Services (CMS) defines the requirement this way: The practice must "Protect electronic health information created or maintained by the certified EHR technology through the implementation of appropriate technical capabilities and conduct or review a security risk analysis per 45 CFR 164.308(a)(1), implement updates as necessary and correct identified security deficiencies as part of the eligible providers risk management process . . . "

After completing a risk analysis, policies and procedures must be put in place to document and mitigate these risks.

Do you really understand what that means? If not, you are not alone.

A lack of technology expertise is the problem. You are not an IT guru and must depend on others, who may not be protecting your best interests.

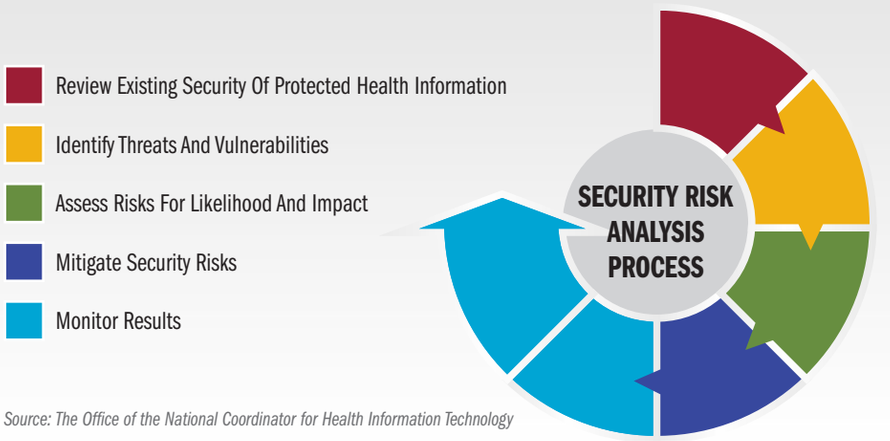
To make a simplistic medical analogy, a security risk analysis is the examination and testing you do to assess clinical risk and diagnose a clinical condition applied to your practice's information technology infrastructure and operations.

Just as you use a diagnosis and other clinical data to plan treatment, you will use the risk analysis to create an action plan to make your practice better at protecting patient information.

Further, privacy and security are like chronic diseases that require treatment, ongoing monitoring and evaluation, and periodic adjustment.

What is a security risk analysis?

A security risk analysis involves analyzing vulnerabilities and threats to your system to safeguard electronic protected health information (EPHI). It means reviewing your policies, practices, and systems and correct any issues that may make EPHI vulnerable.



Source: The Office of the National Coordinator for Health Information Technology

SECURITY RULE

A security risk analysis is a systematic and ongoing process of both:

- **Identifying and examining potential threats and vulnerabilities to protected health information in your medical practice.**
- **Implementing changes to make patient health information more secure than at present, then monitoring results (i.e., risk management).**

The HIPAA Security Rule requires covered entities to conduct a risk analysis to identify risks and vulnerabilities to electronic protected health information (EPHI). Risk analysis is the first step in an organization's Security Rule compliance efforts.

Following HIPAA risk analysis guidelines will help you establish the safeguards you need to implement based on the unique circumstances of your health-care practice.

After completing a risk analysis—which will identify areas of risk—policies and procedures must be put in place to document and mitigate these risks. Risk analysis is an ongoing process that should provide your medical practice with a detailed understanding of the risks to the confidentiality, integrity, and availability of EPHI.

HIPAA requires that covered entities "implement policies and procedures to prevent, detect, contain, and correct security violations" by conducting "an accurate and thorough assessment of the potential risks and vulnerabilities to the confidentiality, integrity, and availability of EPHI held by the [organization]."

Providers should develop a risk analysis that addresses these criteria by evaluating the impact and likelihood of potential breaches, implementing security features, cataloguing security features, and maintaining security protections.

HIPAA OMNIBUS FINAL RULE SUMMARY

There are three areas that physicians will need to focus on to comply with the new HIPAA rules:

- **Privacy, security, and breach notification policies and procedures (and in some cases, new workflows and forms).**
- **Notice of privacy practices.**
- **Business associate agreements.**

All of these forms must be updated. This updated documentation to identify your risks and how you will address them must be dated during the attestation period, not after.

The bottom line is this: If you do not document it, you did not do it. ■

MARK NORRIS *is chief executive officer of Medical Record Services Inc., which works with practices on meaningful use compliance, privacy and security, and attestation. He is former executive director of NEO HealthConnect, one of The Ohio Health Information Partnership's (OHIP) seven Regional Extension Centers (REC). He oversaw 350 primary-care physicians on issues of meaningful use compliance and attestation.*

Fiscal strategies for setting salaries, dealing with raise requests in practice

Tips help managers fine-tune pay scales and build merit into compensation plans

By Keith Borglum, CHBC

TAKE-HOME

- ***Handle raise requests from staff by researching what pay level the market supports. Use it to set pay accordingly and educate staff. Merit pay increases can be a better way to handle raises than simply increasing pay because it will increase worker productivity.***

IT IS OFTEN DIFFICULT to determine how much to pay a particular staff person, and how much to pay that member in relation to other staff in the office. This difficulty can be compounded by many factors.

Both employers and employees sometimes confuse salary and wages. Salaries are fixed amounts of pay per month. A wage is an hourly dollar amount. Most full-time staff work 2,000 to 2,200 hours per year.

When paying a salary, you would think that you have a dependable, fixed amount for your budget, but that's often not the case depending on the job description and the laws of your state. And job descriptions and laws are commonly in flux.

Many states have laws about which staff can be on a fixed salary. Often, salaried staff have to be either licensed personnel using their licensed skills more than 50% of the time on their job, or managers supervising at least five persons whose jobs the manager does not perform.

It can be tricky. Is an RN actually doing tasks requiring an RN license, or is he or she acting primarily in the role of a unlicensed medical assistant more than half time? Or do they spend time as a manager? If your office manager is managing five other staff, and you do a "reduction in force" by one person, what do you do? In both of these cases, you might need to be paying overtime wages, whether or not these persons are salaried.

Salaried-staff are often due overtime wages by law if overtime is worked. Just putting them on a fixed salary does not circumvent the labor laws of your state. These are questions best answered by a labor attorney in your state, or more cost-effectively by just reading the employer guides provided free by your state Labor Board, Chamber of Commerce, or private vendors.

FACTORS AFFECTING PAY

Practices in high cost of living and urban locations often need to pay more to attract good staff than do practices in suburban locations.

Practices in rural locations may pay more or less depending on the availability of staff; since in some locations there is a commuting population that may accept less pay for a local job. In other rural locations a practice may need to pay more to attract staff from urban or suburban centers due to a lack of local qualified staff. Local or regional unemployment can be a big factor in any setting, as can the closure of a hospital.

The skills of individual team members can also affect compensation. Of course, licensure has an effect but so do experience and on-the-job skills. "Time-in-grade"—or how long the person has been employed in the practice—also has some impact, even though it often shouldn't since doing a job badly for a long time rarely results in decreasing pay.

DEALING WITH RAISE REQUESTS

Staff often have unrealistic expectations about earning capacity and wages.

A staff member might have heard others bragging about their wages. Your worker mentally converts that top decile into a belief that it represents the median. Then the person comes to you and says: "Dr. Newguy's physician assistants are getting $18 per hour, and I'm only getting $12 per hour, so I deserve a raise or I quit."

Do you give it? What if Dr. Newguy is a specialist and you are a primary-care practice? Budgets differ. What if the only way that Dr. Newguy can keep staff is to grossly overpay? Do you still try to compete on pay with Dr. Newguy?

Rather than just acquiescing to the raise, or denying it outright, the following response might be more fruitful: "I'm willing to consider a raise if I am underpaying. Let's try to find some statistically relevant data on compensation and benefits over the next week or so, and meet again next Wednesday to discuss it."

Then go find the data. This is highly educa-

Continues on page 50 : ***Salary***

3 Steps for Controlling Staff Costs

1 ESTABLISH A BUDGET

The first step is to look at benchmark data for practices that are similar to yours. According to the National Society of Certified Healthcare Business Consultants, median staffing for solo and small practices is three to four full-time equivalent support staff per doctor, presuming no nonphysician providers or ancillary services and approximately 20 to 25 patient office visits per day. The budget for this level of staffing typically is about 20% to 24% of gross collections.

2 ADJUST FOR YOUR PRACTICE

Determine the proper staff size for your practice by adjusting the benchmarks you find for staff count and costs to account for any special circumstances related to your practice, such as staff productivity, payer mix, capitation payments, use of quality measures, and local wage levels. Once you have tailored the benchmarks to suit your circumstances, you will have a custom benchmark that you can use to evaluate staff costs and easily can update it annually to compare with the national surveys.

3 OBTAIN STAFF INPUT

Discuss your findings with your staff members and solicit their input for staying within budget, then review the data monthly. The benefit of investing in the effort of budgeting, just as it is in investing in other good practice-management behavior, is a flowing, more profitable, and less stressful practice. ■

SALARY

(Continued from page 49)

tional for both staff and the boss. Maybe you are underpaying, and if you don't come up to market rates, you'll lose good team members.

The primary way workers express their unhappiness is through requests for raises. . . . Happy staff members stay on the job, often at lower pay.

There are a number of free resources online to help find the pay rates in your community, or you can refer to local studies or purchased reports.

I prefer Salary.com because it graphically displays data by zip code, and as a curve, and is easily understood. Some of the medical-specialist accounting and consulting firms whose members belong to the National Society of Certified Healthcare Business Consultants (find them at NSCHBC.org) perform annual local studies in their communities that are available to clients or for a fee. Those studies also often provide detailed job descriptions to which you can compare.

Don't make the mistake, though, of misapplying the data. A registered nurse working as a physician assistant should be paid as an PA, not as an RN.

MERIT AND PRODUCTIVITY

If a raise is indicated, try to tie it to a merit or productivity bonus rather than a wage.

A merit bonus might be, "If you become a certified medical assistant, I'll pay for half the schooling and give you a $5,000 per year raise when you graduate." Note that $5,000 per year sounds like a lot more than the $2.50 per hour it represents.

A productivity bonus might be: If you are seeing 18 to 20 patients a day, and have capacity for 22 patients per day, tell your staff that every day the practice sees 22 patients, each staff person gets a $10 bonus. Like magic, you will be seeing 22 patients per day, paying some bonuses, but your productivity and profitability will increase.

STAFF HAPPINESS AND RAISES

The issue may not really be about dollars. The primary way workers express their unhappiness is through requests for raises. Studies have found that employees who threaten quitting as a tactic to get a raise often end up quitting within 6 months anyway. Happy staff stay on the job, often even at lower pay.

If you have lots of turnovers or raise requests, try finding out what might be making your staff unhappy, and fix it.

You might then save a few dollars, and end up with a happier place to work. ■

For Products & Services advertising information, contact: **Karen Gerome** at 800-225-4569, ext 2670 • Fax 440-756-5271 • Email: kgerome@advanstar.com

For Recruitment advertising information, contact: **Joanna Shippoli** at 800-225-4569, ext 2615 • Fax 440-756-5271 • Email: jshippoli@advanstar.com

PRODUCTS & SERVICES

BILLING SERVICES

PM Medical Billing & Consulting

Exclusive Ophthalmology Billers
Expert Ophthalmology Billers
Excellent Ophthalmology Billers
Triple E = Everything gets Paid

Concentrating on one Specialty makes the difference.

We are a Nationwide Ophthalmology Billing Service. We have been in business over twenty years. Our staff consists of billers who are certified Ophthalmic Techs, Ophthalmic assistants, and fundus photographers who are dual certified ophthalmic coders and billers. This combination of clinical backgrounds in ophthalmology with the certified coding degree is the ideal combination of expertise that you need to dramatically increase your revenue. We will get you paid on every procedure every single time. No more bundling, downcoding or denials…

Primary, Secondary, Tertiary and Patient Billing
Relentless and meticulous follow up.

- Experts in Forensic Billing .Specializing in old AR cleanup
- Credentialing and Re credentialing our Specialty. We have a separate Credentialing Department who has cultivated years of contacts to expedite the process as well as getting providers on plans that are technically closed.
- We can offer you our own Practice Management software at no cost to you or we can VPN into your system if that is what you prefer.
- Totally Hippa compliant. We are certified Hippa and have invested in the most secure Hippa connection that Google and Cisco use.
- Monthly custom reports provided.

We presently work on all of the following Practice Management systems :

NextGen, MD Office, Centricity, Medisoft, Office Mate, MD Intellus, Medware, Medcomp, Management Plus, ADS, Revolution EHR, EyeMd EMR, Next Tec, Open Practice Solutions , Cerner Works and more….

All of our clients were paid the PQRI and E-prescribe bonuses and we are ready for the ICD-10 change

Our staff has years of Attendance at AAO and ASCRS and attends all ongoing Ophthalmology billing and Practice Management continuing education classes. We are always knowledgeable and prepared for all government and commercial changes.

On staff MBA consultants

Call today to schedule a free on site consultation.

We will travel to you anytime to evaluate your AR and show you how we can dramatically increase your Revenue.

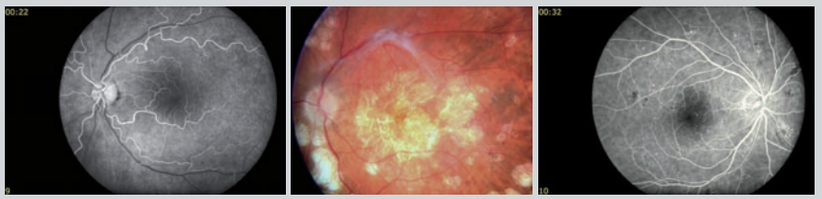
Call toll free at 1-888-PM-BILLING (1-888-762-4554)
Email: pmmedbill@aol.com
Web: www.pmophthalmologybilling.com
24 hours: 516-830-1500

Our Prestigious National Ophthalmology Clients reference list will be provided at your request

PM (Practice Management) Billing will keep an EYE on your Billing so you can keep an EYE on your patients.

DIGITAL IMAGING

DOES YOUR DIGITAL IMAGING SYSTEM CAPTURE IMPRESSIVE 21MP IMAGES?



FUNDUS PHOTO DOES!

Learn more at www.itsthisgood.com 314.533.6000

MARKETPLACE ADVERTISING WORKS!

Call Karen Gerome
to place your
Products & Services ad at
800-225-4569, ext. 2670
kgerome@advanstar.com

EQUIPMENT

HANNA TREPHINE SYSTEM

Only used one time. In perfect condition.
Includes:
#17166 Trephine Receptor, #17167 Setting Key, #17168 Depth Adjust. Key, #17169 Donor Punch, #17170 Supporting Suction base with Teflon Well, #22517172 anodized Alum. Box, 18 Trephine blades sizes 7.0-8.5 mm in unopened packaging.

Contact: **jphollid@bellsouth.net.**

Can send photos.
Price new **$15115.**
$8999 immediate purchase. OBO in 1 month.

Buying and Selling
Pre-owned Ophthalmic
Instrumentation.
Contact Jody Myers at
(800) 336-0410 or
visit www.floridaeye.com

FLORIDA EYE EQUIPMENT
Since 1989

PRODUCTS & SERVICES

GRANTS

FELLOWSHIP AND RESEARCH PROGRAMS

The Benign Essential Blepharospasm Research Foundation (BEBRF) is pleased to offer a research fellowship to support the training of exceptionally qualified physicians or scientists who wish to focus on benign essential blepharospasm with and without oromandibular dystonia. Fellowships will be awarded in the amount of up to $75,000 per year for two years. The BEBRF also offers funds of up to $150,000 annually to fund research into new treatments, pathophysiology and the genetics of benign essential blepharospasm (BEB) and Meige Syndrome (cranial and oromandibular dystonia). Research into photophobia, dry eye and apraxia of eyelid opening as they relate to BEB and Meige and their treatment will also be considered for funding.

Deadline to apply for a Fellowship is June 30, 2014.
Deadline to apply for a research grant is August 31, 2014.
Fellowship applications and grant guidelines can be obtained by email: bebrf@blepharospasm.org or downloaded from: www.blepharospasm.org

RECRUITMENT

FLORIDA

OCULOPLASTIC FELLOWSHIP

Offered by Dr. Roger E. Bassin of The Bassin Center For Plastic Surgery One year fellowship. Learn about face lift, lazerlift, blepharoplasty, brow lift, cheek lift, laser resurfacing, fat transfer and body liposuction as well as basic oculoplastic surgery.

Please submit resumes to:
christine@drbassin.com

KENTUCKY

Once in a
Lifetime Opportunity

Experienced, skilled refractive cataract and LASIK surgeon wanted for well-established Midwest group practice. The new surgeon can expect to start with 35 cataract procedures weekly earning $350+K with ultimate earnings potential in 7 figures. Candidate must have excellent people skills and be able to work well with co-managing optometric referral base.

Contact with CV to
MidwestSurgerygroup@gmail.com

MICHIGAN

Seeking Ophthalmologist to join our growing practice in Hazel Park, Michigan near Detroit.

Please contact
Emad Nakkash at 248-336-3937
for immediate consideration

TEXAS

- Do you own a pair of red tights?
- Do you own a cape?
- Are you faster than a speeding bullet?
- Are you able to leap tall buildings in a single bound?

If so, we are a busy ophthalmology practice located in **warm, sunny El Paso, Texas** and we are looking for a **"Super"** Doc.

Please contact us at **(915) 545-2333** or email your CV to **dlemaster@dralpern.com**

Repeating an ad ***ENSURES*** it will be seen and remembered!

