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REVIEW® OF OPTOMETRY

January 15, 2016

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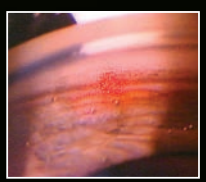

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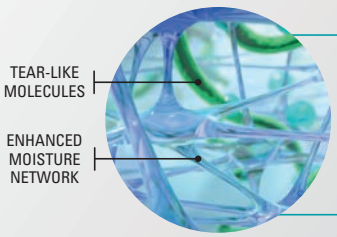

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VOL. 153 NO. 1 ■ JANUARY 15, 2016

IN THE NEWS

A new policy statement issued by the **American Academy of Pediatrics** emphasizes the importance of including instrument-based devices for **pediatric vision screening** for infants as young as 12 months, which should be repeated from ages two through five. The updated schedule also recommends **direct visual acuity testing** for ages four and five, and even cooperative three-year-olds.

The $1.1 trillion omnibus spending bill recently passed by Congress and signed into law by President Obama includes a **two-year suspension of the 2.3% medical device excise tax**. According to the agreement, the medical device excise tax will not be eligible for reinstatement until the 2018 fiscal year.

A study recently published in the *Journal of Pain* found a link between **dry eye and chronic pain syndromes**. Researchers at Bascom Palmer Eye Institute evaluated 154 dry eye patients and found they reported **higher levels of ocular and non-ocular pain** associated with chronic pain syndromes, and had lower scores on depression and quality-of-life indices. The findings suggest a **multidisciplinary approach** used for chronic pain treatment may also benefit patients with dry eye.

When pairs of study participants held each other's gaze, researchers at the National Institute of Physiological Science noted a **synchronization of eye-blinks** and enhanced **inter-brain synchronization** in the right inferior frontal gyrus. The findings suggest **mutual eye contact** might be a crucial component for human **face-to-face social interactions**.

New Technology for Dry Eye Treatment

An implantable device that stimulates tear production could offer hope for those suffering from DED.

By Michael Riviello, Associate Editor

Stanford University investigators recently unveiled a device that electronically stimulates tear production, hoping it will one day provide relief to patients with dry eye.

They implanted the wirelessly controlled device into rabbit eyes below the inferior lacrimal gland. It successfully increased tear generation by approximately 57%, according to the study.

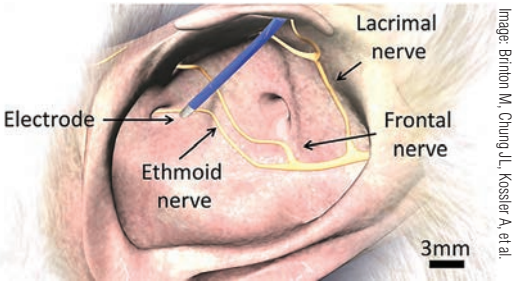

Image: Brinton M, Chung JL, Kossler A, et al.

A monopolar electrode was inserted through the caudal supraorbital incisure and advanced behind the globe toward the ethmoid nerve foramen.

First, the research group stimulated the lacrimal gland directly, which increased tear secretion by engaging efferent parasympathetic nerves, according to the study. Tearing increased proportionally with an electronic pulse of increasing strength, duration and frequency. The most effective form of stimulation was determined by measuring the tear secretion rate using the Schirmer test.

They also discovered that activating the ethmoid nerve prompted reflex tearing and offered an even more efficient way to enhance tear production.

The next phase of the research will be to evaluate the quality of the tears produced, according to the study. The device is currently being studied in clinical trials to determine maximum efficiency and safety, which the researchers hope will lead to FDA approval.

"I hope to see it on the market in the next year," said Daniel Palanker, PhD, author of the study and professor at Stanford University, in a press release. "Meanwhile, we're continuing research into the mechanisms of the tearing response, its enhancement and quality of the tears produced by neural stimulation."

Dr. Palanker believes these devices could be the way of the future. "We think that these types of implants can be used in many other indications, especially in the peripheral neural system, including afferent (signaling) and efferent (controlling the organs and muscles) nerves," says Dr. Palanker.

Brinton M, Chung JL, Kossler A, et al. Electronic enhancement of tear secretion. J Neural Eng. 2015;13(1).

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New OD School Debut Sparks Debate

Growth within a profession is usually a celebrated event, but not everyone applauded as the University of Pikeville-Kentucky College of Optometry (KYCO) announced it is recruiting for its inaugural class in 2016. Though it may serve a regional need, some ODs have concerns over its national impact.

"Acceptance rates for medicine and other health care professions are around 40%, and at the moment, optometry has an acceptance rate of 70%," says Dominick Maino, OD, MEd, a professor at Illinois College of Optometry. "Although this has not appeared to affect the quality of our entering classes, at some point I would suspect that quality will suffer."

Another major concern is the influx of graduates.

"I think we are already crowded [in the profession], and you have to add in, of course, the market forces that are going on," says Bill Potter, OD, chief of Optometry and Contact Lens Services at Millennium Eye Care in West Freehold, NJ. "Health care incomes don't seem to be going up, so if you start to drown the market with job candidates, it's not going to get any better. It's a good possibility that, long-term, they are going to drive down average incomes."

Despite these concerns, KYCO has some key selling points. It's the only optometry school in Kentucky, West Virginia, Virginia, North Carolina, South Carolina or Georgia and hopes to address a growing need in rural Appalachia, a region with the highest incidence of severe vision loss, according to a University press release.

"The theory is, if you put the school in a relatively underserved regional area, it will help," Dr. Potter says. While that's a noble goal that seeks to fulfill a public health need, Dr. Potter wonders whether or not the region will be able to retain those new ODs when they enter practice. "People are so mobile these days that I am not convinced it is going to pump up the region."

The location also offers unique learning options.

"Given that the University of Pikeville-Kentucky College of Optometry was coming to the area, the board and key leaders in optometry in Kentucky felt it must be a best-in-class educational institute," says Paul M. Karpecki, OD, director of clinical research and head of the ocular surface disease clinic at the Koffler Vision Group in Lexington, Ky. "Because of the expanded scope of practice in Kentucky, students will be proficient in advanced diagnostics, including selective laser and periocular surgical procedures."

This could be a key selling point, says Dr. Potter.

"That is a big positive, at least in terms of potential, because it is a drawback in states that have optometry schools historically where the laws were restrictive. If the school is already up and running with privileges, that is a big positive for sure."

Yet, many ODs are still unsure. "Speaking as an individual, I have to wonder why any university at this time would want to consider building a new school or college of optometry," Dr. Maino says. "In 2014, there were 2,604 applicants for 1,789 seats; if this trend continues, schools and colleges of optometry will be fighting to fill a class with qualified students."

"I think skepticism on this is healthy," Dr. Potter concludes. "The benefit of this needs to be shown, and I'm just not positive it will have the desired effects. The negative effect, of course, is if you are pumping in more grads, something's gotta give, and what's going to give is going to be the incomes."

Sight Gags By Scott Lee, OD

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Physicians Skipping Funduscopy

According to a recent study published in *Frontiers in Neurology*, patients are receiving funduscopic evaluations at insufficient rates from physicians in disciplines other than eye care.[1]

The retrospective study reviewed 163 randomly selected charts of patients who presented to the emergency department (ED) with complaints of headaches, altered mental states and visual symptoms such as diplopia and vision loss. For patients complaining of headaches, only 25% were tested with funduscopy, visual symptoms only 26% and altered mental state only 5%.

"To an emergency doctor, a headache represents a neurological complaint," says Andrew S. Gurwood, OD. "When tasked with examining a patient with a chief complaint of headache, they know looking inside the eye may provide corroborating information regarding the status of the patient's general health and whether or not disc edema is present. However, incident stabilization is their priority."

"One possible explanation for ophthalmoscopy being omitted is the team approach," Dr. Gurwood adds. "Emergency rooms often have access to eye care departments with experienced practitioners on call. Asking for a consult may, in their minds, ensure the most accurate data is gleaned along with an expert interpretation. Also, emergency physicians not in the practice of doing funduscopy on a routine basis may not have the expertise necessary to view a fundus through an undilated pupil or in the non-optimal environment of the ED."

The study accounted for that, too, finding that the ophthalmology department was called in for only 53.4% of the visual symptom cases and 12.5% of headache cases. Possible reasons for this may include insufficient exam time, inadequate practitioner skills, lack of available equipment and a general belief that the technique is not useful.[2]

Dr. Gurwood suspects the issue is multifaceted. "Since undilated funduscopy is a practiced skill that requires repetition under the best of conditions, because emergency doctors are not willing to dilate patients in the ED and EDs have 'phone call' access to eye care professionals, it's just easier to ask for a consult to get that data," Dr. Gurwood says. "I'll bet they try funduscopy, but when they don't see inside the eye well, they don't record that. Instead, they recognize they need that data and make an easy phone call. Looking inside the eye is valuable, no one disputes that; I feel confident no eye care professional would omit the procedure in these cases."

1. Golombievski E, Doerrier MW, Ruland SD, et al. Frequency of direct funduscopy upon initial encounters for patients with headaches, altered mental status and visual changes: a pilot study. Front Neurol. 2015;(6):233.
2. Roberts E, Morgan R, King D, Clerkin L. Funduscopy: a forgotten art? Postgrad Med J. 1999;75(883):282-4.

Heart Drug With AMD Connection

The newly FDA-approved heart medication Entresto (valsartan/sacubitril, Novartis) contains an enzyme that may be linked to the development of age-related macular degeneration (AMD), according to an editorial recently published in *JAMA*.

The medication includes a neprilysin inhibitor. Although studies show that inhibiting neprilysin does prevent progression of left ventricular dysfunction, the authors point out that neprilysin "plays a critical role in maintaining the homeostasis of amyloid-β peptide in the brain." By inhibiting neprilysin, the article posits, the patient may experience an accumulation of amyloid-β peptide. Because research shows that an accumulation of amyloid-β peptide may contribute to the development of AMD, they conclude that, while the medication does assist in heart conditions, it has the potential to increase the risk of AMD and Alzheimer's disease.

"I applaud the *JAMA* editorial for calling for more rapid assessment of AMD and Alzheimer's disease through collaborative partnerships," says A. Paul Chous, OD, whose practice focuses on diabetes eye care and education. However, he says, the risk may be worthwhile. "Evidence shows that, in patients diagnosed with heart failure, only one in three survive more than five years. This mortality statistic mitigates, at least to some extent, the potential ocular and neurologic harm posed by increased amyloid-β with this combination of an angiotensin blocker and neprilysin inhibitor." Increased amyloid-β peptide is associated with beta cell failure as seen in Type 2 diabetes mellitus and glaucoma, he adds.

"It also makes sense to carefully monitor patients for these sequelae," he says. ■

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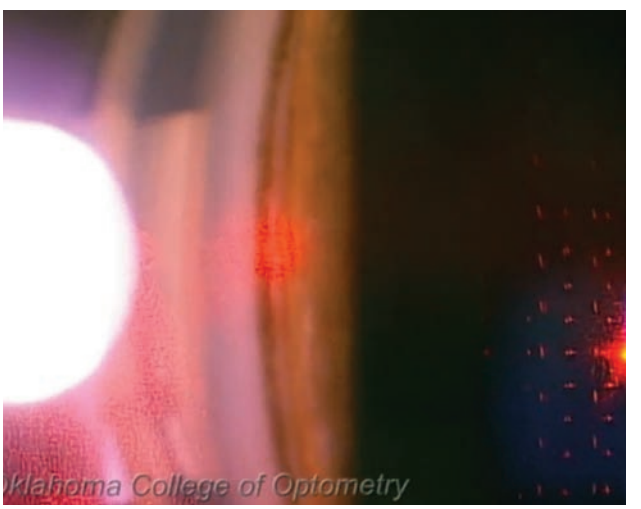

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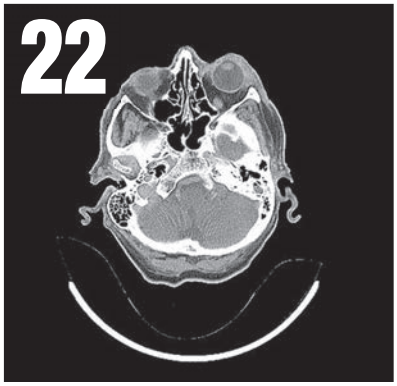

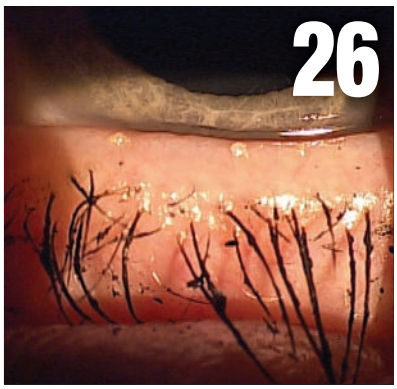

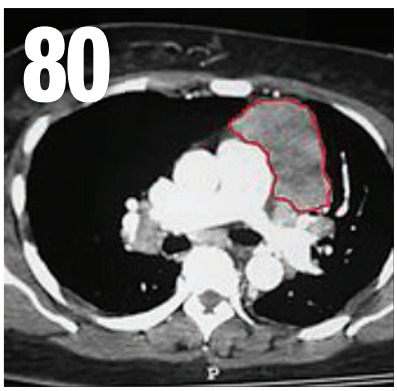

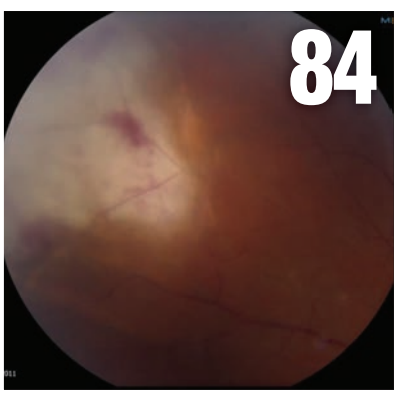

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Down, Boy.

Help Tame Postoperative Ocular Inflammation and Pain With LOTEMAX® GEL

Indication

LOTEMAX® GEL (loteprednol etabonate ophthalmic gel) 0.5% is indicated for the treatment of post-operative inflammation and pain following ocular surgery.

Important Safety Information about LOTEMAX® GEL

- LOTEMAX® GEL is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.
- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. If this product is used for 10 days or longer, IOP should be monitored.
- Use of corticosteroids may result in posterior subcapsular cataract formation.
- 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, and where appropriate, fluorescein staining.
- 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 infection.
- Use 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 exacerbate the severity of many viral infections of the eye (including herpes simplex).
- 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.
- Patients should not wear contact lenses when using LOTEMAX® GEL.
- The most common ocular adverse drug reactions reported were anterior chamber inflammation (5%), eye pain (2%) and foreign body sensation (2%).

Please see brief summary of Prescribing Information on adjacent page.

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to prescribe Lotemax Gel safely and effectively. See full prescribing information for Lotemax Gel.

Lotemax (loteprednol etabonate ophthalmic gel) 0.5%

Rx only
Initial Rx Approval: 1998

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.

