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CLINICAL DIAGNOSIS | SURGERY | DRUG THERAPY

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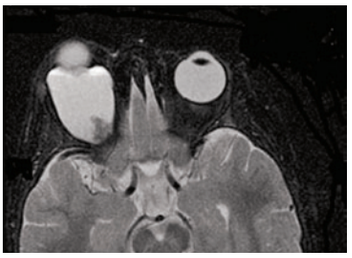
Surgery

TREATMENT TACTICS FOR LYMPHATIC MALFORMATIONS



COLUMBUS, OH :: **A DECADE** of follow-up indicates percutaneous drainage and ablation of lymphatic malformations is a safe and effective treatment. "We're able to achieve permanent remission and decrease the progression of the fibrotic component of these lesions," said Kenneth V. Cahill, MD, FACS.

*(See story on page 13 : **Lesions**)*

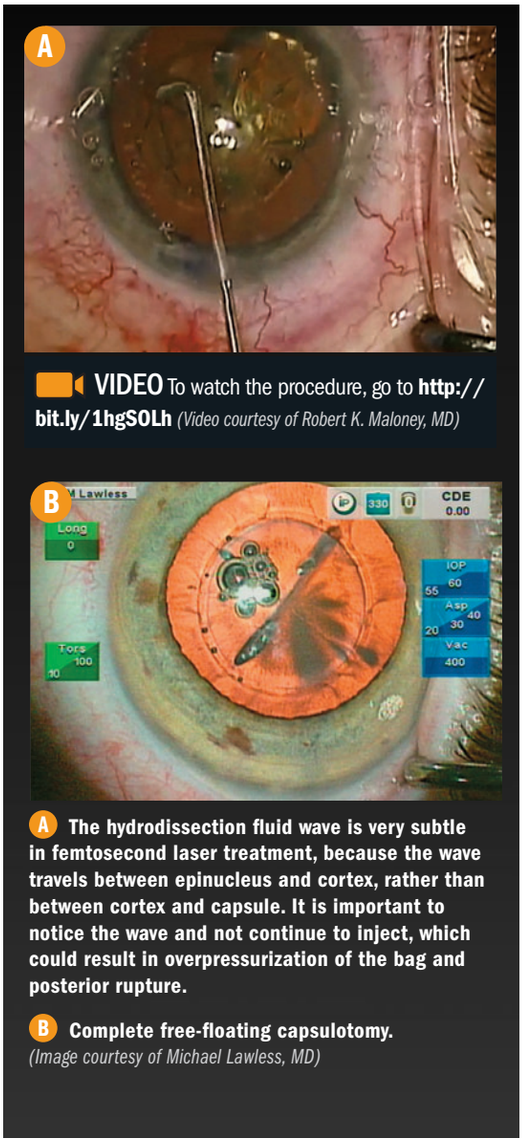
Special Report

ALGORITHM GIVES BOOST TO ALLERGIC CONJUNCTIVITIS

NEW BRUNSWICK, NJ :: **AN ALGORITHM** for the management of allergic conjunctivitis aims to increase consensus among a variety of specialists who may be dealing with ocular allergy. The algorithm also addresses comorbidities such as dry eye and the possible impact on the ocular surface of medications customarily used to treat allergies, said Leonard Bielory, MD.

*(See story on page 21 : **Allergy**)*

Laser refractive lens surgery RIVALS MANUAL TECHNIQUE



A The hydrodissection fluid wave is very subtle in femtosecond laser treatment, because the wave travels between epinucleus and cortex, rather than between cortex and capsule. It is important to notice the wave and not continue to inject, which could result in overpressurization of the bag and posterior rupture.

B Complete free-floating capsulotomy.
(Image courtesy of Michael Lawless, MD)

Femtosecond laser brings both advantages and distinct challenges to lens procedure

By Cheryl Guttman Krader;
Reviewed by Michael Lawless, MD, and Robert K. Maloney, MD

ACCUMULATING DATA PUBLISHED in the peer-reviewed literature demonstrate that laser refractive lens surgery (LRLS) performed with a femtosecond laser offers certain safety advantages compared with manual surgery.

However, surgeons who undertake the laser-assisted procedure must be aware that unique safety issues accompany it, making appropriate patient selection critical.

"If we can remove unpredictable events, perform specific tasks with greater precision, decrease the chance of damage to collateral structures, introduce previously impossible maneuvers, and do all of that reproducibly, then we have a safer operation," said Michael Lawless, MD, medical director, Vision Eye Institute, Chatswood, NSW, Australia, and clinical senior lecturer, Department of Ophthalmology, Sydney University Medical School.

POINT: SAFER THAN MANUAL?

"There is now a body of evidence in the peer-reviewed literature from which we can say that LRLS has been shown to be or is likely to be safer than a manual procedure," Dr. Lawless said.

At the time of his discussion, he identified 74 papers reporting on outcomes of LRLS, of which four were randomized controlled trials, 12 were controlled longitudinal studies, seven were considered to provide grade A or B evidence, and seven would be given a grade C evidence rating.

Summarizing the findings, Dr. Lawless said that use of the laser creates more precise and more pre-

*(Continues on page 18 : **Safety**)*

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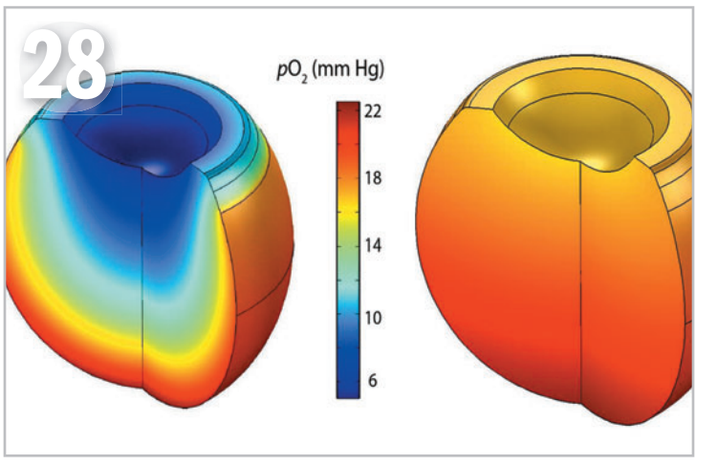

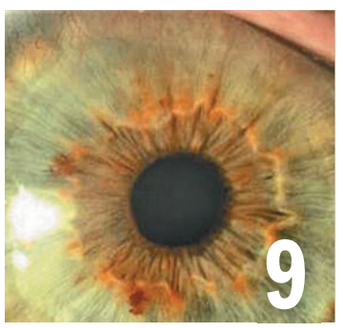

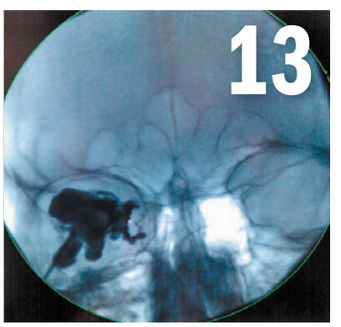

Special Report on page 21

CLINICAL CONCEPTS IN OCULAR ALLERGY

Surgery

In Every Issue

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Drug Therapy

InDispensable

Practice Management

‘Best’ ways to die?

Two ophthalmologists go for a walk and contemplate death

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*.

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“The fear of death follows from the fear of life. A man who lives fully is prepared to die at any time.”
—Mark Twain

A RECENT ARTICLE in *The New York Times*[1] suggests that physicians—because we understand the implications of a serious illness diagnosis and the implications of treatment and associated morbidity—die “better” than do non-physicians. Also, a study of graduates of my medical school showed these doctors were much more likely to have advanced directives (“living wills”) than other American adults.

Perhaps reading that article put me in the frame of mind to contemplate my own mortality while taking a walk for exercise with another ophthalmologist. Although my ophthalmologist friend practices in a city literally on the other side of the world from my own, we shared the same concerns:

Will our children be okay? Will our savings be adequate to provide for the needs of our loved ones? How should we make investments today so that—if something bad happens to us tomorrow—people who count on us and may not have much financial sophistication will understand what to do?

BEING PREPARED

We discussed ways to allocate our investments and prepare for the small chance that—despite our both being healthy today and at the youngest end of the baby boomer generation—some sort of catastrophic injury or illness might lurk around the corner.

“This is what fathers like us have to do,” my friend said.

“If something bad happens to me, will you help my family understand what to do?” I asked my friend.

“Certainly,” he replied. “And will you do the same for mine?”

“Of course,” I said.

GOOD AND BAD WAYS

We then contemplated that if doctors really do die better than other people, what would be the better and worse ways. Our list of good and bad ways to “buy the farm” included:

- **Being bored to death listening to billing and coding experts. (Bad way to die.)**
- **Being annoyed to death by the transition to ICD-10. (Even worse.)**
- **Death from laughing. (This has been documented to occur, and strikes me as a relatively good way to go.)**
- **Death from embarrassment. (Although I frequently hear people say they were so embarrassed they nearly died, I am not aware of this having actually occurred.)**
- **Death on the toilet (like Elvis Presley). (We agreed this is not a great way to go, but definitely not the worst.)**
- **Death in a whirlpool bath (like Orville Redenbacher). (Respect for the dead prevents me from making a joke about this, but I assume the whirlpool bath was more comfortable and pleasant than Elvis’ toilet seat.)**

“Death from laughter has been known to occur since the time of ancient Greece,” I told my friend. “People who write about the phenomenon suggest it may result in either a heart attack or asphyxiation.”

“I see now why you studiously avoid any semblance of humor in your editorials,” he replied.

“Everyone says the best way to pass on is probably quietly in one’s sleep. So that is probably going to be my preference,” I told my friend.

“Nonsense,” was his reply. “The best way to die is to follow the example of Nelson Rockefeller.” ■

Reference

1. How doctors die. *The New York Times*, Nov. 20, 2013

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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.

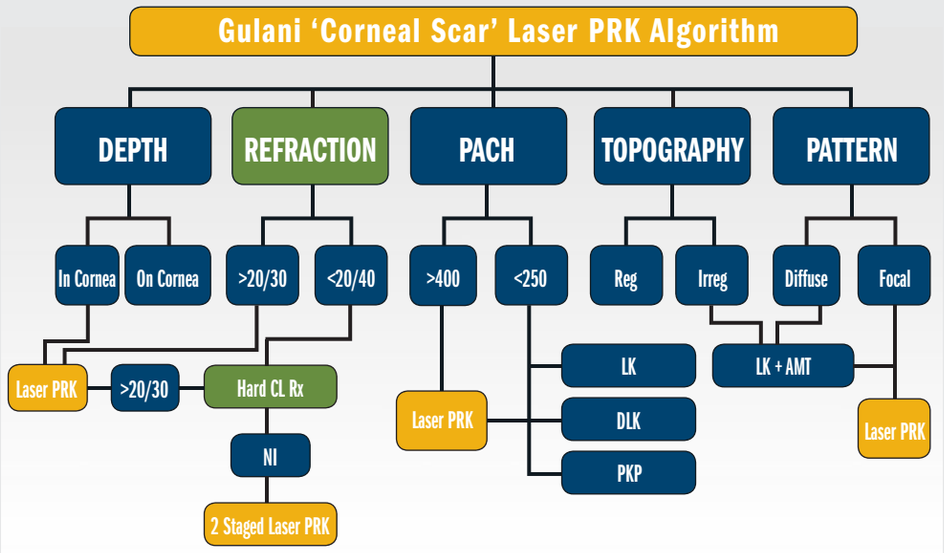
Decoding corneal scars: Straight to 20/20 vision

First of a two-part article focuses on addressing anterior corneal scars with laser PRK

Gloves Off with Gulani **By Arun C. Gulani, MD**

TAKE-HOME

- ***Arun C. Gulani, MD, explains his concept of addressing anterior corneal scars with laser PRK (not PTK) straight to 20/20. In the next article, Dr. Gulani will explain how to build the cornea with various modalities in presenting it for laser PRK.***



The refraction is the mainstay of the corneal scar algorithm, where vision better than 20/30 suggests straight laser PRK and where vision less than 20/40, following a hard contact lens trial, can determine staged laser in two stages or a scar peel, followed by myopic ablation.

My desire in these columns is simple—to change ophthalmologists' mindset! To free eye surgeons from the burden of technology and terminology.

When looking at a corneal scar, the inherent mindset is: "There is the culprit. Let's eradicate it."

Numerous diagnostic technologies are then deployed to "understand the scar and its obviously criminal impact on vision."

Then, many ophthalmologists go through an elegant and complicated thought process to determine whether to choose laser PTK (an optically incorrect surgery), diamond burr application (a barbaric procedure on an elegant visual organ), or a corneal transplant (a relatively interventional procedure that should be the last resort, very much like having to open the entire abdomen to get to the gall bladder) as the correct treatment for this corneal scar.

What I suggest instead is to look at the corneal scar and ask, "How can I use this or modify this to help the patient see better with the least intervention?" and "Is it necessary to remove this and at what cost?"

By cost, I mean, the cost in "vision" currency. Chasing the scar at the cost of vision is not acceptable.

In this article focusing on corneal scars, I will explain my concepts of addressing anterior corneal scars with laser PRK (not PTK) straight to 20/20. In part 2, I shall explain how to build the cornea with various modalities in presenting it for laser PRK.

HOW CORNEAL SCAR AFFECTS VISION

Anterior corneal scars affect vision directly by blocking the optical pathway and indirectly, by altering the shape, and hence the refractive status. Using "Corneoplastique" principles, we can use these very factors and reverse them to our advantage.

In the Gulani 5S algorithm, surgeons can see the impact of the corneal scar on vision and determine the patterned approach of corneal rehabilitation and laser or direct laser, and straight reshaping to vision. The refraction is the mainstay of the corneal scar algorithm, where vision better than 20/30 suggests straight laser PRK and where vision less than 20/40, following a hard contact lens trial, can determine staged laser in two stages or a scar peel, followed by myopic ablation.

For the sake of simplicity, I have divided corneal scars into "on-cornea" scars, which are above the Bowman's membrane and lead to a camouflaged topography and misleading refractive error and "in-cornea" scars, which actually become part of the cornea and are directly responsible for the topography, and have a direct correlate to the refractive error. These can be lasered through.

Instead of laser PTK, which chases the scar and distorts the shape (costing us in vision currency), why not reshape the cornea and take it straight to vision (in many cases, despite a residual scar)?

For example, one of my patients presented with a case of dense corneal scar following herpetic infection 20 years ago. After removal of epithelium and confirming "in-cornea" status (herpetic scars usually become part of the cornea, thus producing a smooth surface once the epithelium is removed), I proceeded

Continues on page 9 : ***Corneal scars***

For the treatment of elevated IOP

UNLOCK TREATMENT POSSIBILITIES

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

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

INDICATIONS AND USAGE

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

Dosage and Administration

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

IMPORTANT SAFETY INFORMATION

Contraindications

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

Warnings and Precautions

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

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

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

Adverse Reactions

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

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

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

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

Learn more at myalcon.com/simbrinza

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

ONE BOTTLE. MANY POSSIBILITIES.

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

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BRIEF SUMMARY OF PRESCRIBING INFORMATION
INDICATIONS AND USAGE

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

DOSAGE AND ADMINISTRATION

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

DOSAGE FORMS AND STRENGTHS

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

CONTRAINDICATIONS

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

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

WARNINGS AND PRECAUTIONS

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

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

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

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

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

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

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

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

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

ADVERSE REACTIONS

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

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

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

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

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

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

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

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

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

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

DRUG INTERACTIONS

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

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

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

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

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

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

USE IN SPECIFIC POPULATIONS

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

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

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

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

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

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

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

OVERDOSAGE

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

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

PATIENT COUNSELING INFORMATION

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

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

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

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

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

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

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

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

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CORNEAL SCARS

(Continued from page 6)

with a refractive laser ablation, and applied mitomycin-C for 30 seconds to the central cornea. Upon application of balanced saline solution, the light reflex had become circular, which translates to vision. This patient ended with uncorrected vision of 20/25+ and was thrilled with her outcome.