RECRUITMENT

CONNECT

with qualified leads and career professionals

Post a job today

Medical Economics Careers
www.modernmedicine.com/physician-careers

Joanna Shippoli
RECRUITMENT MARKETING ADVISOR
(800) 225-4569, ext. 2615
jshippoli@advanstar.com

Networking in a changing environment

Why providing service to others may be most important component of staying connected

The OWL Quarterly **By Beth A. Marsh**

TAKE-HOME

- ***Be intentional about ongoing networking with customers and colleagues by setting aside time to talk about potential business opportunities and share clinical concerns.***

SOME PEOPLE THINK of networking as something you do when looking for a new job. True networking is not about one-way, one-time contacts made only when you need something—it is an ongoing process that many leaders say is a critical element of their success.

Authors from the Center for Creative Leadership (CCL), a national leadership development organization, describe networking as "building relationships and making alliances in service of others and in service of your organization's work and goals."[1]

Good networkers continually gain wisdom and insights by staying connected to others in their field, regardless of any immediate personal benefit. As the CCL's definition points out, providing service to others may be the most important component of networking.

Perhaps that means mentoring a younger colleague or introducing a friend to a great vendor. When you refer others, you build alliances. When you solve a problem for someone, you contribute to a long-term relationship—one that may someday be able to benefit you or your organization.

TAPPING INTO POWER OF CONNECTING

In my career, I have worked for five different ophthalmic pharmaceutical and medical device companies. In each case, the new opportunities were ones I never would have known about had I not stayed connected to former co-workers.

I'm also involved with Ophthalmic Women Leaders (OWL), a networking and professional development organization dedicated to the advancement of women throughout ophthalmology.

These connections have made me more well-rounded, helped me understand some of the new and exciting things that are going on in our industry, and now help support my consulting business.

On LinkedIn, 500 first-degree connections can translate into more than 5 million second- and third-degree connections.

Ophthalmology is a relatively small field. Most networking is done the old-fashioned way—in person, over dinner or coffee, or a round of golf. Opportunities for networking are large conferences, such as the American Academy of Ophthalmology and the American Society of Cataract and Refractive Surgery, as well as scores of other meetings.

Industry attendance at major ophthalmic meetings, however, has changed considerably in recent years.

Due to budget cuts and other trends, companies that would once have sent the majority of employees to meetings have cut back on who attends and how long they stay.

New pharmaceutical and device regulations have also changed how industry interacts with customers at the meetings, with sharp reductions in industry-sponsored social activities, dinners, and parties. Industry-supported breakfast and lunch symposia are now funded by grants and planned entirely by independent medical education providers.

Finally, everyone has gotten more specialized, with some people attending only the pre-meeting add-ons that are most relevant to them, such as Glaucoma Subspecialty Day or the Ophthalmology Innovation Summit.

With all these changes, staying connected cannot be as incidental as it used to be. It is no longer enough to hope you run into someone. Rather, one has to be intentional about networking with customers and colleagues and setting aside time to talk about potential business opportunities, share clinical concerns, and catch up on personal news.

NETWORKING RESOURCES ABOUND

One way to be intentional about this process is to use meeting breaks to connect with the people attending the conference that you want to see, instead of spending that break time calling the office or checking e-mail.

Also, schedule your time to allow you to attend important networking events for any community you are part of—whether that be a university alumni group or a professional development organization.

OWL hosts regular "OWL Monday" receptions and a slate of educational and professional development sessions at major meetings, as well as informal gatherings at meetings like the Association for Research in Vision and Ophthalmology (ARVO) and Hawaiian Eye.

Some meetings offer opportunities to volunteer or support nonprofit organizations by participating in a Habitat for Humanity project or the Run for Vision. Not only do these support good causes, but they are great opportunities to have fun and connect with like-minded people in the ophthalmic community in a unique way.

BEYOND THE BIG MEETINGS

Many professional associations have local or regional chapters, which can be great resources for staying connected with colleagues close to home. We are just beginning to create OWL chapters; the first launched in southern California in 2013.

Additionally, OWL has a formalized mentoring and coaching program that allows members to extend the connections they

Continues on page 54 : **Networking**

NETWORKING

(Continued from page 53)

make in person through longer-term mentoring or coaching relationships.

I believe it is also important to use your network as your eyes and ears at conferences that you don't attend in person. A post-meeting lunch or call, for example, can be a great way to find out what you missed. Ask contacts what they learned, what's going on in the industry, and what the "buzz" was about at the meeting.

Ophthalmic publications also have useful video reporter segments and written summaries that can help you get up to speed even if you couldn't be there in person. Reading the publications regularly helps you to be more conversational across all levels and areas of specialization in this industry.

USE TECHNOLOGY TO YOUR ADVANTAGE

Electronic or social networks like Facebook and LinkedIn have networking as their very foundation. On LinkedIn, for example, 500 first-degree connections can translate into more than 5 million second- and third-degree connections, because you are indirectly linked to everyone that your contacts (and their contacts) know. This makes it easy to network.

As these online communities have matured, they have become far more robust than just lists of friends, with additional resources like specific interest groups and comment forums.

There are many LinkedIn groups specific to ophthalmology; ASCRS and AAO offer online chat or subspecialist communities, as well as their own Twitter feeds and other opportunities to connect with or follow thought leaders. OWL also offers online resources, such as on-demand web seminars, to help people connect and learn from a distance.

Of course, it takes time to participate in these online communities in a meaningful way. One chief executive officer I know told me she schedules 2 hours every month for e-connecting. She uses that time to send congratulatory e-mails, respond to posts on LinkedIn, or add new connections so that she is routinely keeping in touch.

I agree that it is well worth it to devote some of our most precious resource—time—to networking. That time will enrich current relationships and expand the networks we depend on personally and to meet our organizations' goals for years to come. ■

Reference

1. Grayson C, Baldwin D. Leadership networking: Connect, collaborate, create. Center for Creative Leadership, 2007.

BETH A. MARSH *is vice president, strategic marketing and business development, for Aciex Therapeutics; principal of BAM Ophthalmology Consulting; and a board director for Ophthalmic Women Leaders. Learn more about OWL at www.owlsite.org.*

CMS site offers tips for ICD-10

By Donna Marbury

BALTIMORE :: **A NEW WEBSITE CREATED BY** the Centers for Medicare and Medicaid Services (CMS) aims to help practice owners come up with a plan to implement the International Statistical Classification of Diseases-10th Revision (ICD-10.)

Called "Road to 10" (*http://www.roadto10.org/*), the website walks practitioners through a five-question quiz that assesses their type of practice and size, types of vendors and payers, and ICD-10 readiness.

From there, a downloadable action plan is developed that outlines training, interoperability, and testing processes.

The site also features testimonials from physicians in various specialties who are in the process of implementing ICD-10. Other helpful information—including web seminars, frequently asked questions, and charts highlighting the differences between ICD-9 and ICD-10—is also on the website. ■

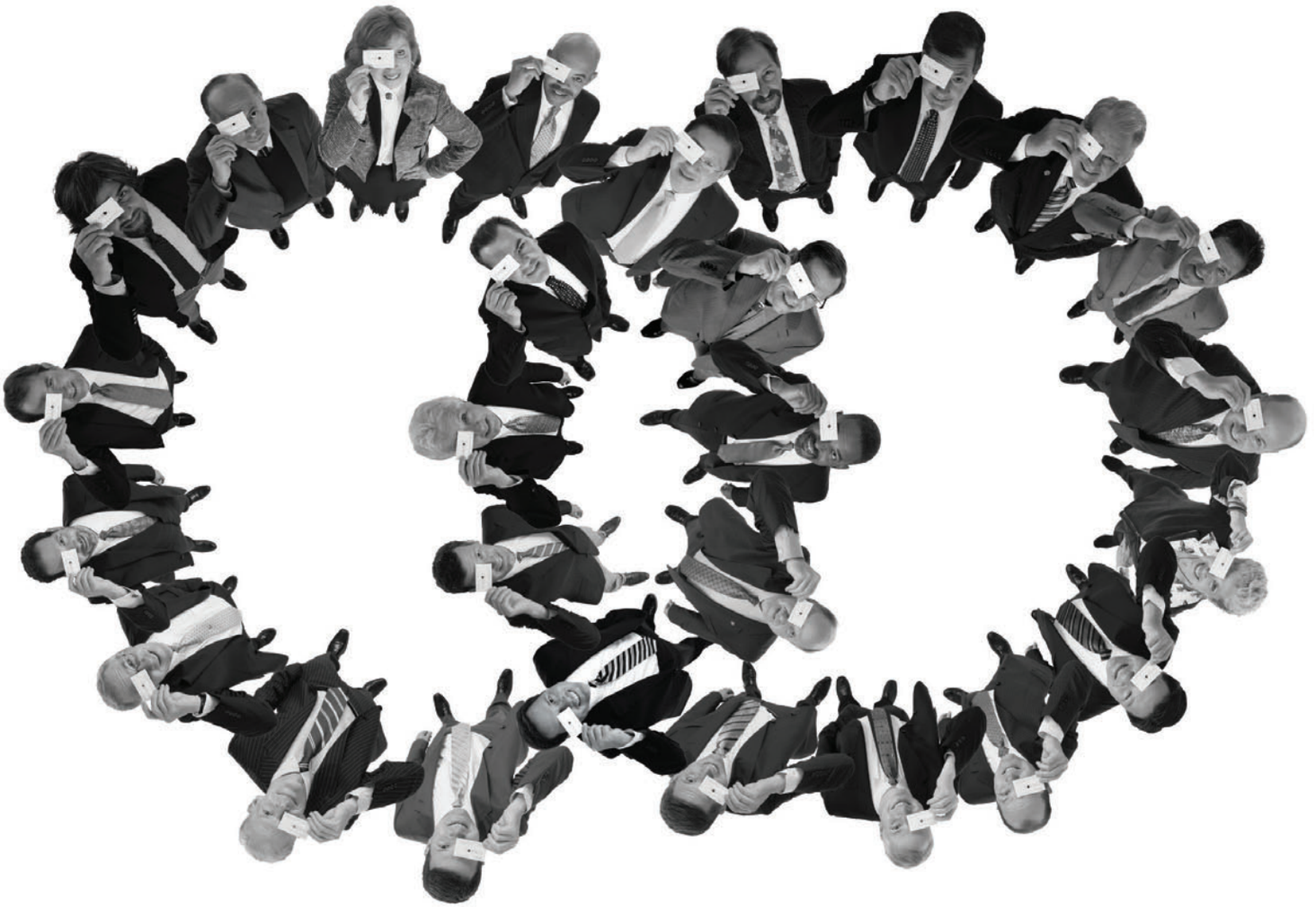
Advertiser Index

Advertiser	Page
Alcon Laboratories Inc. **P:** 800/862-5266 www.alcon.com	CV2, 3, 33-34, CV4
Allergan Inc. **P:** 714/246-4500 **F:** 714/246-4971 www.allergan.com	19-20, 25-26, 29-30
Ellex **P:** 800/824-7444 www.slt-ellex.com	23
Glaukos **P:** 800/452-8567 www.glaukos.com	CV3
Houston Methodist Hospital **P:** 310/280-7800 www.hmleadingmedicine.com	43
Maine Society of Eye Physicians **P:** 207/445-2260 www.maineeyemds.com	45
Ophthalmic Women Leaders **P:** 415/751-2401 **E:** info@owlsite.org www.owlsite.org	44
Rhein Medical **P:** 800/637-4346 www.rheinmedical.com	5
Santen www.santeninc.com	17
Sucampo Pharma Americas www.sucampo.com	13-14
TearLab Corp. **P:** 855/832-7522 www.tearlab.com	7
ThromboGenics **P:** 732/590-2900 www.thrombogenics.com	9-10
TTI Medical **P:** 800/322-7373 www.ttimedical.com	35

This index is provided as an additional service.

The publisher does not assume any liability for errors or omissions.

OPHTHALMOLOGY TIMES (Print ISSN 0193-032X, Digital ISSN 2150-7333) is published semi-monthly (24 issues yearly) by Advanstar Communications Inc., 131 W First Street, Duluth, MN 55802-2065. Subscription rates: $200 for one year in the United States & Possessions, Canada and Mexico; all other countries $263 for one year. Pricing includes air-expedited service. Single copies (prepaid only): $13 in the United States & Possessions, Canada and Mexico; $20 all other countries. Back issues, if available are $25 in the U.S. $ Possessions; $30 in Canada and Mexico; $35 in all other countries. Include $6.50 per order plus $2 per additional copy for U.S. postage and handling. If shipping outside the U.S., include an additional $10 per order plus $5 per additional copy. **Periodicals postage paid** at Duluth, MN 55806 and additional mailing offices. **POSTMASTER:** Please send address changes to OPHTHALMOLOGY TIMES, P.O. Box 6009, Duluth, MN 55806-6009. Canadian G.S.T. number: R-124213133RT001, Publications Mail Agreement Number 40612608. Return undeliverable Canadian addresses to: Pitney Bowes PO Box 25542 London, ON N6C 6B2 CANADA. Printed in the U.S.A.



GLAUCOMA
SPECIALISTS

COMPREHENSIVE
OPHTHALMOLOGISTS

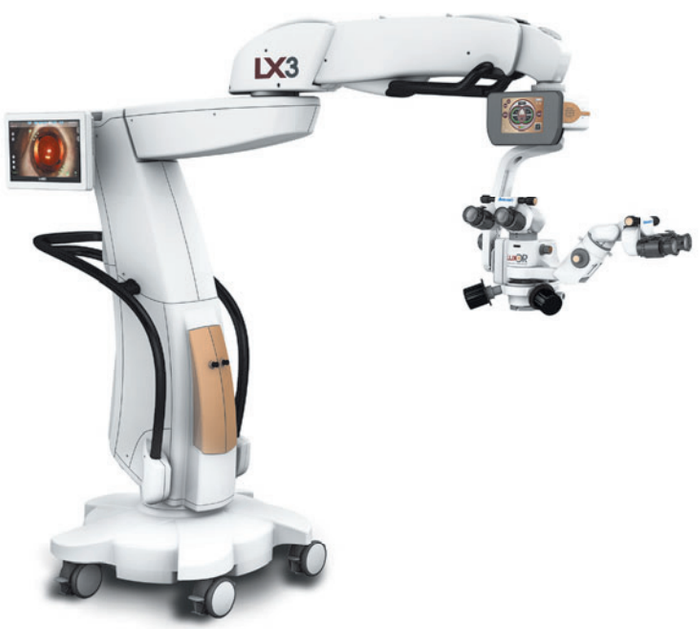
NOT A HOLE.
A COMMON GOAL.

Micro Invasive Glaucoma Surgery (MIGS) procedures meet the patient-focused treatment goals of both glaucoma specialists and comprehensive ophthalmologists. That's because MIGS procedures utilize an *ab interno* micro-incisional approach that allows for early intervention into glaucoma progression and significantly reduce IOP. Indicated for use in conjunction with cataract surgery for the reduction of intraocular pressure in adult patients with mild to moderate open-angle glaucoma currently treated with hypotensive medicine, the iStent® Trabecular Micro-Bypass Stent is a singular advancement in care that addresses the needs of multiple audiences.

To learn more contact Glaukos at 800.452.8567 or visit www.glaukos.com.

MIGS GLAUKOS®
Changing Perspectives

SUPERIOR VISUALIZATION.[1]
NOTHING IS HIDDEN.



Experience the superior visualization of the LuxOR™ LX3 with Q-VUE™ Ophthalmic Microscope. It delivers superior red reflex stability and greater depth of focus, revealing every facet of your procedures in crisp, brilliant detail.[1]

1. Data on file, Alcon Laboratories, Inc.

LuxOR™ | LX3
with Q-VUE™ Ophthalmic Microscope

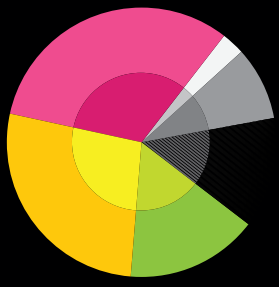
Alcon®
a Novartis company

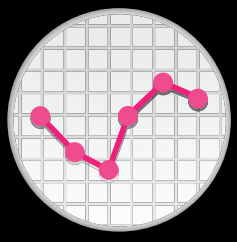
Ophthalmology Times
CLINICAL NEWS & ANALYSIS

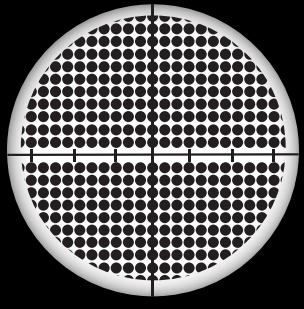
OphthalmologyTimes.com

CME Monograph

Visit www.MedEdicus.com for online testing and instant CME certificate.