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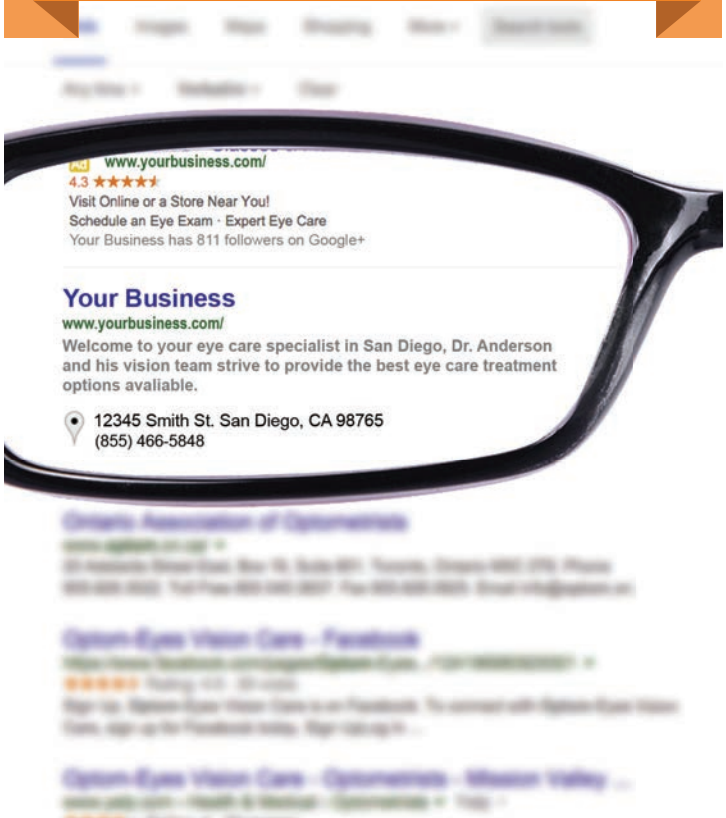

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Looking Back, and Ahead

This year, we celebrate our 125th anniversary—and the stunning rise of optometry. **By Jack Persico, Editor-in-Chief**

Boy, if Frederick Boger could see us now. The founding editor of this publication gave his creation the mission of being "a fountain-head of reliable information—a monthly visitor, in whose columns will be found a clear exposition of all the latest ideas." Authors were tasked with "knowing all that the text book has taught and applying that knowledge to daily occurrences." The year was 1891.

Every word of that mission statement rings true a century and a quarter later. We still strive to fill these pages with educational pieces that are academically sound but written with practical purposes in mind. So, Boger would find much that's familiar in this modern descendent of the publication, originally called *The Optician* at launch. What might bemuse (and, hopefully, please) him is the huge scope of it.

The profession of optometry has changed radically in the last 125 years, most notably because it didn't even exist back in 1891. Jewelers fit glasses and ophthalmologists treated eye disease. Boger had a vision (excuse the easy pun) of a new profession distinct from the jewelry trade. He's said to have coined the word "optometry"—and surely he popularized it through use in this publication month after month.

From Boger's day on, *Review of Optometry* has consistently been an advocate for optometry's evolution. Editors, publishers and optometric leaders lobbied in these pages for the acceptance of contact lenses, diagnostic and therapeutic drugs, surgical comanagement, you name it.

As we begin our anniversary year, the topics covered in this issue show just how big the footprint of optometry has grown.

First, we begin with four features that comprise our annual series on pharmaceuticals. Whereas once we might have talked on a more basic level, this year's education addresses high-level concerns like medication use in pregnant patients, ocular adverse effects of systemic meds, a review of psychotropic drugs and a CE course on managing ocular pain.

After that, we return to the very roots of optometry—refraction—with a detailed protocol you can use to standardize your office's approach, as a means of reducing errors and improving precision. This comes courtesy of our friends at the University of Iowa, who developed it at their institution and report that it saves chair time and frustration.

We've tried to not lose sight of bread-and-butter topics like refraction even as we help our readers embrace new frontiers in clinical care. That's certainly where our features conclude this month, as Oklahoma's Nate Lighthizer, OD, provides step-by-step instructions on how to perform selective laser trabeculoplasty, for ODs in states progressive enough to allow it (and those to come). Somewhere, I'll bet, Frederick Boger is smiling. ■

This July, look for a special commemorative issue that tells the story of optometry (and RO's role in it) from 1891 to 2016. If you'd like to share your opinions and stories for possible inclusion, drop me a line at jpersico@jobson.com.

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Watch Your Mouth!

Eventually, a patient will call you out on your B.S.—trust me, I know. But every once in a while, B.S. is worth its weight in gold. **By Montgomery Vickers, OD**

You have to be *so* careful when talking to patients these days. They may just believe what you say but, had they met you in college, they would know better. Remember when you told your friend, Rich, that you knew how to surf? OK, maybe that was just me and it was last month and maybe it was that I know karate but, well, you get the drift.

The point is that you should do what my dad told me from the time I was born: *watch your mouth*!

The problem is, it's quite difficult to actually watch your mouth. Just try it right now. You'll see.

One time, to make a point about how stupid this patient was being by taking such poor care of her contact lenses, I told her there were "seven bodily fluids that are safer to use as contact lens solution than saliva."

She made me name them. It was like she was planning to make an informed decision about which particular bodily fluid she would start using instead of her spit. As you can imagine, I found myself quickly running out of bodily fluids I could actually name. By the end, I think I listed "crosius," "leotine" and the ever-important, life-enhancing "gawasch," which I defined as the substance that makes mucous eventually turn into boogers.

Trust me, save yourself the pain and watch your mouth. I wish I had listened to my dad. We have to listen to my dad, y'all!

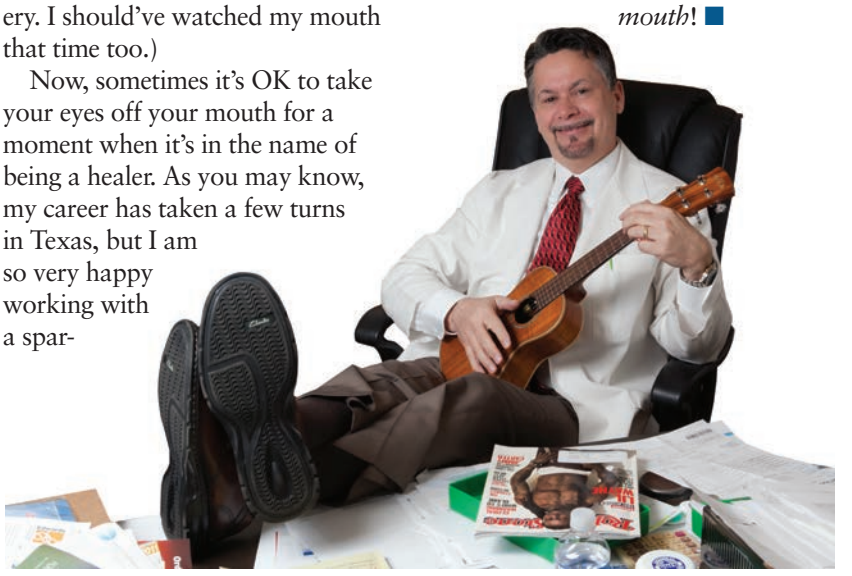
It's OK to just keep your mouth shut when you don't know. You don't know why the patient's second cousin went blind for two weeks and then never needed glasses again. If you did, in fact, know this, you would patent it, open a clinic, offer the procedure and put all of your colleagues out of business. And just the fact that you are, right this second, considering how rich and famous you would be if this came to pass shows you really don't give a hoot about your colleagues in the first place. Let 'em eat cake!

But back to my point. Watch your mouth! It gets you in trouble. Don't promise Mrs. Quiver that she will absolutely love her first pair of PALs at age 78. She might be OK, or she might just want her good ol' ST-28s set at 3 below like she has happily worn since Elvis was on Ed Sullivan. (Oh, this reminds me. Rich, I actually never met Elvis in the Philadelphia airport baggage claim. That autograph on my Ramones T-shirt is a complete forgery. I should've watched my mouth that time too.)

Now, sometimes it's OK to take your eyes off your mouth for a moment when it's in the name of being a healer. As you may know, my career has taken a few turns in Texas, but I am so very happy working with a sparkling crew of colleagues a couple days each week providing extremely important care in nursing homes all over the Dallas metroplex. Once, we needed to evaluate a lady who was bedridden, had terminal cancer and who kept her eyes clamped shut. I could tell she was a fighter because two strong men could not pry this lady's eyes open with a crowbar. My assistant said it was OK—I would never be able to check her eyes. I leaned in close to the patient's ear and quietly said this: "I'll bet everyone you ever met said something about your beautiful blue eyes."

It was a good guess because she instantly popped her tired eyes open, and I was glad I didn't watch my mouth that time. Those eyes were indeed blue and beautiful. Every now and then, when you do open your mouth, something righteous might jump out.

But most of the time, *watch your mouth*! ■





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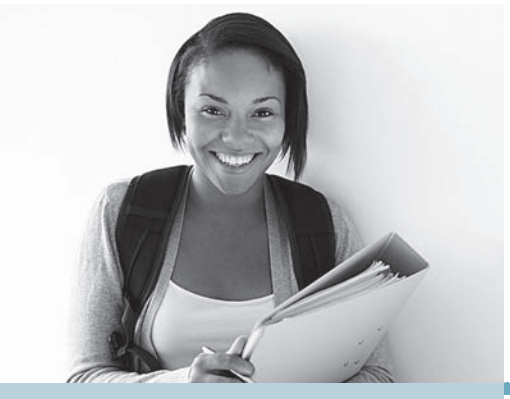

About Rick

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

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

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Referral Notes: Red Herring?

Assumptions and failure to dilate can lead to missed diagnoses. Start from scratch and catch what the specialist missed. **Edited by Paul C. Ajamian, OD**

Q A former patient contacted me recently complaining of visual disturbance. A retina specialist told her she needed a corneal evaluation for keratoconus, and sent her to yet another specialist. She called me to try and sort out the confusion. When I see a patient who just saw a specialist, am I off the hook from dilating?

A "We know that you cannot assume the patient is giving you the entire story. In this case, the retinal specialist 'said nothing about the fundus.' However, you should never trust the history, or the assessment and plan of another eye doctor, until you verify it with your own eyes," says Scott Moscow, OD, of Roswell Eye Clinic in Roswell, Ga. Doctors can miss things, or something new could have developed between visits. "You never know the full story without looking at the eye from front to back," says Dr. Moscow.

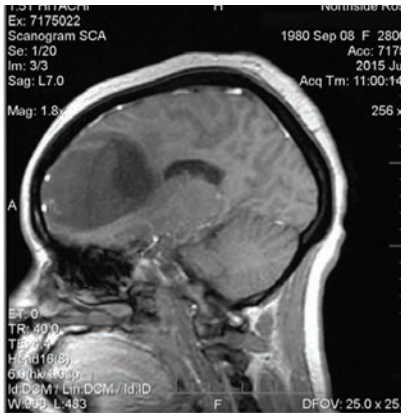
To do this, Dr. Moscow advises dilating every patient who experiences unexplained vision loss. "The dilated fundus exam showed bilateral swollen discs! Who knows how long my patient would have gone on thinking she was losing vision from keratoconus?" Do not simply rely on the previous specialist—perform a dilated fundus exam on every new patient.

Trust Your Gut

Other than mild headaches and slight lethargy, Dr. Moscow's patient didn't have neurological symptoms. Statistically, due to her age, weight and sex, he suspected idiopathic intracranial hypertension. "There were a few red flags that had me concerned," Dr. Moscow says. The first: her visual acuities were 20/200-1 OD and 20/250 OS. Second, her visual fields were severely constricted. "Anecdotally, I don't see visual acuities that poor, or visual fields constricted to that extent, when dealing with a case of idiopathic intracranial hypertension," says Dr. Moscow.

Given these warning signs, Dr. Moscow scheduled the patient for an appointment with a neurologist the next day. "Although the next available appointment was more than three weeks away, I persisted and got her in after bypassing the receptionist, asking to speak directly to the doctor," says Dr. Moscow. "I arranged an MRI that morning, prior to her appointment, in order to avoid further delays." The patient did have intracranial hypertension, but it was not idiopathic: it was secondary to a space-occupying frontal lobe lesion.

Dr. Moscow emphasizes the critical importance of developing a relationship with any doctor to whom you refer your patients. "Direct communication was the key to getting a timely appointment and definitive diagnosis for this patient," says Dr. Moscow. It is also important to make the appointment for the patient, and not leave it up to them. "She would have been told that the earliest appointment was almost a month away, and she might have had to accept that," says Dr. Moscow. He says that it is also vital to listen to 'your gut'—what your brain is telling you the data could mean. "My patient's fundus appearance was stereotypical of 'benign' intracranial hypertension, if there is such a thing; however, the reduced visual acuities and fields were very atypical."



The patient's constricted visual fields were due to a grade 3 astrocytoma of the left frontal lobe.

In this case, Dr. Moscow says it was most important to look at the back of her eye rather than rely entirely on the patient and a previous specialist, who said that she was there "only to be fit with contact lenses for keratoconus."

"Many, many problems can occur in the back of the eye that can only be viewed when dilated," says Dr. Moscow. Just because they are under the care of someone else for another issue doesn't mean that you abdicate responsibility or assume anything. "When a patient presents to your office, you are officially responsible for every problem they come in with." ■

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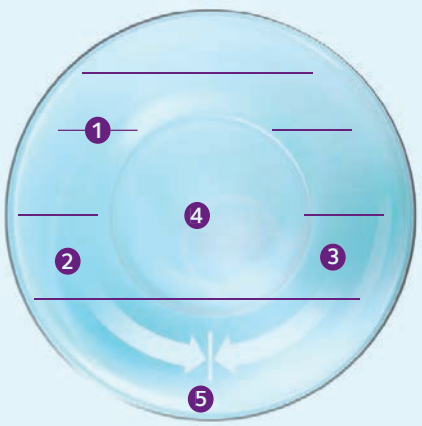

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Ring The Alarm Bell's

Incomplete eyelid closure secondary to left facial nerve paralysis reveals squamous cell carcinoma of the mandible. **By Michael Trottini, OD, and Michael DelGiodice, OD**

A 70-year-old male patient was referred for evaluation of lagophthalmos. The patient described a progressive and painful left facial droop with incomplete eyelid closure, facial numbness, hearing deficit and an inability to open the left half of his mouth. In addition, he reported difficulty eating over the course of four months and subsequent weight loss. His social histories were positive for chronic tobacco and alcohol use.

Best-corrected visual acuity measured 20/30 OU. Pupil testing was normal without afferent defect. Intraocular pressures were 15mm Hg OU. Extraocular motilities were full and smooth. Biomicroscopy revealed complete absence of left eyelid closure with a good Bell's phenomenon. Anterior segment evaluation revealed severe keratopathy in the left eye secondary to chronic exposure. The lens showed 1+ nuclear sclerosis, and the vitreous was attached in both eyes. The optic nerves measured 0.20 OU, and the maculae were flat.

A physical evaluation of the motor functions of the seventh nerve revealed the inability to retract the left side of the face when asked to smile, close the left eye, wrinkle the forehead or open the left side of the mouth. Additional testing revealed normal function of cranial nerve five (CN-V), but reduced hearing in the left ear was consistent with cranial nerve eight (CN-VIII) dysfunction.

Due to the patient's history of chronic alcohol and tobacco use and the involvement of multiple cranial nerves (VII and VIII), emergent computed tomography (CT) of the head and neck was ordered. An immediate read by the radiologist revealed a large, infiltrative and enhancing, ill-defined mass centered on the ramus of the left mandible; additional CT of the brain was unremarkable.

To determine malignancy, a biopsy was taken of mucosal tissues from the left floor of the mouth and from the left retromolar trigone. Histopathology revealed poorly differentiated stage IV squamous cell carcinoma (SCC) of the left retromolar trigone. Ultimately, positron emission tomography (PET) revealed metastatic lung cancer. Both surgical and medical management of the tumor was considered; however, due to the progressive nature of the condition and its late staging, surgical resection would be unfavorable, and chemotherapy could not be performed secondary to poor nutritional status. From an ocular standpoint, the patient was prescribed viscous ophthalmic lubrication for use every few hours along with instructions on taping the outer one-third of the eyelid to reduce exposure; however, ultimately the patient was placed in palliative care and passed away one month after the initial diagnosis.

Table 1. Motor Innervation of CN-VII:

Innervation	Function	Test
Frontalis	Draws the scalp forward and wrinkles the forehead	Patient raises their eyebrows to wrinkle their forehead
Orbicularis oculi	Eyelid closure	Attempt to open forcibly closed eyelids while noting any weakness between the two eyes
Orbicularis oris	Closes the lips	Have the patient attempt to smile
Buccinator	Puckers the lips	Have the patient attempt to puff the cheeks out
Platysma	Wrinkles the surface of the skin in the neck, increases the diameter of the neck during rapid respiration, assists in depressing the angle of the mouth, improves venous flow	Have the patient attempt to contract the muscles of the neck
Posterior belly of the digastric	Assists in opening the jaw	Have the patient attempt to open the mouth
Muscles of the middle ear	Dampens sound to loud noises	Acoustic reflex impedance testing

Discussion

CN-VII palsy is a relatively common neurologic condition. The rate of incidence in the general population is estimated to be 2% to 15%, with 75% to 90% attributed to idiopathic facial nerve paralysis (Bell's palsy).[1] The remaining causes of CN-

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*Efficacy for this organism was studied in fewer than 10 infections.