ON-CORNEA AND IN-CORNEA SCARS

On-cornea scars can be peeled off right under the laser using the cornea as what I call a "resistance-guided platform" which is comprised of pulling on the scar, making sure to remove it completely, in one piece, using the rest of the cornea as your resistance platform. This is followed by refractive PRK (always with mitomycin-C application) as single stage or myopic PRK to be followed by stage two for refractive PRK to emmetropia.

Deeper on-cornea scars can also be peeled off using patience and a resistance-guided technique as well to peel them gently off of the rest of the cornea. Once again, try to maintain the entire piece as a single removal technique. Once it clears the visual axis, you can proceed with refractive laser PRK ablation, followed again by the application of mitomycin-C. This can result in complete central clarity, to an excellent outcome.

In this case, the patient's on-cornea scar was peeled of gently using the cornea as a resistance-guided platform followed by myopic laser application with mitomycin-C for 20 seconds, resulting in an outcome of 20/20 uncorrected vision.

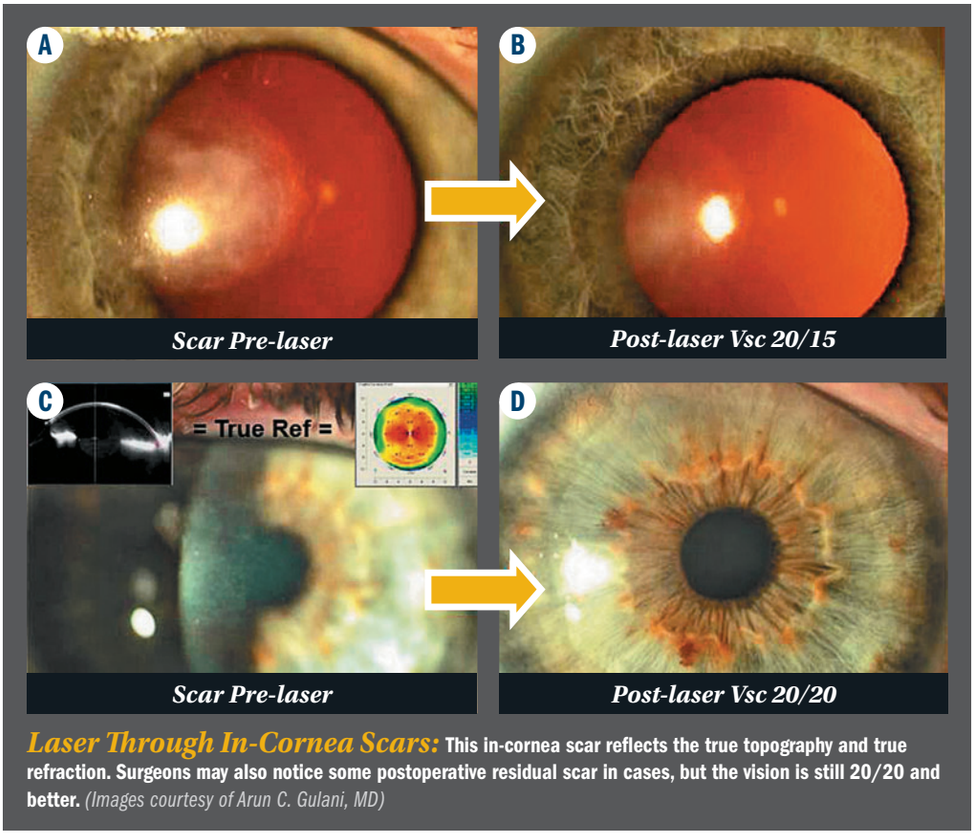
In summary, in-cornea scars can be lasered directly in the PRK mode, shaping the cornea, and indirectly removing the scar, straight to a visual outcome.

In cases of on-cornea scars, the scar can be gently peeled off, maintaining all the principles we discussed about using the corneal platform as a resistance-guided technique in lifting the entire scar gently, in full completion, off the remaining cornea.

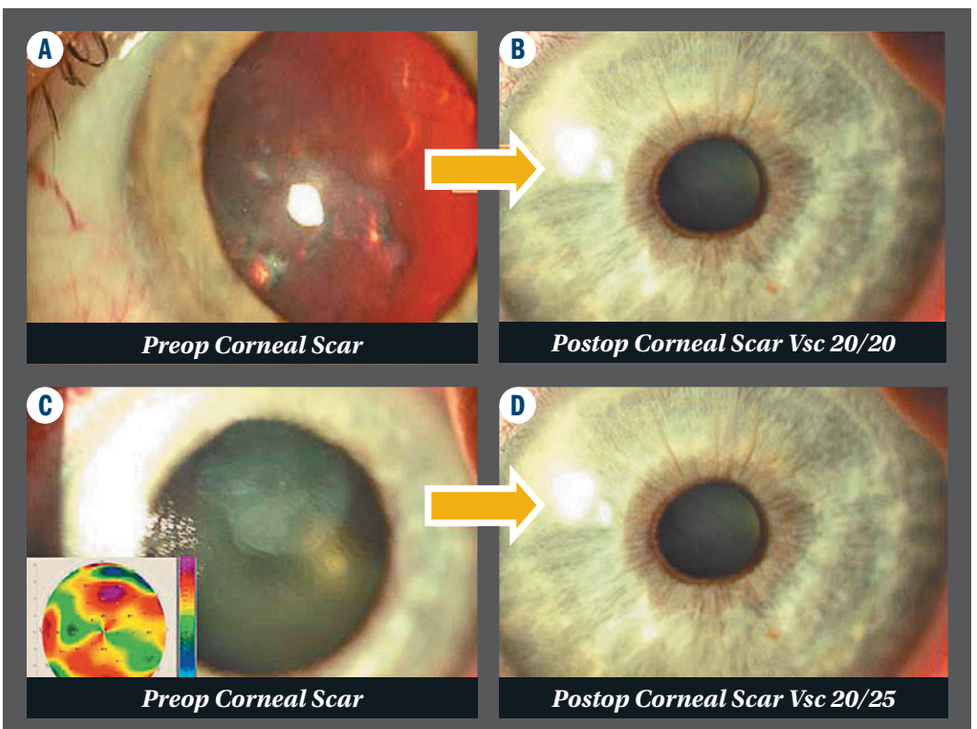
This is followed by laser PRK with mitomycin-C and a bandage contact lens to reach tremendous visual outcomes (single or two-staged).

Intraocular optical manipulation in the form of lens based (pseudophakic and phakic implants) techniques can be combined to aim for myopic PRK before or after as second stage (the endpoint always being emmetropia, with an indirect goal of scar removal).

No matter how bad the scar looks, let us use our algorithm to insist on taking patients straight to vision, with the most elegance possible, maintaining the principles of "Corneoplastique" surgery—topical, brief, aesthetically pleasing, and visually promising.



Laser Through In-Cornea Scars: **This in-cornea scar reflects the true topography and true refraction. Surgeons may also notice some postoperative residual scar in cases, but the vision is still 20/20 and better.** *(Images courtesy of Arun C. Gulani, MD)*



Laser + Scar Peel (On-Cornea): **Notice how the topography is a camouflage due to the on-cornea scar with false refractive error prior to laser refraction.** *(Images courtesy of Arun C. Gulani, MD)*

Continues on page 12 : ***Laser PRK***

Today, she presents
with dry eye symptoms.

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Ophthalmic Diagnostics

Sjögren's Syndrome Foundation

www.nicox.com

What will she look like by the time she is diagnosed?

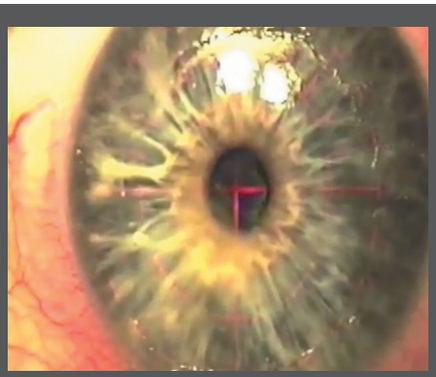
For millions of dry eye patients, their symptoms could be an early sign of a progressive autoimmune disease.[1,2]

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]

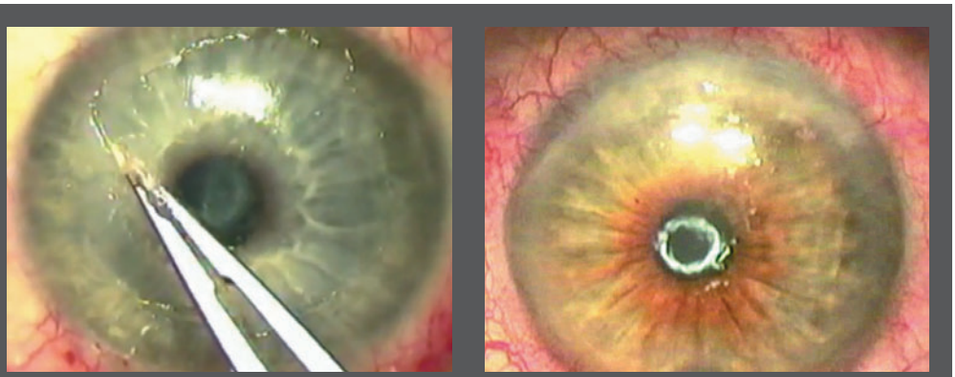
Today, it takes an average of 4.7 years to receive an accurate diagnosis.[2] Together with the Sjögren's Syndrome Foundation, Nicox is out to change that.

Join us in the fight at **morethandryeye.com**, or call **1.855.MY.NICOX** (1.855.696.4269) to learn more.

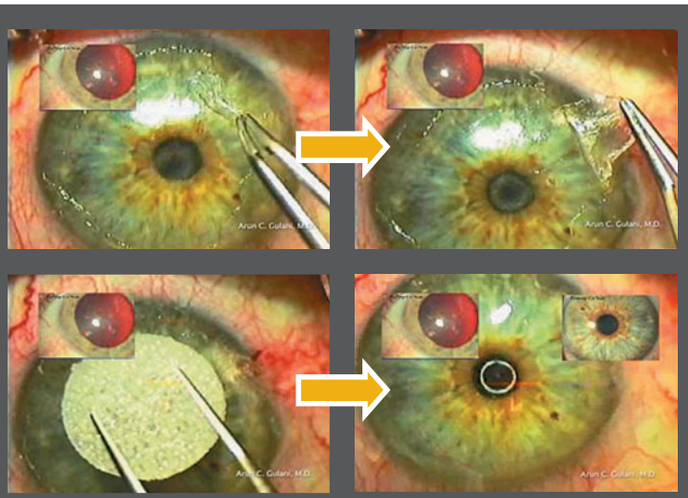
References: 1. Kassan SS, Moutsopoulos HM. Clinical manifestations and early diagnosis of Sjögren syndrome. *Arch Intern Med.* 2004;164:1275-1284. **2.** Sjögren's Syndrome Foundation. Sjögren's Syndrome Foundation. 2001. Available at http://www.sjogrens.org. Accessed September 5, 2013. **3.** Liew M, 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 LS, Massafra U, Migliore A. Sjögren's syndrome: an under-diagnosed disorder. *CLI.* May 2004.



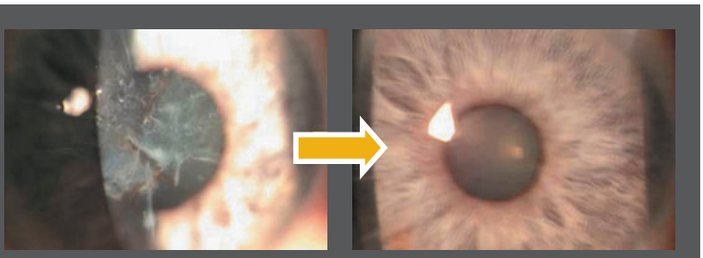
Arun C. Gulani, MD, explains his concept of addressing anterior corneal scars with laser PRK (not PTK) straight to 20/20 vision. Go to **http://bit.ly/1bJtAg0**



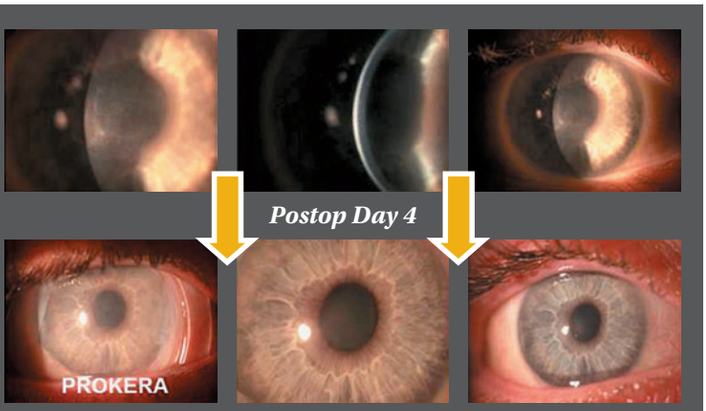
Both of these video clips show two unique cases of corneal scars with what is considered "irreparable" and yet can be corrected to 20/20 in a matter of minutes, according to Arun C. Gulani, MD. Go to **http://bit.ly/1kyJYcm** and **http://bit.ly/1h81PGz**. *(Videos courtesy of Arun C. Gulani, MD)*



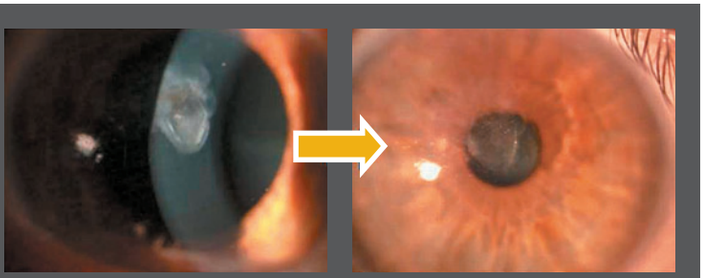
Laser + Scar Peel (On-Cornea): **Scar peel in action.**



Corneal Scar Before/Clear Cornea After Laser:
Left: Dense central scarring in post-RK cornea. Right: Clear postoperative cornea.



Stem Cell Scar: **Laser PRK to 20/20.**



Herpes Scar: **Dense herpetic scar with divot corrected with laser PRK to 20/30.** *(Images courtesy of Arun C. Gulani, MD)*

LASER PRK

(Continued from page 9)

Refractive laser PRK surgery—when practiced as an art—not only can address virgin eyes with all levels of ametropia, but also reverse and correct complex as well as complicated cases with corneal scars back to 20/20. Refractive surgery truly then can come to its own rescue! ■

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ARUN C. GULANI, MD, *is director of the Gulani Vision Institute, Jacksonville, FL. Dr. Gulani has no financial interests to declare.*

Tactics for lymphatic malformations

Percutaneous drainage and ablation minimally invasive, preferable to surgical resection

By Nancy Groves; *Reviewed by Kenneth V. Cahill, MD, FACS*

TAKE-HOME

- ***Percutaneous ablation of lymphatic malformations is a safe, effective alternative to surgical resection, based on extensive follow-up of a large series of cases performed at a leading pediatric hospital in the United States.***

COLUMBUS, OH ::
MORE THAN A DECADE of follow-up indicates that percutaneous drainage and ablation of lymphatic malformations is a safe and effective treatment approach.

"We find that we're able to achieve permanent remission and decrease the progression of the fibrotic component of these lesions," said Kenneth V. Cahill, MD, FACS, in practice in Columbus, OH.

Observation of a series of more than 80 patients followed up to 12 years demonstrates that the best road map for treatment is T2 images on magnetic resonance imaging, judicious use of fluoroscopy with radiation minimization, and ultrasonography for evaluation and treatment, Dr. Cahill said.

This minimally invasive outpatient procedure is preferable to surgical management, he added.

HOW THE PROCEDURE WORKS

The approach that Dr. Cahill, William E. Shiels II, DO, and others at Nationwide Children's Hospital, Columbus, pioneered to manage lymphangioma macrocysts (>1 cm) is to enter the lesion with an angiocatheter through which a flexible pigtail catheter is introduced.