The Science and Art of Glaucoma Management Today

Faculty

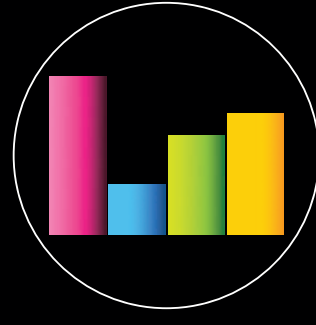
Donald L. Budenz, MD, MPH (Chair)
Kittner Family Distinguished Professor and Chairman
Department of Ophthalmology
University of North Carolina School of Medicine
Chapel Hill, North Carolina

Robert D. Fechtner, MD
Professor of Ophthalmology
The Institute of Ophthalmology and Visual Science
Rutgers New Jersey Medical School
Newark, New Jersey

Leon W. Herndon, MD
Professor of Ophthalmology
Medical Director
Duke Eye Center
Durham, North Carolina

Tony Realini, MD, MPH
Associate Professor of Ophthalmology
West Virginia University Eye Institute
Morgantown, West Virginia

Kuldev Singh, MD, MPH
Professor of Ophthalmology
Department of Ophthalmology
Stanford University School of Medicine
Palo Alto, California



Jointly sponsored by **New York Eye and Ear Infirmary of Mount Sinai** and MedEdicus LLC

New York Eye and Ear Infirmary of **Mount Sinai**

MedEdicus LLC

This continuing medical education activity is supported through an unrestricted educational grant from Alcon, Inc.

Alcon a Novartis company

Distributed with Ophthalmology Times

ORIGINAL RELEASE: March 15, 2014
LAST REVIEW: February 25, 2014
EXPIRATION: March 31, 2015

The Science and Art of Glaucoma Management Today

LEARNING METHOD AND MEDIUM
This educational activity consists of a supplement and ten (10) study questions. The participant should, in order, read the learning objectives contained at the beginning of this supplement, read the supplement, answer all questions in the post test, and complete the Activity Evaluation/Credit Request form. To receive credit for this activity, please follow the instructions provided on the post test and Activity Evaluation/Credit Request form. This educational activity should take a maximum of 1.5 hours to complete.

CONTENT SOURCE
This continuing medical education (CME) activity captures content from a CME symposium held on November 17, 2013, in New Orleans, Louisiana.

ACTIVITY DESCRIPTION
It is well-accepted that decreasing intraocular pressure (IOP) is the only proven strategy to protect the optic nerve and reduce progressive loss of the visual field in patients with glaucoma who have pressures above or within normal range. Many advances in the medical and surgical management of IOP have occurred. Using case presentations, this monograph presents an update on some of the recent advances and expert approaches to managing patients with glaucoma.

TARGET AUDIENCE
This educational activity intends to educate general ophthalmologists and glaucoma specialists.

LEARNING OBJECTIVES
Upon completion of this activity, participants will be better able to:

- Meet IOP goals for patients with treatments that provide effective 24-hour IOP control
- Describe the effects of preservatives in IOP-lowering treatments on ocular surface health
- Incorporate appropriate multitherapy or fixed-combination therapy into individualized regimens
- Discuss the role of minimally invasive glaucoma procedures in effective management of IOP

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 through the joint sponsorship of **New York Eye and Ear Infirmary of Mount Sinai** and MedEdicus LLC. **New York Eye and Ear Infirmary of Mount Sinai** is accredited by the ACCME to provide continuing medical education for physicians.

In July 2013, the Accreditation Council for Continuing Medical Education (ACCME) awarded New York Eye and Ear Infirmary of Mount Sinai "Accreditation with Commendation," for six years as a provider of continuing medical education for physicians, the highest accreditation status awarded by the ACCME.

AMA CREDIT DESIGNATION STATEMENT
New York Eye and Ear Infirmary of Mount Sinai designates this enduring material for a maximum of 1.5 *AMA PRA Category 1 Credits*™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

GRANTOR STATEMENT
This continuing medical education activity is supported through an unrestricted educational grant from Alcon, Inc.

DISCLOSURE POLICY STATEMENT
It is the policy of **New York Eye and Ear Infirmary of Mount Sinai** that the faculty and anyone in a position to control activity content disclose any real or apparent conflicts of interest relating to the topics of this educational activity, and also disclose discussions of unlabeled/unapproved uses of drugs or devices during their presentation(s). **New York Eye and Ear Infirmary of Mount Sinai** has established policies in place that have identified and resolved all conflicts of interest prior to this educational activity. Full disclosure of faculty/planners and their commercial relationships, if any, are noted below.

DISCLOSURES
Donald L. Budenz, MD, MPH, had a financial agreement or affiliation during the past year with the following commercial interests in the form of *Consultant/Advisory Board:* Alcon, Inc; Ivantis Inc; and Santen Pharmaceutical Co, Ltd; *Honoraria from promotional, advertising or non-CME services received directly from commercial interests or their Agents (eg, Speakers Bureaus):* Merck & Co, Inc.

Robert D. Fechtner, MD, had a financial agreement or affiliation during the past year with the following commercial interests in the form of *Consultant/Advisory Board:* Alcon, Inc; and Allergan, Inc; *Honoraria from promotional, advertising or non-CME services received directly from commercial interests or their Agents (eg, Speakers Bureaus):* Alcon, Inc; Allergan, Inc; and Merck & Co, Inc.

Leon W. Herndon, MD, had a financial agreement or affiliation during the past year with the following commercial interests in the form of *Consultant/Advisory Board:* Alcon, Inc; *Honoraria from promotional, advertising or non-CME services received directly from commercial interests or their Agents (eg, Speakers Bureaus):* Alcon, Inc; and Glaukos Corporation.

Tony Realini, MD, MPH, had a financial agreement or affiliation during the past year with the following commercial interests in the form of *Consultant/Advisory Board:* Alcon, Inc; Sensimed; and Sucampo Pharmaceuticals, Inc; *Contracted Research:* Alcon, Inc; *Honoraria from promotional, advertising or non-CME services received directly from commercial interests or their Agents (eg, Speakers Bureaus):* Alcon, Inc; and Lumenis Ltd.

Kuldev Singh, MD, MPH, had a financial agreement or affiliation during the past year with the following commercial interests in the form of *Consultant/Advisory Board:* Alcon, Inc; Allergan, Inc; Bausch + Lomb Incorporated; Ivantis Inc; Santen Pharmaceutical Co, Ltd; Sucampo Pharmaceuticals, Inc; and Transcend Medical, Inc.

PEER REVIEW DISCLOSURE
Ted Gerszberg, MD, has no relevant commercial relationships to disclose.

EDITORIAL SUPPORT DISCLOSURES
Cynthia Tornallyay, RD, MBA, CCMEP; Kimberly Corbin, CCMEP; Barbara Aubel; and Vivian Fransen, MPA, have no relevant commercial relationships to disclose.

DISCLOSURE ATTESTATION
The contributing physicians and instructors listed above have attested to the following:

1) that the relationships/affiliations noted will not bias or otherwise influence their involvement in this activity;
2) that practice recommendations given relevant to the companies with whom they have relationships/affiliations will be supported by the best available evidence or, absent evidence, will be consistent with generally accepted medical practice; and
3) that all reasonable clinical alternatives will be discussed when making practice recommendations.

OFF-LABEL DISCUSSION
This activity includes off-label discussion of dosing of ocular antihypertensives and azithromycin for ocular surface disease. Please refer to the official prescribing information for discussion of approved indications, contraindications, and warnings.

FOR DIGITAL EDITIONS
System Requirements:
When viewing this activity online, please ensure the computer you are using meets the following requirements:

- **Operating System:** Windows or Macintosh
- **Media Viewing Requirements:** Flash Player or Adobe Reader
- **Supported Browsers:** Microsoft Internet Explorer, Firefox, Google Chrome, Safari, and Opera
- **A good Internet connection**

New York Eye and Ear Infirmary of Mount Sinai Privacy & Confidentiality Policies
CME policies: http://www.nyee.edu/cme-enduring.html

Hospital policies: http://www.nyee.edu/website-privacy.html

CME Provider Contact Information
For questions about this activity, call 212-979-4383.

TO OBTAIN *AMA PRA CATEGORY 1 CREDIT*™
To obtain *AMA PRA Category 1 Credit*™ for this activity, read the material in its entirety and consult referenced sources as necessary. Complete the evaluation form along with the post test answer box within this supplement. Remove the Activity Evaluation/Credit Request page from the printed supplement or print the Activity Evaluation/Credit Request page from the Digital Edition. Return via mail or fax to Kim Corbin, Director, ICME, **New York Eye and Ear Infirmary of Mount Sinai**, 310 East 14th Street, New York, NY 10003 or fax to (212) 353-5703. Your certificate will be mailed to the address you provide on the Activity Evaluation/Credit Request form. Please allow 3 weeks for mailed/faxed forms to be processed. There are no fees for participating in and receiving CME credit for this activity.

Alternatively, we offer instant certificate processing and support Green CME. Please take this post test and evaluation online by going to **www.MedEdicus.com**, **Educational Activities** tab, and clicking the **Post-Test & CME Certificate** button. Upon passing, you will receive your certificate immediately. You must score 70% or higher to receive credit for this activity, and may take the test up to 2 times. Upon registering and successfully completing the post test, your certificate will be made available online and you can print it or file it.

DISCLAIMER
The views and opinions expressed in this educational activity are those of the faculty and do not necessarily represent the views of **New York Eye and Ear Infirmary of Mount Sinai**; MedEdicus LLC; Alcon, Inc; or *Ophthalmology Times*.

Introduction

Our knowledge of glaucoma and its treatment is constantly evolving. New diagnostic tools, novel therapies, and insights from clinical trials continue to inform our practice patterns. Clinicians need to stay abreast of all these advances for optimal evaluation and management of their patients with glaucoma. In this educational program, our expert panel of respected glaucoma specialists from across the country will present interesting cases from their practices. We will discuss the cases, identify learning points, and review the science that guides our management decisions. In the process, we hope you will gain insight into the ever-changing art and science of glaucoma management today.

—Donald L. Budenz, MD, MPH,
Program Chair, on behalf of the faculty

Case 1: Glaucoma Progression Despite Apparently Adequate IOP Control

Dr Singh: I present the hypothetical case of a 71-year-old white woman with moderate bilateral primary open-angle glaucoma. Her best corrected visual acuity (BCVA) is 20/25 in each eye. Over the past 2 years, her intraocular pressure (IOP) has been in the range of 12 to 15 mm Hg, with most readings 12 or 13 mm Hg in each eye. The diagnosis, however, is not normal-tension glaucoma because the IOP was in the 20s when therapy was initiated a few years ago. The optic nerves show moderate glaucomatous damage, with a cup-disc ratio of 0.7 in the right eye and 0.65 in the left eye plus neuroretinal rim thinning bilaterally. While the IOP for both eyes might be considered acceptably low by some clinicians, the patient has demonstrated reproducible progression of her visual field in the right eye, with a worsening arcuate defect. She is currently treated with a regimen that includes a fixed-combination agent with a beta-blocker and a carbonic anhydrase inhibitor (CAI) dosed twice daily in both eyes, as well as an alpha agonist dosed 3 times daily. The patient has hazel eyes and has elected not to use a prostaglandin analogue because she does not wish to risk the possibility of iris color change, despite a lengthy discussion regarding the benefits of prostaglandin analogue therapy. In summary, the patient has demonstrated progressive glaucomatous optic neuropathy despite apparently reasonable IOP control. She claims to be adherent to all of her medications faithfully in the morning, although she admits to occasionally missing an evening dose. She takes the morning drops consistently between 8:00 AM and 8:30 AM, and prefers to have her office appointments shortly thereafter.

Dr Budenz: Is it common to see patients who appear to have well-controlled IOP and yet are so clearly progressing?

Dr Fechtner: It is common, and it is very frustrating. We all have patients who are on maximal medical therapy, have had laser surgery, and whose IOP at office visits is in the low teens; they should be stable but they are progressing. I see patients on maximal tolerated therapy. I have performed laser surgery on them. I am doing everything I can. They seem to be well controlled, and yet they are progressing. Over the years, I have begun looking at the optic nerve at every visit, dilated or not, and I am surprised at the number of patients apparently well controlled in whom I find a disc hemorrhage, which is a critical sign of active disease.

Dr Budenz: What is in your differential diagnosis for patients progressing at normal or low pressures? Are there specific issues you think about when evaluating these patients?

Dr Realini: I think about central corneal thickness. Is it extremely low? If so, we may be underestimating true IOP using Goldmann tonometry, and her real IOP may be significantly higher—she may not be controlled as well as we think. In these patients, a target IOP in the mid to high single digits is not unreasonable—if they have thin corneas, their IOP can often get that low with medications, and they may need to be that low to prevent further progression. Also, gonioscopy is important. If the patient described in Case 1 is phakic, she may have relative pupillary block and could be slipping into intermittent subacute angle closure. She could be progressing in small increments during periods of angle closure. We are very good at performing gonioscopy at our initial evaluations, but we do not always remember to repeat the gonioscopy periodically. We should probably repeat gonioscopy every 3 to 5 years to be sure the patient's open angles are staying open over time. I also consider if this patient is having significant circadian IOP variability. Is she peaking at night or at the end of her dosing intervals? She may not be as well controlled as we think—but we have limited tools for assessing her IOP outside of the office as well as outside of normal office hours.

Dr Singh: Her corneal thickness is average in both eyes, approximately 550 microns OU. Her angles are open, and we have no additional information available regarding any circadian IOP behavior.

Dr Herndon: It is important to see our patients at different times of the day. Patients often develop the habit of scheduling appointments at consistent times of the day—the most astute ones want appointments early in the clinic session before we have a chance to fall behind in our schedules. We should be vigilant in

noticing this behavior so we can encourage our patients to schedule appointments at different times of the day. By doing this, we can look across several visits and construct a diurnal IOP curve. Of course, to do this, we must note in the chart what time IOP measurements are taken.

Dr Fechtner: In fact, there is a Current Procedural Terminology code for diurnal IOP assessment (ie, 92100) that provides a small payment for performing this evaluation. In addition, conducting various provocative tests can provide some insight into circadian IOP variability. One test is to have the patient lie back in the supine position and measure IOP after 2 to 3 minutes. This test can give a rough estimate of peak nocturnal IOP.[1] Of course, you will have to use a handheld tonometer because the Goldmann tonometer does not work in that position. I prefer the pneumotonometer, but you could also use a tonopen. Another provocative test that has been suggested is the water-drinking challenge: Ask your patients to consume a half to a full liter of water quickly, then measure the patient's IOP every 15 minutes for the following hour. The higher the IOP variability during the water-drinking test, the more likely the patient is to experience glaucoma progression.[2,3] This can also provide some insight into what might be going on at night when the patient is lying down asleep, although we have not adopted this test in our practice.

Dr Singh: I agree that some form of diurnal IOP assessment may be diagnostically beneficial in such a patient. Options include a 1-day serial tonometry session or a series of visits at which the patient's IOP is assessed at different times of the day. There is also value in checking her IOP first thing in the morning, before her morning medication dosing, to help determine whether or not her nighttime drops are still effective at that time. It is much more difficult to measure nocturnal IOP as it may be inconvenient for both the patient and the clinician. Some devices currently being evaluated are designed to continuously measure IOP over a 24-hour period. However, at present, our best options include stressing better adherence to therapy and revisiting prostaglandin use. The patient's resistance to prostaglandin therapy may diminish, given that the alternative option of trabeculectomy is associated with substantial risk. Likewise, her adherence with the current regimen may improve once she understands her condition is becoming worse. In a collaborative study with investigators at the University of California, San Francisco, including Dr Shan Lin, we found that disease severity may be the best predictor of compliance: Patients with advanced disease refilled their medications more regularly than those with largely asymptomatic early or moderate disease.[4]

Case 2: Medication Intolerance

Dr Fechtner: I provided care for an 86-year-old white man who has had glaucoma since 1998. He has a family history of glaucoma in several sisters. He is a known steroid responder. His medical history is significant for systemic hypertension, a cerebrovascular accident, and heart disease, and he is anticoagulated. Despite these issues, he is generally healthy and lives independently. His visual acuity in the right eye is poor following a branch retinal vein occlusion after cataract surgery, and his visual acuity is 20/50 in his left eye. His IOP is poorly controlled on multiple medications including bimatoprost, timolol/brimonidine fixed-combination therapy, and oral methazolamide. He reports he is allergic to essentially every glaucoma medication. When he stops his medications, his vision improves, but his IOP increases to 30 mm Hg. When he takes his medications, his IOP is well controlled but his vision becomes so poor he cannot read. His external appearance is shown in **Figure 1**.

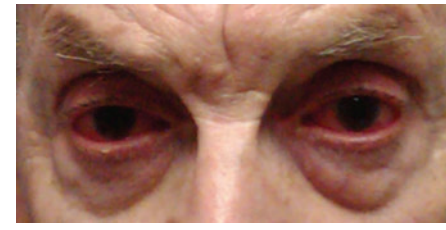


Figure 1. External appearance of the patient described in Case 2. *Photo courtesy of Robert D. Fechtner, MD*

On examination, he had erythematous lid margins with telangiectasia. His meibomian glands have inspissated secretions. He is also using cyclosporine topically for this ocular surface disease. His conjunctiva is injected, the cornea has punctate staining, the anterior chambers are quiet, and he has well-positioned intraocular lenses in both eyes. He also has an afferent pupillary defect in the right eye. His IOP is 19 mm Hg because he has been taking his medications. He has an average central corneal thickness of 560 microns in the right eye and 553 microns in the left eye. His optic nerve is cupped severely in the low-vision right eye after the vein occlusion and is approximately 0.5 in the sighted left eye. His visual fields are given in **Figure 2** and demonstrate advanced glaucoma. To summarize, we have a generally healthy 86-year-old man with profound ocular surface disease, advanced glaucoma, and intolerance to his IOP-lowering medications.

Dr Budenz: How common is it for glaucoma and ocular surface disease to coexist? Does this represent a small minority of our patients?