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- BESIVANCE® is for topical ophthalmic use only, and should not be injected subconjunctivally, nor should it be introduced directly into the anterior chamber of the eye.
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- Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with BESIVANCE®.
- The most common adverse event reported in 2% of patients treated with BESIVANCE® was conjunctival redness. Other adverse events reported in patients receiving BESIVANCE® occurring in approximately 1-2% of patients included: blurred vision, eye pain, eye irritation, eye pruritus and headache.
- BESIVANCE® is not intended to be administered systemically. Quinolones administered systemically have been associated with hypersensitivity reactions, even following a single dose. Patients should be advised to discontinue use immediately and contact their physician at the first sign of a rash or allergic reaction.
- Safety and effectiveness in infants below one year of age have not been established.

Please see brief summary of Prescribing Information on adjacent page.

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References: 1. BESIVANCE® Prescribing Information, September 2012. **2.** At 12 hours, the concentration of besifloxacin in tears was >10 µg/mL. Proksch JW, Granvil CP, Siou-Mermet R, Comstock TL, Paterno MR, Ward KW. Ocular pharmacokinetics of besifloxacin following topical administration to rabbits, monkeys, and humans. *J Ocul Pharm Ther.* 2009;25(4):335-344. **3.** Comstock TL, Paterno MR, Usner DW, Pichichero ME. Efficacy and safety of besifloxacin ophthalmic suspension 0.6% in children and adolescents with bacterial conjunctivitis: a post hoc, subgroup analysis of three randomized, double-masked, parallel-group, multicenter clinical trials. *Paediatr Drugs.* 2010;12(2):105-112.

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Besivance (besifloxacin ophthalmic suspension) 0.6%

Sterile topical ophthalmic drops
Initial U.S. Approval: 2009

1 INDICATIONS AND USAGE

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*Efficacy for this organism was studied in fewer than 10 infections.

2 DOSAGE AND ADMINISTRATION

Invert closed bottle and shake once before use.

Instill one drop in the affected eye(s) 3 times a day, four to twelve hours apart for 7 days.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Topical Ophthalmic Use Only NOT FOR INJECTION INTO THE EYE.

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5.2 Growth of Resistant Organisms with Prolonged Use As with other anti-infectives, prolonged use of Besivance (besifloxacin ophthalmic suspension) 0.6% may result in overgrowth of non-susceptible organisms, including fungi. If super-infection occurs, discontinue use and institute alternative therapy. Whenever clinical judgment dictates, the patient should be examined with the aid of magnification, such as slit-lamp biomicroscopy, and, where appropriate, fluorescein staining.

5.3 Avoidance of Contact Lenses Patients should not wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with Besivance.

6 ADVERSE REACTIONS

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

The data described below reflect exposure to Besivance in approximately 1,000 patients between 1 and 98 years old with clinical signs and symptoms of bacterial conjunctivitis.

The most frequently reported ocular adverse reaction was conjunctival redness, reported in approximately 2% of patients.

Other adverse reactions reported in patients receiving Besivance occuring in approximately 1-2% of patients included: blurred vision, eye pain, eye irritation, eye pruritus and headache.

8 USE IN SPECIFIC POPULATIONS

8.1 Pregnancy Pregnancy Category C. Oral doses of besifloxacin up to 1000 mg/kg/day were not associated with visceral or skeletal malformations in rat pups in a study of embryo-fetal development, although this dose was associated with maternal toxicity (reduced body weight gain and food consumption) and maternal mortality. Increased post-implantation loss, decreased fetal body weights, and decreased fetal ossification were also observed. At this dose, the mean C_{max} in the rat dams was approximately 20 mcg/mL, >45,000 times the mean plasma concentrations measured in humans.

The No Observed Adverse Effect Level (NOAEL) for this embryo-fetal development study was 100 mg/kg/day (C_{max}, 5 mcg/mL, >11,000 times the mean plasma concentrations measured in humans).

In a prenatal and postnatal development study in rats, the NOAELs for both fetal and maternal toxicity were also 100 mg/kg/day. At 1000 mg/kg/day, the pups weighed significantly less than controls and had a reduced neonatal survival rate. Attainment of developmental landmarks and sexual maturation were delayed, although surviving pups from this dose group that were reared to maturity did not demonstrate deficits in behavior, including activity, learning and memory, and their reproductive capacity appeared normal.

Since there are no adequate and well-controlled studies in pregnant women, Besivance should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers Besifloxacin has not been measured in human milk, although it can be presumed to be excreted in human milk. Caution should be exercised when Besivance is administered to a nursing mother.

8.4 Pediatric Use The safety and effectiveness of Besivance® in infants below one year of age have not been established. The efficacy of Besivance in treating bacterial conjunctivitis in pediatric patients one year or older has been demonstrated in controlled clinical trials *[see CLINICAL STUDIES (14)]*.

There is no evidence that the ophthalmic administration of quinolones has any effect on weight bearing joints, even though systemic administration of some quinolones has been shown to cause arthropathy in immature animals.

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

12 CLINICAL PHARMACOLOGY

12.1 Mechanism of Action Besifloxacin is a fluoroquinolone antibacterial *[see CLINICAL PHARMACOLOGY (12.4)]*.

12.3 Pharmacokinetics Plasma concentrations of besifloxacin were measured in adult patients with suspected bacterial conjunctivitis who received Besivance bilaterally three times a day (16 doses total). Following the first and last dose, the maximum plasma besifloxacin concentration in each patient was less than 1.3 ng/mL. The mean besifloxacin C_{max} was 0.37 ng/mL on day 1 and 0.43 ng/mL on day 6. The average elimination half-life of besifloxacin in plasma following multiple dosing was estimated to be 7 hours.

12. Microbiology

Besifloxacin is an 8-chloro fluoroquinolone with a N-1 cyclopropyl group. The compound has activity against Gram-positive and Gram-negative bacteria due to the inhibition of both bacterial DNA gyrase and topoisomerase IV. DNA gyrase is an essential enzyme required for replication, transcription and repair of bacterial DNA. Topoisomerase IV is an essential enzyme required for partitioning of the chromosomal DNA during bacterial cell division. Besifloxacin is bactericidal with minimum bactericidal concentrations (MBCs) generally within one dilution of the minimum inhibitory concentrations (MICs).

The mechanism of action of fluoroquinolones, including besifloxacin, is different from that of aminoglycoside, macrolide, and β-lactam antibiotics. Therefore, besifloxacin may be active against pathogens that are resistant to these antibiotics and these antibiotics may be active against pathogens that are resistant to besifloxacin. *In vitro* studies demonstrated cross-resistance between besifloxacin and some fluoroquinolones.

In vitro resistance to besifloxacin develops via multiple-step mutations and occurs at a general frequency of $< 3.3 \times 10^{-10}$ for *Staphylococcus aureus* and $< 7 \times 10^{-10}$ for *Streptococcus pneumoniae*.

Besifloxacin has been shown to be active against most isolates of the following bacteria both *in vitro* and in conjunctival infections treated in clinical trials as described in the INDICATIONS AND USAGE section:

*Aerococcus viridans**, CDC coryneform group G,

*Corynebacterium pseudodiphtheriticum**, *C. striatum**, *Haemophilus influenzae, Moraxella catarrhalis**, *M. lacunata**, *Pseudomonas aeruginosa**, *Staphylococcus aureus, S. epidermidis, S. hominis**, *S. lugdunensis**, *S. warneri**, *Streptococcus mitis* group, *S. oralis, S. pneumoniae, S. salivarius**

*Efficacy for this organism was studied in fewer than 10 infections.

13 NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility Long-term studies in animals to determine the carcinogenic potential of besifloxacin have not been performed.

No *in vitro* mutagenic activity of besifloxacin was observed in an Ames test (up to 3.33 mcg/plate) on bacterial tester strains *Salmonella typhimurium* TA98, TA100, TA1535, TA1537 and *Escherichia coli* WP2uvrA. However, it was mutagenic in *S. typhimurium* strain TA102 and *E. coli* strain WP2(pKM101). Positive responses in these strains have been observed with other quinolones and are likely related to topoisomerase inhibition.

Besifloxacin induced chromosomal aberrations in CHO cells *in vitro* and it was positive in an *in vivo* mouse micronucleus assay at oral doses × 1500 mg/kg. Besifloxacin did not induce unscheduled DNA synthesis in hepatocytes cultured from rats given the test compound up to 2,000 mg/kg by the oral route. In a fertility and early embryonic development study in rats, besifloxacin did not impair the fertility of male or female rats at oral doses of up to 500 mg/kg/day. This is over 10,000 times higher than the recommended total daily human ophthalmic dose.

14 CLINICAL STUDIES

In a randomized, double-masked, vehicle controlled, multicenter clinical trial, in which patients 1-98 years of age were dosed 3 times a day for 5 days, Besivance was superior to its vehicle in patients with bacterial conjunctivitis. Clinical resolution was achieved in 45% (90/198) for the Besivance treated group versus 33% (63/191) for the vehicle treated group (difference 12%, 95% CI 3% - 22%). Microbiological outcomes demonstrated a statistically significant eradication rate for causative pathogens of 91% (181/198) for the Besivance treated group versus 60% (114/191) for the vehicle treated group (difference 31%, 95% CI 23% - 40%). Microbiologic eradication does not always correlate with clinical outcome in anti-infective trials.

17 PATIENT COUNSELING INFORMATION

Patients should be advised to avoid contaminating the applicator tip with material from the eye, fingers or other source.

Although Besivance is not intended to be administered systemically, quinolones administered systemically have been associated with hypersensitivity reactions, even following a single dose. Patients should be advised to discontinue use immediately and contact their physician at the first sign of a rash or allergic reaction.

Patients should be told that although it is common to feel better early in the course of the therapy, the medication should be taken exactly as directed. Skipping doses or not completing the full course of therapy may (1) decrease the effectiveness of the immediate treatment and (2) increase the likelihood that bacteria will develop resistance and will not be treatable by Besivance or other antibacterial drugs in the future.

Patients should be advised not to wear contact lenses if they have signs or symptoms of bacterial conjunctivitis or during the course of therapy with Besivance.

Patients should be advised to thoroughly wash hands prior to using Besivance.

Patients should be instructed to invert closed bottle (upside down) and shake once before each use. Remove cap with bottle still in the inverted position. Tilt head back, and with bottle inverted, gently squeeze bottle to instill one drop into the affected eye(s).

Manufactured by: Bausch & Lomb Incorporated
Tampa, Florida 33637

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U.S. Patent Nos. 6,685,958; 6,699,492; 5,447,926
†DuraSite is a trademark of InSite Vision Incorporated

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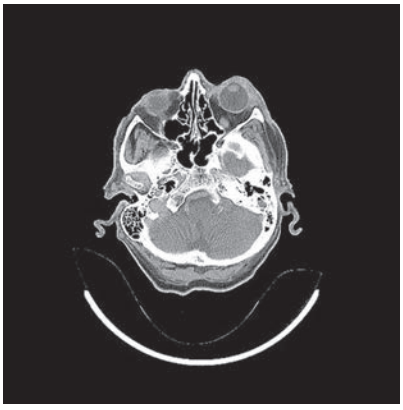
VII palsy include: infection, inflammation, trauma, facial diplegia , iatrogenic and neoplasm (*Table 1*).[1]

The most common benign neoplastic cause of CN-VII palsy is facial nerve schwannoma and the most common malignant neoplasm is SCC.[2] Neoplasm is responsible for a mere 5% of all cases of CN-VII dysfunction.[3] In the United States, SCC of the head and neck represents 4% of all malignancies, but is responsible for more than 90% of all head and neck cancers.[3] An epithelial-derived tumor, SCC is most commonly associated with alcohol and tobacco use, with significantly less incidence in those who neither smoke nor drink.[4] The most common sites for SCC are: the floor of the mouth, tongue, soft palate, anterior tonsillar pillar and retromolar trigone, the last of which is aggressive and carries a poor prognosis.[5]

The facial nerve (FN) emerges from the brainstem between the pons and the medulla. It is predominantly responsible for the majority of all facial movement (*Table 1*) and, to a lesser extent, sensory function. It shares an anatomic locale with both major and minor salivary glands, mostly the parotid and submandibular glands. Disruption of the facial nerve at any location may result in sensory deprivation and partial or complete loss of facial function.

Presentations of FN weakness warrant comprehensive workup with special attention to the cranial nerves. Testing both upper and lower facial motor function helps differentiate between upper and lower motor neuron lesions; upper motor neuron (supranuclear) lesions result in contralateral facial weakness. Testing will show sparing of the upper face with paralysis of the contralateral lower face. For example, a patient with a right CN-VII palsy from a left upper motor neuron lesion will present with lower FN weakness on the right side with sparing of the frontalis and orbicularis oculi muscles. The patient will be able to furrow their forehead and close their eyelid, but will show weakness when asked to puff the cheeks, smile, open their mouth and pucker their lips. A lower motor lesion, as seen in our patient, affects the main trunk of the facial nerve and causes ipsilateral weakness in both upper and lower facial regions. FN paralysis involving a history of pain, multiple CN involvement and recalcitrant behavior should be investigated with MRI or CT of the head and neck to exclude tumor, demyelination and stroke, and laboratory testing to exclude infection and inflammation.



Large infiltrative and enhancing ill-defined mass of the left mandible and face, deviating the airway to the right.

The ocular management of CN-VII paresis may include both medical and surgical therapies. If the patient cannot close their eye, lubrication of the cornea is necessary to prevent secondary-exposure keratitis and subsequent corneal ulceration. The mainstays of therapy are nonpreserved artificial tears used frequently while awake and ophthalmic ointments at bedtime. If significant lagophthalmos exists, the palpebral aperture can be narrowed by applying transparent, medical-grade tape to the lateral aspect of the lower eyelid, then directing the tape upward and laterally, securing it to the orbital rim; this will act as a temporary tarsorrhaphy.

External eyelid prostheses can also be used as short-and long-term treatment for patients with temporary facial paralysis and as a trial before implantation of eyelid gold weights. Moisture chamber goggles and punctal occlusion can also provide additional moisture. In the presence of severe keratopathy or corneal ulceration, a bandage contact lens and amniotic membrane may be helpful.[6,7] In the event of persistent corneal decompensation, treatment options may include complete or partial tarsorrhaphy, gold-weight insertion in the affected upper eyelid to induce a ptosis and surgical intervention with a lateral canthal strengthening procedure (canthoplasty) to repair ectropion.[8]

This case represents an atypical, low prevelance cause of facial nerve paralysis; however, a careful history, review of systems, physical examination and proper neuroimaging increase the odds of a timely and accurate diagnosis. ■

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The Dry Eye Deluge

Last year saw an explosion of advancements in the world of ocular surface disease—and we are finding more every day. **By Paul M. Karpecki, OD**

Given modern dry eye disease (DED) risk factors such as computer, smartphone and tablet use, we can only anticipate this disease will increase in frequency. Fortunately, ophthalmic companies are working at a feverish pace to address this situation.

Diagnostic Technology

Point-of-care devices for osmolarity and inflammation testing, such as TearLab and InflammaDry (RPS), help clinicians provide a positive diagnosis; in particular, osmolarity can track progress and help determine the most appropriate therapy. More importantly, it can help determine who doesn't have DED.