The catheter remains in place to withdraw fluid and instill radiocontrast to confirm the extent of the cyst, make sure there is no communication of cysts within the orbit, and check for leakage around the catheter. Ultrasound can be used instead of fluoroscopy to document the catheter placement.

Once the macrocyst has been drained and its extent and intactness have been evaluated, sodium morrhuate is introduced then withdrawn and rinsed after its dwell time.

The second step is introduction of absolute alcohol, which is also then withdrawn and rinsed. Next, the catheter that had been left in place is attached to a suction bulb.

"We find that draining out any serous fluid that leaks from the de-endothelialized cyst decreases postoperative swelling and seems to improve the success rate of collapsing these cysts," Dr. Cahill said.

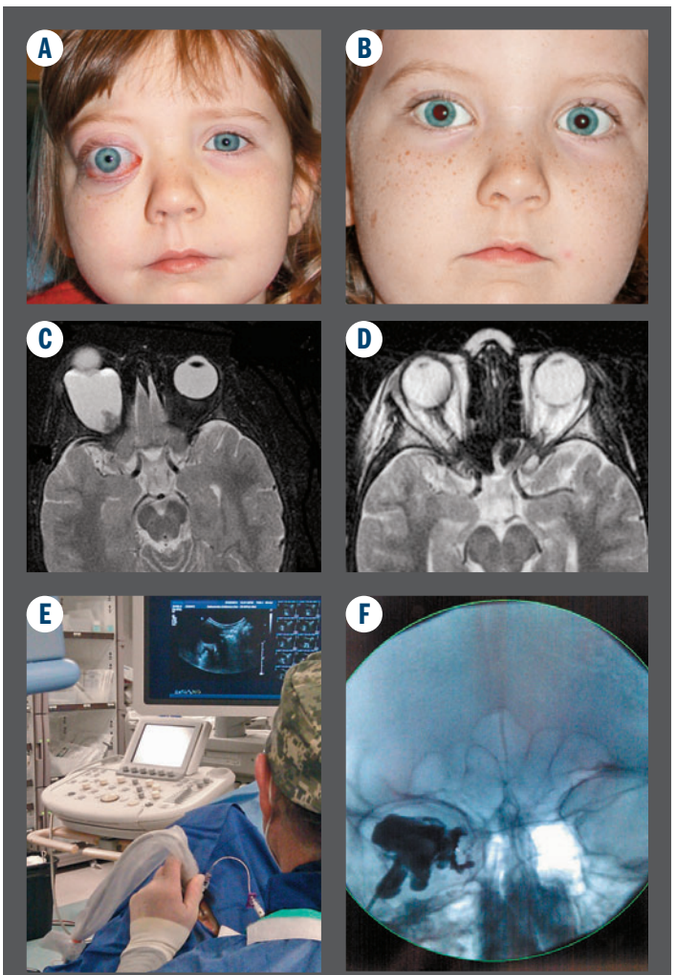
Follow-up includes ophthalmic exams and B-scan ultrasound to monitor recovery. More than one treatment is necessary for most patients.

OTHER TREATMENT PROTOCOLS

Variation in lesions may alter the treatment protocol. Some are labeled venolymphatic, a clinical rather than histopathological description. In these cases, a bloody fluid rather than serous fluid slowly reaccumulates in the cavity, and no vascular communication can be detected radiographically. Patients with a microscopic amount of blood in their cystic fluid tend to require more treatments than those who have "pure" lymphangiomas or a non-bloody fluid.

Pupil dilation is a side effect that may occur with treatment of large retrobulbar cysts, but in all cases it has fully resolved, Dr. Cahill said.

Continues on page 20 : ***Lesions***



A Pre-treatment clinical photo showing severe right proptosis and hypoglobus with conjunctival injection.

B Post-treatment photo after two sclerotherapy treatments with sodium tetradecyl sulfate and ethanol showing significant reduction in proptosis and hypoglobus.

C Pre-treatment T2 magnetic resonance imaging (MRI) in the axial plane showing a large macrocyst occupying the majority of the right orbit causing severe proptosis.

D Post-treatment T2 MRI in the axial plane after sclerotherapy showing resolution of the macrocyst.

E Intraoperative photo using ultrasound-guided aspiration and injection of the orbital lymphatic malformation.

F Intraoperative fluoroscopic image during treatment of a large macrocyst with injection of contrast through a pigtail catheter to define the extent of the lymphatic malformation and ensure no extravasation into normal orbital tissue and no active vascular communication. *(Images courtesy of Kenneth V. Cahill, MD, FACS)*

Long-term data for corneal inlay expanding outcomes for presbyopia

Monocular uncorrected near visual acuity improved by an average 3.4 lines at 3 years

By Lynda Charters; *Reviewed by John A. Vukich, MD*

TAKE-HOME

- ***Long-term clinical trial data for a small-aperture corneal inlay (Kamra, AcuFocus) for presbyopia turned in superb results.***

MADISON, WI ::

A SMALL-APERTURE corneal inlay (Kamra, AcuFocus) for presbyopia yielded superb results in an analysis of long-term data.

Monocular uncorrected near visual acuity (UNVA) improved by an average 3.4 lines, intermediate visual acuity improved slightly, and distance visual acuity was unchanged—all of which is very encouraging for patients with presbyopia, said John A. Vukich, MD, surgical director, Davis Duehr Dean Center for Refractive Surgery, Madison, WI.

Dr. Vukich

Dr. Vukich highlighted 3-year data from the prospective, non-randomized U.S. clinical trial with the inlay that included 507 patients who were naturally occurring presbyopic emmetropes (age range, 45 to 60 years).

> ‘It is important that there was no loss of intermediate vision during the follow-up period.’
>
> *— John A. Vukich, MD*

Refractive errors in this patient population were low levels of myopia and hyperopia (–0.75 and 0.5 D) with no more than 0.5 D of astigmatism.

All patients had UNVA worse than 20/40 and better than 20/100. Best-corrected distance visual acuity was 20/20 or better bilaterally.

Implantation of the corneal inlay—a monocular procedure that is performed in the non-dominant eye—is performed during an intralamellar dissection that resembles a pocket into which the device is positioned over the pupil.

Eyes with the inlay had an average gain in monocular UNVA of 3.4 lines preoperatively to 36 months after implantation, Dr. Vukich noted.

36-MONTH FOLLOW-UP PERIOD

“Importantly, this gain in vision was a sustained improvement that was maintained over the 36-month follow-up period,” Dr. Vukich said.

All study eyes completed the 36-month follow-up examination.

An important consideration in patients with presbyopia is the status of intermediate vision. In the study eyes, monocular uncorrected intermediate visual acuity (UIVA) improved, but as expected not to the same extent as near vision. The mean UIVA was 20/25.

“It is important that there was no loss of intermediate vision during the follow-up period,” he said.

In addition, monocular uncorrected distance visual acuity was maintained over the course of the study in the eyes with the inlay.

“The average distance visual acuity remained better than 20/20,” Dr. Vukich said.

Excellent uncorrected distance binocular visual acuity also was maintained at an average of 20/16 over the duration of the study.

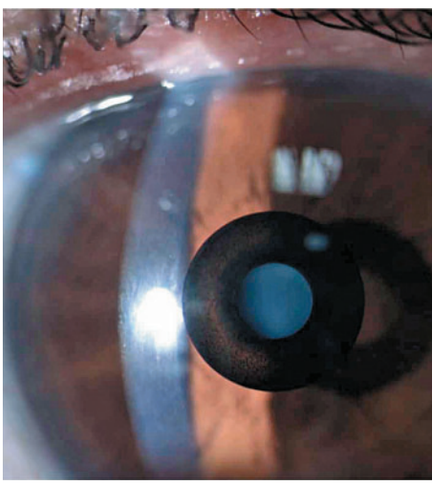
Long-term results showed that UNVA improved from a mean of J8 to J2 in the eyes with the inlay from preoperatively to 1 month postoperatively and was maintained to 5 years after surgery. The vision in the eye with the inlay and in both eyes was unaffected by the progression of presbyopia, Dr. Vukich said.

He noted that—while 5 years after surgery, normal progression of presbyopia would be expected as a result of lessening of the accommodative ability—the patients continue to do well despite natural presbyopic progression.

“This indicates that the vision is unaffected by the continuing presbyopic changes,” Dr. Vukich said. “This is certainly encouraging.” ■

OphthalmologyTimes.com *Online Exclusive*

PHYSICIAN-PATIENT RECEIVES CORNEAL INLAY IN HIS OWN EYE



TURNING THE TABLES to become a corneal inlay patient himself, Jeffrey Machat, MD, FRSCS, underwent implantation of the presbyopic device (Kamra, AcuFocus) in his own eye. To learn more about Dr. Machat’s surgery and the visual outcomes, go to http://bit.ly/1dOPM8Y.

JOHN A. VUKICH, MD

E: *javukich@gmail.com*

Dr. Vukich is a consultant to and chairman of the medical advisory board of AcuFocus. The device is investigational and not available commercially in the United States.

Monotherapy Maintained.

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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.

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3 surgical tips for ECP combined with phaco

Pearls focus on maximizing endoscopic cyclophotocoagulation with cataract surgery

By Cheryl Guttman Krader; *Reviewed by Robert J. Noecker, MD, MBA*

TAKE-HOME

- ***Thorough treatment of the ciliary processes—combined with measures for minimizing postoperative IOP spikes and inflammation—will lead to improved outcomes when performing endoscopic cyclophotocoagulation with cataract surgery.***

FAIRFIELD, CT :: **ENDOSCOPIC CYCLOPHOTOCOAGULATION (ECP)** can be performed in combination with cataract surgery without any need for surgeons to modify their standard cataract technique.

Dr. Noecker

To optimize both the efficacy and safety of ECP, however, surgeons should take care to treat the ciliary processes fully, avoid postoperative IOP spikes, and minimize inflammation, said Robert J. Noecker, MD, MBA, director of glaucoma, Ophthalmic Consultants of Connecticut, Fairfield, CT.

1 FULLY TREAT THE CILIARY PROCESSES.

Dr. Noecker observed that inadequate treatment of the ciliary processes is perhaps the biggest mistake surgeons make when performing ECP in combination with cataract surgery.

To enable 360° treatment of the ciliary processes, Dr. Noecker said he inserts the laser through two incisions—the primary temporal cataract incision and a superonasal incision made 120° away.

However, he also pointed out that treatment of the posterior aspect of the ciliary processes is another component to achieving thorough treatment, and that can be accomplished by treating through the capsule.

"When performing ECP through an anterior approach, it is impossible to treat all of the ciliary epithelium because the anatomy limits full access," Dr. Noecker explained. "That is the reason why surgeons are sometimes disappointed with the outcome of ECP in phakic patients.

"Therefore, a good tip when combining ECP with cataract surgery is to treat the ciliary processes through the capsule," Dr. Noecker continued.

2 AVOID POSTOPERATIVE IOP SPIKES.

All cataract surgeons recognize the importance of meticulous removal of viscoelastic at the end of the case in order to avoid postoperative IOP spikes, and the need is even greater when combining cataract surgery with ECP for two reasons.

Dr. Noecker explained that the combined procedure involves placing more viscoelastic into the eye—into the capsular bag as well as in the area of the zonules.

In addition, there is no buffer against viscoelastic-related IOP spikes with ECP because—unlike some other glaucoma procedures that may be combined with cataract surgery—ECP does not increase outflow and lead to an immediate decrease in IOP.

Since the zonules are semipermeable to the viscoelastic, surgeons should be spending about twice as much time as they normally would during irrigation and aspiration to remove viscoelastic.

Thoroughness may also necessitate going behind the iris, Dr. Noecker said.

Also to minimize IOP spikes, Dr. Noecker recommended aggressive prophylaxis with IOP-reducing medications, including oral acetazolamide and topical agents.

In addition, existing glaucoma medications should be continued while awaiting the onset of the ECP treatment effect.

3 MINIMIZE INFLAMMATION.

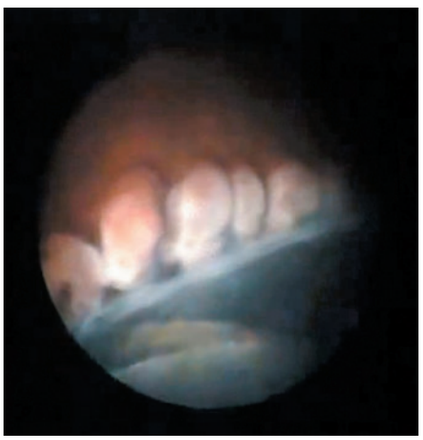
With recognition of the importance of minimizing inflammation when performing ECP, the first consideration for surgeons is to be careful in their technique.

"If you see bubbles when performing ECP, you are overtreating," Dr. Noecker said. "The patient may still get a benefit from the procedure, but you will have given something up by causing inflammation."

Secondly, surgeons should be aggressive with their approach to anti-inflammatory treatment. To suppress inflammation and improve patient comfort, Dr. Noecker recommended having the anesthesiologist administer intravenous dexamethasone.

In addition, Dr. Noecker administers dexamethasone by intracameral injection at the end of the procedure and treats aggressively postoperatively with a potent topical corticosteroid. ■

ECP AND PHACO



VIDEO To watch a video clip showing endoscopic cyclophotocoagulation performed in combination with cataract surgery, go to **http://bit.ly/1g6Rzeu**.
(Video courtesy of Robert J. Noecker, MD, MBA)

Weigh in on the discussion about performing endoscopic cyclophotocoagulation with cataract surgery at **Facebook.com/OphthalmologyTimes.**

ROBERT J. NOECKER, MD, MBA

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Dr. Noecker is a paid consultant to and on the speakers' bureau for Endo Optiks. He is also a paid consultant to, speakers' bureau member, and/or receives research support from other companies with products for glaucoma management.

SAFETY

(Continued from page 1)

dictable corneal incisions. It can also be stated unequivocally that the capsulotomy created with the laser is more precise relative to a manual capsulorhexis and has equivalent if not better strength.

Dr. Lawless noted some studies have suggested the laser-created capsulotomy is inferior in terms of smoothness of the cut surface. That research, however, was conducted with older laser technology and higher energies than are currently used. A recent study [Mastropasqua L, et al. *J Cataract Refract Surg*. 2013;39:1581-1586] showed irregularity of the cut surface was similar comparing manual and laser capsulotomies when the latter was performed with a low-energy setting of just 7 microJ.

TAKE-HOME

- ***Surgeons with experience using the femtosecond laser for refractive lens surgery discuss the safety benefits and challenges accompanying its use.***

"We are now in a low-energy environment with the use of our lasers, and many systems are even operating below 7 microJ," Dr. Lawless said, adding that he expects the quality of the capsulotomy edge created with the laser will soon be as good or exceed that of the manual capsulorhexis for most systems. How edge quality relates to capsule integrity is still to be determined.

Multiple studies investigating the effect of laser-assisted surgery on ultrasound energy usage show effective phaco time is reduced 40% to 90% relative to a manual procedure. Moreover, the reduction in ultrasound energy has been directly related to a benefit for minimizing endothelial cell loss, according to several studies.

In addition, two studies and various case reports show macular thickening is reduced by use of the laser, and there are case series describing use of the laser to facilitate surgery in difficult cases, including eyes with white cataract, phacomorphic glaucoma, a corneal graft, and those requiring mechanical pupil enlargement.

SURGICAL COMPLICATIONS

Focusing on surgical complications, Dr. Lawless cited a paper from his practice group that analyzed outcomes in a prospective cohort of 1,500 eyes consecutive eyes [Roberts TV, et al. *Ophthalmology*. 2013;120:227-233].

Using published data for manual surgery to benchmark the results, Dr. Lawless observed that the rates of posterior capsular tears, including events with and without vitreous loss, and of anterior capsular tears were lower than the best published historical results.

The rate of posterior capsule complications using the laser (0.08% or 0.23% for cases with vitreous loss) were also far better than the 2% rate reported in an analysis of data from 600,000 eyes in the Swedish National Cataract Register, Dr. Lawless said.

"In my personal series of 981 eyes, I have a 0.1% anterior capsular tear rate and a 0% rate of posterior capsule tears," he added. "I could never achieve those outcomes with manual surgery."