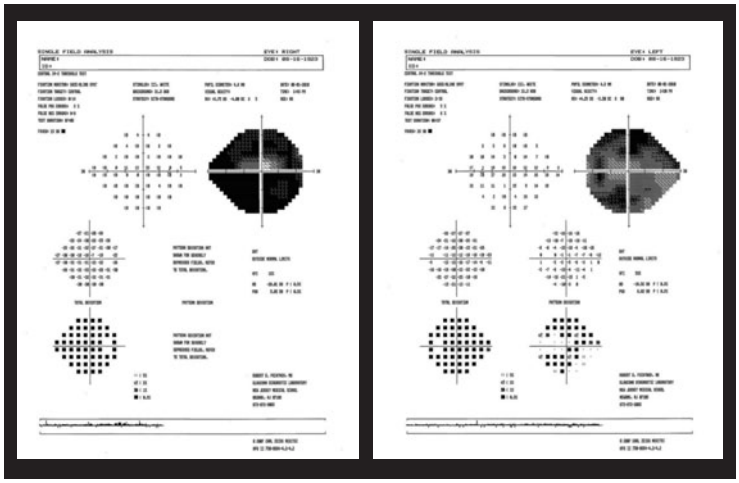


Figure 2. Visual fields from the patient described in Case 2.
Images courtesy of Robert D. Fechtner, MD

Dr Fechtner: We know from several studies that ocular surface disease is prevalent in patients who are treated for glaucoma. I think we underestimate the prevalence because in a busy clinical setting, we do not want to take the time to address the issue if the patient does not raise the complaint. We conducted a multicenter study of more than 600 patients treated for glaucoma and ocular hypertension, using the Ocular Surface Disease Index as our outcome measure. Surprisingly, we found almost 50% of these patients had symptoms consistent with mild, moderate, or severe ocular surface disease.[5] A similar study conducted in southern California found a similar number of patients—59%—had symptoms consistent with mild, moderate, or severe ocular surface disease.[6] These patients are in our practices. They are not uncommon at all.

Dr Budenz: What are our options for this patient?

Dr Herndon: He is intolerant to his medications, has significant ocular surface disease, and is monocular. We have to be aggressive in lowering his IOP to preserve both his remaining visual function and his quality of life. This patient may require surgery. In this setting, however, with such ocular surface inflammation, he may be at high risk for failure of filtering surgery. Another option would be to transition him to preservative-free medications and see if that improves the ocular surface. Preservatives such as benzalkonium chloride (BAK) have been implicated in ocular surface disease[7] and may reduce the success of eventual glaucoma surgery.[8] This patient may benefit from reducing or eliminating his exposure to these excipient ingredients that are found in most of our eye drop medications.

Dr Realini: I agree that surgery is both a reasonable option and potentially his best option. I share Dr Herndon's concern that the current status of his ocular surface may predispose him to failure of glaucoma surgery. One approach I have found helpful in this setting is to stop all topical medications for 30 days and treat instead with an oral CAI for temporary IOP control. With a little luck, the eye drop holiday lets the ocular surface quiet down so surgery can be performed with a better chance for success. In this case, the patient is already on an oral CAI. There may be room to increase the dose or switch to acetazolamide, which may or may not be more effective.

Dr Singh: Surgical therapy appears to be a reasonable choice as the medications are clearly causing profound adverse effects. While it is difficult to study compliance, it is reasonable to assume that, all other things being equal, patients who report burning, stinging, and other symptoms associated with the use of glaucoma medications are going to be less likely to be compliant with these medications relative to those who do not experience such symptoms.

Dr Fechtner: Like my colleagues on the panel, I suspected that BAK may be at least partially responsible for this clinical picture. True allergy to BAK is rare. More common, however, is intolerance, and I believe this is dose-dependent. I have seen many patients tolerate the first BAK-preserved medication, and even the second one, but when the patient begins using the third medication—and now we may be up to 5 or 6 drops per day—the intolerance manifests. In these patients, I try to either eliminate or at least reduce the BAK load. Fixed-combination formulations can help reduce this BAK load by delivering 2 medications in a single drop. In this patient's case, I would like to eliminate BAK if possible. We are fortunate that in our modern era we have many more BAK-free options than ever before.

Dr Budenz: Dr Fechtner, how did you manage this patient?

Dr Fechtner: I switched him from the BAK-preserved prostaglandin analogue to SofZia-preserved travoprost. I discontinued his preserved fixed-combination therapy and placed him on preservative-free timolol; this patient came to me before the release of the preservative-free dorzolamide/timolol fixed-combination formulation. I also tried to increase his oral CAI dose but he was intolerant of the higher dose. At the same time that we changed his IOP-lowering regimen, we also changed our approach to his ocular surface disease. I continued the cyclosporine but added lid hygiene as well as azithromycin (off label) to his lid margins. On follow-up, he began to feel better, but his IOP was still elevated. We added pilocarpine, 1%, and his IOP has now been well controlled in the low to mid teens; he looks, feels, and sees better.

Case 3: Optimizing the Multidrug Regimen

Dr Realini: A 57-year-old patient of mine was recently diagnosed with open-angle glaucoma during a routine eye examination. She has normal visual acuity and a normal anterior segment examination. Her IOP at the referring optometrist's office during the 3 visits before referral was consistently in the 26 to 27 mm Hg range before any treatment. She has moderate optic disc changes, with a 0.65 cup-disc ratio in the right eye and a 0.7 in the left eye. She has early and reproducible visual field loss in both eyes. Systemically she is quite healthy, having only moderate hypertension for which she takes an oral beta-blocker. She was started on a prostaglandin analogue in both eyes and referred to me for further evaluation and management. On the prostaglandin analogue, her IOP was in the range of 20 to 21 mm Hg during 2 consecutive visits to my office, with normal central corneal thickness in both eyes. Based on her optic nerve and visual field damage, I set a target IOP to achieve a 40% reduction from her untreated baseline. This means we needed to lower her IOP to approximately 16 mm Hg. A prostaglandin alone has not gotten us there.

Dr Budenz: In this case, will you switch to a different monotherapy agent or add adjunctive therapy to the prostaglandin analogue?

Dr Realini: I have a 2-step decision process for switching vs adding treatment agents. First, I ask if the medication has been well tolerated. I agree completely with Dr Singh that any degree of intolerance should prompt us to seriously consider switching therapy, because if the patient complains and you ignore the complaint, the patient is going to ignore using the medication. If the medication is tolerated, I next ask whether or not the medication delivered what I expected from it. If a medication performs less well than I had hoped, I consider that the patient may be a suboptimal responder and may do better with a different monotherapy agent. One caveat: I never make decisions about medication responsiveness based on a single on-treatment IOP measurement. IOP is too variable for clinicians to discern meaningful trends with only 1 data point, and I do not want to rush to declare a patient nonresponsive to prostaglandin therapy because this class of medications is the most effective, safe, and conveniently dosed class that we have. In this patient's case, I knew from the start that a 40% reduction from baseline was likely to require a multidrug regimen because no single medication consistently delivers that much IOP reduction. We should not discontinue a medication for failing to meet our target if the target was beyond the medication's reach. I chose to continue the prostaglandin because it resulted in IOP reductions of 6 to 7 mm Hg, which is what I expected.

Dr Singh: The challenge is in selecting effective adjunctive therapy. We know much more about how a medication works as monotherapy than as adjunctive therapy. It is a mistake to assume that an agent will work as well when added to a prostaglandin relative to when used as a monotherapeutic option. Beta-blocker use is a perfect example in which IOP lowering of 5 to 6 mm Hg is common with monotherapy; yet even half of this effect cannot be counted on when used adjunctively with a prostaglandin. Likewise, selective laser trabeculoplasty may not be as additive to a prostaglandin as it is when used as initial therapy or when added to other medications.

Dr Realini: Adjunctive therapy to a prostaglandin is a challenge because no single medication we have adds much in terms of effectiveness. Numerous studies have evaluated the additivity of the common second-line therapies to a prostaglandin analogue (**Table 1**). To summarize them briefly, the best we can hope for is 2 to 3 mm Hg of additional IOP-lowering with the addition of a beta-blocker, CAI, or adrenergic agonist.[9-12] In selecting therapy, I also consider the circadian cycle. We know from work done primarily in the laboratory of Liu and Weinreb that IOP is highest at night, when we are lying down asleep.[13,14] We would like to select therapies that will be effective for the full 24-hour cycle, including this important nocturnal period. Prostaglandins effectively lower IOP throughout the 24-hour circadian cycle. Of the adjunctive options, however, only CAIs lower IOP during the nocturnal period[15]—neither beta-blockers[15] nor adrenergic agonists[16] lower IOP at night. So we are now in a quandary: We need an additional 5 mm Hg of IOP reduction, and there is no single medication that is likely to provide this result.

Table 1. Additivity of Various Adjunctive Therapies to Prostaglandins (using mm Hg as a measure for comparison)

Study	O'Connor[9]	Feldman[10]	Reis[12]	Bournias[11]
Design	Retrospective	Prospective	Prospective	Prospective
PGA	Latanoprost	Travoprost	Travoprost	Any
Timolol	2.5		3.9	
Dorzolamide	3.9			3.4 P 2.8 T
Brinzolamide		2.7	4.0	3.4 P 2.6 T
Brimonidine	2.0	2.1	2.3	4.8 P 3.8 T

PGA=prostaglandin analogue; P=peak; T=trough

Dr Singh: On average that is true. These IOP reductions from adjunctive therapy are mean values. Some patients will respond better than average, and others will respond less well than average. The question is whether or not it is worth trying 1 adjunctive agent when it is unlikely to lower IOP to a level that you hope to reach.

Dr Realini: It is certainly reasonable to have that discussion with this patient and to try this treatment approach. However, she lives a long way from our medical office, and winter is coming. West Virginia winters keep patients away from the office. She requests that we lower her IOP to target in as few visits as possible.

Dr Budenz: Is it ever the right step to go straight to a fixed-combination formulation as second-line therapy?

Dr Fechtner: Yes. We have all been taught to add medications 1 at a time so we can know their effect and assess each agent's efficacy independently. This means we add only 1 of the 2 components of a fixed-combination formulation, and if IOP drops significantly but not enough, we can add a third drug by replacing the adjunctive single agent with fixed-combination therapy. I have followed this exact pattern for years, and I think I have wasted a lot of time doing so. In fact, it would appear the US Food and Drug Administration (FDA) is changing its view on this issue as well. The dorzolamide/timolol fixed-combination formulation is still labeled for use only in patients inadequately controlled on—or unable to take—a beta-blocker. But the timolol/brimonidine and brinzolamide/brimonidine fixed-combination formulations can be started as first-line therapy or as first adjunctive therapy, according to their prescribing information.

Dr Budenz: Do we have any data on the additivity of fixed-combination formulations to prostaglandins?

Dr Realini: Three prospective studies have evaluated this clinical question. The findings from 2 of these studies were quite consistent, demonstrating 5 to 8 mm Hg of additional IOP reduction when a fixed-combination formulation was added to a prostaglandin.[17,18] One study is an obvious outlier, suggesting that the additivity of dorzolamide/timolol to latanoprost provides less than 1 mm Hg of additional IOP reduction.[19] I have read this study carefully and cannot find any methodological errors; I believe it is only a statistical blip and should be disregarded as it does not represent common clinical experience. Overall, I think IOP reductions of 5 to 8 mm Hg are a more reasonable expectation when adding a fixed-combination formulation to a prostaglandin.

Dr Budenz: Dr Realini, what did you decide to do for your patient?

Dr Realini: Together we elected to continue her prostaglandin therapy and go straight to a fixed-combination formulation as adjunctive therapy. We discussed laser surgery but she was not interested. In selecting a fixed-combination formulation from the 3 options available, I made my decision based on 2 key points: (1) beta-blockers add poorly to prostaglandins; and (2) this patient has systemic hypertension, for which she was taking an oral beta-blocker. Oral beta-blockers achieve partial beta-blockade within the eye. In patients taking an oral beta-blocker, topical timolol works approximately 25% less well than for patients not taking an oral beta-blocker.[20] It made little sense to me to add a fixed-combination formulation that contained a beta-blocker. So we started the newest fixed-combination formulation, brinzolamide/brimonidine. It is labeled for 3 times daily dosing, but I prescribed it off label for twice-daily dosing. Over the next several visits, her IOP stabilized between 15 and 17 mm Hg, and we were very happy that she was meeting her IOP target using 3 drops a day of these agents from 2 bottles.

Dr Budenz: Are there circumstances when you might add a beta-blocker to a prostaglandin for a patient on oral beta-blocker therapy?

Dr Herndon: Of course. It depends on what the alternative is. If a patient will otherwise require filtration surgery, it is worth trying a beta-blocker first.

Case 4: A Patient Who Needs Glaucoma Surgery

Dr Herndon: A 79-year-old woman from my practice suffers from severe primary open-angle glaucoma in her right eye with moderate damage in her left eye. She has a history of retinal detachment in the right eye and has received pars plana vitrectomy with a scleral buckle in this eye. She subsequently underwent a Baerveldt implant with scleral patch graft placement to this right eye over a year ago with good maintenance of IOP control in the low teens. The right eye, despite these many issues and operations, is now stable. The left eye—her better eye—now has gradual vision loss, progressive cataract changes, and IOP measurements in the 26- to 29-mm Hg range despite 3 medications. Her visual fields are given in **Figure 3**.

The right eye is evaluated using a 10-2 algorithm because she only has a small residual central island of vision; even that has split fixation with dense superior loss. The left visual field shows a reproducible inferior nasal step on the 24-2 algorithm. Likewise, she has significant inferior nerve fiber layer thinning on optical coherence tomography (OCT) in the right eye, as well as early superior nerve fiber layer dropout in the left eye corresponding to her inferior field defect (**Figure 4**).

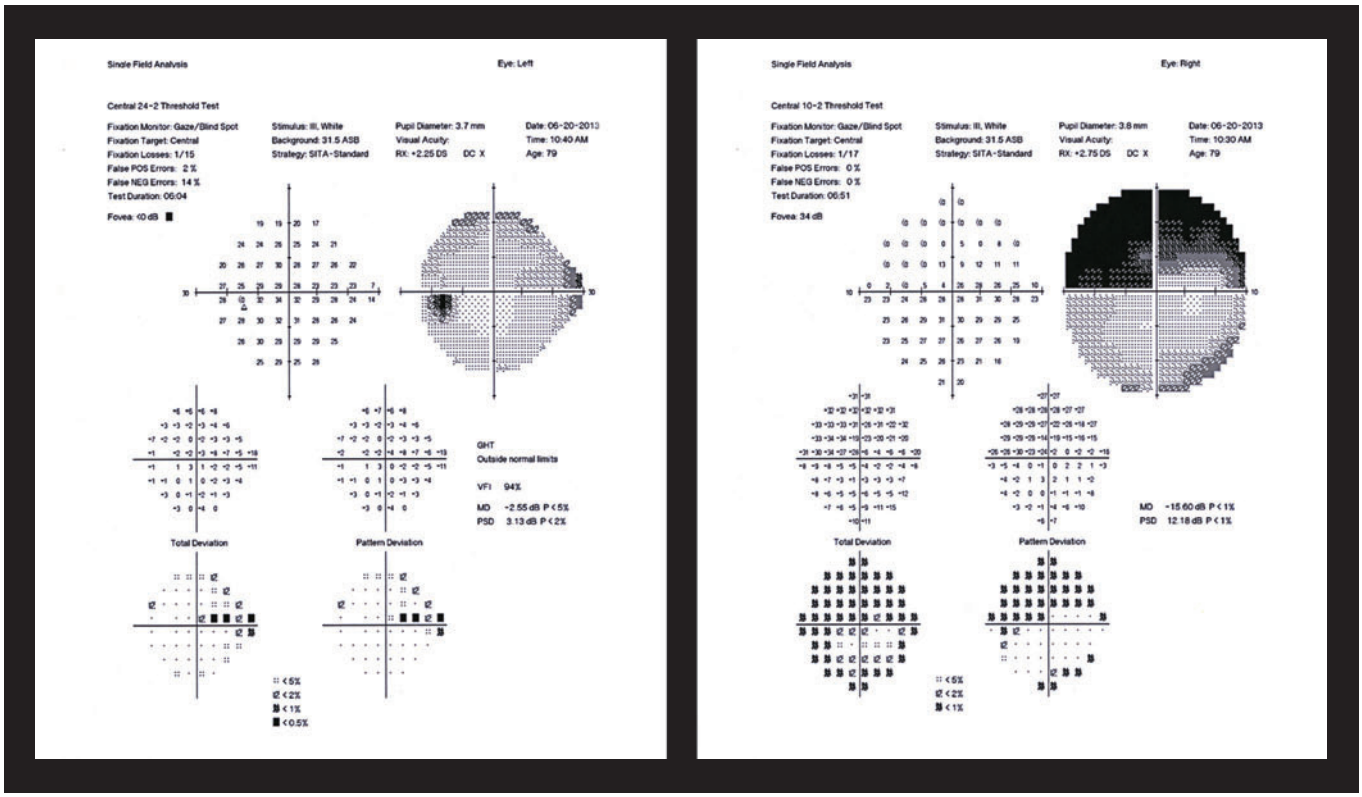


Figure 3. Visual fields of the patient presented in Case 4. Note that the right field is a 10-2 algorithm and the left field is a 24-2 algorithm.
Images courtesy of Leon W. Herndon, MD