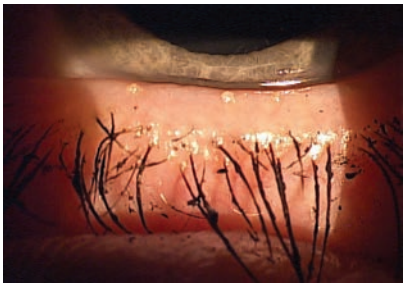
The new LipiView with dynamic meibomian imaging (TearScience) shows high definition imaging of the meibomian glands, tracks blink rates and has interferometry to provide lipid layer thickness measurements.

Oculus has combined some of its advanced testing (meiboscan, non-invasive break-up time, tear meniscus height measurements, redness grading, etc.) to produce a report that displays the data gathered from the Keratograph 5M dry eye exams and such as osmolarity, blink rate and OSDI dry eye questionnaires.

Topcon recently introduced a meibographer feature as part of its SL-D701 slit lamps.

Lid Margin Disease

Less than 10 years ago, DED experts published findings suggesting that lid margin disease was critical to dry eye; they also thought non-lid margin disease was the most common presentation.[1] However, today we know that lid margin disease represents the single largest category of DED.[2]



Dry eye disease is on the rise, and more treatment options are on the way.

A number of advances address the new understanding of the disease, including Lid Scrub Plus Platinum (OcuSoft), which is an extra-strength eyelid cleanser containing phytosphingosine. Research indicates phytosphingosine has both antibacterial and anti-inflammatory properties.[3] Phytosphingosine lipids inhibit microorganisms and their second-messenger function, and are considered part of the body's natural defense system. A recent study also shows it acts as an anti-inflammatory at concentrations as low as 0.1%.[4]

iLast (Paragon BioTeck) is a new eyelid product containing retinol palmitate and hyaluronic (HA), which has been shown to bind up to 1000 times its weight in water.[5] Retinol palmitate appears to be able to prevent keratin formation, which may play a role in meibomian gland obstruction.[6]

The use of hypochlorous acid has also been advantageous for patients suffering from *Staphylococcal* blepharitis and can be obtained via a prescription for Avenova with Neutrox 0.01% HOCL (NovaBay) or over the counter with Hypochlor gel 0.02% HOCL (OcuSoft).

Another advancement in meibomian gland dysfunction (MGD) management is the new Bruder Moist Heat Compress (Bruder Healthcare) with antimicrobial properties, improved design and consistent hydrating heat release for 10 to 12 minutes or longer.

In-office, mechanical, thermal pulsation has become more accessible to practitioners with a reduction in the price of LipiView and single-use activators for the LipiFlow (TearScience) treatment platform. In multiple studies, LipiFlow has been shown to significantly improve mean meibomian gland secretions and reduce mean dry eye symptoms to approximately half of the pre-procedure level and for up to three years.[7-9]

BlephEx (RySurg)—a handheld device that allows doctors to perform in-office microblepharoexfoliation—is a significant advancement in blepharitis and MGD management. It safely removes the inflammatory biofilm and its associated *Staph.* toxins that build up along the margin of the eyelid. These toxins cause various stages of chronic inflammatory blepharitis of the lid margin, leading to dry eye and MGD.[10] Removing these toxins every four to six months can help maintain clean, healthy, lid margins and eventually normalize and maintain natural tear function.

Eye Drop Technology

One of the newer formulation tears on the market is Retaine MGD (OcuSoft), which is a preservative-free ophthalmic emulsion for moderate to severe dry eye. The formula's cationic emulsion is the delivery of two or more immiscible liquid ingredients (e.g., oil and water) through the electrostatic attraction between the positively charged drops and the negatively charged ocular surface.

Recently, Allergan launched Optive gel drops, which are an improved version of Liquigel. The new drops contain the same osmoprotectants as Optive and the same polymer blend as Liquigel. The key innovation is the benefit of protecting cells with intracellular solutes (osmoprotection via compatible solutes) to maintain proper osmolarity levels and reduce stress on the ocular surface.[11]

Allergic Eye Disease

On the prescription side, Pazeo (0.7% olopatadine hydrochloride, Alcon) for the treatment of itching associated with allergic conjunctivitis was recently approved. The drug achieved a 24-hour approval and was shown to be statistically superior not only to the placebo at 24 hours, but to Pataday (0.2% olopatadine, Alcon).[12]

Cool compress masks from Bruder Healthcare and hydrating sinus masks are two new allergy treatment additions as well.

New Technologies

Another exciting advancement in DED management is a forthcoming amniotic membrane treatment with a clear 6mm central aperture, called Prokera Clear (Bio-Tissue), which allows clinicians to treat the disease and preserve vision. It's designed to maintain visual acuity throughout the treatment period while providing excellent efficacy. The device elutes the active biologic properties and provides anti-inflammatory properties and high-quality regenerative healing.

Another simple, but I feel significant, advancement is extended duration punctal plugs. Permanent intracanalicular punctal plugs have risks—including the development of pyogenic granuloma and, rarely, irritation on the ocular surface with surface plugs—and an ideal solution is a dissolving intracanalicular plug. Extended duration plugs can now last anywhere from 90 to 180 days. The Extend plug (Beaver-Visitec) offers diameter sizes ranging from 0.2mm to 0.5mm in 0.1mm steps. Other 180-day dissolving punctal plugs include the ComfortTear Lacrisolve (Paragon BioTeck) and the Quintess six-month dissolvable lacrimal plug (OcuSoft).

Another technology aims to improve your eye health while working on a computer. The primary features of Dr. i-Coach's (Eyes4Lives) sensor and software package are a blink rate analyzer, computer time, distance and posture monitor, and vision self-tests. Tracking and alerting the user of improper computer habits reduces eyestrain and minimizes the effects of prolonged digital device use.

New Studies and Products

Allergan announced the purchase of a new device called Oculeve—currently in FDA clinical trials—that may stimulate a patient's own tears. Shire announced OPUS 3 study results of its dry eye drug candidate, lifitegrast. Preliminary results indicate that the primary endpoint was met with significant improvement in patient-reported symptoms in the group receiving lifitegrast. Additional endpoints evaluating symptoms at days 14 and 42 were also met. Other studies include TheraTears' (Akorn) effect on hyperosmolarity and FreshKote drops (Focus Laboratories) for the management of central corneal staining. Finally, Abbott plans to introduce Blink Lid-Clean wipes, which are preservative-free, hypoallergenic, contain chamomile and are approved for use with children.

With an estimated 30 million Americans suffering from DED, these continued advances are a welcome addition to our practices to help us successfully treat many patients.[13-15] ■

Dr. Karpecki is a consultant/advisor to: AMO, Alcon Labs, Allergan, Akorn, Bausch + Lomb/Valeant, BioTissue, Bruder Healthcare, Beaver-Visitec, Cambium Pharmaceuticals, Essilor, Eyemaginations, Eyes4Lives, Focus Laboratories, Glaukos, iCare USA, Ocusoft, Konan Medical, Optometric Medical Solutions, Reichert, Shire Pharmaceuticals, RySurg, Science Based Health, SightRisk, TearLab, TearScience, TLC Vision, Topcon and Vmax.

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PEER • REVIEWED • PRA • ARTICLE •

Pregnancy Precautions: HOW TO PRESCRIBE SAFELY FOR NEW AND EXPECTANT MOTHERS

While patients who are pregnant or breastfeeding make challenging cases for many optometrists, new guidelines may make things easier. **By Jill Autry, OD, RPh**

Many clinicians panic when confronted with a patient who is pregnant or nursing and needs treatment for an ocular condition. In my experience, unfounded fears, a historically confusing and simplistic FDA classification system and limited data on ophthalmic medications often cause eye care practitioners to withhold treatment or undertreat this patient population.

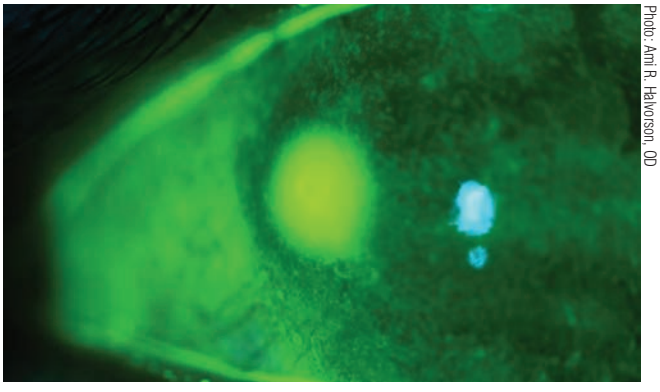

Photo: Ami R. Halvorson, OD

Tobramycin, with a historical FDA category B rating, is commonly used for pregnant patients diagnosed with bacterial keratitis.

However, compiled data suggest the majority of severe birth defects are due not to drug side effects, but to genetic or chromosomal abnormalities.[1,2] Additionally, most teratogenic birth defects are due to alcohol, illicit drug consumption or infective teratogens and not the use of over-the-counter (OTC) and FDA-approved medications.[1,2] Finally, the risk of birth defects resulting from topically-applied medications is extremely low, suggesting that, although prescribing for the pregnant patient requires an increased level of caution, especially in gestational weeks two through 10, there are a variety of relatively safe options available for most ocular disease conditions.[3]

This article discusses the use of ophthalmic medications during pregnancy and lactation, and what practitioners should take into consideration when treating patients who are pregnant or breastfeeding.

Considerations for Breastfeeding Patients

When prescribing for breastfeeding patients, clinicians must weigh the benefits of medication use for the mother against the potential risks to the infant, such as the repercussions of not breastfeeding the infant or exposing the infant to the medications. A drug considered safe for patients who are pregnant may not be safe for patients who are nursing.[4] Clinicians can limit the breastfed infant's exposure to medication by prescribing medications to the mother with poor oral absorption, educating the mother to avoid breastfeeding during times of peak maternal serum drug concentration and prescribing topical therapy when possible.

Mothers with medically fragile infants may need different dosing to minimize drug accumulation and toxicity in the infant.[4]

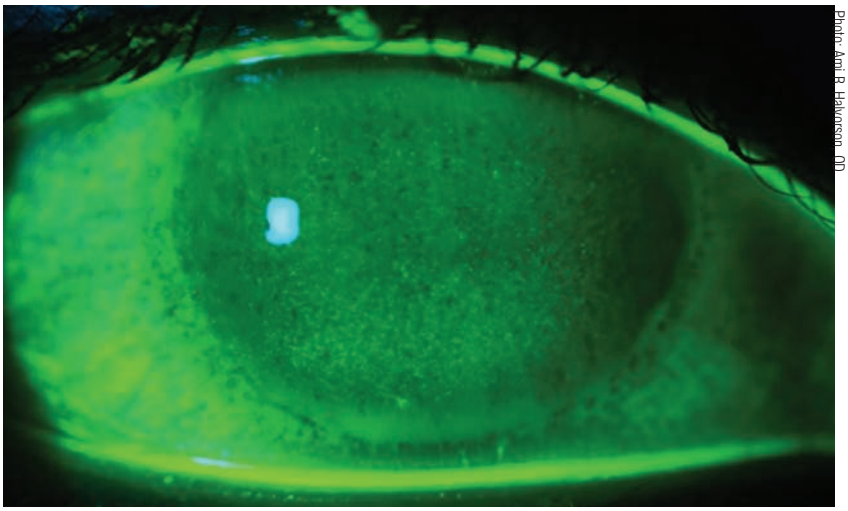

Photo: Ami R. Halverson, OD

Patients who are pregnant and have dry eye will often notice a worsening of their symptoms.

Dilating

Another concern is the use of dilating drops during the course of pregnancy and breastfeeding. The consensus is occasional dilation is acceptable, but that repeated use of these agents should be avoided if possible.[5-7] Due to an increased half-life, clinicians should avoid the use of longer duration parasympatholytics such as atropine, scopolamine and homatropine. The shorter acting agents such as tropicamide or cyclopentolate are considered safer for use in pregnancy and lactation. The ophthalmic sympathomimetic phenylephrine should be avoided unless dilation with tropicamide only is inadequate and a dilated retinal examination is necessary for the treatment or evaluation of a current ocular condition.[5-7]

Oral Antibiotics

Pregnant and nursing women develop skin and soft tissue infections just like any other patient. Expect at some point in your career to examine a pregnant or nursing patient with a hordeolum, dacryocystitis, preseptal cellulitis or similar presentation. We should not undertreat this patient by avoiding oral antibiotic therapies with the historic category B FDA rating such as Augmentin (amoxicillin/clavulanic acid, GlaxoSmithKline), erythromycin, azithromycin and amoxicillin, as they are used routinely during pregnancy and are approved by obstetricians for infections from gestation through breastfeeding.[6-9]

All of these choices provide the broad-spectrum coverage we generally seek in treating lid and ocular adnexa infections. However, just as in the pediatric population, it is prudent to avoid tetracycline and fluoroquinolone derivatives when treating pregnant and lactating patients, as they offer increased risks to the developing fetus or infant.[10,11] Tetracycline and its derivatives—including doxycycline and minocycline—have been known to cause discoloration of teeth and maternal liver toxicity.[12] Fluoroquinolone derivatives such as oral ciprofloxacin, moxifloxacin or levofloxacin have been associated with lab animal fetal cartilage-forming defects, and their use in pregnant patients is controversial despite data to suggest relative safety.[13]

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Topical Treatments

For topical antibiotics, such as those needed to treat bacterial keratitis, tobramycin has the historical FDA category B rating and has been used extensively in pregnancy as a topical ophthalmic antibiotic.[14] The use of topical fluoroquinolones during pregnancy has not been well studied; however, because of their undisputed efficacy in the treatment of corneal ulcers, these medications may be necessary if the benefits outweigh the potential risk to the developing fetus.

Fortified topical cephalosporin antibiotics, such as cefazolin and ceftazidime, have an excellent

An Update on the FDA's Pregnancy and Lactation Labeling

By Ami R. Halvorson, OD, and Erica Wiegandt, OD

The Food and Drug Administration (FDA) passed the Pregnancy and Lactation Labeling Final Rule (PLLR) in December 2014. The new rule changed the labeling requirements for prescription medication as it pertains to women who are pregnant and breastfeeding, as well as men and women of reproductive age. The new guidelines are to assist health care providers in determining risk and benefit to an expecting or lactating mother when pharmaceutical therapy is needed.

The new labeling system took effect on June 30, 2015. According to the FDA website, any new prescription drugs or biologic agents that are submitted for FDA approval after this date will be labeled with the new labeling system. Any drugs or agents that are subject to the Physician Labeling Rule—drugs that were FDA approved after June 30, 2001—will be gradually phased into the system within the next three to five years. Manufacturers are required to remove the lettering category within the next three years for any product approved before June 30, 2001. Clinicians will continue to see prescription drugs labeled with the older lettering system until they are updated.

Currently, no topical ophthalmic medications are consistent with the new labeling rule. Manufacturers of the prescription drugs are responsible for relabeling their medications as data for pregnant and breastfeeding women become available. The manufacturers are not subject to conduct new studies to evaluate risks to pregnant or lactating women, but they are required to evaluate up-to-date medical literature and revise their labeling accordingly.[1] Over the counter (OTC) medications are not subject to the PLLR and will not be relabeled.

The new labeling system has three categories: Pregnancy, Lactation and Females & Males of Reproductive Potential. The chart below compares previous labeling to the new labeling to illustrate the changes that took place.

- ***Pregnancy.*** The Pregnancy subsection, termed 'subsection 8.1', no longer includes the pregnancy categories (A, B, C, D, X, N) but instead includes a narrated section on risk summary, clinical considerations and data for a given drug. In addition to these sections, a pregnancy exposure registry, when available, is also required—something that was only recommended in the past.
- ***Lactation.*** The Lactation subsection, termed 'subsection 8.2', contains pertinent information about a medication as it applies to a nursing mother, such as the amount of prescription medication in the breast milk and possible effects on the child. This subsection also has the risk summary, clinical considerations and data subheadings.
- ***Patients of Reproductive Potential.*** The Females and Males of Reproductive Potential subsection, termed 'subsection 8.3', is a brand new category that provides information on a given medication and the need for pregnancy testing, contraception recommendations and information on infertility. The location for this information on a particular drug has not been consistently categorized before.