COUNTERPOINT: NOT SAFER

Robert K. Maloney, MD—director, Maloney Vision Institute, and clinical professor of ophthalmology, Jules Stein Eye Institute/UCLA, Los Angeles—first established his preference is for using the laser.

Dr. Maloney has been performing LRLS routinely for 2 years and has experience with three of the four systems available in the United States, he noted.


Dr. Maloney

However, Dr. Maloney said he has encountered complications using all three systems and emphasized that the laser introduces different safety issues.

He cited the paper from Dr. Lawless to highlight the learning curve for the laser-assisted procedure.

In addition, Dr. Maloney reviewed the potential for anterior capsule tears using the laser along with the challenges of cortex removal and operating on eyes with small pupils.

"I try to avoid the femtosecond laser procedure in patients with small pupils because I think it makes a challenging situation even more difficult," Dr. Maloney said. "In addition, surgeons should know that cortical removal is more difficult in 100% of eyes in procedures done with the laser, and that is an issue rarely spoken about."

He explained that in the laser-assisted procedure, the hydrodissection wave separates cortex from the epinucleus, not from the capsule, and after the laser-created capsulotomy, there are no cortical tags to grab onto with the irrigation/aspiration port.

OT OphthalmologyTimes.com
Online Exclusive

EPITHELIAL REMOVAL BY PTK BENEFICIAL FOR PERFORMING CXL

STUDIES EVALUATING TREATMENT OF PROGRESSIVE KERATOCONUS with corneal crosslinking (CXL) show greater benefit using an epithelium-off versus epithelium-on technique. However, epithelial removal by laser-assisted phototherapeutic keratectomy (PTK) may give better results than manual debridement, according to a study presented by Ronald N. Gaster, MD. Go to **http://bit.ly/1l0oE0a**.

Discussing a laser-assisted case, Dr. Maloney pointed out how the cortex peels off in tiny fragments and the particular difficulty of removing subincisional cortex.

Discussing anterior capsular tears, Dr. Maloney observed that with improved technology and surgeon experience, the rate of anterior capsular tears with LRLS has been dramatically reduced.

This complication has not been eliminated, however, he said.

Dr. Maloney explained that the tears can arise if the laser has not created a free-floating capsulotomy because any irregularity in the rim can radialize as the surgeon works to break the adhesions.

However, the tear can also develop even before the eye is opened because the nucleus might prolapse forward due to pressure created by intralenticular gas bubbles.

Dr. Maloney also highlighted cases where the anterior capsule tear extended to the posterior capsule, and depending on their extent, necessitated a change in the plan for IOL implantation.

Despite these challenges, Dr. Maloney said he still believes that LRLS is the safest way to perform cataract surgery in most patients. ■

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Dr. Maloney is a consultant for Abbott Medical Optics.

Dr. Lawless and Dr. Maloney each were assigned to discuss opposing views of the relative safety of laser refractive lens surgery during Refractive Surgery Subspecialty Day at the 2013 meeting of the American Academy of Ophthalmology.

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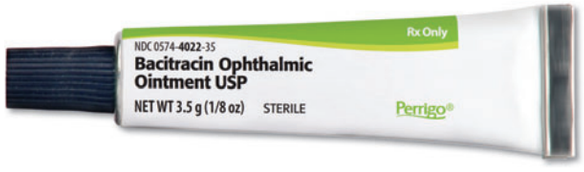

www.perrigobacitracin.com

Please see adjacent page for full prescribing information.

References: 1. Kempe CH. The use of antibacterial agents: summary of round table discussion. *Pediatrics*. 1955;15(2):221-230. **2.** Kowalski RP. Is antibiotic resistance a problem in the treatment of ophthalmic infections? *Expert Rev Ophthalmol*. 2013;8(2):119-126. **3.** Recchia FM, Busbee BG, Pearlman RB, Carvalho-Recchia CA, Ho AC. Changing trends in the microbiologic aspects of postcataract endophthalmitis. *Arch Ophthalmol*. 2005;123(3):341-346. **4.** Freidlin J, Acharya N, Lietman TM, Cevallos V, Whitcher JP, Margolis TP. Spectrum of eye disease caused by methicillin-resistant *Staphylococcus aureus*. *Am J Ophthalmol*. 2007;144(2):313-315. **5.** Hecht G. Ophthalmic preparations. In: Gennaro AR, ed. *Remington: the Science and Practice of Pharmacy*. 20th ed. Baltimore, MD: Lippincott Williams & Wilkins; 2000. **6.** Bacitracin Ophthalmic Ointment [package insert]. Minneapolis, MN: Perrigo Company; August 2013. **7.** Data on file. Perrigo Company.

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LESIONS

(Continued from page 13)

Smaller cysts also require a slightly different approach. Instead of the pigtail probe, a small-gauge angiocatheter or double-lumen needle is used.

Dual-agent therapy and prolonged drainage are not feasible. In these cases, ultrasound is very helpful to determine the presence and accuracy of placement of the needle.

DOXYCYCLINE OR BLEOMYCIN FOAM

Another useful strategy is to use bleomycin foam mixed with albumin to monitor placement of the fluid; the foam shows prominently on the treatment ultrasound.

The foam is also beneficial because it can fill the cyst and contact the endothelial tissue lining the cyst with less of the bleomycin, Dr. Cahill said.

This decreases the chance of extravasation, and the amount of bleomycin used can stay below toxic dose levels even when extensive lesions are treated.

Doxycycline foam can also be used, following the same principles as bleomycin foam, Dr. Cahill said. There is no toxicity, but doxycycline foam may cause more inflammation.

Conjunctival cysts—usually classified as microcysts—are treated with direct visualization of needle placement, using doxycycline or bleomycin foam.

"Regardless of the size, the cyst may require more than one treatment, and we may not be able to treat all cysts during a single session," Dr. Cahill said. "There's variable interconnectivity of cysts, and it's best to treat the more superficial ones rather than to go through one to treat a deeper one.

"Sometimes it is necessary to limit the amount that's treated in one session because we're dealing with a closed space and we do not want to create a compartment syndrome," he said.

SIDE EFFECTS

Side effects that may occur include edema around cysts, hemorrhage from needle tracts, and serous transudate or hemorrhage inside cysts from denuded endothelial linings. Systemic corticosteroids following treatment can make the recovery easier.

In all of the cases that Dr. Cahill and colleagues have treated over the years, complications have been temporary. These include double vision, corneal exposure, increased IOP, mydriasis, optic nerve compromise, and one incident of corneal penetration.

The treatment protocol has several shortcomings, he said.

At this time, it is not possible to treat all apical cysts and intraconal cysts safely. When treatment is possible, multiple treatments may be needed—usually at 1- to 3-month intervals—and recovery from each treatment takes about 1 month, Dr. Cahill concluded. ■

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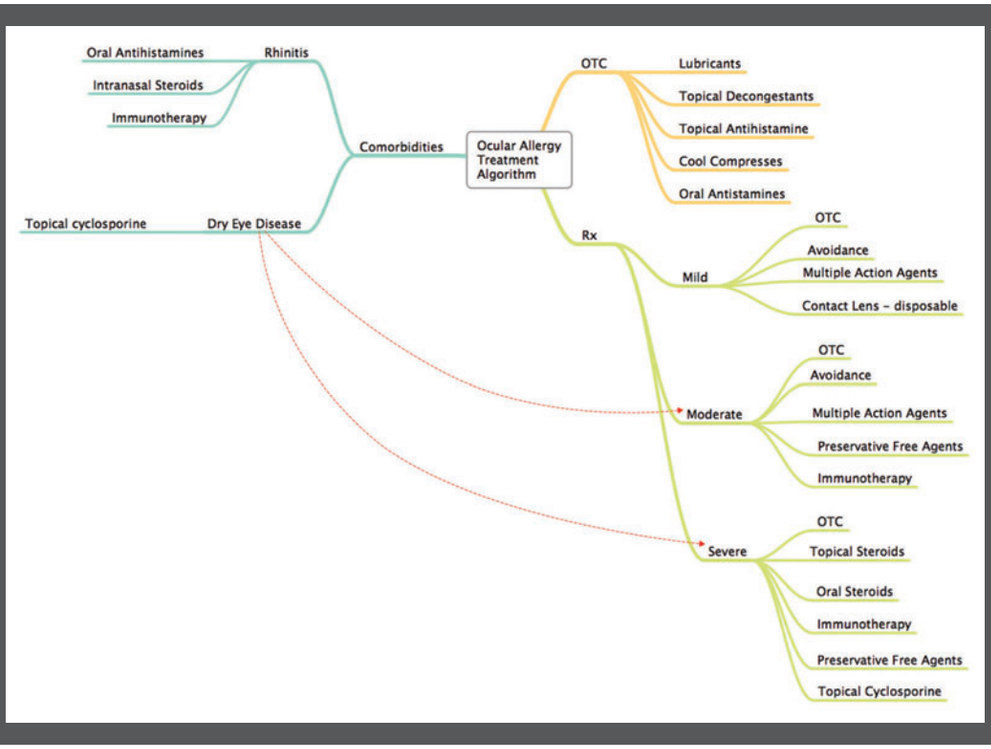
Dr. Cahill did not report any financial disclosures.

Eye health, allergies resource available

JACKSONVILLE, FL ::
AS THE SPRING ALLERGY SEASON APPROACHES, Johnson & Johnson Vision Care is offering an educational brochure, "Eye Health and Allergies." The complimentary brochure is designed to provide patients with useful information on how eye allergies occur, common signs and symptoms, and practical advice on how to treat eye allergies.

The brochure also includes helpful information about eye allergies and contact lenses, including advice on the benefits of daily disposable contact lenses.

Digital copies can be downloaded from the Patient Education section of *www.Acuvue-Professional.com*. Eye-care professionals may also order bulk copies for the office by sending an e-mail request with their name and mailing address to *eyeallergybrochure@rprny.com*. ■



Current Best Practices

The algorithm presented outlines current best practices regarding diagnosis and treatment of allergic conjunctivitis based on recent medical findings and expert opinion similar to those provided for asthma and allergic rhinitis. Greater awareness of the allergic conjunctivitis disease state and knowledge of treatment options for symptom relief can improve patient management and encourage healthcare providers to further collaborate in assisting patients to reach closer to their objective of ameliorating the symptoms of ocular allergy. The ocular allergy treatment algorithm includes over-the-counter (OTC) agents and then progresses to include a stepwise approach using prescription medications that build on the various complementary mechanisms of action of therapeutic agents including topical lubricants, cool compresses, decongestants, antihistamines, nonsteroidal anti-inflammatory drug (NSAID), mast cell stabilizers, corticosteroids, and subcutaneous (and potentially sublingual*) immunotherapy, but also include the treatment of comorbid conditions such as allergic rhinitis and tear film dysfunction (dry eye disease). (*Not FDA approved.)

(Source: Allergy Asthma Proc. 2013;34:1–13.)

ALGORITHM ADDRESSES ALLERGIC CONJUNCTIVITIS

Management approach urges collaboration, consensus among specialists, non-specialists

By Nancy Groves; *Reviewed by Leonard Bielory, MD*

take-home

- **A new algorithm for the management of allergic conjunctivitis encourages collaboration and consensus among colleagues with different expertise as well as greater emphasis on ocular signs and symptoms by physicians who are not eye-care specialists.**

NEW BRUNSWICK, NJ ::

An algorithm for the management of allergic conjunctivitis aims to increase consensus among a variety of specialists who may be dealing with ocular allergy.

The algorithm is a stepwise approach that also addresses comorbidities such as dry eye and the possible impact on the ocular surface of medications customarily used to treat allergies.

In addition, it includes immunotherapy as an alternative treatment approach in patients whose symptoms are more severe.

"It's basically about the ability to collaborate and communicate in improving the care of the patient," said Leonard Bielory, MD, an allergist-immunologist in the Department of Medicine, Rutgers University, Robert Wood Johnson University Hospital, New Brunswick, NJ, and longtime advocate of a more holistic approach to managing allergic conjunctivitis.

Dr. Bielory et al. reported their recommendations in *Allergy and Asthma Proceedings* (2013;34:1-13).

Dr. Bielory, whose co-authors included several optometrists, explained that subspecialists are trained to concentrate on one organ. While specialists in areas other than eye care may regularly treat patients with ocular allergies, they do not necessarily place sufficient emphasis on ocular signs and symptoms.

"The ocular condition is probably equivalent at times, if not more, than the nasal congestion that is the reason most patients are referred to an allergist," he said.

The allergist will primarily assess the nasal, skin, and respiratory aspects of the disease, whereas the eye-care specialist will center on the eye, with less focus on the other aspects of allergic conjunctivitis.

Continues on page 25 : ***Algorithm***

Can immunotherapy play a role in future approaches to ocular allergy therapy?

Treatment strategy explores desensitization, suppression of allergen-specific IgE production

By Paul Gomes

Recent clinical trials of immunotherapies for allergic conjunctivitis or allergic rhinitis

ALLERGEN	CLINTRIALS/SPONSOR	PRIMARY ENDPOINT	CONJUNCTIVITIS ENDPOINT	STUDY RESULTS
Grass (phase III)	**NCT00409409 Stallergenes**	Total Symptom Score (TSS[1])	Itching, watery eyes component of TSS	Complete, not reported
Grass (phase III)	**NCT00550550 Merck**	Total Symptom Score (TCS[2])	Gritty/itchy/red eyes component of DSS[3]	Met primary endpoint versus placebo
Grass (phase IIb/III)	**NCT00367640 Stallergenes**	Total Symptom Score (TSS[1])	Itching, watery eyes component of TSS	Complete, not reported
A total of 91 studies found in Clintrials database using SLIT/AIT and grass				
Ragweed (phase III)	**NCT01353079 Greer Labs**	Total Symptom Score (TCS[2])	None specified	Complete, not reported
Ragweed (phase II)	**NCT01198613 Circassia Ltd.**	Total Symptom Score (TCS[2])	Ocular symptom score	Met primary endpoint versus placebo
Ragweed (phase III)	**NCT00770315 Merck**	Total Symptom Score (TCS[2])	Gritty/itchy/red eyes component of DSS[3]	Met primary endpoint versus placebo
A total of 23 studies found in Clintrials database using immunotherapy and ragweed				

TSS[1]: a combination of 6 scores: sneezing, rhinorrhoea, nasal itch, nasal congestion, ocular itch, and watery eyes. TCS[2]: the sum of rhinoconjunctivitis daily symptom score (DSS) and rhinoconjunctivitis daily medication score (DMS) averaged over the entire grass pollen season. DSS[3]: includes a "gritty/itchy/red eyes" component. (Source: www.clinicaltrials.gov)

THERAPEUTIC APPROACHES TO ocular allergic disease are at a crossroad. Topical and systemic antihistamines have evolved to once-daily treatments that provide effective symptomatic relief to a large segment of the population, but for another group—perhaps as many as one-third of the 40 million people in the United States with seasonal or perennial allergy—none of the current treatments provide consistent relief.

One therapeutic strategy common outside the United States is immunotherapy, a technique of re-training or desensitizing the immune system so that responses to common allergens, such as pollen, animal dander, or dust mites, are attenuated. Multiple immunotherapy trials are under way or recently completed in the United States, so it is a good time to consider this new technique and how it might impact therapy of allergic conjunctivitis (AC).

Diseases such as atopic dermatitis, rhinitis, and AC are a related group of disorders that—together with asthma—comprise what has been referred to as the atopic march. All of these conditions involve development of a type-2 regulatory T-cell response to common environmental allergens, leading to an inappropriate IgE production and immunological sensitization.

take-home

- **Numerous clinical trials are under way that may help to define the role of immunotherapy in ocular allergy.**

When subsequently exposed to the allergenic culprit, these antibodies can initiate mast cell degranulation and the entire sequela of an allergic response. If the same antigen is exposed to dendritic cells or other antigen-presenting cells at low concentrations, it is possible to initiate a shift in the regulatory balance between the type-2 T-regs and the non-allergenic type-1 T-cells.