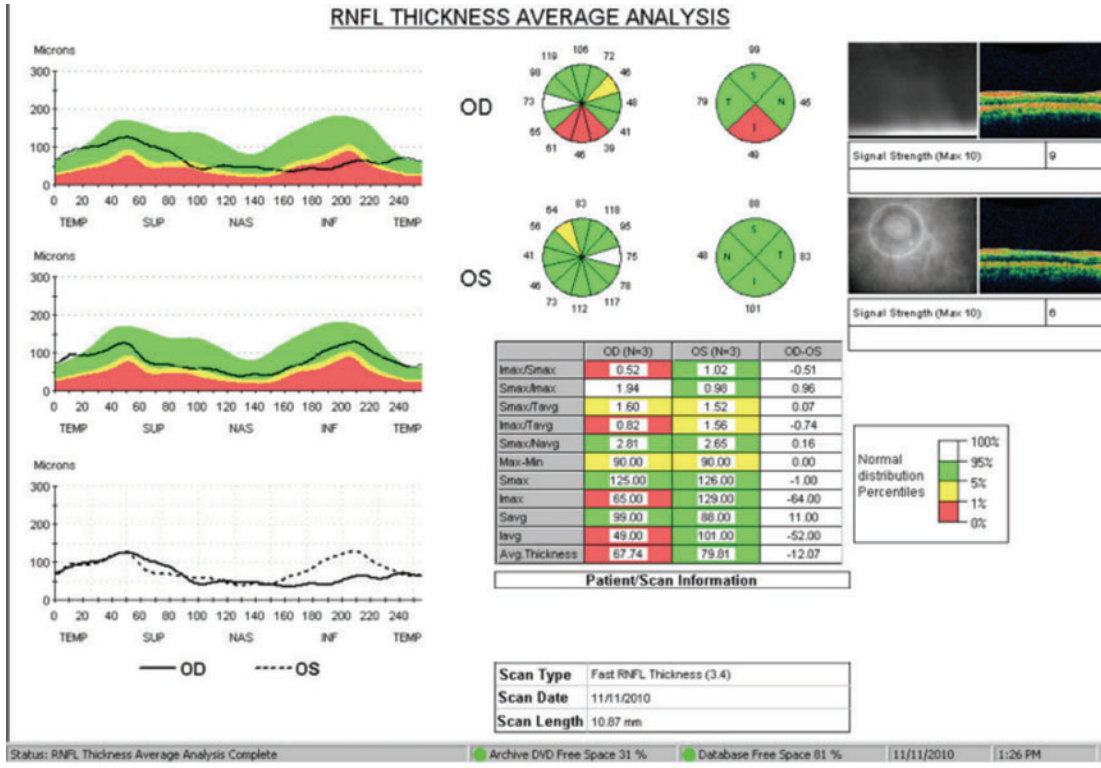


Figure 4. The OCT images from Case 4, demonstrating significant inferior nerve fiber layer dropout in the right eye and early dropout superiorly in the left eye.
Images courtesy of Leon W. Herndon, MD

Dr Budenz: Her right eye shows us what is in store for her left eye unless we intervene. This patient is poorly controlled on 3 medications and has required surgery in the fellow eye for adequate disease control. Panel, what would be your next step?

Dr Realini: She needs an IOP-lowering procedure. We can also remove the cataract at the same time. I vote for a combined procedure. Numerous glaucoma procedures can be paired with a cataract operation. In her case, given the preoperative IOP and her use of 3 medications, I would likely proceed with a combined cataract and trabeculectomy procedure. Several minimally invasive glaucoma surgery (MIGS) devices are available. Based on my interpretation of the data from clinical trials,[21,22] these MIGS are not likely to provide significant IOP reductions compared with cataract surgery alone—perhaps only 2 to 3 mm Hg. They can help reduce the medication burden for 1 or 2 years postoperatively, but after that many patients are right back where they started in terms of the number of medications needed to control IOP.

Dr Fechtner: There are several considerations when selecting a glaucoma procedure. One factor is the concern for postoperative IOP elevations. Without an alternate aqueous outflow pathway, there are few options for blunting a postoperative IOP spike. Also, because this patient is essentially monocular, we want to optimize visual rehabilitation so she can function independently postoperatively. I agree that the MIGS may not provide the level of IOP control that we need for this patient. Also, they cannot be manipulated like a trabeculectomy or a non-valved implant in the event of a postoperative IOP spike. My preference for this patient's care would be a trabeculectomy using the Ex-PRESS implant to standardize the sclerostomy size, minimize postoperative hypotony, and provide a reasonable chance for both IOP reduction and rapid visual recovery postoperatively.

Dr Budenz: One lesson we have learned from the MIGS clinical trials, among other studies, is that cataract surgery alone is an effective IOP lowering procedure for some patients. Is there a role for cataract surgery alone in this patient?

Dr Singh: The Ocular Hypertension Treatment Study demonstrated an approximate 4-mm Hg IOP reduction from baseline in the untreated group at 1 year postoperatively.[23] While there are patients in whom IOP drops significantly with cataract surgery alone, there are those patients in whom urgent trabeculectomy is required in the early postoperative period when an IOP spike occurs. If it were my eye, I would want to have cataract surgery alone without trabeculectomy along with meticulous removal of viscoelastic at the end of the case and the use of postoperative oral CAI therapy to minimize the risk of an early IOP spike. Despite this, I expect there will be a high likelihood of requiring future trabeculectomy; but even a small chance of avoiding, or at least delaying, glaucoma filtration surgery is worth considering as an option.

Dr Budenz: Three panelists have given 3 different strategies for managing this patient. This underscores that the optimal practice pattern for the surgical management of glaucoma is evolving. Dr Herndon, what did you elect to do for this patient?

Dr Herndon: I considered all of these options (**Table 2**). For cataract surgery alone, the best data suggest a 4-mm Hg IOP reduction at 1 year and as little as a 2-mm Hg reduction at longer follow-up.[23] I also considered a standard trabeculectomy with or without the Ex-PRESS implant. The Ex-PRESS implant does not seem to improve success rates over trabeculectomy alone, although it may offer a slightly safer early postoperative course and faster vision rehabilitation than trabeculectomy alone.[24] Two MIGS are approved by the FDA for use in the United States. Trabectome, which performs trabecular ablation somewhat similar to a goniotomy, is a procedure that lowers IOP an average of 4.5 mm Hg at 12 months, with some blood reflux possible in the early postoperative period.[21] The iStent, which is approved for use at the time of cataract surgery and provides typically similar IOP reductions to cataract surgery alone, can reduce the number of glaucoma medications needed by the patient.[22] It is also a safe procedure, with some small risk of blood reflux and of device obstruction if not placed appropriately.

Table 2. Surgical Alternatives to Trabeculectomy or Tube-Shunt Procedures for the Management of Glaucoma

	Efficacy	Safety
Cataract alone	Mean -4.1 mm Hg through 12 months[23]	No additional risk
Trabectome	Mean -4.5 mm Hg through 12 months[21]	Blood reflux
iStent	Same IOP reduction as cataract surgery alone (-8.5 mm Hg) but with fewer medications (mean 0.2 vs 0.4 medications per patient)[22]	Stent obstruction
Ex-PRESS	Compared with trabeculectomy: – Qualified success OR 1.00 – Complete Success OR 0.93[24]	Better tolerated than trabeculectomy; substantially more risk than cataract alone

OR=odds ratio

Given all of these options, I elected to perform a cataract procedure with implantation of an iStent device. This decision was based largely on the safety factors, including a low risk of early complications and a rapid visual rehabilitation. I counseled the patient that she may need a more invasive glaucoma surgical procedure in the future, but that this was a reasonable plan. For this procedure, I remove the cataract first and then implant the device. The iStent is a snorkel-shaped tube that bypasses the trabecular meshwork and allows aqueous humor to flow directly into Schlemm's canal. It comes preloaded on an inserter. The long end of the snorkel is passed through the meshwork and seated in Schlemm's canal, and the short end stents the meshwork, allowing aqueous to flow through. I place the iStent in the inferonasal quadrant when possible, as there may be more collector channels in that region. Eventually, we may be approved by the FDA to place more than 1 device at a time, and we can take advantage of multiple quadrants and different populations of outflow collector channels. For now, only 1 device per procedure is approved, although trials with 2 or more devices are ongoing; this approach is approved in other global markets. In this patient's case, the procedure went well, and at last follow-up nearly a year postoperatively, her IOP in that eye is consistently in the mid-teens without the use of medications.

Summary

Dr Budenz: We have discussed 4 challenging patients and heard the experts share their clinical management tips, techniques, and pearls. Some of our patients will progress despite apparently well-controlled IOP because factors such as central corneal thickness, the status of the angle, the possibility of IOP spikes outside routine office hours, and the potential for nonadherence to therapy. We are fortunate to have so many medical options for lowering IOP, but we must remain vigilant for patients who cannot tolerate medications because allergies to the medication itself or to preservatives and other inactive ingredients in the formulations. In these patients, formulations with alternate preservation systems or no preservatives at all may be appropriate, and we are fortunate these days that there are several from which to choose. We can also reduce exposure to eye drops by using fixed-combination formulations, which have the added benefit of simplifying complex multidrug regimens. For our patients who cannot be controlled adequately with medications alone, several novel MIGS have been developed, and others are on the way, offering us a better opportunity than ever before to individualize therapy even in the operating room. Overall, familiarity with the IOP-lowering options available today will allow us to artfully apply the science to the treatment plans that meet our patients' needs and lifestyles.

References

1. Mosaed S, Liu JH, Weinreb RN. Correlation between office and peak nocturnal intraocular pressures in healthy subjects and glaucoma patients. *Am J Ophthalmol*. 2005;139:320-324. **2.** Susanna R Jr, Hatanaka M, Vessani RM, Pinheiro A, Morita C. Correlation of asymmetric glaucomatous visual field damage and water-drinking test response. *Invest Ophthalmol Vis Sci*. 2006;47:641-644. **3.** Susanna R Jr, Vessani RM, Sakata L, Zacarias LC, Hatanaka M. The relation between intraocular pressure peak in the water drinking test and visual field progression in glaucoma. *Br J Ophthalmol*. 2005;89:1298-1301. **4.** Ung C, Zhang E, Alfaro T, et al. Glaucoma severity and medication adherence in a county hospital population. *Ophthalmology*. 2013;120:1150-1157. **5.** Fechtner RD, Godfrey DG, Budenz D, Stewart JA, Stewart WC, Jasek MC. Prevalence of ocular surface complaints in patients with glaucoma using topical intraocular pressure-lowering medications. *Cornea*. 2010;29:618-621. **6.** Leung EW, Medeiros FA, Weinreb RN. Prevalence of ocular surface disease in glaucoma patients. *J Glaucoma*. 2008;17:350-355. **7.** Pisella PJ, Pouliquen P, Baudouin C. Prevalence of ocular symptoms and signs with preserved and preservative free glaucoma medication. *Br J Ophthalmol*. 2002;86:418-423. **8.** Broadway DC, Grierson I, O'Brien C, Hitchings RA. Adverse effects of topical antiglaucoma medication. II. The outcome of filtration surgery. *Arch Ophthalmol*. 1994;112:1446-1454. **9.** O'Connor DJ, Martone JF, Mead A. Additive intraocular pressure lowering effect of various medications with latanoprost. *Am J Ophthalmol*. 2002;133:836-837. **10.** Feldman RM, Tanna AP, Gross RL, et al. Comparison of the ocular hypotensive efficacy of adjunctive brimonidine 0.15% or brinzolamide 1% in combination with travoprost 0.004%. *Ophthalmology*. 2007;114:1248-1254. **11.** Bournias TE, Lai J. Brimonidine tartrate 0.15%, dorzolamide hydrochloride 2%, and brinzolamide 1% compared as adjunctive therapy to prostaglandin analogs. *Ophthalmology*. 2009;116:1719-1724. **12.** Reis R, Queiroz CF, Santos LC, Avila MP, Magacho L. A randomized, investigator-masked, 4-week study comparing timolol maleate 0.5%, brinzolamide 1%, and brimonidine tartrate 0.2% as adjunctive therapies to travoprost 0.004% in adults with primary open-angle glaucoma or ocular hypertension. *Clin Ther*. 2006;28:552-559. **13.** Liu JH, Zhang X, Kripke DF, Weinreb RN. Twenty-four-hour intraocular pressure pattern associated with early glaucomatous changes. *Invest Ophthalmol Vis Sci*. 2003;44:1586-1590. **14.** Liu JH, Kripke DF, Twa MD, et al. Twenty-four-hour pattern of intraocular pressure in the aging population. *Invest Ophthalmol Vis Sci*. 1999;40:2912-2917. **15.** Liu JH, Medeiros FA, Slight JR, Weinreb RN. Comparing diurnal and nocturnal effects of brinzolamide and timolol on intraocular pressure in patients receiving latanoprost monotherapy. *Ophthalmology*. 2009;116:449-454. **16.** Liu JH, Medeiros FA, Slight JR, Weinreb RN. Diurnal and nocturnal effects of brimonidine monotherapy on intraocular pressure. *Ophthalmology*. 2010;117:2075-2079. **17.** Fechtner RD, Harasymowycz P, Nixon DR, et al. Twelve-week, randomized, multicenter study comparing a fixed combination of brimonidine-timolol with timolol as therapy adjunctive to latanoprost. *Clin Ophthalmol*. 2011;5:945-953. **18.** Konstas AG, Mikropoulos D, Dimopoulos AT, Moumtzis G, Nelson LA, Stewart WC. Second-line therapy with dorzolamide/timolol or latanoprost/timolol fixed combination versus adding dorzolamide/timolol fixed combination to latanoprost monotherapy. *Br J Ophthalmol*. 2008;92:1498-1502. **19.** Hatanaka M, Reis A, Sano ME, Susanna R Jr. Additive intraocular pressure reduction effect of fixed combination of maleate timolol 0.5%/dorzolamide 2% (Cosopt) on monotherapy with latanoprost (Xalatan) in patients with elevated intraocular pressure: a prospective, 4-week, open-label, randomized, controlled clinical trial. *J Glaucoma*. 2010;19:331-335. **20.** Schuman JS. Effects of systemic beta-blocker therapy on the efficacy and safety of topical brimonidine and timolol. Brimonidine Study Groups 1 and 2. *Ophthalmology*. 2000;107:1171-1177. **21.** Francis BA, Minckler D, Dustin L, et al. Combined cataract extraction and trabeculotomy by the internal approach for coexisting cataract and open-angle glaucoma: initial results. *J Cataract Refract Surg*. 2008;34:1096-1103. **22.** Samuelson TW, Katz LJ, Wells JM, Duh YJ, Giamporcaro JE. Randomized evaluation of the trabecular micro-bypass stent with phacoemulsification in patients with glaucoma and cataract. *Ophthalmology*. 2011;118:459-467. **23.** Mansberger SL, Gordon MO, Jampel H, et al. Reduction in intraocular pressure after cataract extraction: the Ocular Hypertension Treatment Study. *Ophthalmology*. 2012;119:1826-1831. **24.** Wang W, Zhou M, Huang W, Zhang X. Ex-PRESS implantation versus trabeculectomy in uncontrolled glaucoma: a meta-analysis. *PLoS ONE*. 2013;8:e63591.

CME Post Test Questions

The Science and Art of Glaucoma Management Today

To obtain *AMA PRA Category 1 Credit*™ for this activity, complete the CME Post Test by writing the best answer to each question in the Answer Box located on the Activity Evaluation/Credit Request form following. Alternatively, you can complete the CME Post Test online at http://www.MedEdicus.com, Educational Activities tab, and click the Post-Test & CME Certificate button.

See detailed instructions at To Obtain *AMA PRA Category 1 Credit*™ on page 2.

1. Possible explanations for a patient with glaucoma who is progressing despite apparently well-controlled IOP include:
   a. Low central corneal thickness masking higher true IOP
   b. Peak IOP outside office hours
   c. Open iridocorneal angles
   d. Both a and b

2. Provocative tests to estimate peak nocturnal IOP include:
   a. Withdrawal of IOP-lowering medications
   b. Water-drinking test and supine IOP
   c. Water-drinking test and diurnal curve
   d. None of the above

3. What percent of the patients with glaucoma also have symptoms of ocular surface disease?
   a. 25% to 30%
   b. 35% to 40%
   c. 50% to 60%
   d. 75% to 80%

4. Some ways of reducing exposure to preservatives in patients with glaucoma include all of the following, except:
   a. Using fixed-combination formulations
   b. Using oral carbonic anhydrase inhibitors
   c. Using topical cyclosporine therapy
   d. Using preservative-free formulations

5. Adding a single adjunctive agent to a prostaglandin analogue typically results in an incremental IOP reduction of:
   a. 1 mm Hg
   b. 2 mm Hg to 3 mm Hg
   c. 5 mm Hg to 7 mm Hg
   d. 8 mm Hg to 10 mm Hg

6. IOP reduction from topical beta-blockers is blunted in patients concurrently using:
   a. Brimonidine
   b. Prostaglandins
   c. Oral beta-blockers
   d. Both a and c

7. Nocturnal IOP reduction is not expected from:
   a. Beta-blockers
   b. Carbonic anhydrase inhibitors
   c. Prostaglandins
   d. All of the above

8. Minimally invasive glaucoma surgeries include:
   a. Trabeculectomy and iStent
   b. Ahmed valves and Trabectome
   c. Trabectome and iStent
   d. Trabectome and trabeculectomy

9. Benefits of iStent implantation include:
   a. IOP reduction of approximately 5 mm Hg to 8 mm Hg
   b. No complications
   c. Reduction of medications for 1 to 2 years
   d. Surgeons with 20 years of experience performing the procedure

10. In patients with ocular hypertension, cataract surgery alone can lower their IOP by:
    a. 2 mm Hg
    b. 4 mm Hg
    c. 6 mm Hg
    d. 8 mm Hg

Activity Evaluation/Credit Request

The Science and Art of Glaucoma Management Today

Original Release: March 15, 2014
Last Review: February 25, 2014
Expiration: March 31, 2015

To receive *AMA PRA Category 1 Credit*™, you must complete this **Evaluation** form and the **Post Test**. Record your answers to the **Post Test** in the **Answer Box** located below. Mail or Fax this completed page to **New York Eye and Ear Infirmary of Mount Sinai**–ICME, 310 East 14th Street, New York, NY 10003 (Fax: 212-353-5703). Your comments help us to determine the extent to which this educational activity has met its stated objectives, assess future educational needs, and create timely and pertinent future activities. Please provide all the requested information below. This ensures that your certificate is filled out correctly and is mailed to the proper address. It also enables us to contact you about future CME activities. Please print clearly or type. Illegible submissions cannot be processed.