New Labeling Benefits

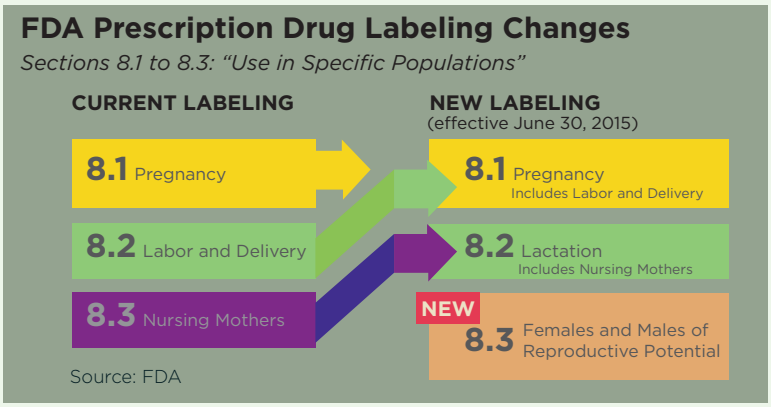
The new labeling system was created because it was felt that the older lettering system, implemented in 1979, was overly simplistic and perhaps did not convey the potential drug risks to the prescribing care provider. The former lettering system was thought to be misinterpreted as a grading system that was often confused by practitioners. Hopefully, the new narrated system will better convey risks involved in prescribing.

A definite advantage to the new PLLR is that it takes the gestational age of the pregnancy into consideration. With the lettering categories, it was assumed that a medication was equally safe or equally dangerous throughout the pregnancy. The PLLR addresses timing of exposure during specific trimesters.[2]

The PLLR also addresses the widespread lack of data on many medications, since pregnant women are often excluded from clinical trials due to the ethics of the unknown. Much of the teratogenic data obtained is through observational or epidemiological studies. A 2011 study reviewed the safety of 172 drugs that were FDA approved from 2000 to 2010 and found that 168 (97.7%) of the drugs scrutinized lacked enough data to determine the teratogenic effects of the medications during a pregnancy.[3]

In efforts to collect more information, there are many pregnancy registries that collect data on already approved medications that are often used during pregnancy. They compare the data to the same population not taking the medication to look for trends. As of December 2014, the FDA has a labeling rule that requires drug manufacturers to include pregnancy registry contact information on the medication label. This should help physicians and pregnant patients easily participate in the registry, which can lead to improved

safety profile and can be made into ophthalmic preparations by a compounding pharmacist for severe bacterial keratitis if tobramycin isn't acceptable, the fluoroquinolones are of concern, or neither provide adequate coverage. For less severe infections, such as bacterial conjunctivitis or prophylaxis against infection, erythromycin, polymixin B and topical azithromycin are other safe options.[15-17]



data collection for medications.[4]

There are over six million pregnancies in the United States each year, and it is estimated that a woman takes three to five medications during her pregnancy.[5] Because many comorbidities during pregnancy require treatment, optometrists are bound to be in a position to prescribe for a pregnant or breastfeeding patient. The FDA's new labeling system should help optometrists have a clearer understanding of the safety profiles and risks involved with the medications they prescribe. As with virtually all practitioners, optometrists have to make informed decisions based on the risks vs. benefits to a patient in need of diagnostic or therapeutic medications. The new labeling system will provide the prescriber more organized data on the potential risks and benefits to the mother, the fetus, the breastfeeding child and to men and women of reproductive ages.

Of course, consulting with a woman's obstetrician is always a potential option when considering prescribing medications during pregnancy. Protecting a pregnant or breastfeeding patient from unintentional adverse effects of diagnostic and therapeutic medications is undoubtedly every practitioner's intent and the new labeling system should make this easier than before.

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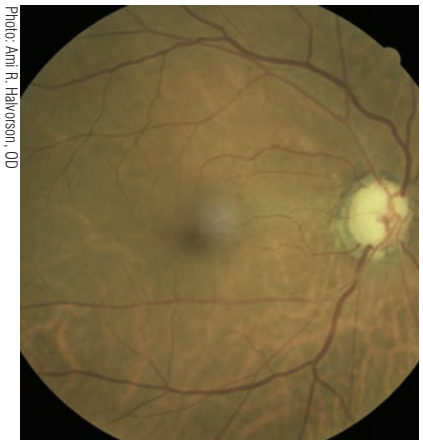

Photo: Ami R. Halvorson, OD

Because oral carbonic anhydrase inhibitors are contraindicated during pregnancy, consider using labetalol as a topical glaucoma treatment.

Pain Management

There are situations when a patient who is pregnant may need pain control for an ocular issue. Corneal abrasions or lid lacerations are certainly reasons for considering oral pain management. Aspirin and other oral nonsteroidal anti-inflammatory agents are a concern during pregnancy, and acetaminophen alone, although generally acceptable for short-term use during pregnancy, may not give the level of relief necessary.[18]

Although prolonged and heavy use of opioid agents has been shown to affect the fetus, opioids such as acetaminophen with codeine are routinely used by obstetricians for short-term relief from painful conditions during pregnancy.[19]

During breastfeeding, the synthetic codeine derivative hydrocodone is preferred, as genetic differences exist between patients, which can cause more conversion of codeine to morphine, resulting in opioid overdose in a breastfed infant. Therefore, hydrocodone bitartrate and acetaminophen may be the preferred agent.[19]

Systemic Antiviral Meds

Ocular herpes simplex can present in patients who are pregnant as well, and recurrences may be more common during pregnancy given the stressed systemic state and decreased immunity. Periocular herpetic lesions, corneal dendritic ulcerations or herpes-induced conjunctivitis can prompt the need for antiviral therapy.

Because oral antivirals such as acyclovir have been used by obstetricians for the prevention of pregnancy-induced genital herpes outbreaks and transmission of the virus to the fetus, these medications have been found to be well-tolerated in pregnant women and can be used when necessary for ocular herpetic conditions.[20] In fact, oral antivirals such as acyclovir, valacyclovir and famciclovir have the historic FDA pregnancy category B rating, while topical antivirals such as Viroptic (trifluridine, Pfizer) and Zirgan (ganciclovir, Bausch + Lomb) have the historic FDA category C rating. This is likely because they have been less frequently prescribed and observed than their oral counterparts. Oral acyclovir has also been approved by the American Academy of Pediatrics for lactating women.[21]

Managing Ocular Surface Disease

Dry eye patients often experience worsening of their ocular surface disease during pregnancy. Restasis (topical ophthalmic cyclosporine, Allergan), is typically used as a primary treatment; however, although not found in the bloodstream after topical administration during the FDA trials, it is historically designated as category C. Therefore, avoid cyclosporine when possible and instead recommend an increase in frequency of nonpreserved artificial tears, gels and ointments, as well as punctal plugs for the pregnant patient with dry eye.

Associated ocular allergies can be treated with Lastacaft (alcaftadine 0.25%, Allergan) safely. Other similar allergy drops that have a comparable mechanism of action to Lastacaft, such as Pataday (olopatadine 0.2%, Alcon) and Pazeo (olopatadine hydrochloride 0.7%, Alcon), have the historic FDA category C rating and are not recommended for use in patients who are pregnant or breastfeeding. Such a disparity between medications highlights the need for the FDA's updated labeling system (*see "An Update on the FDA's Pregnancy and Lactation Labeling," pg. 30*).

As many ocular conditions have associated inflammation, eye care practitioners often desire to prescribe a topical steroid. The use of a topical corticosteroid is indicated for conditions such as contact lens-induced inflammation, iritis and sterile infiltrative keratitis. Although many practitioners are concerned about the use of topical steroids in pregnancy given their side effect profile, ophthalmic steroids are approved by obstetricians for ocular inflammation because of the low amounts of systemic absorption.[22] Check with the patient's physician, however, for oral steroid treatment.

Glaucoma During Pregnancy

To treat glaucoma during pregnancy, oral carbonic anhydrase inhibitors (CAIs), such as Diamox (acetazolamide, Lederle), are contraindicated.[23,24] Although adverse effects on the fetus are unproven, it may be prudent to avoid topical CAIs such as Trusopt (dorzolamide, Merck) and Azopt (brinzolamide, Alcon) and prostaglandins such as Xalatan (latanoprost, Pfizer),

Lumigan (bimatoprost, Allergan) and Travatan (travoprost, Alcon). Although it is unlikely prostaglandins would cause harm as a once-daily ocular drop, their use is often avoided due to their important role in the induction of labor.[25]

Although topical glaucoma treatments in pregnancy have been poorly studied, labetalol is commonly used orally during pregnancy for the treatment of hypertension.[25] If used, topical beta-blockers should be avoided in the first trimester. Alphagan (brimonidine, Allergan) is the only topical ocular hypotensive agent with the historically more preferable FDA category B pregnancy rating. Brimonidine should be avoided, however, in lactation, as its use has been associated with inducing apnea and central nervous system depression in the breastfeeding infant.[26]

Consider surgical options such as trabeculectomy or selective laser trabeculoplasty if these medications are not controlling the patient's IOP, or if medications must be avoided entirely.

While some treatments are safe and effective during pregnancy and lactation, for some patients the best treatment may be no treatment. Many practitioners and their patients choose close observation without therapy because IOP is naturally and progressively lower during each trimester of pregnancy due to an increase in circulating prostaglandins and hormonal changes. ■

Dr. Autry received her pharmacy degree from the University of North Carolina at Chapel Hill. She practiced in critical care before returning for her optometry degree at the University of Houston. Following graduation, she performed a residency in ocular disease at the Eye Center of Texas ophthalmology center, where she is a partner today.

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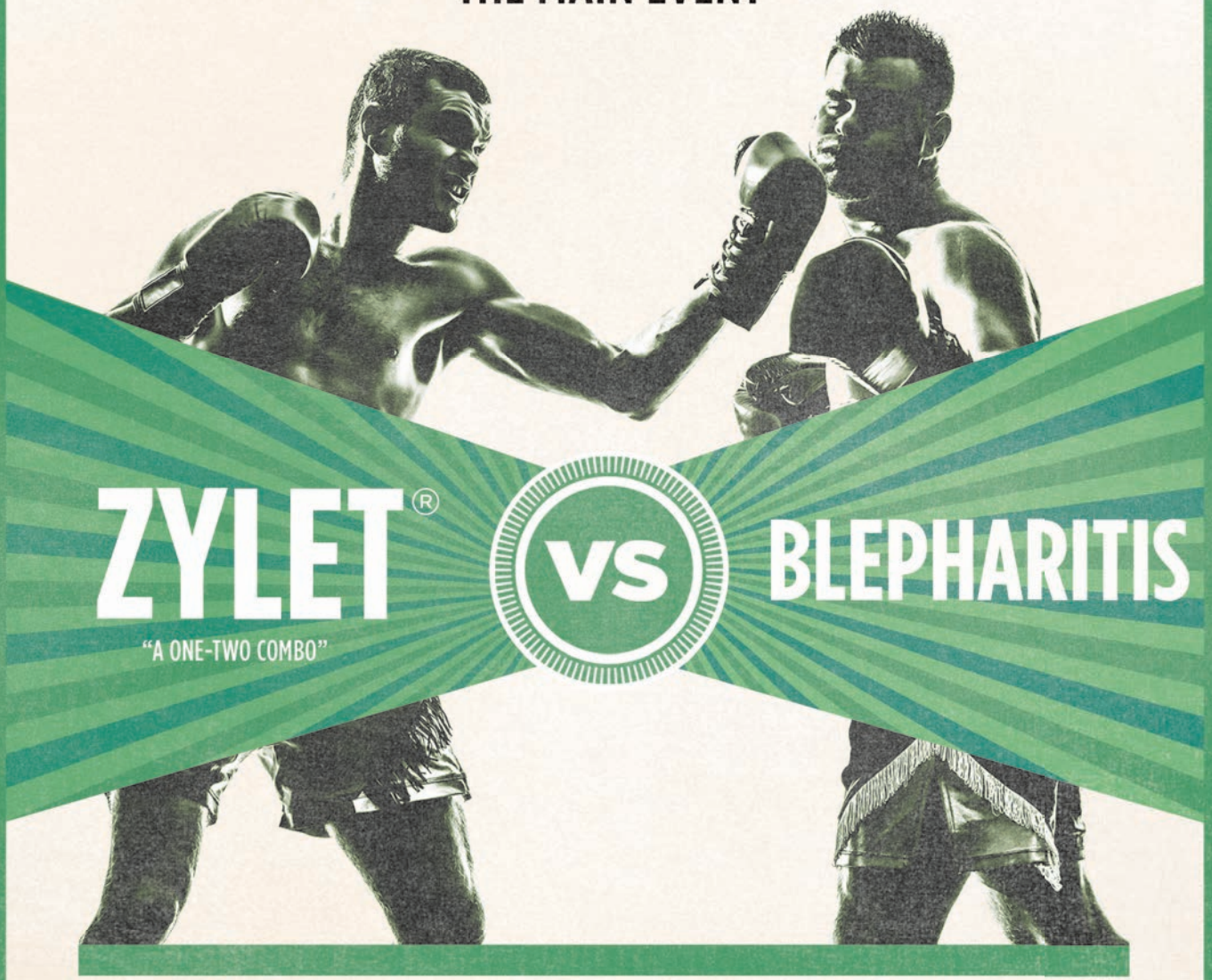

HELP PUT RELIEF IN YOUR CORNER

INDICATIONS AND USAGE

ZYLET® (loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension) is a topical anti-infective and corticosteroid combination for steroid-responsive inflammatory ocular conditions for which a corticosteroid is indicated and where superficial bacterial ocular infection or a risk of bacterial ocular infection exists.

Please see additional Indications and Usage information on adjacent page, including list of indicated organisms.

INDICATIONS AND USAGE (continued)

Ocular steroids are indicated in inflammatory conditions of the palpebral and bulbar conjunctiva, cornea and anterior segment of the globe such as allergic conjunctivitis, acne rosacea, superficial punctate keratitis, herpes zoster keratitis, iritis, cyclitis, and where the inherent risk of steroid use in certain infective conjunctivitides is accepted to obtain a diminution in edema and inflammation. They are also indicated in chronic anterior uveitis and corneal injury from chemical, radiation or thermal burns, or penetration of foreign bodies.

The use of a combination drug with an anti-infective component is indicated where the risk of superficial ocular infection is high or where there is an expectation that potentially dangerous numbers of bacteria will be present in the eye.

The particular anti-infective drug in this product (tobramycin) is active against the following common bacterial eye pathogens: *Staphylococci*, including *S. aureus* and *S. epidermidis* (coagulase-positive and coagulase-negative), including penicillin-resistant strains. *Streptococci*, including some of the Group A-beta-hemolytic species, some nonhemolytic species, and some *Streptococcus pneumoniae*, *Pseudomonas aeruginosa, Escherichia coli, Klebsiella pneumoniae, Enterobacter aerogenes, Proteus mirabilis, Morganella morganii*, most *Proteus vulgaris* strains, *Haemophilus influenzae*, and *H. aegyptius, Moraxella lacunata, Acinetobacter calcoaceticus* and some *Neisseria* species.

IMPORTANT SAFETY INFORMATION

- ZYLET® is contraindicated in most viral diseases of the cornea and conjunctiva including epithelial herpes simplex keratitis (dendritic keratitis), vaccinia, and varicella, and also in mycobacterial infection of the eye and fungal diseases of ocular structures.
- Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. 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.
- Use of corticosteroids may result in posterior subcapsular cataract formation.
- 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 a slit lamp biomicroscopy and, where appropriate, fluorescein staining.
- Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infections. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
- Employment 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 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.
- Most common adverse reactions reported in patients were injection and superficial punctate keratitis, increased intraocular pressure, burning and stinging upon instillation.

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

With a one-two combo in the treatment of blepharitis and other steroid-responsive ocular conditions with the risk of bacterial infection, PRESCRIBE ZYLET® TODAY.

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Zylet®
loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension

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BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use Zylet safely and effectively. See full prescribing information for Zylet.