Although this desensitization process is not completely understood, suppression of allergen-specific IgE production is also thought to be important in immunotherapy.[1]

SCIT AND SLIT MODALITIES

Any type of immunotherapy involves a repeated presentation of small amounts of antigen. In the United States, subcutaneous injection (SCIT) has been the method of choice for these treatments. The protracted nature of the treatment regimes has limited this therapy to the most severely allergic patients.

In contrast, European physicians have used both oral and topical delivery of antigen for many years. Both of these treatment modalities have shown similar efficacy and safety profiles when compared with SC antigen delivery. Recent large-scale trials in the United States have focused on sublingual allergen delivery (SLIT), a modality that has the potential to expand the use of immunotherapy to a much greater patient population.[2]

A sample of recent trials in the United States is summarized in the table above. Note that few of these studies use any primary measures of allergic conjunctivitis as endpoints.

There is a good deal of misinformation surrounding the use of immunotherapy, particularly with respect to its safety profile. In a recent meta analyses of SLIT that included thousands of subjects over a wide range of allergen doses and delivery protocols, there are only a handful of reported incidents of anaphylaxis.

*Continues on page 25 : **Immunotherapy***

In the face of elevated IOP after monotherapy

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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.

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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

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

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ALLERGAN

IMMUNOTHERAPY

(Continued from page 22)

These trials have established that significant relief from signs and symptoms of allergy can develop with weeks of therapy initiation, and that this relief is sustained even after a discontinuation of allergen. On the other hand, despite the large number of trials, there still seems considerable debate over dosing issues.

In addition, the high numbers of recent trials for grass, ragweed, and dust mite allergens have been unable to address specifically the efficacy of SLIT for AC.

Patients with allergies commonly experience a spectrum of symptoms that includes ocular itching, hyperemia, and chemosis. More than 80% of allergy sufferers report experiencing some ocular symptomology. Despite this, several recent trials have only limited measures of ocular symptoms often included in scores, based upon "gritty eyes or watery eyes." None of the scores appear to include direct measures of ocular itching, the hallmark symptom of AC.[3]

Of greater impact is the lack of a positive comparator group, such as antihistamine or steroid therapy. Most studies include rescue drug usage (either systemic, nasal, or ocular) as a secondary endpoint, but this does not provide a direct comparison between immunotherapy and established allergy treatments. This study design may be a reflection of the low statistical power inherent in all environmental trials.[4]

A MEASURE OF EFFICACY

Allergen challenge has been used to measure efficacy of allergen desensitization, and can provide an objective measure of the treatment effects on either nasal or ocular symptoms. In addition, conjunctival allergen challenge protocols (such as the CAC) are validated metrics that have been used in FDA assessment of AC therapies. So it is hard to understand why metrics like the CAC have not been employed to develop immunotherapeutics.

The few studies that include conjunctival challenge data suggest that ocular itching may be a more sensitive measure of efficacy. In recent reports, ocular itching was reduced 30% to 48% from placebo, whereas the threshold for conjunctival response to allergen provocation was significantly increased.[5]

When compared with the best reported nasal or ocular symptom score improvements of 24% to 28%, it seems as if some of these early studies may have omitted a valuable endpoint from their trials. The medical community will know more when the decisions of the FDA on this new approach to allergic diseases, such as AC, are announced later this year. ■

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PAUL GOMES *is vice president, allergy at Ora Inc., Andover, MA.*

ALGORITHM

(Continued from page 21)

But even when the ocular symptoms seem predominant, chances are extremely high that the patient also has nasal allergy, and vice versa, Dr. Bielory said, adding that the outcomes would probably be better if allergists retained their broad approach of evaluating the nasal, respiratory, dermal, gastrointestinal, and ocular symptoms but had heightened awareness of the ocular aspects and more appreciation of the role that ophthalmologists or optometrists could play in co-managing patients.

As chairman of a joint task force of the American Academy of Allergy Asthma and Immunology and the American College of Allergy, Asthma and Immunology focusing on ocular allergy practice parameters, Dr. Bielory often lectures on this topic and is regularly approached by colleagues who want to learn more about managing ocular allergy and dry eye.

COLLABORATION WORKS BOTH WAYS

"There is increasing appreciation by ophthalmologists—who normally use a variety of medications in the treatment of patients who come in complaining of ocular allergy and after a time realize that there is no response and that they need further assessment as to what is either the allergen bothering them or that this is not an allergic response—that perhaps skin testing and a further assessment would reveal that they're not dealing with an allergic response," Dr. Bielory said. "That would be important before adding more and more medications that don't work."

The algorithm that Dr. Bielory et al. developed begins with patient history and examination evaluating for severity of itching and whether the itch is intermittent or persistent. Other ocular symptoms, such as foreign body sensation, tearing, burning, and redness, should also be addressed.

Symptom duration and prior treatments are also noted. Each symptom is classified by severity level, with appropriate first-line and alternative treatment recommendations and follow-up guidelines.

STEP 1 Treatment of patients with mild, intermittent itching may involve nonpharmaceutical measures, over-the-counter medication, or an ocular antihistamine/mast cell stabilizer.

STEP 2 Patients with mild or intermediate to severe itching but no severe redness or concurrent ocular conditions should be treated with a topical ocular antihistamine/mast cell stabilizer, or in some cases, corticosteroids.

STEP 3 Patients with moderate to severe symptoms and redness should be treated with a topical ocular antihistamine/mast cell stabilizer, a topical ocular corticosteroid, or both.

The other concept within the algorithm is the addition of immunotherapy for those who have chronic allergic disorders in addition to nasal and respiratory symptoms. Immunotherapy has been shown to assist in improving the overall quality of life while reducing the frequency and amount of other medications for the treatment of allergies and asthma. ■

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Dr. Bielory is a consultant for Allergan and Bausch + Lomb, is on the committees of Merck and GlaxoSmithKline, and has received financial support from Sanofi and grants from Allergan.

Why once-daily drug is physician's 'go-to' therapy for ocular allergy

Medication a reliable choice for safe and effective control of seasonal allergic conjunctivitis

By Cheryl Guttman Krader; *Reviewed by Alan G. Kabat, OD*

MEMPHIS, TN ::

TOPICAL ANTIHISTAMINE-MAST cell stabilizers are regarded as the mainstay treatment for seasonal allergic conjunctivitis (SAC) because of their safety, tolerability, and ability to provide prompt and ongoing relief.

Though this class of dual-acting agents contains several medications, including over-the-counter (OTC) and prescription agents, Alan G. Kabat, OD, said that olopatadine hydrochloride ophthalmic solution 0.2% (Pataday, Alcon Laboratories) is his "go-to" product for managing patients with mild-to-moderate SAC.


Dr. Kabat

"There are other safe and effective options for treating SAC," said Dr. Kabat, professor, Southern College of Optometry, Memphis, TN. "However, I like the science supporting olopatadine. It is a highly selective H1 antagonist and has demonstrated superiority for efficacy and tolerability when compared with multiple other anti-allergy agents in head-to-head trials.

"The published study results mirror my clinical practice experience," he said. "I use olopatadine 0.2% to treat my own ocular allergy, and when I prescribe it for patients with SAC, I know I can rely on it to be successful 99% of the time."

Dr. Kabat noted that the comparator trials were conducted using the original formulation of olopatadine that contained 0.1% of the active ingredient. Results of a clinical trial using a conjunctival allergen challenge model established that olopatadine 0.2% once-daily dosing was as effective as olopatadine 0.1% twice a day for preventing ocular itching associated with allergic conjunctivitis [*Curr Eye Res*. 2007;32:1017-1022].

"Olopatadine 0.2% is just one of two antihistamine-mast cell stabilizers that is approved for once-daily dosing," Dr. Kabat said. "Patients like the convenience of that schedule and it is particularly nice for contact lens wearers who do not have to remove their lenses during the day to instill a second dose.

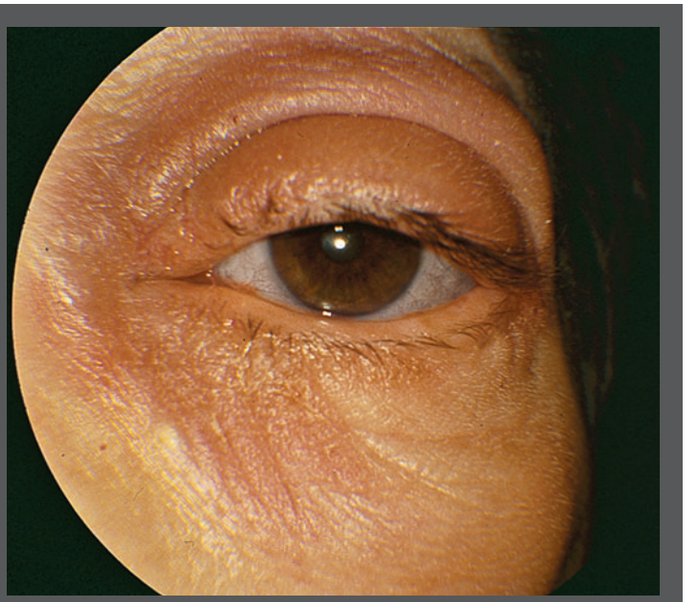
"Contact lens wearers whose eyes are irritated and uncomfortable toward the end of the day may find particular benefit from instilling their daily drop of olopatadine 0.2% in the evening after they take out their lenses," he said.

In a worst-case scenario where the environmental allergen load is extremely high, patients might achieve better round-the-clock allergy control if they use olopatadine 0.2% twice a day, he added. Patients with a more severe flare-up of their allergy may need treatment with a topical corticosteroid.

SAFETY ALLOWS SELF-TREATMENT

Taking into account the efficacy and favorable safety of olopatadine 0.2%, Dr. Kabat said that for demonstrated trustworthy patients who regularly return for follow-up visits, he is very comfortable writing a prescription for olopatadine 0.2% with open refills. Patients are instructed to begin using the medication a few weeks prior to the onset of allergy season and to continue using it for the duration of the season.

"Ideally, patients who are known to have SAC should start using their antihistamine-mast cell stabilizer as a preventive strategy before allergen levels begin to increase," he said. "The reality is that most patients turn to their allergy medication as rescue therapy only after they are bothered by their signs and symptoms."



This patient presented with a severe allergic reaction affecting both the conjunctiva and lids. Olopatadine 0.2% alleviated symptoms within 24 hours, according to Alan G. Kabat, OD. *(Image courtesy of Alan G. Kabat, OD)*

"In either case, it is helpful to allow dependable patients to have medication on hand so that they can self-treat," he said. "This approach will also reduce the possibility that they turn to OTC anti-allergy medications, which are attractive because of their convenience but not as effective as olopatadine 0.2% and other prescription antihistamine-mast cell stabilizers."

take-home

Alan G. Kabat, OD, discusses why olopatadine 0.2% is his preferred anti-allergy medication for managing mild-to-moderate seasonal allergic conjunctivitis.

DISPELLING DRY EYE MYTH

Although there has been some discussion about differential antimuscarinic effects of ophthalmic antihistamines, Dr. Kabat noted there has never been any translational work showing that these pharmacologic differences are clinically meaningful with respect to propensity to cause or exacerbate dry eye.

In a randomized, double-masked clinical trial including 52 patients with allergic conjunctivitis and dry eye who were assigned to use olopatadine 0.2% or saline once daily for 1 week, there were no significant differences between treatment groups at the end of the study in evaluations of tear film break-up time, corneal and conjunctival staining, tear volume and flow, Schirmer test, injection, or symptom evaluations [*Curr Med Res Opin.* 2008;24:441-447].

"Oral antihistamines—and particularly older-generation agents, such as diphenhydramine—act at the level of the autonomic nervous system and can cause drying of the ocular surface," Dr. Kabat explained. "However, it has never been shown conclusively that any topical medications with antihistaminic activity cause or worsen dry eye.

"In contrast, it is my anecdotal observation that patients with allergic conjunctivitis and comorbid dry eye have a reduction in their dry eye symptoms when using a medication that effectively controls their ocular allergy." ■

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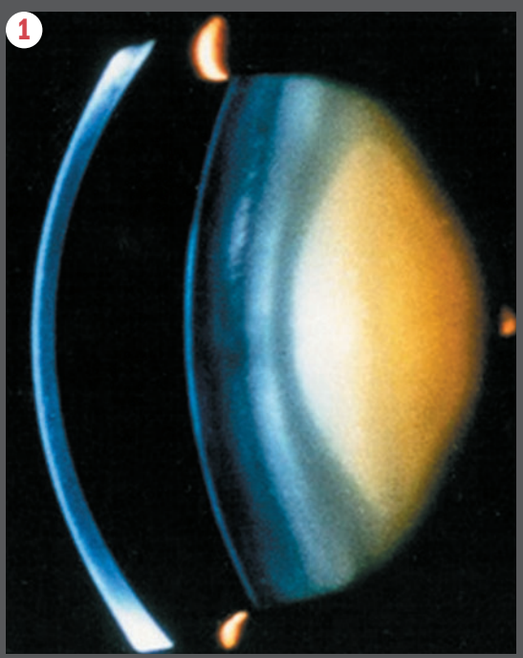
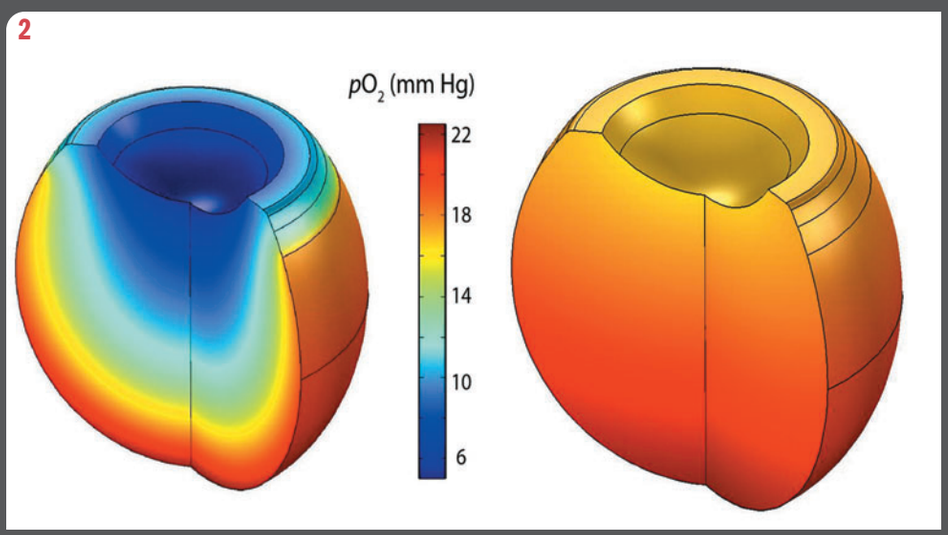
The vitreous: Orphan of the eye

Reversing degenerative changes could help protect retina, crystalline lens, trabecular meshwork

Eye on Research **By David C. Beebe, PhD,** *Special to* Ophthalmology Times





1 **Color Scheimpflug photo of a nuclear cataract.**

2 **Diagram of oxygen distribution in the eye before (left) and after (right) vitrectomy.**
(Images courtesy of David C. Beebe, PhD)

TAKE-HOME

- ***Degeneration of the vitreous is implicated not only in retinal conditions, but also in cataract and glaucoma, suggests ongoing laboratory research at the University of Washington–St. Louis.***

The vitreous body—the clear, jelly-like substance that fills the posterior segment—is a rather neglected segment of the eye. It is discarded after vitrectomy and considered of little interest in a healthy eye.

Few researchers have studied it directly. We know that the vitreous is a non-regenerative tissue that undergoes slow liquefaction with age. At the advanced stages of this degeneration, the risk of retinal tears, retinal detachment, and macular holes is increased.

Ongoing research in my lab at the University of Washington–St. Louis suggests that degeneration of the vitreous is implicated, not only in these retinal conditions, but in cataract and glaucoma as well. We've come to this recognition through a combination of eye bank tissue research and collaborations with observant clinicians who have provided access to human subjects undergoing vitreoretinal surgery.

THE LENS AND THE VITREOUS

With age, the human crystalline lens nucleus hardens and the rate of nutrient diffusion to the proteins in the center of the lens slows down dramatically. As cataract surgeons know, that harder nucleus is typically surrounded by a softer outer cortex. The cortex is full of viable cells with high levels of the protective antioxidant glutathione.