PARTICIPANT INFORMATION (*Please Print*) ❑ Home ❑ Office

Last Name _____ First Name _____

Specialty _____ Degree ❑ MD ❑ DO ❑ OD ❑ PharmD ❑ RPh ❑ NP ❑ RN ❑ PA ❑ Other _____

Institution _____

Street Address _____

City _____ State _____ ZIP Code _____ Country _____

E-mail _____ Phone _____ Fax _____

Please note: We do not sell or share e-mail addresses. *They are used strictly for conducting post-activity follow-up surveys to assess the impact of this educational activity on your practice.*

Learner Disclosure: To ensure compliance with the US Centers for Medicare and Medicaid Services regarding gifts to physicians, **New York Eye and Ear Infirmary of Mount Sinai** Institute for CME requires that you disclose whether or not you have any financial, referral, and/or other relationship with our institution. **CME certificates cannot be awarded unless you answer this question.** For additional information, please call NYEE ICME at 212-979-4383. Thank you.

❑ Yes ❑ No I and/or my family member have a financial relationship with **New York Eye and Ear Infirmary of Mount Sinai** and/or refer Medicare/Medicaid patients to it.

❑ **I certify that I have participated in the entire activity and claim 1.5 *AMA PRA Category 1 Credits*™.**

Signature Required _____ **Date Completed** _____

OUTCOMES MEASUREMENT

❑ Yes ❑ No **Did you perceive any commercial bias in any part of this activity? IMPORTANT! If you answered "Yes," we urge you to be specific about where the bias occurred so we can address the perceived bias with the contributor and/or in the subject matter in future activities.**

_____

Circle the number that best reflects your opinion on the degree to which the following learning objectives were met:
5 = Strongly Agree 4 = Agree 3 = Neutral 2 = Disagree 1 = Strongly Disagree

Upon completion of this activity, I am better able to:

• Meet IOP goals for patients with treatments that provide effective 24-hour IOP control	5	4	3	2	1
• Describe the effects of preservatives in IOP-lowering treatments on ocular surface health	5	4	3	2	1
• Incorporate appropriate multitherapy or fixed-combination therapy into individualized regimens	5	4	3	2	1
• Discuss the role of minimally invasive glaucoma procedures in effective management of IOP	5	4	3	2	1

1. Please list one or more things, if any, you learned from participating in this educational activity that you did not already know. _____

_____

2. As a result of the knowledge gained in this educational activity, how likely are you to implement changes in your practice?
4=definitely will implement changes 3=likely will implement changes 2=likely will not implement any changes 1=definitely will not make any changes

4 3 2 1

Please describe the change(s) you plan to make: _____

_____

3. Related to what you learned in this activity, what barriers to implementing these changes or achieving better patient outcomes do you face?

_____

_____

4. Please check the Core Competencies (as defined by the Accreditation Council for Graduate Medical Education) that were enhanced for you through participation in this activity. ❑ Patient Care ❑ Practice-Based Learning and Improvement ❑ Professionalism ❑ Medical Knowledge ❑ Interpersonal and Communication Skills ❑ Systems-Based Practice

5. What other topics would you like to see covered in future CME programs? _____

_____

ADDITIONAL COMMENTS _____

_____

_____

POST TEST ANSWER BOX

1	2	3	4	5	6	7	8	9	10

Ophthalmology Times
CLINICAL NEWS & ANALYSIS

OphthalmologyTimes.com

iTech
BUILDING THE OPHTHALMIC TECH'S COMMUNITY OF PRACTICE

ENSURING PATIENT SUCCESS WITH CONTACT LENSES

KEEP YOUR PATIENTS SAFE WITH STRICT WEAR AND CARE REGIMENS

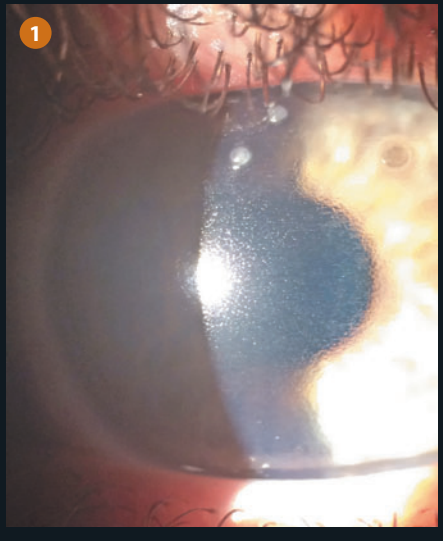


Figure 1. Soft contact lens overwear; note the "jelly bump" deposit superiorly and the overall poor condition of the lens.

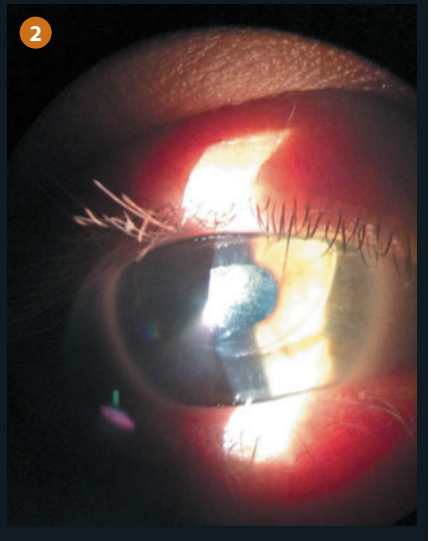


Figure 2. Rigid gas permeable lens overwear; note the central deposit.

INSIDE:
Contact lenses
The power of recommendation
You know what is best for your patient, and you should make the call. Don't let him make his decisions about healthy contact lens wear and care—make a reccomendation. Our recommendations have a strong influence on patient choice, and they are there to promote patients' best interests.
PAGE 10

Note correction on page 14. Images were mislabeled in the Winter 2013 issue; they are shown again with correct captions.

By Ernie Bowling, OD, FAAO
Chief Optometric Editor

Contact lenses are a large part of any general eye care practice. It is one source of great pride and satisfaction when a patient new to contact lenses first sees clearly without his spectacles, and we all enjoy seeing that epiphany. Yet, like with all experiences, the new soon wears off, and those patients who started out with the best of intentions regarding their contact lens wear and care can slip into some not-so-healthy habits. Overall rates of non-compliance with contact lens wear and care are routinely cited as ranging from 40%-91%.[1,2]

During the course of a busy clinic day, patients presenting for contact lens follow-up are often given the perfunctory

See **Contact lenses** on page 3

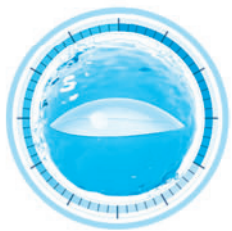
THIS IS WHY YOU CAN give your patients comfort that lasts.

ATTACHING AND
FORMING A HYDROPHILIC ENVIRONMENT
across the surface of the lens[1,2,4]

Proprietary HydraGlyde®
Moisture Matrix

CREATING A UNIQUE BARRIER
that reduces lipid deposition
and removes protein deposits[1-3]

PROVIDING MOISTURE
from morning till night[1,2,4]



OPTI-FREE® PureMoist® MPDS with HydraGlyde® Moisture Matrix

TALK TO YOUR PATIENTS ABOUT THE BENEFITS OF **OPTI-FREE®** BRAND PRODUCTS.
LEARN MORE AT **MYALCON.COM**

REFERENCES:
1. Data on file, Alcon Research Ltd. **2.** Lally J, Ketelson H, Borazjani R, et al. A new lens care solution provides moisture and comfort with today's CLs. *Optician* 4/1/2011, Vol 241 Issue 6296, 42 -46. **3.** Campbell R, Kame G, Leach N, et al. Clinical benefits of a new multi-purpose disinfecting solution in silicone hydrogel and soft contact lens users. *Eye & Contact Lens* 2012:38(2);93-101. **4.** Davis J, Ketelson HA, Shows A, Meadows DL. A lens care solution designed for wetting silicone hydrogel materials. Poster presented at: ARVO; May 2010; Fort Lauderdale, FL.

Alcon®
a Novartis company

Contact lenses

Continued from page 1

vision check and slit lamp evaluation and sent on their merry way. This means some of those non-compliers may be slipping through the cracks and will continue with their bad habits—until the day they show up in the clinic with a red eye or corneal ulcer.

"An ounce of prevention is worth a pound of cure," so the old saying goes, and the best way to prevent a contact lens adverse event is by strict adherence to established wear and care regimens. The best way to have patients comply is through continual reinforcement of good habits, and the best time to emphasize these habits is at the regular contact lens follow-up visits.

The contact lens technician can play a pivotal role in this regard, as more often than not, the tech spends far more time with the patient than the doctor—time that can be pivotal in evaluating your contact lens wearers and heading off any potential problems.

Opening questions

Before the doctor ever sees the patient, some perfunctory questions will help assess the patient's attitude about her contact lens experience.: Some considerations:

- **Does the patient smoke? If she does, advise her to stop. Studies have shown that contact lens wearers who smoke have more problems than those who don't.[3]**
- **Look at the patient's fingernails; short and smooth fingernails help avoid damaging contact lenses or scratching the eye on lens application and removal.**
- **Does the patient have any spectacles? This can become important if the patient develops some ocular irritation or redness with contact lens wear but continues to wear the contact lenses and worsen the condition all because she had no other method of vision correction. Spectacles allow the eyes to have a break from contact lens wear.**

Contact lens patients should remember the "3 goods." When wearing contact lenses:

1. The contact lenses should feel good
2. The patient ought to see good
3. The eyes ought to look good (i.e. no redness)

Lens types and wear schedules

The next question is what type of contact lens is the patient wearing? Even though you may have that information in front of you in the chart, it is important for the patient to know what type of contact lens she has on her eye. I am always amazed at the number of patients who have no clue about what contact lens they are wearing, and I am not alone; a study conducted at the Centre for Contact Lens Research (CCLR) found that only half of the study participants were able to recall from memory the brand names of their habitual contact lenses.[4]

Also inquire about the patient's wearing schedule. Is he wearing his lenses daily wear only? If so, how many hours per day are the lenses on the eye? Is he wearing the lenses for extended wear? If so, how many days continuously is he wearing the lenses? It is also confounding to find that patients often wear a lens designed for strict daily wear for extended overnight periods. A recent study reported that 6% of contact lens patients wear their lenses overnight, despite being advised to wear them for daily wear only.[5] Many times the patient will be hesitant to admit to overnight wear, yet if the question is asked in a non-confrontational way, the patient will often confess to extending his contact lens wearing schedule. I often remind patients who are sleeping in their lenses that this practice is associated with a 10-fold increased risk of microbial keratitis over contact lenses worn as strictly daily wear.[6]

Lens replacement

Likewise, patients should be asked about their replacement regimen. Many patients will wear their contact lenses beyond the recommended replacement schedule. It has been well established that lens replacement is the most commonly reported aspect of contact lens non-compliance.[7] There are as many excuses for the practice as there are contact lenses on the market. Some feign forgetfulness, some ignorance, and some will tell you they see no reason "to throw away a perfectly good contact lens." I often liken this to the "last razor" analogy. I am pretty good about replacing my disposable razors regularly, but that last one

See **Contact lenses** on page 4

"An ounce of prevention is worth a pound of cure," so the old saying goes, and the best way to prevent a contact lens adverse event is by strict adherence to established wear and care regimens.

11%–49%

of patients always fail to wash their hands before handling their lenses[11]

Contact lenses

Continued from page 3

in the package seems to last about twice as long as the others.

Replacing contact lenses at recommended intervals allows for better comfort. A study conducted by the Centre for Contact Lens Research shows that silicone hydrogel lens patients who are compliant with manufacturer-recommended replacement schedule have better comfort and vision at the end of the day than noncompliant patients.[8] Using lenses beyond their recommended replacement schedules has been associated with a 4-fold increased risk in infections compared with lenses replaced at appropriate intervals (see Figures 1 and 2).[9]

It doesn't hurt to remind your patients that contact lenses are medical devices and are regulated by the U.S. Food and Drug Administration—they aren't buying shoes here. Smartphone-based applications and electronic reminder services are a great way to help tech-savvy patients remember when to replace their lenses. Acuminder from Acuvue lets patients sign up for free text messages or e-mail reminders to change their lenses or schedule an appointment.

In addition to wearing times and replacement schedules, inquire about other high-risk habits. Does the patient shower in her lenses? Wear them swimming or in a hot tub? I don't ever recommend patients swim in their contact lenses or wear them when showering or in a hot tub. Many patients are surprised at that recommendation. Knowing that many will not comply with that recommendation, I suggest they use protective goggles and, immediately after swimming, remove and clean their contact lenses before wearing them again.

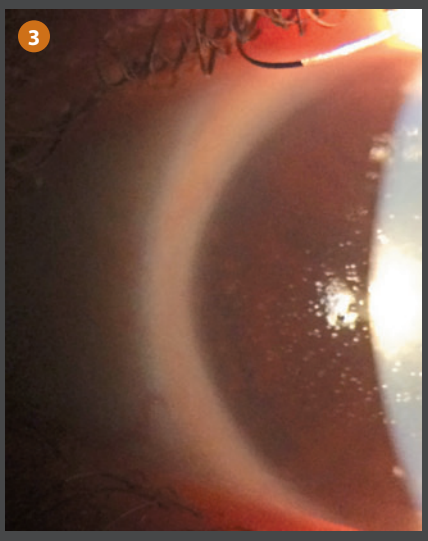


Figure 3. Contact lens from a patient presenting with an infectious corneal ulcer.

Figure 4. Contact lens-related Staph corneal ulcer.

Lens care

Regardless of the type of lens worn and the wearing schedule, proper lens care is essential to maintaining good ocular health. The patient should be asked about her lens care regimen. I find this to be a huge area of non-compliance. While many patients can't tell you what brand of lens they are wearing, fewer still can tell you the brand of contact lens cleaning and storage solution they use.

A visual aid may be helpful. Our office keeps a display of various contact lens solutions—if the patient has no idea about her care system, she will be asked if one in our display is the brand she is using. In many cases, it is not the brand recommended at the time the lenses are dispensed. Patients may start out with good intentions and follow the doctor's recommendations at the onset but quickly switch to an off-brand or generic due to cost considerations. Again, it is helpful for ancillary staff to gently remind the patient that the doctor has recommended a particular brand of solution based on the patient's needs and suggest the patient adhere to the doctor's recommendations.

The doctor's recommendation is important. Studies have shown that patients are more likely to comply if the doctor has made a strong recommendation—not only about solutions but wearing times and replacement schedules.[10] Does the patient wash his hands before handling contact lenses? It sounds like a

See **Contact lenses** on page 6

Today, she presents with dry eye symptoms.

What will she look like by the time she is diagnosed?

For millions of dry eye patients, their symptoms could be an early sign of a progressive autoimmune disease.[1,2]

As many as **1 in 10** patients with dry eye also have Sjögren's Syndrome, a chronic condition of deteriorating exocrine glands that can have significant systemic ramifications.[2-4]

Today, it takes an average of **4.7 years** to receive an accurate diagnosis.[2] Together with the Sjögren's Syndrome Foundation, Nicox is out to change that.

Join us in the fight at **morethandryeye.com**, or call **1.855.MY.NICOX** (1.855.696.4269) to learn more.

nicox
Ophthalmic Diagnostics

Sjögren's Syndrome Foundation

www.nicox.com

References: 1. Kassan SS, Moutsopoulos HM. Clinical manifestations and early diagnosis of Sjögren syndrome. *Arch Intern Med.* 2004;164(12):1275-1284. **2.** Sjögren's Syndrome Foundation. Sjögren's Syndrome Foundation. 2001. Available at http://www.sjogrens.org. Accessed September 5, 2013. **3.** Liew M, Zhang M, Kim E, et al. Prevalence and predictors of Sjögren's syndrome in a prospective cohort of patients with aqueous-deficient dry eye. *Br J Ophthalmol.* 2012;96:1498-1503. **4.** Martin-Martin LS, Massafra U, Migliore A. Sjögren's syndrome: an under-diagnosed disorder. *CLI.* May 2004.

40%-75%

of contact lens wearers fail to rub and rinse with their multi-purpose solutions[12]

Contact lenses

Continued from page 4

no-brainer, but, again, take nothing for granted. Between 11%-49% of patients always fail to wash their hands before handling their lenses;[11] and there is a 1.5-times increased risk for developing microbial keratitis and 2-times greater risk for developing sterile keratitis in patients who fail to wash their hands.[3,6] Recommend the patient use a non-cosmetic soap because soaps with oils or lotions in them can transfer to the contact lens and cause irritation on lens application along with blurred vision.