Zylet® (loteprednol etabonate 0.5% and tobramycin 0.3% ophthalmic suspension)

Initial U.S. Approval: 2004

DOSAGE AND ADMINISTRATION

2.1 Recommended Dosing

Apply one or two drops of Zylet into the conjunctival sac of the affected eye every four to six hours. During the initial 24 to 48 hours, the dosing may be increased, to every one to two hours. Frequency should be decreased gradually as warranted by improvement in clinical signs. Care should be taken not to discontinue therapy prematurely.

2.2 Prescription Guideline

Not more than 20 mL should be prescribed initially and the prescription should not be refilled without further evaluation [*see Warnings and Precautions (5.3)*].

CONTRAINDICATIONS

4.1 Nonbacterial Etiology

Zylet, as with other steroid anti-infective ophthalmic combination drugs, 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

5.1 Intraocular Pressure (IOP) Increase

Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision. 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.

5.2 Cataracts

Use of corticosteroids may result in posterior subcapsular cataract formation.

5.3 Delayed Healing

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

5.4 Bacterial Infections

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

5.5 Viral Infections

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

5.6 Fungal Infections

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

5.7 Aminoglycoside Hypersensitivity

Sensitivity to topically applied aminoglycosides may occur in some patients. If hypersensitivity develops with this product, discontinue use and institute appropriate therapy.

ADVERSE REACTIONS

Adverse reactions have occurred with steroid/anti-infective combination drugs which can be attributed to the steroid component, the anti-infective component, or the combination.

Zylet:

In a 42 day safety study comparing Zylet to placebo, ocular adverse reactions included injection (approximately 20%) and superficial punctate keratitis (approximately 15%). Increased intraocular pressure was reported in 10% (Zylet) and 4% (placebo) of subjects. Nine percent (9%) of Zylet subjects reported burning and stinging upon instillation.

Ocular reactions reported with an incidence less than 4% include vision disorders, discharge, itching, lacrimation disorder, photophobia, corneal deposits, ocular discomfort, eyelid disorder, and other unspecified eye disorders.

The incidence of non-ocular reactions reported in approximately 14% of subjects was headache; all other non-ocular reactions had an incidence of less than 5%.

Loteprednol etabonate ophthalmic suspension 0.2% - 0.5%:

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.

In a summation of controlled, randomized studies of individuals treated for 28 days or longer with loteprednol etabonate, the incidence of significant elevation of intraocular pressure (≥10 mm Hg) was 2% (15/901) among patients receiving loteprednol etabonate, 7% (11/164) among patients receiving 1% prednisolone acetate and 0.5% (3/583) among patients receiving placebo.

Tobramycin ophthalmic solution 0.3%:

The most frequent adverse reactions to topical tobramycin are hypersensitivity and localized ocular toxicity, including lid itching and swelling and conjunctival erythema. These reactions occur in less than 4% of patients. Similar reactions may occur with the topical use of other aminoglycoside antibiotics.

Secondary Infection:

The development of secondary infection has occurred after use of combinations containing steroids and antimicrobials. Fungal infections of the cornea are particularly prone to develop coincidentally with long-term applications of steroids.

The possibility of fungal invasion must be considered in any persistent corneal ulceration where steroid treatment has been used.

Secondary bacterial ocular infection following suppression of host responses also occurs.

USE IN SPECIFIC POPULATIONS

8.1 Pregnancy

Teratogenic effects: Pregnancy Category C. Loteprednol etabonate has been shown to be embryotoxic (delayed ossification) and teratogenic (increased incidence of meningocele, abnormal left common carotid artery, and limb fixtures) 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 at 0.5 mg/kg/day (6 times the maximum daily clinical dose) during organogenesis did not result in any reproductive toxicity. Loteprednol etabonate was maternally toxic (significantly reduced body weight gain during treatment) when administered to pregnant rats during organogenesis at doses of ≥5 mg/kg/day.

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

Reproductive studies have been performed in rats and rabbits with tobramycin at doses up to 100 mg/kg/day parenterally and have revealed no evidence of impaired fertility or harm to the fetus. There are no adequate and well controlled studies in pregnant women. Zylet should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

8.3 Nursing Mothers

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

8.4 Pediatric Use

Two trials were conducted to evaluate the safety and efficacy of Zylet® (loteprednol etabonate and tobramycin ophthalmic suspension) in pediatric subjects age zero to six years; one was in subjects with lid inflammation and the other was in subjects with blepharoconjunctivitis.

In the lid inflammation trial, Zylet with warm compresses did not demonstrate efficacy compared to vehicle with warm compresses. Patients received warm compress lid treatment plus Zylet or vehicle for 14 days. The majority of patients in both treatment groups showed reduced lid inflammation.

In the blepharoconjunctivitis trial, Zylet did not demonstrate efficacy compared to vehicle, loteprednol etabonate ophthalmic suspension, or tobramycin ophthalmic solution. There was no difference between treatment groups in mean change from baseline blepharoconjunctivitis score at Day 15.

There were no differences in safety assessments between the treatment groups in either trial.

8.5 Geriatric Use

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

NONCLINICAL TOXICOLOGY

13.1 Carcinogenesis, Mutagenesis, Impairment of Fertility

Long-term animal studies have not been conducted to evaluate the carcinogenic potential of loteprednol etabonate or tobramycin.

Loteprednol etabonate was not genotoxic *in vitro* in the Ames test, the mouse lymphoma TK assay, a chromosome aberration test in human lymphocytes, or in an *in vivo* mouse micronucleus assay.

Oral treatment of male and female rats at 50 mg/kg/day and 25 mg/kg/day of loteprednol etabonate, respectively, (500 and 250 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender. No impairment of fertility was noted in studies of subcutaneous tobramycin in rats at 100 mg/kg/day (1700 times the maximum daily clinical dose).

PATIENT COUNSELING INFORMATION

This product is sterile when packaged. Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the suspension. If pain develops, redness, itching or inflammation becomes aggravated, the patient should be advised to consult a physician. As with all ophthalmic preparations containing benzalkonium chloride, patients should be advised not to wear soft contact lenses when using Zylet.

MANUFACTURER INFORMATION

BAUSCH & LOMB INCORPORATED

TAMPA, FLORIDA 33637 USA

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Based on 9007705-9004405 Revised 08/2013 US/ZYL/15/0014

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Managing the Medicine Cabinet

The most common prescription medications pose risks to your patients' ocular health. Spot them on the chart so you can be prepared to rein in their possible side effects. **By Benjamin P. Casella, OD**

In the age of polypharmacy, many patients present with—quite literally—page-long medication lists. Many commonly prescribed systemic medications can affect the eyes and visual system, with adverse effects ranging from mild dryness to blindness.[1] As primary care doctors for the human eye, optometrists often find themselves on the frontlines of health care. This notion, coupled with the reality of an aging patient population makes it paramount that optometrists remain cognizant of the potential side effects associated with the common systemic medications; several of the most commonly used medications are discussed here.

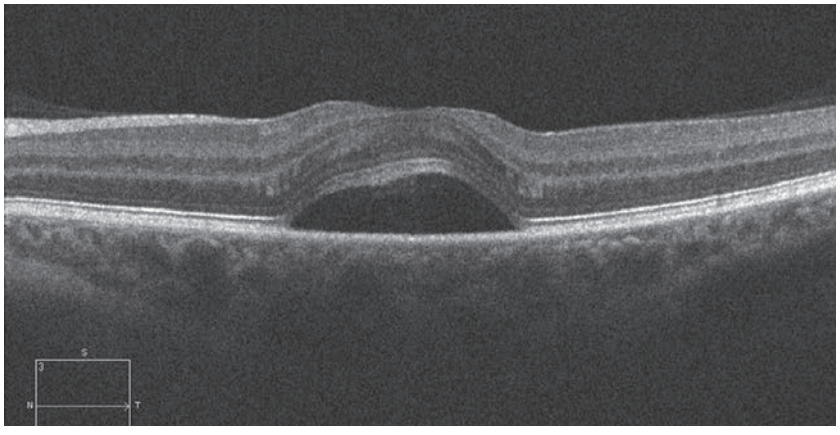

Fig. 1. SD-OCT scan of a 40-year-old female with corticosteroid-induced CSR. The patient presented sudden onset of unilateral blur several weeks after being prescribed oral prednisone for allergies. CSR resolved subsequent to steroid cessation.

Corticosteroids

As the standard for treatment of inflammation, corticosteroids such as prednisone, methylprednisolone, hydrocortisone, dexamethasone, etc., are used for a wide variety of acute and chronic conditions, such as arthritis, inflammatory bowel disease (IBD) and sarcoidosis. These diseases typically mandate long-term treatment and may persist for many years. Even at relatively low doses, long-term treatment with systemic corticosteroids carries risks for several adverse effects.[2]

The formation of posterior subcapsular cataract (PSC) and ocular hypertension are arguably the two most well known effects of both systemic and topical corticosteroid therapy. Research shows corticosteroids dysregulate blood glucose levels, which may cause ophthalmic manifestations such as induced myopia in the presence of diabetes; however, central serous retinopathy (CSR) is also a well-documented adverse ocular effect of corticosteroid use.[3,4] Steroid-induced CSR and steroid-induced ocular hypertension both tend to

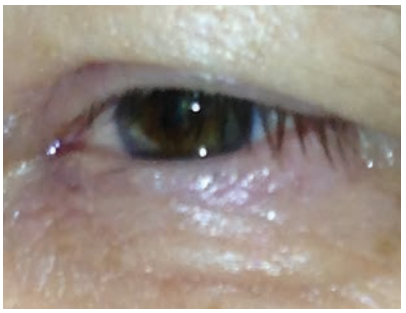

Fig. 2. A 64-year-old white male with mild conjunctival inflammation, angioedema of the eyelids associated with a recent increase in lisinopril dosage.

resolve when the patient discontinues the medication.

Anti-Hypertensives

Systemic hypertension is among the most common chronic diseases in the United States, and the frequency at which anti-hypertensive medications appear on patients' medication lists follow suit.[5] Three of the most common types of hypertension medications are beta-blockers, diuretics and angiotensin-converting enzyme (ACE) inhibitors. Common beta-blockers include atenolol, metoprolol and carvedilol. Just as topical beta-blockers suppress aqueous humor production, they may also suppress tear production, potentially leading to symptomatic dry eye disease.[6,7] Conjunctival inflammation may also occur or worsen with beta blocker use. Diuretics, such as hydrochlorothiazide, furosemide and triamterene, can also cause or exacerbate dry eye disease.[8] Uncommonly, supportive therapy may not be enough to quell the dry eye, and changing to another class of anti-hypertensive therapy may be necessary.

Common ACE inhibitors include lisinopril, benazepril and enalapril. Conjunctival inflammation with or without angioedema of the eyelids has been reported with ACE inhibitor use. *Figure 2* is the left eye of a 64-year-old male who presented with conjunctival inflammation and angioedema of both eyelids, which worsened around the same time that his lisinopril (a commonly prescribed ACE inhibitor) dosage was increased from 5mg to 10mg QHS. Interestingly, his ocular condition did not readily respond to topical corticosteroid therapy, but his symptoms did subside with his medication being changed to Cozaar (losartan potassium, Merck), an angiotensin II receptor antagonist, after a brief conversation with the prescribing doctor.

This case highlights the potential for adverse reactions even at relatively low concentrations.

Statins

Hypercholesterolemia is a major contributor to cardiovascular disease (one of the leading causes of death worldwide).[9] Statins, such as atorvastatin, lovastatin, and simvastatin, work well to reduce elevated cholesterol levels, and their side-effect profiles are relatively desirable—their systemic side effects are not as common as with other medications.

Commonly, muscle weakness or soreness may occur with statin use, which researchers attribute to induced mitochondrial dysfunction at the cellular level.[10] Myopathic symptoms may present to the optometrist first as diplopia, ptosis or soreness around the eyes. When new-onset myopathic symptoms occur in the presence of statin use, the statin should be considered a potential cause, and the prescriber should be made aware so that changes to therapy can be made if need be. Finally, cataract formation has been reported as an uncommon side effect of statin use.

In recent years, investigators have studied the possibility of statin use having a protective effect against the development of open-angle glaucoma.[11,12] There is not enough evidence to change current treatment modalities, but this research will likely continue as the race to find effective so-called "neuroprotective" therapeutic agents for glaucoma continues.

Multiple Sclerosis Medications

Several years ago, Gilenya (fingolimod, Novartis) became the first FDA-approved oral medication for relapsing-remitting multiple sclerosis (MS), the most common form of MS. In recent years, Gileyna has been implicated in the formation of macular edema by increasing vascular permeability.[14-16] For this reason, it is recommended that patients have a baseline ophthalmic examination, including dilated fundus evaluation, and a second examination three to four months subsequent to the first, since studies indicate that adverse effects tend to manifest after four

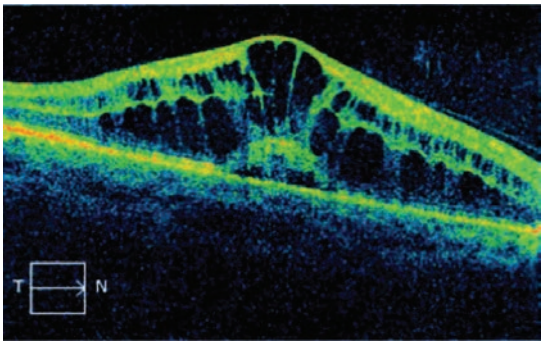

Fig. 3. Drug-induced macular edema is uncommon, but a potentially sight-threatening side effect of fingolimod therapy.

Ocular Adverse Reactions of Systemic Drugs

By Len V. Koh, OD, Midwestern University and Arizona College of Optometry

(IND: indications, OAR: ocular adverse reactions, REC: recommendations)