In the center of the aged lens, there is much less glutathione overall, and what is there is more likely to be the oxidized form rather than the protective reduced form of glutathione. These changes in the lens nucleus are responsible for presbyopia and nuclear cataracts, and likely play a role in the development of cortical cataracts, as well.

Yet, we understand little about what triggers this process.

A series of clues led us to suspect vitreous degeneration as the key to lens changes. The first clue was the discovery, while I was doing some research into lens development, that the genes expressed in 6-day-old chicken embryo lenses were characteristic of cells under hypoxic conditions.

Then, clinicians in Sweden observed that patients undergoing intensive hyperbaric oxygen therapy for systemic conditions, such as artherosclerosis, over a period of >1 year had interesting ophthalmic side effects. All of the subjects became more myopic, with increased nuclear opacity, and about half developed frank nuclear cataracts.[1]

This suggests that oxygen, if it gets to high enough concentrations on the lens, becomes toxic and can somehow push the lens toward nuclear cataracts. (Figure 1)

It is also well known that patients undergoing vitrectomy for retinal surgery will generally develop nuclear cataracts within 2 years.

Based on all these clues—hypoxic chick embryo lenses and the rapid onset of nuclear cataract in eyes exposed to hyperbaric oxygen or vitrectomy—we proposed that the vitreous body keeps the lens in the hypoxic environment it needs to remain healthy.

TESTING THE HYPOTHESIS

To test this theory, my associates and I collaborated with Nancy Holekamp, MD, a vitreoretinal surgeon in our department. Using a fiber optic device, we measured oxygen levels adjacent to the lens and in the mid-vitreous in patients undergoing retinal surgery. Measures were obtained before and after vitrectomy. We found that the lenses in the post-vitrectomy eyes were exposed to significantly more oxygen.[2] (Figure 2 on Page 28)

The increased exposure to oxygen occurs as a result of removing the vitreous and is independent of the gauge of vitrectomy instrumentation.[3]

> 'We proposed that the vitreous body keeps the lens in the hypoxic environment it needs to remain healthy.' — *David C. Beebe, PhD*

Next, we examined the state of the vitreous in eye bank globes. The eyes were graded by the percentage of vitreous liquefaction and degree of lens opacity. It turns out that the state of the vitreous is an even better predictor of nuclear cataract than age in eyes of donors between 50 to 70 years old.[4]

As the vitreous liquefies with age, I believe it gradually exposes the lens to more oxygen and that this exposure is largely responsible for the development of age-related nuclear cataract. It is still not clear why the vitreous degenerates earlier and more rapidly in some eyes and less rapidly in others, but it appears that the latter category of people are protected against nuclear cataracts until later in life.

In subsequent studies we noted that diabetics had lower levels of oxygen around the lens and in the vitreous, which could be protective if oxygen is the culprit in the development of nuclear cataract.[5]

It also turns out that diabetic eyes with ischemic retinopathy—clear evidence that the retina is hypoxic—show no significant progression of nuclear opacification for up to one year after vitrectomy.[6]

Nondiabetic and nonischemic diabetic eyes progress to cataract at the same rates, but the intraocular environment in the ischemic retinopathy eyes continues to be hypoxic even after vitrectomy.

BEYOND THE LENS

Loss of the vitreous may also affect the trabecular meshwork. Stanley Chang, MD, noticed that his patients had a higher risk of primary open-angle glaucoma after vitrectomy and cataract surgery.

We were able to show that he was right: Oxygen levels in the posterior chamber, anterior to the IOL, and in the anterior chamber angle were much higher in patients who had had both vitrectomy and cataract surgery.[7]

We also found some important racial differences in oxygen levels in the anterior segment. Prior to ocular surgery, African Americans have much higher intraocular oxygen levels, on average, than European Americans.[8]

This could be expected to increase oxidative damage to the outflow system over their lifetime. We don't know whether the higher oxygen in African American eyes is due to genetic or environmental factors, but it could partly explain the large racial discrepancies in glaucoma incidence and risk.

CHALLENGES AHEAD

These are fascinating studies, but there is much more to be done. Donor eyes and lenses will be a critical resource in the future, as we examine whether vitreous and lens changes can be prevented or reversed.

For example, we are now investigating whether specific compounds can be injected into the vitreous to restore its structure as a gel. The first clinical application for such compounds would likely be in cases where a very limited vitrectomy is being performed, but ideally, it could be injected even before there is separation from and damage to the retina. Initial feasibility studies are being conducted in animal eyes, but in order to translate this into human clinical trials, we'll need to test the compound in donor eyes, as well.

We also hope to compare proteomic analysis of the structural components of the aged vitreous with that of vitreous from very young eyes to understand better how the vitreous body changes over time.

Much of our work to date has been done with local donor eyes not suitable for transplant. As we begin to require more specialized tissue (such as the very young eyes), there may be opportunities to work with the Lions Eye Institute for Transplant and Research (LEITR), which provides extensive resources for ocular tissue research and actively works to facilitate collaboration among scientists, clinicians, and industry. (See "About this series," above)

Certainly, there are challenges inherent in dealing with ocular tissue or with patients in a clinical setting. The variability in human eyes is disconcerting to basic scientists who are used to tightly controlling variables. But we also learn a great deal from this variability about real-world applications.

Furthermore, our experience demonstrates how much we all have to gain from collaboration with one another. So often, observant clinicians have provided the key in-

Continues on page 30 : ***Vitreous***

About this series

EYE ON RESEARCH is a quarterly series of articles highlighting cutting-edge ophthalmic research with the potential to have significant impact on vision and ocular health worldwide. The series is supported by the Lions Eye Institute for Transplant and Research Inc. (LEITR), a nonprofit organization dedicated to the recovery, evaluation, and distribution of eye tissue for transplantation, research, and education. Located in Tampa, FL, LEITR is the only combined eye bank and ocular research center in the world. LEITR provides fresh donor globes, corneas, lenses, trabecular meshwork, and other tissues from diseased and healthy human eyes—often within 4 to 6 hours of death—to researchers for immediate use in their own labs or in its on-site research facility. For more information, contact *info@LionsEyeInstitute.org* or visit *LionsEyeInstitute.org*. ■

Uncovering a neurologic defect: The importance of visual field testing

In this case, neurological deficit may point to patient's postoperative visual complaints

By Lynda Charters; *Reviewed by Bradley J. Katz, MD, PhD*

TAKE-HOME

- ***Visual field testing is indispensable in diagnosing neurologic visual deficits.***

SALT LAKE CITY ::
WHEN A PATIENT presents with the complaint that he or she is slowly losing vision, what course of action does a general ophthalmologist take?

That was the task given Bradley J. Katz, MD, PhD, neuro-ophthalmologist, John A. Moran Eye Center, University of Utah School of Medicine, Salt Lake City.

CASE REPORT

A 68-year-old man presented to Dr. Katz and described gradual painless loss of vision bilaterally. Best-corrected visual acuity (BCVA) levels were 20/40 in the right eye and 20/50 in the left eye. The examination was normal with the exception of 2+ nuclear sclerotic cataracts bilaterally.

The patient underwent two uncomplicated cataract surgeries 2 weeks apart by Dr. Katz. Recovery was uneventful, and postoperative uncorrected visual acuity was 20/30 in both eyes with BCVA of 20/25 in both eyes. However, the patient insisted that there was no improvement in his vision compared with preoperatively.

"My first thought when a patient complains of no visual acuity improvement is dry eye syndrome, and my second thought is cystoid macular edema—but the patient had neither," he said.

DIAGNOSTIC OPTIONS

When choosing a diagnostic tool, options include: topography, multifocal electroretinography, visual field testing, or magnetic resonance imaging (MRI) of the brain and orbits.

A poll of ophthalmologists indicated that 85% would order visual field testing to rule out a central scotoma and hemianopsia. A panel of experts also recommended color vision testing. The goal of testing, they pointed out, is to determine if there is a neurogenic origin of the vision loss, according to Joseph Rizzo, III, MD.

Dr. Rizzo recommended that visual field testing be part of a standard visual evaluation. With simple confrontation field testing consisting of finger counting and presentation of a small object on either side of the midline, 70% of neurologic field defects can be identified.

Optical coherence tomography may or may not be useful because some conditions are not characterized by an abnormal retinal nerve fiber layer (RNFL) early in the disease process and simple myopia can cause thinning of the RNFL. In support of this recommendation, Dr. Katz commented that another cataract patient of his had a homonymous hemianopsia, which would have had a normal RNFL.

Dr. Katz discussed that visual field testing demonstrated a substantial bitemporal visual field defect that was worse inferiorly, which suggested superior compression of the chiasm.

Dr. Rizzo noted the need for MRI imaging of the brain with and without contrast focused on the chiasmal region.

To avoid missing a lesion, conveying clinical information to the radiologist is critical. Computed tomography is inadequate in such a case, because it is not as sensitive in the chiasmal region compared with MRI, added Mark Moster, MD. He also emphasized the importance of telling the radiologist that there is a bitemporal hemianopia.

"If a plain MRI brain scan without contrast is ordered, the result may be normal and the patient can progressively go blind because the lesion was missed," he said.

Continues on page 31 : ***Visual field***

VITREOUS

(Continued from page 29)

sights that sparked new areas of inquiry for our laboratory.

In return, the basic science work that we do with eye bank tissue helps to move new therapies closer to clinical reality. ■

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DAVID C. BEEBE, PHD, *is the Janet and Bernard Becker Professor of Ophthalmology and Cell Biology at Washington University of St. Louis, MO. Dr. Beebe has no financial interest in the eye banks discussed or referred to in the article. Readers may contact him at 314/362-1621 or beebe@vision.wustl.edu.*

VISUAL FIELD

(Continued from page 30)

The case under discussion was that of chronic visual loss, which can be diagnosed on an outpatient basis.

In cases of acute visual loss with head pain and the threat of pituitary apoplexy, the patient should undergo urgent imaging because of the potential for mortality and endocrine complications, Dr. Rizzo said.

Dr. Katz's patient has undergone transsphenoidal resection of the pituitary tumor and is doing well. He emphasized the importance of not dismissing patient complaints about blurry vision after uncomplicated cataract surgery. Doing so may result in missing an important neurologic defect: in this case, a pituitary tumor. ■

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Dr. Katz presented this case report for discussion during Neuro-Ophthalmology Subspecialty Day at the 2013 meeting of the American Academy of Ophthalmology.

Prevent Blindness seeks award applications

By Rose Schneider

CHICAGO ::

PREVENT BLINDNESS IS NOW accepting applications for its 2014 Joanne Angle Investigator Award.

The award—which was recently renamed to honor Joanne Angle, who served with the Association for Research in Vision and Ophthalmology, as well as the national Board of Directors for Prevent Blindness—is a research grant provided annually to a public health project that seeks to help save sight.

The investigator award program has awarded more than $1 million to eye and vision research projects since its inception in 2003.

The deadline for the 11th annual investigator award is March 31. Grants are for a 1-year period, up to $30,000, reviewed by a panel of scientists, and commence on July 1.

"Supporting eye and vision research today is crucial to finding the answers to blinding eye diseases and conditions," said Hugh R. Parry, president and chief executive officer of Prevent Blindness. "By starting the next decade of this sight-saving program, we can help to make a real difference in the lives those who have, or potentially could have, significant vision loss.

"By renaming this initiative as the Joanne Angle Investigator Award, we honor Ms. Angle's legacy as a pioneer and leader in this important field," he added. ■

New drugs and devices advance strabismus treatment to next level

Innovations aim to create permanent change, not cause inflammation or collateral damage

By Nancy Groves; *Reviewed by Stephen P. Christiansen, MD*

TAKE-HOME

- ***The surgical procedures and botulinum toxin A injections widely used today to treat strabismus may be supplanted within a decade or two by new drugs and devices that are more effective.***

BOSTON :: **THOUGH STRABISMUS TREATMENT** in children is generally effective, investigators have taken action to improve the success rate further by exploring new drugs and developing new devices.

Currently, ophthalmologists seeking to reassure parents of children requiring treatment for strabismus often cite an 80% success rate for the surgical procedure.

This is "simply inaccurate," said Stephen P. Christiansen, MD, noting that the overall reoperation rate for infantile esotropia is about 34%, and for exotropia it approaches 80%.

"We have seen some changes in the way we treat patients over these last few years," said Dr. Christiansen, chairman and professor of ophthalmology and pediatrics, Boston University School of Medicine. "But I expect that within 20 years or so the way we treat patients with strabismus will have changed dramatically.

"We have to recognize that if we are doing a mechanical operation for a disease that is principally electrical, there are going to be long-term changes in eye alignment because the electrical system changes over time," he said.

DEVELOPMENT OF DEVICES

On the devices front, one of the promising new approaches is a titanium T-plate anchoring platform system that could be particularly helpful as a means for ocular alignment in patients with severe paralytic and restrictive strabismus, Dr. Christiansen said.

The plate is attached to the nasal orbital wall, and the extraocular muscle insertion is tethered to the posterior plate. Hilda Capo, MD, and David T. Tse, MD, both of Bascom Palmer Eye Institute, University of Miami Miller School of Medicine, developed the T-plate system, introduced in 2010.

ANOTHER LOOK AT PHARMACEUTICALS

Among pharmaceutical approaches, botulinum toxin A (BTX-A) has been used in strabismus treatment for more than 30 years, but it is time for re-assessment, Dr. Christiansen suggested. BTX-A may lack the power to control the alignment in patients with large angles adequately—especially with a single injection—although it may still be appropriate in patients with smaller angles, residual strabismus after recession, or consecutive strabismus.

Analyzing all cases of strabismus treatment with BTX-A, about 50% of children with infantile esotropia will require re-injection. But in children who have smaller angles (< ±35 prism diopter [PD]), reports are as good as 63% alignment within 8 PD of straight (range 34 to 63).

In a study by Tejedor and Rodriguez (*IOVS*, 2001), the success rate was 53% aligned for patients with acquired esotropia following a single injection (mean ET = 35 PD). Analysis by A. de Alba et al. (*Archives of Ophthalmology, 2010*) demonstrated that use of BTX-A has an extremely low rate of consecutive exotropia, <3% for all treated patients.

"Although these patients haven't been followed for long periods, it looks like BTX-A may result in good long-term alignment with relatively low consecutive exodeviations," Dr. Christiansen said.

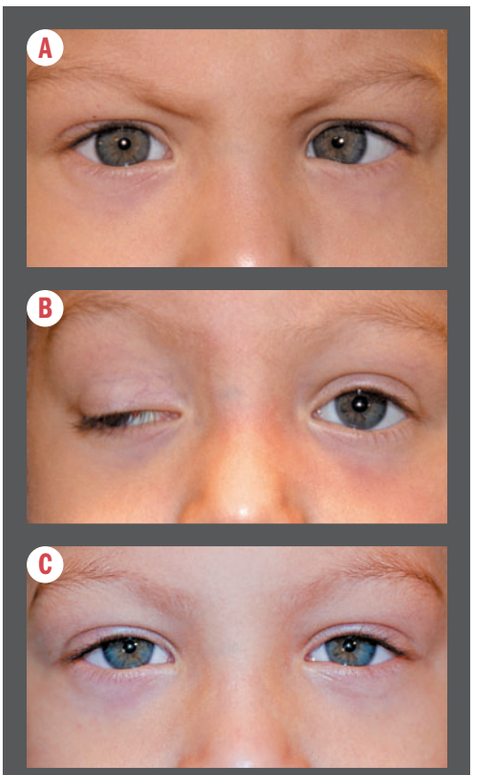
BTX-A treatment has limitations as well as advantages. For instance, it has a limited duration of action and can only weaken, not strengthen, the extraocular muscles. It also has a relatively modest effect on alignment with a single injection, and there are no long-term decreases in force generation.

As a result, many patients need re-injections.

"Parents do not like that," Dr. Christiansen said. "They want their child taken care of in a single operation."