Is the patient using the solution properly? Does the patient rub and rinse his contact lenses daily with the recommended solution (not water or—God forbid—saliva)? Tap water should never come into contact with soft contact lenses, and saliva contains numerous microbes that can lead to an ocular infection. If I had a nickel for every time I've heard a patient say, "But the bottle says, 'no rub,'" I'd be a rich man. My standard answer: "no rub" doesn't mean no rub. Fortunately, most multi-purpose solutions no longer advertise "no rub."

Have the patient demonstrate how he cares for his lenses. Ask the patient to clean each lens by rubbing it gently with his index finger in the palm of his other hand, then rinsing the contact lens before placing it in the storage case. This "rub and rinse" cleaning method is sufficient with most multi-purpose solutions in use, yet not all patients perform the practice. Some 40%-75% of contact lens wearers fail to rub and rinse with their multi-purpose solutions.[12] Do not allow the tip of the solution bottle to come into contact with any surface, and instruct the patient to keep the solution bottle tightly closed when not in use. Likewise, patients need to understand that sterile saline is not a disinfectant, nor are contact lens rewetting drops.

Speaking of solution, is the patient dumping the solution out daily and using fresh solution or simply "topping off' the solution in the case? A reported 22% of wearers top off their lens case occasionally, frequently, or almost every night.[4] In an attempt to save money, this practice is one shown to contribute to ocular infections.[13] Old solution should never be re-used.

Also, remind patients that transferring solution from one container to a smaller-travel size container should be discouraged. This is another compliance concern that is often neglected in lens care while traveling, and it has been identified as a risk factor for infection among contact lens wearers. Restrictions on liquids in carry-on luggage when flying mean that re-usable lens wearers may be tempted to transfer solutions into smaller containers. Such a transfer can affect the sterility of the contact lens care solution. Use the smaller size bottles of solution when travelling. If hygiene is difficult to ensure, consider refitting the patient into a daily disposable lens.

Be sure patients inspect their lenses before application. Patients should look for nicks along the lens edge, torn lenses, or visible breaks. Damaged lenses can damage the eye, so advise patients to discard the lens and use a fresh one.

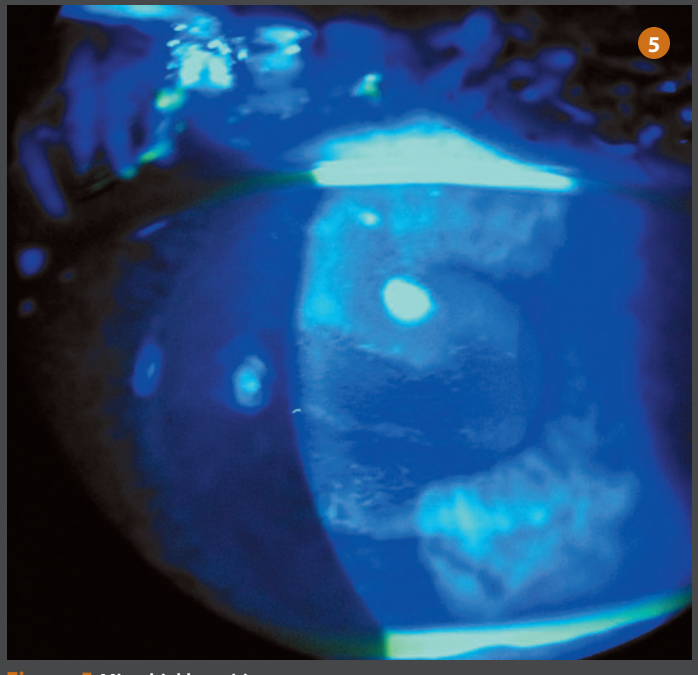


Figure 5 Microbial keratitis.

Lens case

Of all the components of contact lenses, lens cases represent the most common source of contamination and have been shown to include a host of pathogenic microorganisms, including bacteria, amoeba, and fungi.[14]

So, we need to ask our patients about their lens storage case. Do they ever clean it? Some 61%-79% of contact lens wearers fail to clean their case daily (see Figure 3).[15] The storage case should be rinsed out daily with storage solution—never water—then wiped with a clean tissue and allowed to air dry. Because *Acanthamoeba* cysts may be present in tap water and can survive for years after drying,[16] I recommend using only contact lens disinfecting or multi-purpose solution for this step. Recent studies suggest that wiping your case with a clean tissue and/or placing it upside-down on another clean tissue may be additional good steps in keeping bacteria biofilms off the case.[15,17]

Does the patient regularly replace her storage case? Storage cases should be replaced every 1-3 months or if the case is damaged or cracked. One surefire way to see how well the patient manages her contact lenses is to ask the patient bring in her contact lenses, solutions, and storage case when she comes in to the office for her appointment. Much like your medical doctor wants you to bring in your medications at your physical exam, asking the patient bring in her contact lens paraphernalia can show how diligent she is in caring for her lenses.

Wear and care handouts

There is no statistically significant difference between patients receiving both verbal and written instructions and those receiving only oral instructions.[18] But it is best to give the patient a double dose of positive reinforcement, not only with the spoken word but with a nice handout outlining the patient's lens type, the recommend lens wearing schedule, and the recommended solution type. Keep a copy of these recommendations in the patient's chart—that way patients can't say they haven't been warned. Failure to follow recommendations and poor hygiene can increase the risk of ocular infections such as microbial keratitis. Examples of handouts are available online from the American Optometric Association or the Association of Contact Lens Educators.

If a patient is noncompliant, often this reinforcement of his wear and care will return him to healthy habits. For those who it doesn't, perhaps it is time to change lens type to a daily disposable. In terms of reducing the risk of infection, single-use daily disposable lenses are the safest type of soft contact lens.

What to do when the eye is red

My staff and I tell patients to remember the "3 goods" when wearing their contacts. With the lenses on their eyes:

1. **The contact ought to feel good**
2. **The patient ought to see good**
3. **The eyes ought to look good, i.e., there should be no redness.**

The next point for the patient to remember is if one of these "3 goods" isn't good, she should immediately remove the contact lens and call her eyecare practitioner. This may seem like a no-brainer, but there is an astounding number of patients who present with an adverse event that started out as a minor redness or irritation, but progressed to something far more serious because the patient continued to wear the contact lens (see Figure 4), often because he had no spectacle back up. The contact lens acute red eye (CLARE), which can result from lens wear, has a variety of causes, including an improper fit, lens deposits, damaged lenses, corneal hypoxia, an allergic reaction to lens care solution ingredients, ocular allergy, dry eye, and, in the worst case scenario, infectious keratitis. Eye infections, while infrequent, can be devastating, preventing patients from wearing their contact lenses for extended periods and can result in permanent corneal scarring and vision loss (see Figure 5).

Safe and successful lens wear

Contact lenses are among the safest forms of vision correction when patients follow the proper wear and care instructions. Fortunately, even with high rates of contact lens noncompliance, the incidence of severe complications associated with contact lens wear is relatively low. Why do patients not comply with your instructions? They either:

- **Haven't understood what they've been told**
- **Choose to ignore what they've been told, thinking nothing bad is going to happen to them**
- **Forgot what they've been told**

Compliance, however, is the key to long-term successful lens

See **Contact lenses** on page 8

61%-79%

of contact lens wearers fail to clean their case daily

23%

of patients were unable to later recollect seeing any information regarding the risks and complications associated with lens wear[19]

Dr. Bowling is chief optometric editor of Optometry Times.

Contact lenses

Continued from page 7

wear. Our patients' single best way to avoid eye infections and protect their eyes is to follow recommended lens wear and care guidelines. In particular, the guidelines should include performing a "rub and rinse" step in the lens cleaning process, reducing contact with water while wearing contact lenses, and replacing the lens case frequently.

Recommendations have to be ongoing and continual at each and every visit because patients forget. One study reported that while 88% of patients were given lens care information, 23% were unable to later recollect seeing any information regarding the risks and complications associated with lens wear.[19] To maximize compliance, both verbal and written information should be given and key aspects reinforced during follow-up visits to prevent any misunderstanding.[20]

The patient who choses to ignore a recommendation will likely show up with what I affectionately call the "positive washcloth test," a compress over her eye to lessen the pain and photophobia from her contact lens-related infectious corneal ulcer. I am not above telling these patients that this severe complication from their contact lens abuse is going to keep them out of contact lenses for a prolonged period of time; cost them a tremendous amount of money in office visits, medications, and lost wages; and it all may have been prevented if they had only adhered to the recommended wear and care schedule.

I have noticed this discussion regarding the costs of abuse seems to hit home, or perhaps, it's just that the patient doesn't want to go through that pain again. While the focus of the contact lens follow-up visit is to ensure good vision and ocular health with contact lens wear, our job as eyecare professionals is to constantly reinforce good lens wearing habits and lens care so our patients can enjoy a lifetime of safe, successful contact lens wear.◗

References

1. de Oliveira PR, Temporini-Nastari ER, Ruiz Alves M, et al. Self-evaluation of contact lens wearing and care by college students and health care workers. *Eye Contact Lens*. 2003 Jul;29(3):164–7.

2. Donshik PC, Ehlers WH, Anderson LD, et al. Strategies to better engage, educate, and empower patient compliance and safe lens wear: compliance: what we know, what we do not know, and what we need to know. *Eye Contact Lens*. 2007 Nov;33(6 Pt 2):430–3.

3. Radford CF, Minassian D, Dart JK, et al. Risk factors for nonulcerative contact lens complications in an ophthalmic accident and emergency department: a case-control study. *Ophthalmology*. 2009 Mar;116(3):385-92.

4. Dumbleton KA, Woods CA, Jones LW, et al. The relationship between compliance with lens replacement and contact lens-related problems in silicone hydrogel wearers. *Cont Lens Anterior Eye*. 2011 Oct;34(5):216-22.

5. Jansen ME, Chalmers R, Mitchell GL, et al. Characterization of patients who report compliant and non-compliant overnight wear of soft contact lenses. *Contact Lens Anterior Eye*. 2011 Oct;34(5):229-35.

6. Dart JK, Radford CF, Minassian D, et al. Risk factors for microbial keratitis with contemporary contact lenses: a case-control study. *Ophthalmology*. 2008 Oct;115(10):1647-54.

7. Dumbleton K, Woods C, Jones L, et al. Patient and practitioner compliance with silicone hydrogel and daily disposable lens replacement in the United States. *Eye Contact Lens*. 2009 Jul;35(4):164-71.

8. Dumbleton K, Woods C, et al. Role of compliance with the replacement frequency of silicone hydrogel lenses on subjective comfort and vision. *Optom Vis Sci*. 2009;86:90626.

9. Saw SM, Ooi PL, Tan DT, et al. Risk factors for contact lens-related fusarium keratitis: a case-control study in Singapore. *Arch Ophthalmol*. 2007 May;125(5):611-7.

10. Homedes N. Do we know how to influence patients' behaviour? Tips to improve patients' adherence. *Fam Pract* .1991 Dec;8(4):412-23.

11. Sokol JL, Mier MG, Bloom S, et al. A study of patient compliance in a contact lens-wearing population. *CLAO J*. 1990 Jul-Sep;16(3):209-13.

12. Hickson-Curran S, Chalmers RL, Riley C. Patient attitudes and behavior regarding hygiene and replacement of soft contact lenses and storage cases. *Cont Lens Anterior Eye*. 2011 Oct;34(5):207-15.

13. Stapleton F, Dart JK, Minassian D. Risk factors with contact lens related suppurative keratitis. *CLAO J*. 1993 Oct;19(4):204-10.

14. Hall BJ, Jones L. Contact lens cases: The missing link in contact lens safety? *Eye Contact Lens*. 2010 Mar;36(2):101-5.

15. Wu Y, Carnt N, Stapleton F. Contact lens user profile, attitudes and level of compliance to lens care. *Cont Lens Anterior Eye*. 2010 Aug;33(4):183-8.

16. Sriram R, Shoff M, Booton G, et al. Survival of Acanthamoeba cysts after desiccation for more than 20 years. *J Clin Microbiol*. 2008 Dec;46(12):4045-8.

17. Wu YT, Zhu H, Willcox M, et al. The effectiveness of various cleaning regimens and current guidelines in contact lens case biofilm removal. *Invest Ophthalmol Vis Sci*. 2011 Jul 15;52(8):5287-92.

18. Cardona G, Llovet I. Compliance amongst contact lens wearers: comprehension skills and reinforcement with written instructions. *Cont Lens Anterior Eye*. 2004 Jun;27(2):75-81.

19. Morgan PB. The Science of Compliance: a guide for the eye care professional. 2007.

20. Efron N. The truth about compliance. *Cont Lens Anterior Eye*. 1997;20(3):79-86.


techKNOWlogy
Helping you do what you do best…even better.
Allergan presents TechAlliance—
a program designed for you, the eye care technician, offering:
■ Educational programs
■ Patient education materials
■ Product information
■ Solutions to let you focus on providing patient care
And much, much more.
Register at AllerganTechAlliance.com today for these resources, plus program updates and premium content.
Allergan is proud to offer
TechALLIANCE™
by Allergan
Visit AllerganTechAlliance.com
ALLERGAN ©2013 Allergan, Inc., Irvine, CA 92612 ™ mark owned by Allergan, Inc.
www.AllerganTechAlliance.com APC68UO13 130170

The power of recommendation

Knowing what's best for your patient and making the call

By Martin Carroll, OD, FAAO

There is significant healing power in the doctor-patient relationship. If we work together in these relationships, significant improvement can occur to our patient's quality of life and health status.

The word "fudiciary" is derived from the Latin word for "trust." This "trust" is the basis for the doctor-patient relationship. The bond between the doctor and patient is vital for a successful diagnostic and therapeutic outcome. The patient can trust that communication about her health and her condition is held in confidence and that the doctor follows accepted codes of professional ethics.

The doctor-patient relationship has evolved over the centuries from a paternalistic interaction into a more modern shared decision-making model. This modern model allows for patients to be autonomous and express their views and choices, including no treatment. We must remember that our patients filter our instructions through their existing belief system before coming to a final action.

In the patient's best interest

Remember that competent patients have a right to refuse care, and we must respect their decision. However, under vision- or life-threatening situations, we must strongly encourage specific actions, especially treatment that carries little risk. We can gently persuade the patient by educating him of the harm in avoiding or denying treatment.

Some experts suggest that patients should be the primary decision makers in their own health care and that doctors should not make treatment recommendations, including allowing patients to make their own choice[1] and that doctor's recommendations can be influenced by industry.[2] However, our recommendations have a strong influence on patient choice[3] and are there to promote patients' best interest.[4] Cognitive patient biases affect the choices they make that are contradictive to their own best interest.[5,6] Our recommendations can potentially help our patients overcome these biases.

When people make decisions for others, they hone in on the most important aspect of the decision and are less swayed by other factors that could bias the decision.[7] This confirms how important our recommendations are.

Dr. Carroll graduated from the Southern California College of Optometry and has been in private practice since 1981. He is a member of the Wyoming Optometric Association, the American Optometric Association and the American Academy of Optometry. He is an adjunct assistant professor for the Illinois College of Optometry and adjunct clinic professor for Western University College of Optometry. Dr. Carroll is a Diplomate of the American Board of Optometry.

In the contact lens arena, we have a vast array of contact lens options and modalities to choose from, and the proper contact lens wear and care regimen ultimately depends on our patients following our instructions. Frank recommendations are often required so that our patients' contact lens wear is safe, comfortable, and successful.

The power of a recommendation is often undervalued or overlooked.

How many times have you heard a patient say he is not complying with the practice's written orders for contact lens wear and care, only to discover that the problem is you? I admittedly have. Knowing that one third to one half of patients fail to follow a doctor's written orders[8,9] makes the process of recommending vital to a patient's health. Years ago, I found that bringing a personal touch to my patient relationships allows me to better connect to the patient and enhance my recommendations and my written orders.

I believe that compliance can be vastly improved by allowing patients to share in the decisionmaking for their condition following my recommendations. For example, I might say, "I know that it may be hard to change your lenses at exactly every 2 weeks as I have prescribed. Let's talk about what happens when you don't change your lenses and come up with a solution together. I would suggest that you change them on the first and fifteenth of the month."

While some may argue that patients can choose wisely,[10] I cannot reiterate enough how important it is to make recommendations that ensure healthy contact lens care and wear and not leave it up to our patients to make their own decisions. Otherwise, why would they need us?

Obviously, there is a reason contact lenses are regulated as medical devices and their distribution restricted to licensed professionals, by the Food and Drug Administration (FDA). We know that civil penalties of up to $16,000 per violation can be assessed for the illegal sale of contact lenses. I am preaching to the choir when I say that contact lenses are a prescription device that if fit, worn, used, and taken care of incorrectly can lead to grave outcomes. The challenge is to convey this to our patients.

Making a successful recommendation

A successful recommendation begins with:

- **Reducing barriers to communication**
- **Establishing a comfortable environment for doctor-patient interaction**
- **Small talk to connect on a personal level**
- **Focus on the patients' needs**

Building trust to increase compliance

Our patients can have safe and successful contact lens wear if we provide full-service care and they adhere to our prescribed orders. A few of those orders being:

- **Lenses**
- **Care system**
- **Hygiene**
- **Wearing schedule**
- **Lubrication**
- **Environment**
- **Replacement schedule**
- **Comprehensive eye examination schedule**
- **Cases**
- **Follow-up**
- **Seek care when certain symptoms occur**

Let me give you a common scenario that many of us face daily: you prescribe contact lenses but fail to prescribe the care system, specific wearing schedule, specific replacement schedule and/or follow-up. Your patient ends up in the emergency department with a central corneal ulcer. That was your fault.[11]

Our patients are best served when we are proactive with recommendations.