Adalimumab (Humira) *IND:* Rheumatoid arthritis, ankylosing spondylitis *OAR:* Optic neuritis	**Alendronate** (Fosamax) **Pamidronate** (Aredia) *IND:* Osteoporosis, Paget's disease *OAR:* Uveitis, scleritis or episcleritis	**Amiodarone** (Cordarone) *IND:* Irregular heartbeat, atrial fibrillation, supraventricular tachycardia *OAR:* Photosensitivity, corneal verticillata, thyroid eye disease	**Aripiprazole** (Abilify) *IND:* Schizophrenia, bipolar I disorder, major depression, autistic disorder *OAR:* Diplopia	**Canthaxanthine** (Orobronze) *IND*: Oral tanning agent *OAR:* Crystalline retinopathy
Carbamazepine (Tegretol) *IND:* Epilepsy, trigeminal neuralgia *OAR:* Blurred vision, hallucinations, transient diplopia, oculomotor disturbances, nystagmus	**Cetirizine** (Zyrtec) *IND:* Allergic rhinitis *OAR:* Mydriasis, oculogyric crisis	**Digoxin** (Lanoxin) *IND:* Heart failure, atrial fibrillation *OAR:* Yellow vision, halo effect, retrobulbar neuritis	**Ethambutol** (Mycobutin) *IND:* Pulmonary tuberculosis *OAR:* Optic neuritis, retrobulbar neuritis	**Ezogabine** (Potiga) *IND:* Epilepsy *OAR:* Retinal pigmentary abnormalities *REC:* Baseline and eye exam every six months
Fingolimod (Gilenya) *IND:* Relapsing forms of multiple sclerosis *OAR:* Macular edema *REC:* Baseline eye exam, and three to four months after treatment, then PRN	**Flecainide** (Tambocor) *IND:* Paroxysmal supraventricular tachycardias *OAR:* Eye pain or irritation, photophobia, nystagmus	**Hydrochlorothiazide** (Microzide) *IND:* Hypertension, combined with other anti-hypertensives *OAR:* Acute myopia and secondary angle-closure glaucoma	**Hydroxychloroquine** (Plaquenil) *IND:* Malaria, lupus, and rheumatoid arthritis *OAR:* Retinal toxicity >6.5mg/kg/d *REC*: Baseline and annual eye exam	**Interferons** (Avonex/Intron A) *IND:* Hepatitis B/C, leukemia *OAR:* Macular edema, retinal hemorrhages, optic neuritis *REC:* Baseline and periodic eye exam
Isotretinoin (Accutane) *IND:* Acne *OAR:* Decreased night vision, corneal opacities *REC:* Use caution when driving at night	**Ivabradine** (Corlanor) *IND:* Heart failure *OAR:* Phosphenes first two months *REC:* Use caution when driving	**Linezolid** (Zyvox) *IND:* Pneumonia, skin infections *OAR:* Peripheral and optic neuropathy *REC:* Eye exam for anyone taking linezolid for more than three months, or symptomatic patients	**Methotrexate** (Trexall) *IND:* Neoplasm, psoriasis, rheumatoid arthritis *OAR:* Conjunctivitis, optic neuropathy	**Minocycline** (Solodyn) *IND:* Acne vulgaris *OAR:* Pseudotumor cerebri (unusual headaches), blurred vision
Niacin (Niacor) *IND:* Hypercholesterolemia, hypertriglyceridemia *OAR:* Toxic amblyopia, cystoid macular edema	**Phenothiazines** *IND:* Schizophrenia, nausea and vomiting, *OAR:* Corneal and lens deposits, conjunctival pigmentation, pigmentary retinopathy *REC:* Periodic ocular examination	**Pioglitazone** (Actos) **Rosiglitazone** (Avandia) *IND:* Diabetes mellitus Type 2 *OAR:* Macular edema	**Prednisone** (Deltasone) **Prednisolone** (Pred Forte) *IND:* Inflammation: e.g., iritis, arthritis, rhinitis, asthma, dermatitis *OAR:* PSC, elevated IOP, exophthalmos	**Rifabutin** (Mycobutin) *IND:* Prevention of disseminated *Mycobacterium avium* complex disease *OAR:* Uveitis, peripheral and central corneal deposits
Sildenafil (Viagra) **Tadalafil** (Cialis) **Vardenafil** (Levitra) *IND:* Erectile dysfunction *OAR:* Blue vision, shimmering around objects, CSC, subconjunctival heme, NAION	**Tamoxifen** (Nolvadex) *IND:* Metastatic breast cancer, reduction in breast cancer incidence in high-risk women *OAR:* Cataract, corneal deposits, crystalline retinopathy	**Tamsulosin** (Flomax) *IND:* Benign prostatic hyperplasia *OAR:* Intraoperative floppy iris syndrome, blurred vision	**Topiramate** (Topamax) *IND:* Epilepsy, migraine, weight loss *OAR:* Bilateral acute angle-closure, myopic shift	**Vigabatrin** (Sabril) *IND:* Epilepsy, infantile spasms *OAR:* Bilateral concentric VF constriction *REC:* Baseline eye exam every three months while on therapy, three to six months after therapy

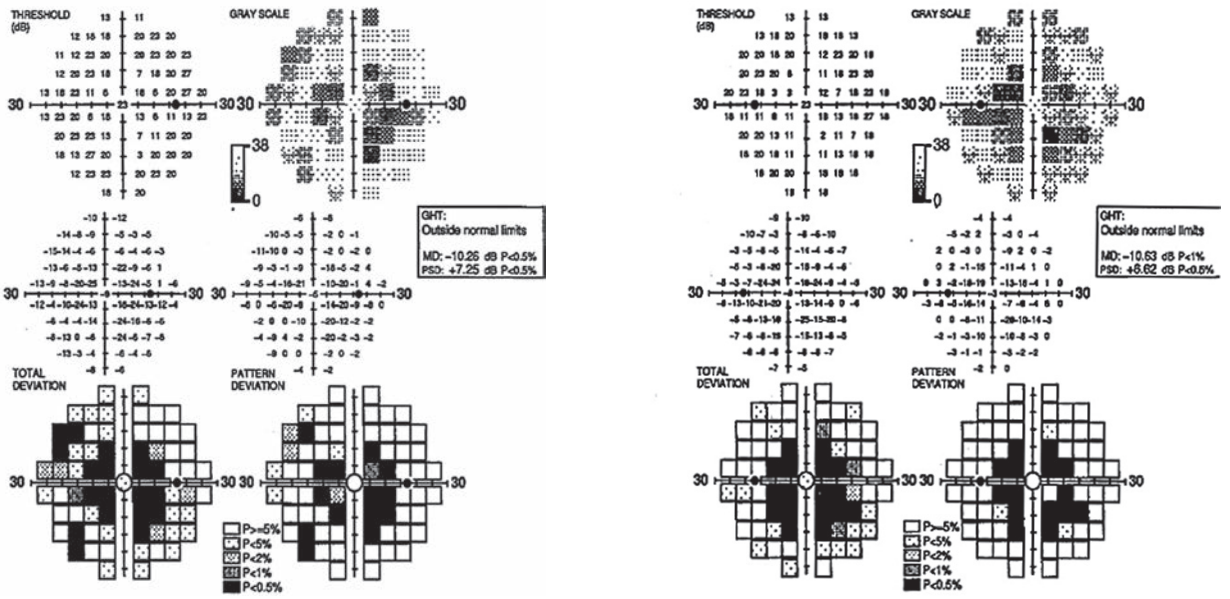

Fig. 4. The visual field study of a 52-year-old black female who presented with central scotomas, which was associated with methotrexate-induced toxic optic neuropathy.

months.[17] OCT studies are highly beneficial in establishing a baseline and monitoring patients who are taking Gilenya. Patients should be counseled on the risks associated with Gilenya (e.g., macular edema), and advised to monitor their vision at home and to call immediately if they experience changes in vision. The edema is thought to resolve, in most cases, with cessation of the medication.[15] Treatment of the edema may be indicated for recalcitrant cases or where the positive effects of this medication are too great to warrant its discontinuation. Although macular edema is not a common side effect of fingolimod therapy, communication regarding these recommendations should be established and maintained with the prescribing doctor.

Migraine Medications

Topamax (topiramate, Janssen Pharmaceuticals) has been widely prescribed for years to prevent the occurrence of migraine headaches. The development of acute angle closure glaucoma is an uncommon, but well-documented side effect of this medication.[18-20] Research shows the risk of topiramate-induced angle closure is five times greater in persons under the age of 50 and is typically bilateral (in contrast to angle closure resulting from pupillary block).[18] Since the cause of topiramate-induced angle closure is edema and effusion of the uvea, pilocarpine should be avoided.

In addition to lowering IOP in the acute phase of the attack, cycloplegics and topical steroids are also indicated to reduce vascular permeability within the uvea itself. Peripheral iridotomy is of no use, as primary pupillary block is not the cause of topiramate-induced angle closure. Myopic shifts may occur as a result of the same mechanism as the angle closure. Acute-onset maculopathy and transient, non-specific visual field defects have also been reported.

DMARDs

Disease-modifying anti-rheumatic drugs, or DMARDs, is a clinically descriptive term designating a family of medications whose therapeutic effects were first associated with rheumatoid arthritis. In fact, DMARDs are used to treat other inflammatory/autoimmune diseases as well, such as psoriasis and Crohn's disease.[21] The member of the DMARD family that is most well-known for its ocular side effects is the antimalarial drug Plaquenil (hydroxychloroquine, Sanofi Canada). Routine evaluations for its characteristic bull's eye maculopathy, and daily visual monitoring on the part of the patient are necessary to prevent this permanent and potentially visually-impairing sequela.

Fundus photography, visual field studies, fundus autofluorescence and multifocal electroretinogram (mfERG) studies have all shown value in detecting bull's eye maculopathy. In the past

Table 1. Selected Side Effects of 10 Common Oral Meds

DRUG	OCULAR SIDE EFFECT
Cordarone (amiodarone, Pfizer)	Vortex keratopathy
Cogentin (benztropine, Merck)	Mydriasis/cycloplegia, dilpopia
Benadryl (diphenhydramine, McNeil-PPC)	Dry eye
Depakote (divalproex, AbbVie)	Blurred vision, mydriasis
Vyvanse (lisdexamfetamine, Shire)	Blurred vision, mydriasis
Viagra (sildenafil, Pfizer)	Cyanopsia, anterior ischemic optic neuropathy
Flomax (tamsulosin, Boehringer-Ingelheim)	Floppy iris syndrome
Tetracycline	Gray scleral discoloration
Mellaril (thioridazine, Novartis)	Dyschromatopsia, pigmentary retinopathy
Coumadin (warfarin, Bristol-Myers Squibb)	Subconjunctival and/or retinal hemorrhages

decade or so, SD-OCT studies have become popular as a means of objectively assessing early retinal damage with a high resolution on the order of just a few microns. In 2011, SD-OCT was added to the American Academy of Ophthalmology's clinical guidelines for detecting hydroxychloroquine and chloroquine toxicity.[22]

Trexall (methotrexate, Barr Laboratories) was first developed as a form of chemotherapy and continues to be used as such; however, this drug has gained popularity as an effective DMARD agent.[23] It has been shown to cause certain ocular side effects even at low doses (a typical dose may be 2.5mg orally two to three times per week), the most significant of which is toxic optic neuropathy (see *Figure 4*).[24] Folic acid supplementation may prevent or lessen some side effects of methotrexate and other DMARDs.[25]

Truly, no medication is without some side effect. However, keeping abreast of the most common ocular side effects of the most commonly prescribed systemic medications will aid in correct and timely diagnoses for your patients, especially since signs and symptoms such as redness, dryness and visual disturbances are often quickly attributed to and treated as sequelae of primary eye conditions.

As well, communication with the prescribers of these medications is important in relaying the fact that, as primary care doctors for the human eye, we, as optometrists, are monitoring for these adverse effects, some of which can be visually devastating if not diagnosed and treated early on. ■

Dr. Casella is the owner of a third-generation private practice in Augusta, GA. He has no financial interest in any of the products mentioned in this article.

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PEER • REVIEWED • PRA • ARTICLE

THE MIND'S EYE:

Ocular Complications of Psychotropic Medications

Most optometrists will see patients who take psychoactive drugs. Know the potential ocular side effects and how to manage these patients. **By Bhawan Minhas, OD**

Psychoactive drugs are prescribed frequently for a variety of conditions that alter mood and emotional status. Whether it's short-term use of an antidepressant to cope with the loss of a loved one or a lifelong reliance on an anti-schizophrenia drug to function normally in everyday life, approximately 46% of Americans will meet the criteria for a DSM-IV and -V (*Diagnostic and Statistical Manual of Mental Disorders*) disorder at some point in their lifetime.[1,2] Furthermore, half of all lifetime cases are known to begin by age 14 and three quarters by age 24.[1]

Although many potential neurological complications exist, the eye is the second most common site to manifest drug toxicity, outshined only by the liver.[4] As such, optometrists should follow individuals placed on these agents diligently. A standardized approach for monitoring ocular toxicities from these medications and others would be helpful. The astute clinician should be aware of these agents and their potential complications so that timely intervention can be started to prevent permanent sequelae.

Proposed ramifications of ocular toxicity include: ocular surface and ocular pigmentation complications, cataracts, accommodative interference, angle closure glaucoma, retinopathy and neuropathy, ocular motility disorders and impaired sensory perception.[4] Two systemic considerations that, although not directly related to the eye, can have ocular consequences include increased risk of metabolic syndrome, specifically diabetes, and cerebrovascular events.

The Ocular Surface

Drug toxicity to the ocular surface can manifest as epithelial keratopathy, corneal edema and altered tear film quantity and quality.[5] Timely and appropriate management of these complications can prevent permanent ocular surface damage and impaired vision. Early recognition can ensure the patient is able to continue the appropriate treatment for their underlying disorder.

Phenothiazines (typical antipsychotics), for example, can cause phototoxic lysis of the corneal endothelium.[6] This is linked to total dosage of medication.[5,6] This can lead to impaired endothelial pump function, causing severe corneal edema and consequent severe visual effects.[6] Visual impairment is irreversible without prompt identification and cessation of the medication.

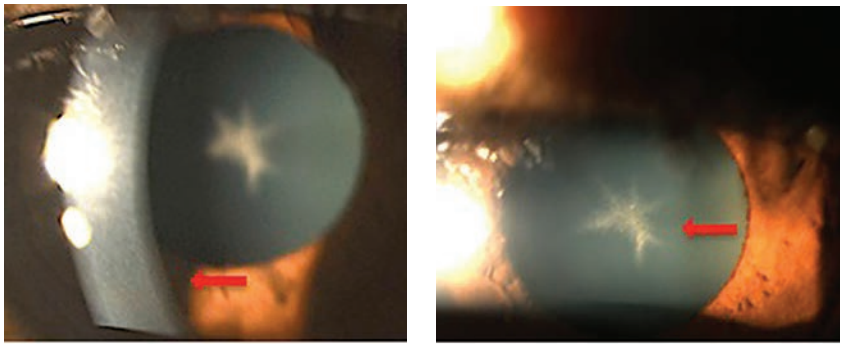
Chlorpromazine in particular, a member of the phenothiazine family, has been noted to cause corneal epithelial keratopathy.[5] The manifestation seen with chlorpromazine use is noted to have a distinctive pattern of swirling lines or fine streaks in the epithelium, reminiscent of Plaquenil (Covis Pharmaceuticals) keratopathy.[5] This presentation has been linked to high dosages (>2g/day) of the medication.[5] The condition elicits minimal visual consequences and usually regresses with appropriate

intervention, such as dose tapering.[5]

Psychiatric medications also can act to alter both the quantity and quality of tears. Medications that have anticholinergic effects, such as tricyclic antidepressants (TCAs), may cause decreased lacrimation.[7,8] One can postulate that any medication with such effects would decrease the quantity of tear production. Although particularly bothersome in CL wearers or post-LASIK patients, appropriate use of artificial tears or prescription cyclosporine can be helpful in such cases.

Clozapine, an atypical antipsychotic medication, is commonly used as an alternative to traditional phenothiazines due to a comparative reduced risk of neurological side effects.[9] However, clozapine exhibits anticholinergic effects by blocking muscarinic and nicotinic receptors, as well as the muscarinic-3 receptors in the conjunctiva and lacrimal gland.[10] This leads to decreased mucous and aqueous secretion.[10] Persistent tear film instability and dry eye syndrome can induce morphological and biomechanical changes at the cellular level, inevitably affecting the ocular surface and vision.[11] Prompt lubrication and tear rehab agents such as cyclosporine are required to prevent desiccation.

Alterations of the tear film quality may also manifest as changes to the chemical components of the tears occur. Lithium, one of the oldest mood stabilizers, has been reported to cause eye irritation during the first few weeks of treatment.[12] A potential etiology may be an increased sodium concentration in lacrimal secretion due to lithium's effects on sodium-chloride cotransport proteins.[12] The increased tear osmolarity may diminish with sustained use as a new equilibrium is established, thus explaining why the toxicity is only seen with medication initiation.



A 54-year-old black female with pertinent history of clozapine 100mg PO daily use for schizophrenia. No previous history of typical antipsychotic medication use. Her best-corrected visual acuity is 20/20 OU. Note the fine golden-brown dust-like deposits on the corneal endothelium, greatest inferiorly, and anterior subcapsular opacity in a stellate pattern in both eyes. No pigmentary retinopathy was noted.

Follow The Pigment

Beyond their effects on the ocular surface, both chlorpromazine and clozapine have been linked to ocular pigmentation; however, the former, a typical antipsychotic, is more likely to cause pigment changes compared with clozapine.[4,13,14] Ocular pigmentation secondary to drug toxicity can be divided into two categories: pigmentation of the skin, conjunctiva, cornea or lens and pigmentation retinopathy.[13,14] The first may cause minimal to no changes to vision, while the latter may lead to irreversible degenerative retinopathy.

Chlorpromazine is known to accumulate in the skin of the eyelid, conjunctiva, posterior corneal stroma, lens and uveal tract.[4,13,14] As the compound is phototoxic, it has been postulated that photosensitization of the tissue proteins occurs in areas of increased sun exposure after accumulation of the drug in these tissues.[13,14] Protective sun wear and reduced sun exposure while on the medication is recommended.