Another issue with BTX-A is orbital leakage accompanying the injection, which can have collateral effects on other extraocular muscles and perhaps on the ciliary ganglion. Tonic pupil has also been reported following BTX-A injection.

These drawbacks have sent investigators in pursuit of an ideal agent for strabismus that would be titratable, last long enough for sensory and motor adaptation to occur, create perma-



A Appearance of a 1-year-old child with infantile esotropia prior to treatment. Prism and alternate cover testing showed a 25 prism-diopter esotropia.

B One week after injection of both medial rectus muscles with 4 units of botulinum toxin A. The child has a large-angle exotropia and bilateral asymmetric ptosis.

C Good long-term alignment was achieved with a single bilateral medial rectus injection of botulinum toxin A.

(Images courtesy of Stephen P. Christiansen, MD)

Continues on page 33 : ***Strabismus***

Pearls for penetrating orbital injury

Advances in imaging technology enhance physicians' understanding about foreign body

By Cheryl Guttman Krader; *Reviewed by James C. Fleming, MD*

MEMPHIS, TN ::

THE NEED FOR INTERVENTION in patients with an intraorbital foreign body depends on the ability to localize the retained material and determine the full extent of injury. Success with each of these measures depends on knowledge of the physics of traumatic injuries, features of orbital anatomy, and the unique characteristics of different foreign body materials and imaging modalities.

Understanding of the physics of traumatic injuries is the basis for understanding the extent of intraocular damage, said James C. Fleming, MD, chairman, Department of Ophthalmology, and the Philip M. Lewis Professor of Ophthalmology, University of Tennessee Health Science Center, Hamilton Eye Institute, Memphis, TN.

The object's mass and velocity affect its ability to penetrate orbital tissues as well as the cavitation effect that is produced, which will determine if there is damage disseminated distant from the site where the foreign body lies.

In terms of anatomic considerations, Dr. Fleming said the orbit is a conically shaped compartment with internal structures, including extraocular muscles and a septal system. Foreign bodies entering the conical orbit are driven back to the apex, and trauma from a penetrating foreign body to the extraocular muscles and septal system can affect ocular movement.

CHARACTERISTICS

The composition of the foreign body determines its visibility on imaging and reactivity within the orbit. Although foreign bodies can be classified based on whether they are inorganic (metal, glass, fiberglass, plastic) or organic (plant material), no generalizations can be made based on those categorizations.

Among inorganic materials, even minimally sized metallic foreign bodies can be detected with plain radiography. Plastic and fiberglass look like air, and the identification of glass fragments depends on their size and whether the glass contains lead or is colored because of metal content (e.g., cobalt or gold).

Dry wood is relatively easy to detect on computed tomography (CT) or magnetic resonance imaging (MRI) where it looks like linear air but with a cylindrical shape. Discriminating between air and wood on CT requires proper setting and understanding of the monitors of the display scale and using "lung" presets on the CT views. As another clue, "linear air" associated with the presence of dry wood will remain if imaging is repeated after a few days, but will have disappeared if it was only air.

However, due to its water content, green wood is difficult to find with either CT or MRI.

"Inflammation will be seen surrounding retained wood and that can be identified with gadolinium enhancement," he said. "We are almost doomed to identifying green wood on imaging only after waiting for inflammation to set up."

Looking for delayed inflammation with repeat imaging is probably also the best way to determine complete success in removing wood foreign bodies, he added.

Whether it is necessary to remove an intraocular foreign body depends in part on the material. Glass, plastic, and many metals are inert and therefore can be left alone if they are not causing problems or anticipated to lead to issues based on their resting location.

Exceptions are in cases of metallic foreign bodies made of pure copper, iron, or lead in its pure form, and for patients with any metallic foreign body needing MRI of the head in the future.

SURGICAL TIPS

When extracting foreign bodies, Dr. Fleming recommended placing a ribbon retractor or some other instrument behind fragments whenever possible to prevent them from being propelled posteriorly during the retrieval attempt. He also advised following the missile track carefully to find the terminal site of injury and to anticipate that multiple fragments are retained.

Intraoperative stereotactic localization with preoperative CT or MRI may not be helpful in guiding foreign body extraction since soft tissue landmarks can change intraoperatively and cannot be tracked. "C" arm localization may be better, but it provides limited soft tissue differentiation.

Intraoperative MRI and CT systems are now available that allow for real-time imaging in the operating room or intensive care unit. ■

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Dr. Fleming reviewed these principles in his delivery of the Wendell Hughes Lecture at the 2013 meeting of the American Academy of Ophthalmology. Dr. Fleming has no relevant financial interests to disclose.

STRABISMUS

(Continued from page 32)

nent change in the globe's rotational position, and would not create significant inflammation or cause unwanted collateral damage, he said.

Growth factors, such as IGF I and II, are showing excellent results so far. These agents increase motor strength, giving surgeons a way to both weaken and strengthen the muscle. Toxins besides BTX-A are being studied, as are immunotoxins (ricin-mAb 35 and other fusion proteins).

Injection of the anesthetic bupivacaine, an off-label use of this agent, is another innovation in strabismus treatment, first advocated by Alan B. Scott, MD, of the Smith-Kettlewell Eye Institute, San Francisco, about 8 years ago. Bupivacaine causes fiber hypertrophy, creating large, stiff muscles.

"Bupivacaine by itself doesn't have a huge effect on alignment, but if you weaken a rectus muscle with BTX-A and strengthen the antagonist with bupivacaine, you do get a significant change in the rotation," Dr. Christiansen said. ■

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Dr. Christiansen did not report any financial interests or relationships.

Anti-VEGF therapy: Safety trends

Clinical data provide limited insights on anti-vascular endothelial growth factor treatment systemic effects

By Cheryl Guttman Krader; *Reviewed by Pravin U. Dugel, MD*

TAKE-HOME

- ***Analyses of data from large clinical trials have been undertaken to determine how patient age and treatment-specific variables may influence the systemic safety of anti-vascular endothelial growth factor treatment.***

Though it is known that intravitreal treatment with anti-vascular endothelial growth factor (VEGF) agents can be associated with systemic effects, a paucity of statistically definitive data is the basis for ongoing controversy about the clinical impact.

"We won't ever have definitive clinical trials on the systemic safety of intravitreal anti-VEGF agents, and so it is all the more important now to look at the totality and directionality of the important trends in what is the most important of all issues for our patients—their safety," said Pravin U. Dugel, MD, managing partner, Retinal Consultants of Arizona, Phoenix.

Dr. Dugel

"We know we should [look] at major arteriothromboembolic events (ATEs), and we know the most vulnerable patients—those 85 years and older—are at increased risk," said Dr. Dugel, also clinical associate professor of ophthalmology, Keck School of Medicine, University of Southern California, Los Angeles.

There appears to be no drug or dose effect with ranibizumab (Lucentis, Genentech), but there may be a treatment regimen effect. There may also be differences in systemic exposure and safety profiles among different anti-VEGF agents.

AT INCREASED RISK?

The question of whether patients aged ≥85 years are at increased risk for ATEs with intravitreal anti-VEGF treatment was investigated in a logistic regression analysis using data from the ranibizumab MARINA and ANCHOR studies.

With patients stratified by age, ATE rates were higher among patients aged ≥85 years than in the younger cohort. This effect of age was confirmed in an analysis pooling data for patients treated with the commercially available dose of ranibizumab 0.5 mg in the MARINA, ANCHOR, PIER, SAILOR, and HARBOR studies.

Additional data analyses from MARINA and ANCHOR showed no drug effect or dose effect comparing patients treated with ranibizumab 0.3 or 0.5 mg. Also, no dose effect was identified in the HARBOR trial comparing groups treated with ranibizumab 0.5 versus 2 mg.

However, an analysis of data from HARBOR showed a treatment regimen effect. Among patients aged ≥85 years, the ATE rate was higher among those receiving monthly injections compared with those being treated as needed.

Whether differences in systemic safety exist among the three most commonly used anti-VEGF agents is perhaps the most controversial question, Dr. Dugel said.

The agents differ structurally—aflibercept (Eylea, Regeneron) and bevacizumab (Avastin, Genentech) contain the Fc portion of IgG1, whereas ranibizumab does not.

Data from the IVAN study showed bevacizumab caused more systemic VEGF suppression than ranibizumab, whereas a study by Yu et al. showed the two Fc-containing agents, aflibercept and bevacizumab, achieve a higher serum concentration than ranbizumab.

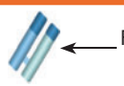
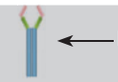
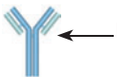
ADVERSE EVENT RATE

Comparative data on serious adverse events (SAEs) was first provided by CATT—bevacizumab-treated groups had a higher SAE rate than ranibizumab groups, and the difference among groups continued to increase over time.

More recently, data from the VIEW studies comparing ranibizumab and aflibercept was released in the European Public Assessment Report. Analyses focusing on patients aged ≥85 years showed that after 1 year, the rate of cardiovascular events was higher among ranibizumab-treated patients whereas the rate of cerebrovascular events was higher among patients treated with aflibercept.

During the second year, the between-treatment difference in cardiovascular rate trended to normalize, but the difference between groups in cerebrovascular event rates remained. ■

Molecular Differences Between VEGF Inhibitors

VEGF INHIBITOR	STRUCTURE	MOLECULAR WEIGHT	MOLECULAR CHARACTERISTICS
Ranibizumab[1]	 Fab	48 kDa	Fab fragment (no Fc portion*)
Aflibercept[2]	 Fc portion	115 kDa	Fusion protein (Fc-containing)
Bevacizumab†[3]	 Fc portion	149 kDa	Full-length monoclonal antibody (Fc-containing)

* Responsible for recycling via the FcRn receptor

† NB: Bevacizumab is not indicated for intravitreal use

VEGF, vascular endothelial growth factor; Fab, antigen binding fragment; Fc , fragment crystallizable region; FcRn, the neonatal Fc receptor for IgG; kDa, kilodalton

1. Highlights of prescribing information. http://www.gene.com/gene/products/information/pdf/lucentis-prescribing.pdf. Accessed May 30, 2012.
2. Highlights of prescribing information. http://www.regeneron.com/Eylea/eylea-fpi.pdf. Accessed May 30, 2012.
3. Highlights of prescribing information. http://www.gene.com/gene/products/information/pdf/avastin-prescribing.pdf. Accessed May 30, 2012.

(Figure courtesy of Pravin U. Dugel, MD)

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Dr. Dugel is or has been a consultant for Genentech, Novartis, and Regeneron.

LED ILLUMINATION
This optical dispensary is enhanced by the use of light-emitting diode (LED) lighting.

DARKER COLORING
The darker wall paint and contrasting cream-colored flooring help make this dispensary's frame boards stand out.
(Images courtesy of Eye Designs)

TRENDING NOW:

Optical dispensary designs, furnishings

How LED lighting, color contrasting, and modernization are transforming optical shop displays

By Rose Schneider, *Content Specialist,* Ophthalmology Times

The design and functionality of an optical dispensary are highly important aspects to an ophthalmologist's practice, but choosing ideal color schemes and fixture plans that will optimize patients' experience is key.

While there are endless options from which to choose, Dan Sloan—a designer for Fashion Optical Displays, Paradise, CA—said he has recently seen a shift to light-emitting diode (LED) lighting, hardwood flooring, color, and furniture schemes that are a mix between traditional and contemporary, and a focus on improving merchandise display organization.

LED LIGHTING

"Lighting is now becoming a crucial component of the optical design," said Melanie Nicholson, an interior designer for Eye Designs, Collegeville, PA. "Proper illumination of the optical (dispensary) can affectively change the mood of the space."

In the past, Sloan said LED lighting was less common than standard halogen lighting because it had high Kelvin ratings, which caused light fixtures to look "awfully funny" in the dispensaries, almost emitting a purplish color.

But with growing technology over the years, he said, LED lighting now produces "that nice

Continues on page 36 : ***Dispensary design***

In Brief

Innovative technology

B + L BEGINS ROLL OUT OF NEW CONTACT LENSES

BRIDGEWATER, NJ :: **BAUSCH + LOMB HAS BEGUN** the initial rollout of its Ultra monthly replacement silicone hydrogel contact lens with MoistureSeal technology.

The new lens technology—which was studied and developed for 7 years—combines a material with new manufacturing processes to produce a contact lens that breaks the cycle of discomfort for comfort all day, according to the company.

"The level of excitement for this new technology among eye-care professionals underscores the increasing need for a lens that breaks the cycle of discomfort and better addresses the demands of today's contact lens user," said Joseph Barr, OD, MS, FAAO, vice president, medical affairs, Pharmaceuticals and Vision Care, Bausch + Lomb. "With patients spending more than 10 hours each day using digital devices, we know that it is critical to surpass current standards for comfort, vision, and eye health. We believe that Bausch + Lomb Ultra does just that."

The Ultra contact lenses are now distributed in select markets with a national rollout scheduled for this spring.

Recognition ceremony

PREVENT BLINDNESS HOSTS PERSON OF VISION AWARDS

NEW YORK :: **PREVENT BLINDNESS** has chosen Zyloware Eyewear's Bob Shyer, chairman, and Henry Shyer, vice chairman, as its 2014 Person of Vision Award recipients. The awards will be presented at the organization's Person of Vision Dinner on March 27 at the New York Palace, New York.

The Person of Vision Award recognizes an individual or corporation for outstanding leadership and dedication in the field of vision and eye health. Zyloware Eyewear is the oldest independent family owned frame supplier in the United States. Bob and Henry Shyer were chosen because of their contributions to the vision industry and for continuing their family legacy and business which now spans decades.

Co-chairpersons of the 2014 Person of Vision Committee are Zyloware's Chris Shyer, president, and Jamie Shyer, chief operating officer. ■

DISPENSARY DESIGN

(Continued from page 35)

warm glow," similar to halogen lighting, but uses less energy and produces less heat.

More physicians are requesting decorative chandeliers, scones, and frame displays with LEDs as well, Nicholson added.

"Using the proper LED lighting can really make the frames and brands that you're featuring pop, drawing customers in and grabbing their attention," she said.

FLOORING

Both Sloan and Nicholson said physicians have begun to lean more toward wood flooring, as opposed to traditional carpeting.

"Hard surfaces make it look more high-end," Nicholson said.

TAKE-HOME

- ***Optical dispensary designers discuss what they have seen this year as far as lighting, fixture plans, visual merchandising, and color scheme trends.***

Flooring color requests have begun to shift toward the dark end of the scale, Sloan said, such as darker stain or espresso coloring, to add more of a contrast between display fixtures and the floor.

"That seems to be trending pretty heavily," Sloan said.

To accomplish the same outcome, Nicholson said she has seen requests for grays and neutral creams, which are accented by the now trending splash of color that can be seen incorporated in seating, imagery, and tile in the practice's reception area.

However, some physicians are opting for wood plank ceramic tile or vinyl plank over hardwood flooring, Nicholson noted, due to pricing.

FURNITURE, ORGANIZATION

Frame boards have had a complete overall, as physicians are now realizing that—to make the process of finding the right pair of frames easier for patients—organization is of the upmost importance.

"Merchandising elements are key to letting your customers know what you are selling and the brands that you carry," Nicholson said. "It is so frustrating to walk into a doctor's practice and see a wall of frames. Frame boards need visual breaks so the eye can rest and give direction to the frames that are meant for them."

Nicholson suggested adding small signage within the frame board to help distinguish gender, styles, and brands.

Joost Bende, president and principal architect for Pacific 33 Architects Inc., San Diego, said he has seen a shift toward opting out of frame boards completely, and instead using glass shelves or other unique displays to help the products stand out to patients.

If the physician would like to stick with frame boards, Sloan suggested breaking up the boards with shelving or putting the frames into collections, which would create better ease for patients.

Feature walls have also become quite popular, according to Nicholson, along with areas to incorporate new products and brand merchandising.

"Offices are adding three-dimensional wall dividers with cutout to create a unique look," she added.

Updating the optical dispensary's overall look to be more up-to-date visually has been a common theme seen by Sloan, Nicholson, and Bende.