A successful recommendation begins with:

- **Reducing barriers to communication**
- **Establishing a comfortable environment for doctor-patient interaction**
- **Small talk to connect on a personal level**
- **Focus on the patients' needs**

To facilitate open communication, some techniques are:

- **Sit down**
- **Lean forward when listening**
- **Listen without interrupting**
- **Make eye contact**
- **Acknowledge feelings**
- **Explain, educate, and reassure**
- **Ask if you covered everything and if patients have any questions**
- **Be sincere**

We have all seen the tragic events that occur when a patient does not follow our

See **Recommendation** on page 14

I am preaching to the choir when I say that contact lenses are a prescription device that if fit, worn, used, and taken care of incorrectly can lead to grave outcomes. The challenge is to convey this to our patients.

Nutrition's role in eye care

Why diet and lifestyle should be part of the exam room conversation

By Steven M. Newman, OD, CNS

Dr. Steve Newman combines his knowledge as an optometric physician, certified personal trainer, and board-certified nutrition specialist to educate his patients and the public on the importance of a healthy lifestyle. With more than 25 years in the health profession, Dr. Newman has advised thousands of patients on health, medicine, nutrition, supplements, and overall well being. E-mail him at drstevennewman@yahoo.com.

What are some common questions our patients expect to hear from us? "How is your vision? Which is better, one or two? How many nights out of the average month do you sleep in your contact lenses?" Sure, these are the easy answers, but when is the last time you surprised your patient with a question about his diet? With all the information available on the benefits of vitamins and supplements, how many of us have changed our case history questions to reflect the times?

We all have patients suffering from cardiovascular diseases like hypertension, diabetes, and heart disease. We all ask our diabetic patients what their last fasting blood sugar measurement was; why not qualify this number with the food intake for the prior 24 hours? Diet and healthy lifestyle choices play significant roles in the treatment of cardiovascular diseases that affect the eye. We inquire about prescription medications, but medicine falls into the category of "what the doctor can do for them." Who's asking the questions about "What are you doing for yourself?" Optometrists and their staffs are in a unique position to ask the proper questions, then form an educated opinion after evaluating critical blood flow to and in the eye.

To be proactive, patients need to be asked a few direct questions, then commit to make small lifestyle changes.

Picture this scenario: a patient goes to his doctor and finds out his cholesterol is high, putting him at risk for heart disease. Instead of recommending eating better and incorporating mild exercise into his life, his doctor has recommended a statin drug. Three months later, the patient's cholesterol numbers are much better, but he doesn't have the energy to get off the couch and walk around the block. This leads to the common case of "healthier blood work/unhealthier patient." We can't place all the blame on the physicians—after all, they've been talking about healthy lifestyle habits for decades, and most patients simply don't want to listen. We've all been out with friends or relatives who would rather eat more now only to take an extra pill later. Breaking down these mental barriers may be futile, but impressing upon our patients the vital role their active participation plays in their own health can often have a more positive, personal result.

Doctor's orders: a healthy diet

The Phototrope study concluded that ubiquinone (CoQ10) combined with omega 3s and acetyl l-carnitine, can slow down or actually reverse early, dry macular degeneration[1] (see Figure 1). The best way to get these is by allowing our bodies to produce the CoQ10 uninhibitedly while consuming the omega 3s and acetyl l-carnitine in a natural manner with proper food. It's been documented how statins, a widely-used cholesterol medication, hinder the liver's ability to produce CoQ10, the fuel source for our cells' mitochondria.[2]

Research confirms the reasons why optometrists and their staff should routinely discuss diet and lifestyle with patients. Areas of studies that have shown beneficial cardiovascular outcomes include:

- **Cinnamon**[3]
- **Vitamins**[4]
- **Exercise**[5]
- **Yoga**[6]
- **Meditation**[7]

Popular television shows, like Dr. Oz, combined with the plethora of information available to anyone with an Internet connection, has increased both knowledge and confusion in our patients' minds. Their general practitioners are spending less and less time with them,

and they may or may not not feel comfortable talking to a technician about their vitamins. And consider that chiropractors have been routinely discussing vitamins with their patients for years, but chiropractors don't see the same demographics of patients that eyecare practitioners do, limiting impact on the general public.

Sooner or later, we all need an optometrist. The impact we and our staffs can have on the future landscape of health care in America can stretch further than previously thought. During a 2004 meeting of the Florida Optometric Association's Regional Board of Directors in Tampa, FL, Leonard Carlson, the former head legal counsel for the Florida Optometric Association, was asked if ODs were putting their licenses at risk for discussing vitamins with their patients. His response may surprise you: "With all the studies concluding the benefits of vitamins and supplements in relationship to eye health, my opinion is that any optometrist *not* discussing vitamins and supplements with their patients is putting their license at greater risk."◗

References

1. Feher J, Kovacs B, Kovacs I, Schveoller M, et al. Improvement of visual functions and fundus alterations in early age-related macular degeneration treated with a combination of acetyl-L-carnitine, n-3 fatty acids, and coenzyme Q10. *Ophthalmologica*. 2005 May-Jun;219(3):154–66.

2. Vaughan RA, Garcia-Smith R, Bisoffi M, Conn CA, et al. Ubiquinol rescues simvastatin-suppression of mitochondrial content, function and metabolism: Implications for statin-induced rhabdomyolysis. *Eur J Pharmacol*. 2013 Jul 5;711(1-3):1-9.

3. Helbowicz J, Dawiche G, Bjorgell O, Almer LO. Effects of cinnamon on postprandial blood glucose, gastric emptying, and satiety in healthy subjects. *Am J Clin Nutr*. 2007 Jun;85(6):1552-6.

4. Seto SW, Lam TY, Or PM, Lee WY, et al. Folic acid consumption reduces resistin level and restores blunted acetylcholine-induced aortic relaxation in obese/diabetic mice. *J Nutr Biochem*. 2010 Sept:21(9):872-80.

5. Panza VS, Wazlawik E, Ricardo Schutz G, Comin L, et al. Consumption of green tea favorably affects oxidative stress markers in weight-trained men. *Nutrition*. 2008 May;24(5):433-42.

6. Howie-Esquivel J, Lee J, Collier G, Mehling W, et al. Yoga in heart failure patients: a pilot study. *J Card Fail*. 2010 Sep;16(9):742-9.

7. Walton KG, Schneider RH, Nidich S. Review of controlled research on the transcendental meditation program and cardiovascular disease. *Cardiol Rev*. 2004 Sep-

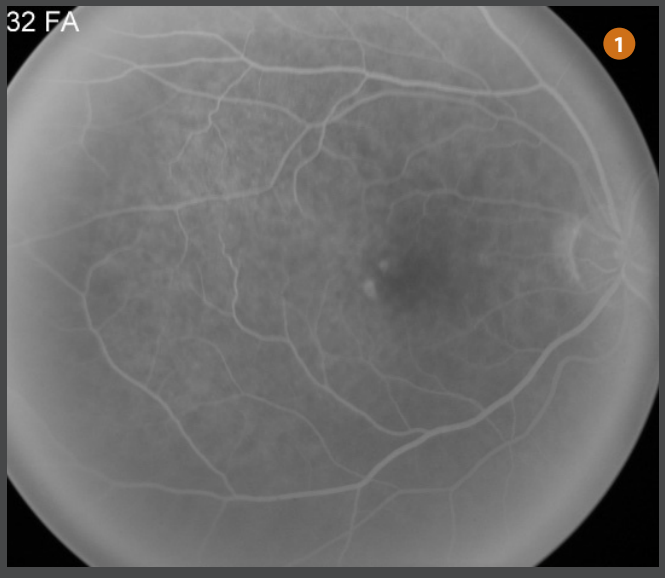


Figure 1. Early dry AMD with fluorescein.

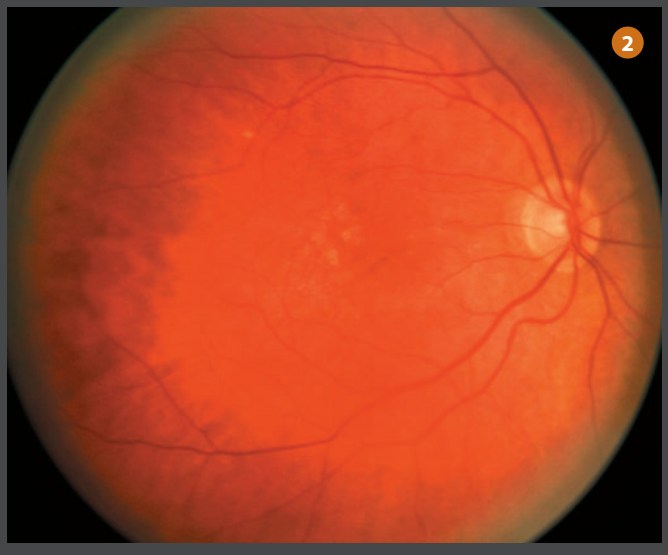


Figure 2. Early dry AMD
(Photos courtesy Harlin Sindu, OD, and Burton Wisotsky, MD)

Sooner or later, we all need an optometrist. The impact we and our staffs can have on the future landscape of health care in America can stretch further than previously thought.

Recommendation

Continued from page 11

recommendations and ruins his vision for a lifetime.

It is of utmost importance that we and our staffs make proper recommendations for our contact lens patients so they comply with our written prescription orders.

You know what is best for your patient, and you should make the call. Don't let them make their own decisions about healthy contact lens wear; recommend.

References

1. Veatch RM. Models for ethical medicine in a revolutionary age: what physician-patient roles foster the most ethical relationship? *Hastings Cent Rep*. 1972 Jun;2(3):5-7.+

2. Quill TE, Brody H. Physician recommendations and patient autonomy: finding a balance between physician power and patient choice. *Ann Intern Med*. 1996 Nov 1;125(9):763-769.

3. +Siminoff LA, Fetting JH. Effects of outcome framing on treatment decisions in the real world: impact of framing on adjuvant breast cancer decisions. *Med Decis Making*. 1989 Oct-Dec;9(4):262-71.+444

4. Ubel PA. "What should I do, doc?": Some psychologic benefits of physician recommendations. *Arch Intern Med*. 2002 May 13;162(9):977-80.+

5. Redelmeier DA, Rozin P, Kahneman D. Understanding patients' decisions: cognitive and emotional perspectives. *JAMA*. 1993 Jul;270(1):72-6.+

6. Ubel PA. Is information always a good thing? Helping patients make "good" decisions. *Med Care*. 2002 Sep;40(9 Suppl):V39-44.+

7. Stone ER, Allgaier L. A social values analysis of self-other differences in decision making involving risk. *Basic Appl Soc Psych*. 2008;30(2):114-29.

8. Osterberg L, Blaschke T. Adherence to medication. *N Engl J Med*. 2005 Aug 4;353(5):487-97. 16

9. Huang ES, Karter AJ, Danielson KK, Wartson EM, et al. The Association Between the Number Prescription Medications and Incident Falls in a Multi-ethnic Population of Adult Type-2 Diabetes Patients: The Diabetes and Aging Study. *J Gen Intern Med*. 2010 Feb;25(2):141-6.

10. Quill TE, Brody H. Finding a balance between recommendations and patient choice. *Ann Intern Med*. 1996 Nov;125(9):763-9.

11. Karpecki PM, Schechtman DL. Microbial threats in CL wear. *Rev Optom*. 2010 Dec;147(12):69-70.

CORRECTION: IMAGES IN THE WINTER 2013 ISSUE WERE MISLABELED. CORRECT IMAGES AND CAPTIONS BELOW.

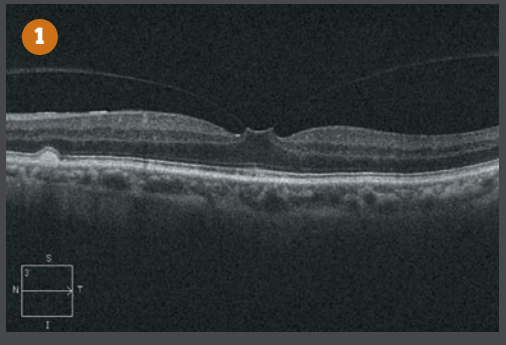


Figure 1
VMA pretreatment 3 months prior to treatment.

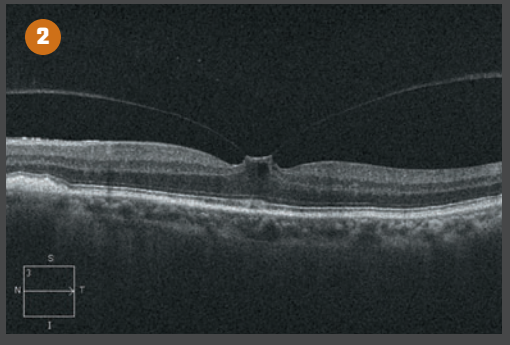


Figure 2
VMA day of treatment with Jetrea.

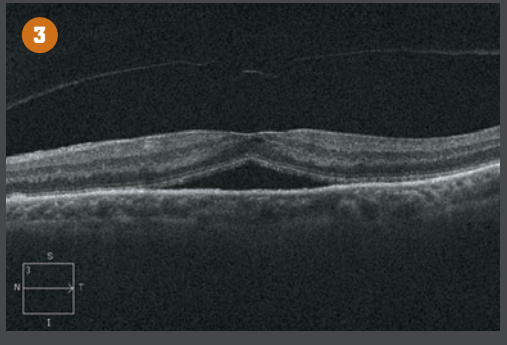


Figure 3
One week after treatment with Jetrea. Note macular edema.

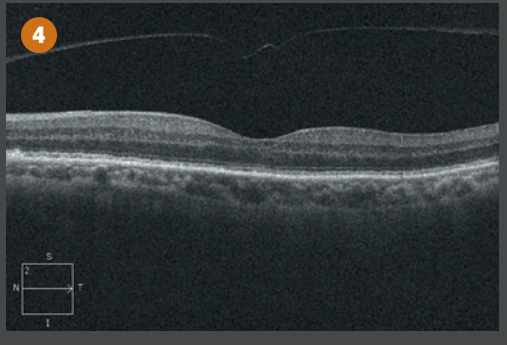


Figure 4
One month after treatment with Jetrea. Note resolution of VMA and macular edema.

Images courtesy of Mark E. Tafoya, OD, MD

Comprehensive Support 4 Patients

For U.S. Audiences Only

EYLEA®
(aflibercept) Injection

4 U℠

EYLEA4U® is a program delivering on Regeneron's commitment to providing comprehensive support for patients and providers

**EYLEA4U ranks high in satisfaction*
9 out of 10 users surveyed are very satisfied with the EYLEA4U program**

*Data on file. EYLEA4U User Experience & Satisfaction Survey conducted in December 2012.

Reimbursement Support
Guidance and assistance with the overall reimbursement process

Patient Support
Helping patients access EYLEA® (aflibercept) Injection whether they are uninsured, lack coverage, or need help with their out-of-pocket costs

Product Support
Assistance with product ordering and returns

Call 1-855-EYLEA4U (1-855-395-3248) Monday-Friday 9am-8pm Eastern Time
Option 4 for Reimbursement and Patient Assistance

More information available at www.EYLEA.com

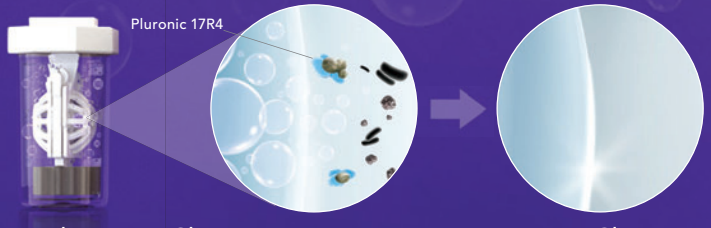
REGENERON

 08/2013 LEA-0151C

THIS IS WHY 4 out of 5 patients agree their lenses feel like new.[1]

The scientifically proven formula of CLEAR CARE® Solution deeply cleans, then neutralizes, to create a gentle saline similar to natural tears. The result is pure comfort and is why CLEAR CARE® has the most loyal patients of any lens care brand.[2]

The Science Behind a Pristine, Clean Lens:



Triple-Action Cleaning

- Patented formula deeply cleans
- Carries away dirt & debris
- Pluronic^ 17R4 lifts away protein

Pristine, Clean Lens

- Less residual H_2O_2[3-5]
- Irritant-free comfort
- No added preservatives

Range of Residual H_2O_2 on Lens:

Recommend CLEAR CARE® Solution and learn more at MYALCON.COM

PERFORMANCE DRIVEN BY SCIENCE™

^Trademarks are the property of their respective owners.

References: 1. A market research study conducted amongst 107 US contact lens wearers representative of CLEAR CARE® purchasers in the United States, 2007. 2. Based on third party industry report 52 weeks ending 12/29/12; Alcon data on file. 3. Alcon data on file, 2009. 4. SOFTWEAR™ Saline package insert. 5. Paugh, Jerry R, et al. Ocular response to hydrogen peroxide. *American Journal of Optometry & Physiological Optics*: 1988; 65:2,91–98.

Alcon®
a Novartis company