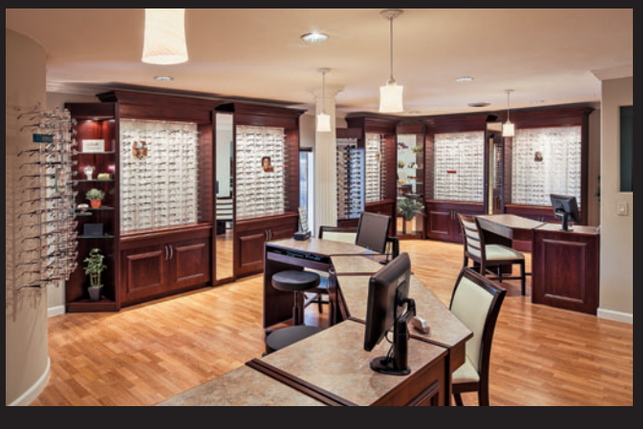
"Overall designs of the office are becoming less clinical and more retain driven," Nicholson said. "People are looking for the cool factor in the design of a new space with more of a contemporary feel."

Bende added that he has seen the trend moving toward a "very modern look, linear and simple," while Sloan said he has seen more combinations of old and new.

"(They) aren't purely traditional or contemporary, but a fusion of the two," he said. ■

ORGANIZING FRAME BOARDS
Frame boards are broken up to make the process of finding the right pair of frames easier.

FUSION STYLING
This dispensary captures a combination of modern and traditional furnishing to create an updated look.



WOOD FLOORS
Wood flooring is utilized in this optical dispensary for a sleeker feel.
(Images courtesy Fashion Optical Displays)

In Brief

Range of applications

ADLENS LAUNCHES VARIABLE-FOCUS EYEWEAR WITH IMPROVED OPTICS

OXFORD, UNITED KINGDOM ::

ADLENS INTRODUCES ADJUSTABLES, its latest variable-focus eyewear product.

Each lens consists of two wave-shaped plates that glide across each another to alter the power of each lens, correcting more than 90% of spherical errors (lens power –6 D to +3 D). Although the improved optics result in an optimized reading zone, Adjustables were designed for a range of applications—such as up-close work, computer use, yard work, and for managing fluctuating vision in diabetes patients or after eye surgery.

Along with enhanced optics, Adjustables offer an aesthetic pair of glasses. The brow bar is more ergonomic for a modern look, the nosepiece is adjustable for a comfortable fit, and the frame and temple arms were designed to give the glasses a lightweight feel. Adlens Adjustables are available in black, blue, gray/black, and red/black, followed soon by a new range of colors.

One-stop service

SANTINELLI BOOSTS ITS LINE OF DISPENSARY TOOLS, SUPPLIES

HAUPPAUGE, NY ::

SANTINELLI INTERNATIONAL HAS used its 40th anniversary to re-launch its optical supplies product line. According to the company, Santinelli offers one-stop service for both dispensary and finishing needs.

Products for in-office labs highlight such staples as nose pads, temple tips, and screws, but also include unique workshop items. One featured line is the Visionary Plier Collection, developed by Breitfeld & Schliekert, a German company known for craftsmanship and functional products.

"We are thrilled to provide our clients the ability to order a wide array of the optical tools and supplies they need to successfully run their practice," said Gerard Santinelli, president and chief executive officer.

An e-catalog is available on the company's website: *www.santinelli.com.* ■

(Images courtesy of Adlens and Viva International Group)

Marciano puts a new spin on sophisticated eyewear

NEW YORK ::

THE MARCIANO optical collection from Viva International Group updates its signature style with colorful modern details.

The dramatic cat-eye silhouette of model GM 199 has satin metal finishes in gold, burgundy, and black. Transparent horn temple tips complement this simple elegant frame in shades of black, burgundy, and tortoise, as well as blue and green horn.

The retro-inspired model GM 201 offers rich jewel-tone horn colorations in teal, purple, brown, and black throughout. Acetate fronts, double-plated metal temples, and acetate temple tips set off the rectangular shape. ■

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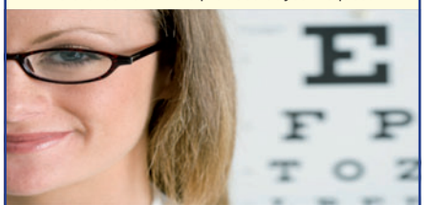

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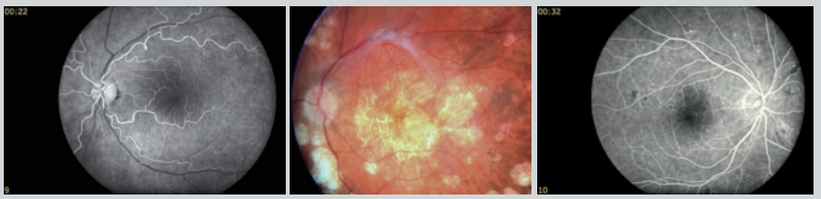

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How 'Obamacare' impacts eye health disparities

Provisions of Affordable Care Act may be able to reduce vision health inequalities

By Rose Schneider, *Content Specialist,* Ophthalmology Times

TAKE-HOME

- ***Vision health disparities are a serious issue in the United States among minorities, and many are hoping provisions in the Affordable Care Act will be able to alleviate the issue.***

DETROIT ::

Disparities in vision and eye health-care opportunities among minorities is a big problem in the United States, according to M. Roy Wilson, MD, MS.

Furthermore, these disparities have resulted in a high number of unnecessary vision loss among American minorities, as 6.9% of African Americans and 9.2% of Hispanics have impaired vision that could be easily remedied with eyeglasses, said Dr. Wilson, president of Wayne State University, Detroit.

"There are a number of ophthalmic diseases for which there are disparities based on either race, ethnicity, or socially economic status," he said.

Though many physicians see the disparities problem as exclusively an access issue, Dr. Wilson said he believes there are more factors that play a role as well.

"There is lots of evidence it's not just access," said Dr. Wilson, who is also the former deputy director for strategic scientific planning and program coordination at the National Institute on Minority and Health Disparities (NIMHD) of the National Institutes of Health (NIH).

"The problem is much more widespread," he continued.

That is where the Affordable Care Act (ACA) will come into play, Dr. Wilson said, as the health-care overhaul has the potential to reduce the dilemma greatly, while addressing its various causes.

ACA IMPACT

There are four areas, Dr. Wilson explained, in which the ACA may have a significant impact on decreasing vision related disparities among minorities:

1. INFRASTRUCTURE: **The ACA has elevated the National Center for Minority Health and Health Disparities into the NIMHD. The act has given the newly formed agency overall responsibility for strategic planning and program coordination for all the health disparities related to research and training for the entire NIH. The act also established the Office of Minority Health in the Health and Human Services Department, as well as in other government offices like the Centers for Disease Control and the Centers for Medicare and Medicaid.**

2. ACCESS: **The health-care overhaul included many increased access provisions, including Medicaid expansion, insurance regulation/the American health benefit exchange, community health centers creation, as well as prevention and wellness additions. These specific changes the ACA brings could turn out to make a large impact on accessibility to health care by minorities—"simply because more minorities (currently) have difficulty with access," he added.**

3. HEALTH-CARE WORKFORCE AND CULTURAL COMPETENCY: **There are a number of provisions associated with this area, as its intent is to improve the diversity of the workforce.**

4. QUALITY IMPROVEMENT: **The ACA will increase data collection and research to improve the quality of health-care for minorities.**

RESEARCH AND DATA COLLECTION

Dr. Wilson said he believes quality of health care, not just access to it, is one of the most critical aspects in regard to vision-related disparities.

"To me, one of the most important things the ACA did with respect to health disparities, is that all federal funded health programs and surveys are now required to collect and report on every patient's race, ethnicity, and language preferences using Health and Human Services definitions with the goal of ultimately reducing disparities," he said.

Another way the ACA is encouraging further data collection and research to combat disparities is through electronic health records (EHRs).

Dr. Wilson explained that many physicians have advocated for some type of national eye health surveillance mechanism to reduce disparities in vision and eye health.

"There's a lot of potential for (EHRs here)," he said.

> Inequities in vision and health care extend beyond access, notes M. Roy Wilson, MD, MS.

This method could still be an issue, because not all physicians have EHRs, Dr. Wilson said.

"(However), the ACA is moving most practitioners in that direction," he said. "There is potential for going from individual data to population data, which will facilitate health surveillance on a population level, which can then be used to track and monitor progression and outcomes of disease better to address health disparities."

But EHRs cannot accomplish this alone, Dr. Wilson said. Some kind of system that brings all the necessary components together and to analyze them is needed.

One of the ways to do this is through clinical data registry, he said.

"This is an area that has much potential, because if you track data by . . . race and ethnicity and language preference, then you're going to get better care all the way around," Dr. Wilson said. "Hopefully, for most of those conditions that you're tracking, you're going to

Continues on page 42 : ***Disparity***

BAUSCH + LOMB

LOTEMAX®

loteprednol etabonate
ophthalmic gel 0.5%

Brief Summary: Based on full prescribing information.

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb at 1-800-323-0000 or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch

INDICATIONS AND USAGE

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

DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once to fill tip before instilling drops.

Apply one to two drops of LOTEMAX into the conjunctival sac of the affected eye four times daily beginning the day after surgery and continuing throughout the first 2 weeks of the post-operative period.

CONTRAINDICATIONS

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

WARNINGS AND PRECAUTIONS

Intraocular Pressure (IOP) Increase

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. Steroids should be used with caution in the presence of glaucoma. If this product is used for 10 days or longer, intraocular pressure should be monitored.

Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

Delayed Healing

The use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification such as slit lamp biomicroscopy and, where appropriate, fluorescein staining.

Bacterial Infections

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

Viral Infections

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

Fungal Infections

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

Contact Lens Wear

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

ADVERSE REACTIONS

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

The most common adverse drug reactions reported were anterior chamber inflammation (5%), eye pain (2%), and foreign body sensation (2%).

USE IN SPECIFIC POPULATIONS

Pregnancy

Teratogenic Effects: Pregnancy Category C.

Loteprednol etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic (increased incidence of meningocele, abnormal left common carotid artery, and limb flexures) when administered orally to rabbits during organogenesis at a dose of 3 mg/kg/day (35 times the maximum daily clinical dose), a dose which caused no maternal toxicity. The no-observed-effect-level (NOEL) for these effects was 0.5 mg/kg/day (6 times the maximum daily clinical dose). Oral treatment of rats during organogenesis resulted in teratogenicity (absent innominate artery at ≥5 mg/kg/day doses, and cleft palate and umbilical hernia at ≥50 mg/kg/day) and embryotoxicity (increased post-implantation losses at 100 mg/kg/day and decreased fetal body weight and skeletal ossification with ≥50 mg/kg/day). Treatment of rats with 0.5 mg/kg/day (6 times the maximum clinical dose) during organogenesis did not result in any reproductive toxicity. Loteprednol etabonate was maternally toxic (significantly reduced body weight gain during treatment) when administered to pregnant rats during organogenesis at doses of ≥5 mg/kg/day.

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

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

Nursing Mothers

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

Pediatric Use

Safety and effectiveness in pediatric patients have not been established.

Geriatric Use

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

NONCLINICAL TOXICOLOGY

Carcinogenesis, Mutagenesis, Impairment Of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate. Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma tk assay, or in a chromosome aberration test in human lymphocytes, or *in vivo* in the single dose mouse micronucleus assay. Treatment of male and female rats with up to 50 mg/kg/day and 25 mg/kg/day of loteprednol etabonate, respectively, (600 and 300 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender.

PATIENT COUNSELING INFORMATION

Administration

Invert closed bottle and shake once to fill tip before instilling drops.

Risk of Contamination

Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the gel.

Contact Lens Wear

Patients should be advised not to wear contact lenses when using LOTEMAX.

Risk of Secondary Infection

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

FOR MORE DETAILED INFORMATION, PLEASE READ THE PRESCRIBING INFORMATION.

Bausch & Lomb Incorporated
Tampa, Florida 33637 USA
US Patent No. 5,800,807

DISPARITY

(Continued from page 40)

reduce the difference between different populations' outcomes."

LOOKING FURTHER

Another route the ACA will utilize research to combat health disparities is through the creation of the Patient-Centered Outcomes Research Institute (PCORI).

Dr. Wilson said PCORI assures that research will address the health-care needs of all patient populations, which is needed, as treatments may not work equally for everyone.

Though Dr. Wilson said he believes these ACA provisions and agency creations will most certainly alleviate eye health disparities, because of the act's difficult rollout, the exact impact is still up in the air.

"One of the issues with the ACA is a lot of it hasn't been implemented and there's been a lot of hold up," he said. "So even though a lot of the provisions have been passed, they haven't been funded.

"Because of political considerations, some of this is still in doubt," he added. "How many of those are actually implemented . . . will depend on a lot of political factors and will ultimately determine how effective the ACA is in addressing health disparities." ■

M. ROY WILSON, MD, MS
P: *313/577-2230* E: *president@wayne.edu*
Dr. Wilson did not indicate a financial interest in the subject matter.

Maneuvering around problems with the ACA

By Lynda Charters

COLUMBIA, MD ::

THE AFFORDABLE CARE ACT (ACA) was designed to provide health insurance for millions of uninsured citizens with no exclusions for pre-existing conditions, expand services like screening and preventive health coverage, and be less costly for patients and the government.

Considering the troublesome initial operation of the ACA sign-up website, David Glasser, MD, who is in private practice in Columbia, MD, speculated about the future of the program.

"My first prediction is that some form of 'Obamacare' will be around long after President Obama leaves office," he said.

However, a number of questions arise when he considers the future of the ACA, such as whether there will be more government regulations, potential loss of patients, limited therapeutic options, and physician reimbursement.

"There are definitely more government 'hoops,'" he noted.

Physicians may also have fewer patients since healthy individuals may not sign up for health coverage because of cost, and with only sick individuals signing up, the insurance will be more expensive.

Dr. Glasser said a cost-cutting measure is to limit provider networks to those willing to discount the cost of coverage heavily.

"The ability to see patients will depend on if the carrier accepts physicians into their network and if the carrier payments are acceptable to physicians," he said.

Therapeutic options may be subject to cost-cutting measures also, he proposed.

"Carriers will start contracting with limited hospitals and ambulatory surgical centers that provide a good deal, which may not be where a physician has privileges," he said.

Dr. Glasser said he wonders if there will be problems with payments for corneal tissue and more adverse medical necessity determinations that may make it more difficult for certain procedures to be performed.

Dr. Glasser advised that physicians simplify when possible. He recommended using the American Academy of Ophthalmology's IRIS Registry to remove the busy work from an electronic health records system, read contracts, and tell the ambulatory surgical centers to analyze their contracts for potential tissue payment issues. ■

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- Cataracts—Use of corticosteroids may result in posterior subcapsular cataract formation
- Delayed healing—Use of steroids after cataract surgery may delay healing and increase the incidence of bleb formation and occurrence of perforations in those with diseases causing corneal and scleral thinning. The initial prescription and renewal of the medication order should be made by a physician only after examination of the patient with the aid of magnification
- Bacterial infections—Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infection. In acute purulent conditions, steroids may mask infection or enhance existing infections
- Viral infections—Use of corticosteroid medication in the treatment of patients with a history of herpes simplex requires great caution. Use of ocular steroids may prolong the course and exacerbate the severity of many viral infections of the eye (including herpes simplex)
- Fungal infections—Fungal infections of the cornea are particularly prone to develop coincidentally with long-term local steroid application. Fungus invasion must be considered in any persistent corneal ulceration where a steroid has been used or is in use
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- The most common ocular adverse drug reactions were anterior chamber inflammation (5%), eye pain (2%) and foreign body sensation (2%)

Please see brief summary of full prescribing information on adjacent page.

*Ophthalmic corticosteroid.

References: 1. LOTEMAX GEL Prescribing Information, September 2012. **2.** Fong R, Leitritz M, Siou-Mermet R, Erb T. Loteprednol etabonate gel 0.5% for postoperative pain and inflammation after cataract surgery: results of a multicenter trial. *Clin Ophthalmol.* 2012;6:1113-1124. **3.** Data on file, Bausch & Lomb Incorporated.

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