Although these pigment changes are not as common with the use of clozapine, there have been a handful of cases with a similar pathology.[14] Although newer, safer alternatives are present in comparison with conventional treatments, clinicians should continue to be aware of potential, less common side effects that may still exist.

Lenticular Opacities and Cataracts

Cataracts that develop through the natural aging process most often cause bilateral clouding of the crystalline lens; however, cataracts secondary to medication use are rarely bilateral and usually asymmetric.[15] This may be due to unequal deposition of a foreign medication in the crystalline lens. Additionally, as certain antipsychotics—namely the atypical variety—can cause metabolic syndrome, hyperglycemic status in these patients can also lead to early diabetic cataract formation.[15] Interestingly, lenticular opacities are often found in conjunction with corneal opacities, yet not all represent true cataractous changes.[15]

Phenothiazines such as chlorpromazine and thioridazine are the most common antipsychotic agents that lead to lenticular opacities.[4,7,8] As described above, posterior corneal pigmentation can be related to anterior subcapsular pigment, which may show a link to alterations in the aqueous humor.[15,16]

Psychiatric Medications

These drugs work by altering levels of particular neurotransmitters in the brain.[3] They can loosely be categorized into six groups:

- Antipsychotics (typical and atypical); the delineation of "typical" vs. "atypical" antipsychotics has less to do with their efficacy and more to do with their side effect profile.[4] Typical antipsychotics are known to have more severe toxicity, which can be related to either high dose or cumulative dosing, depending on the condition being considered.[4,5]
- Antidepressants—tricyclic antidepressants, selective serotonin reuptake inhibitors, serotonin-norepinephrine reuptake inhibitors, norepinephrine reuptake inhibitors and monoamine oxidase inhibitors.
- Anxiolytics (benzodiazepines).
- Mood stabilizers (Lithium).
- Anticonvulsants.
- Stimulants.[3,4]

Although phototoxicity may be a potential mechanism of action, an alternate explanation may be lens discoloration. Endogenous melanin in the eye could be trapping free radicals produced by psychotropic medications, which may show up as lens discoloration in certain cases.[15,16] These opacities may not reverse with cessation of the causative agent, yet any resultant visual disturbance will vary based on the duration of exposure and degree of damage.[15,16]

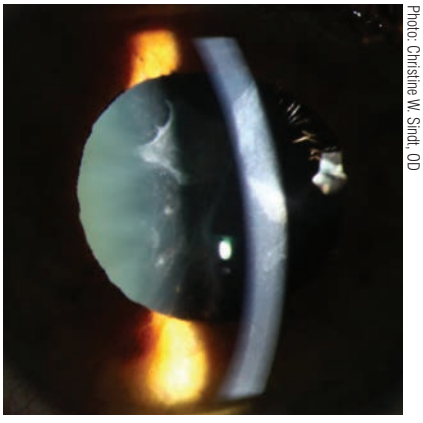
Accommodative Interference

Changes to accommodative status in patients using psychiatric medications occur mainly due to the drugs' anticholinergic effects. The common effects include mydriasis and cycloplegia due to combinations of sympathetic stimulation; TCAs, selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs) and norepinephrine reuptake inhibitors (NRIs) have been shown to cause both mydriasis and cycloplegia in the acute phase of treatment.[17]

Mydriasis—dilation of the pupil due to stimulation of alpha receptors located on the radial muscle of the iris—may cause non-severe and transient visual changes. Cycloplegia, however, has a paretic effect on the ciliary muscle and may lead to blurred vision, mainly at near. Management of accommodative disability may require an appropriate spectacle prescription until the condition improves. Moreover, it can be assumed that any psychotropic medication with strong anticholinergic actions, antiadrenergic actions or both can cause mydriasis and cycloplegia with similar effects.

Along with an anticholinergic effect, SSRIs have multiple actions on the central and peripheral nervous system, including muscles of the iris that cause pupil dilation and constriction. An alternative mechanism of action for mydriasis by SSRIs may be stimulation of 5-HT7 receptors.[18] These receptors are located in the iris sphincter and, when stimulated, cause a passive mydriasis.[18] They are likely also involved in increased intraocular pressure and SSRI-related glaucoma.

Topamax (topiramate, Janssen Pharmaceuticals), for example, is an anticonvulsant that may cause blurred vision secondary to changes caused by idiosyncratic swelling of the ciliary body, leading to a refractive change and myopic shift in prescription.[8,19] The World Health Organization has identified at least 13 adverse ocular side effects of Topamax, classified as "certain," "probable/likely" or "possible."[20] Abnormal vision and acute myopia (up to -8.75D) were categorized as potential side effects of Topamax use.[20] Associated symptoms likely occur within the first month of treatment.[20] Also note that this medication is often used off-label for migraine relief.



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Cataracts secondary to medication are usually asymmetric, perhaps due to unequal deposition of medication in the crystalline lens.

IOP and Angle Closure Glaucoma

Risk factors for acute angle closure glaucoma include: race, increased age, narrow anterior chamber angle, shallow anterior chamber depth, hyperopia, nanophthalmos, previous angle closure of fellow eye, family history, female sex and use of any substance that causes pupillary dilation.[21] Selecting the appropriate treatment for acute angle closure requires a firm understanding of the mechanism in play. Ask yourself: is the condition a result of an anatomically narrow angle further aggravated into pupil block by a medication causing mydriasis and cycloplegia? Or is it due to choroidal effusion, ciliary body swelling and forward displacement of the iris-lens structures, thus crowding the angle and causing angle closure without pupil block? These two situations would require individualized treatment plans.

TCAs, SSRIs, SNRIs, typical antipsychotics and theoretically any psychiatric medication having anticholinergic effects can cause an acute angle closure with pupil block in a patient with anatomically

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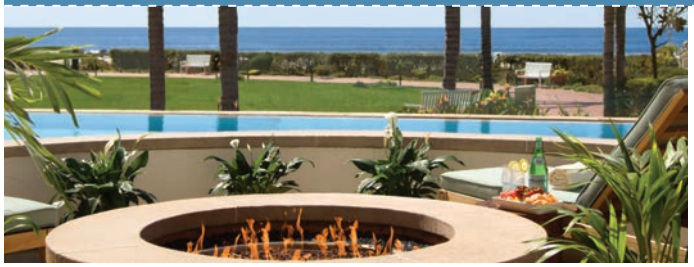

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narrow angles.[8] The mechanism in such a case would be drug-induced mydriasis in an already crowded angle, either active or passive, depending on the drug. Thus, these drugs should be prescribed cautiously in patients with narrow angles. Furthermore, this builds a case for including a comprehensive medication review into routine eye exams and appropriate correspondence with primary care physicians for at-risk patients.

The exact mechanism behind secondary angle closure as related to Topamax remains unclear, although suprachoroidal effusion is likely involved.[19,22] In addition, the sulfa-based molecule could potentially produce an allergic reaction, causing swelling of the lens and ciliary body.[19,22] Here, aggressive cycloplegia is the treatment of choice, as opposed to the traditional line of thinking with an acute angle closure in which mydriasis/cycloplegia would further exacerbate the condition.[22] The perceptive clinician should be able to distinguish between the two and select appropriate treatment. Recently, Topamax has been linked to visual field defects independent of increased intraocular pressure or angle closure attack, causing eye care providers to monitor patients accordingly.[23]

As most of these ocular complications arise in the first 49 days of treatment, and even after the first dose, it is critical for clinicians encountering patients on this treatment modality to establish a length of time on treatment.[20,23] Appropriate correspondence with the neurologist is warranted, as cessation of the medication, with or without initiation of other medical intervention, halts the condition and can save vision.[20,23] A traditional laser peripheral iridotomy (LPI) would not be beneficial in this case, as the mechanism of action differs from a typical acute angle closure attack.[22] Also, patients taking Topamax without ocular complications warrant a yearly evaluation.

Table 1. Psychiatric Medications and their Ocular Complications[8]

Ocular Complication	Medication
Refractive error	Topamax
Increased intraocular pressure	Topamax, antidepressants (TCAs/SSRIs/SNRIs)
Accommodative interference	Topamax, antidepressants (TCAs/SSRIs)
Ocular motor disturbances	Anticonvulsants, Topamax, anxiolytics, lithium
Oculogyric crisis	Typical antipsychotics, atypical antipsychotics, Topamax, anticonvulsants
Tear film changes	Lithium, antidepressants
Corneal or lenticular opacities	Typical antipsychotics, rarely atypical antipychotics
Pigmentary retinopathy	Typical antipsychotics, rarely anticonvulsants and anxiolytics

SSRIs and SNRIs are also linked to increased IOP via a different mechanism involving the 5-HT7, 5-HT2A and 5-HT2C receptors located in the iris-ciliary body complex.[18] These receptors cause an increase in flow to the ciliary body, thereby increasing aqueous humor production and IOP.[18] Coupling this with the active and passive mydriasis caused by these or other medications, angle closure with pupil block can occur concomitantly.[18]

Retinopathy and Optic Nerve Involvement

Because the eye is developmentally and anatomically an extension of the brain and the retina is on that continuum, it can be affected by medications that have psychotropic effects. Also, this thin and fragile tissue can act as a reservoir for deposition of the drug reaching the eye through its vascular supply.[8] As such, drug toxicity can affect both the retinal pigment epithelium (RPE) and the neurosensory retina (mainly, rods and cones).[4,8] Deposited medication in either the RPE or sensory retina is not easily cleared and can lead to potential damage.

Ocular pigmentation caused by phenothiazines, such as thioridazine and chlorpromazine, may take place in the retina. Thioridazine's risk is a function of large daily doses (>800 mg/day), while the risk associated with chlorpromazine is related to daily dose and duration of use.[4,8,24] Pigment has been shown to deposit from the peripheral to central retina.[24] Researchers postulate that phototoxic stress causes peripheral vision loss, nyctalopia, permanent vision loss and complete blindness as damage progresses.[23] Early detection and intervention can prevent permanent visual consequences.

Researchers have hypothesized a possible link to retinal toxicity and melanin binding, as the RPE is rich in melanin. However, studies show that binding affinity of medications to ocular melanin is not predictive of drug toxicity.[25]

Retinal toxicity has been described in conjunction with benzodiazepines in a small number of cases.[26] Clonazepam, an anticonvulsant and anxiolytic, has been linked to a 'white-dot-like' retinopathy that can be seen using ophthalmoscopy and confirmed with fundus autofluorescence.[25] Optic nerve involvement in the form of optic disc swelling causing blurred vision has been documented with therapeutic doses of lithium.[27] Resolution of this

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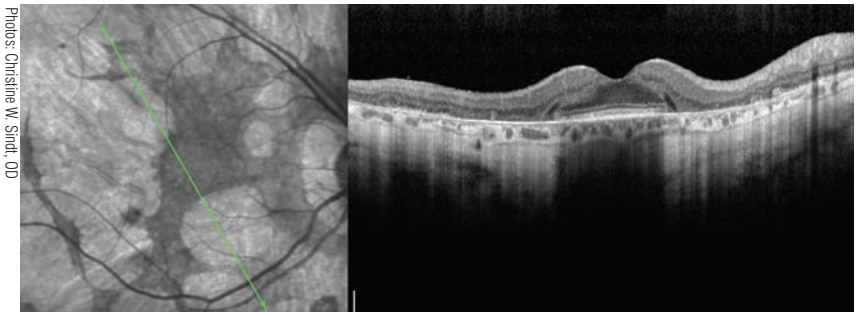

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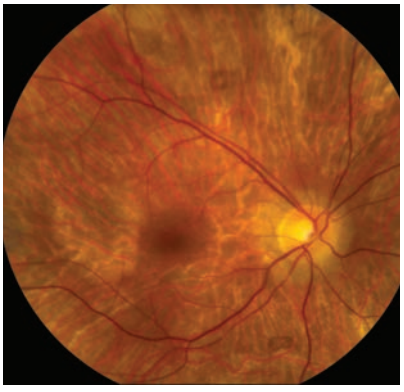

Clinical signs and symptoms of thioridazine toxicity include decreased visual acuity, visual field defects and retinal pigment epithelial disturbances. There is selective uptake of thioridazine in pigmented uveal tissue and the retinal pigment epithelium, which results in toxicity.

pathology has been seen with cessation of the medication. Regardless of exact cause, a need for yearly screening for retinopathy or papillopathy in patients taking high-risk medications is indicated. FAF screening may also be of value.

Ocular Motility Disorders

Oculogyric crisis caused by dystonia is due to involuntary contractions of various extraocular muscles. This may cause any variant of gaze paralysis, can be painful and even life-threatening if systemic muscles become involved.[5] The etiology is complex and likely involves dopamine receptor blockage along with other causes.[6,8] Antipsychotics, carbamazepine, Topamax and SSRIs all have been associated with oculogyric crisis.[4,8] Treatment of ocular dystonia includes anticholinergic agents (i.e., intramuscular benzatropine) and antihistamines (i.e., diphenhydramine) and can be rapidly effective in reversing symptoms.[4,6,8]

Benzodiazepines have been linked to dysfunction of saccades and smooth-pursuits and nystagmus.[28,29] Research has shown a correlation between downbeat nystagmus and lithium use, which can be reversed with termination of the medication; rarely, it may persist after discontinuation.[30] Diplopia, oscillopsia, gaze-evoked nystagmus, gaze palsies, downbeat nystagmus and periodic alternating nystagmus have been associated with carbamazepine use.[31] Lamotrigine (Lamictal, GlaxoSmithKline), an anticonvulsant, can cause a downbeat nystagmus, diplopia and interference with eye movements in overdoses or in combination with carbamazepam.[4,8] Finally, Topamax can induce nystagmus in high doses, although it is not well understood if the cause is idiosyncratic.[4,8] Given the vast array of medications that can cause nystagmus and motility disorders, it is important to consider psychotropic medications in the differentials when evaluating a patient with ocular dysmotility.

Impaired Sensory Perception

Changes to color vision and contrast sensitivity can be noted with use of psychiatric medications. Central and paracentral color vision decrease has been clearly demonstrated with use of carbamazepine; however, the effect is subclinical and requires only monitoring.[32] Contrast sensitivity function can be reduced in patients taking carbamazepine and benzodiazepines.[8] Changes to sensory perception indicate a need for monitoring visual function above and beyond visual acuity. Regular color vision and contrast sensitivity testing should occur in patients using these medications.

Metabolic and Cerebrovascular Implications

Although the literature indicates that newer antipsychotics have safer toxicology profiles compared with typical antipsychotics, newer medications may still cause metabolic syndrome. Specifically, impaired glucose metabolism, exacerbation of existing Type 1 and 2 diabetes, induction of Type 2 diabetes and diabetic ketoacidosis have all been linked to treatment with antipsychotic medications.[15,33] Clinicians should routinely screen for newly forming diabetic retinopathy in patients taking chlorpromazine, clozapine and olanzapine.[15,33]

Lastly, there has been much discussion in the literature regarding the increased risk of cerebrovascular events in elderly patients with dementia treated with antipsychotic medications.[33] Typical antipsychotic agents have been associated with higher risk of cerebrovascular accidents.[34] Statistically significant risk has not been noted with atypical medications and seems to dissipate with discontinuation.[34] ■

Dr. Minhas is a member of the clinical faculty at Salus University in Philadelphia, where she works with both the traditional optometry program and the Scholars Optometry Program.

A special thank you to Andrew Gurwood, OD, for his guidance and mentorship.

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Principles of Ocular Pain Control

Identify the cause of your patients' achy eyes and get familiar with meds that provide relief. **By Julie Tyler, OD**

Ocular pain can occur for many reasons in a clinical care setting. Patients who tend to present most acutely—and usually with greater severity of symptoms—most often have an anterior segment finding (such as dry eye, anterior uveitis or conjunctival irregularities) or angle closure.

However, ocular pain may also be associated with a variety of conditions in the posterior segment, such as optic neuritis, ocular ischemic syndrome (OIS) and ocular complications associated with giant cell arteritis (GCA).

This article reviews nontraumatic, noninfectious causes of ocular pain in both the anterior and posterior segments, and discusses oral and topical management.

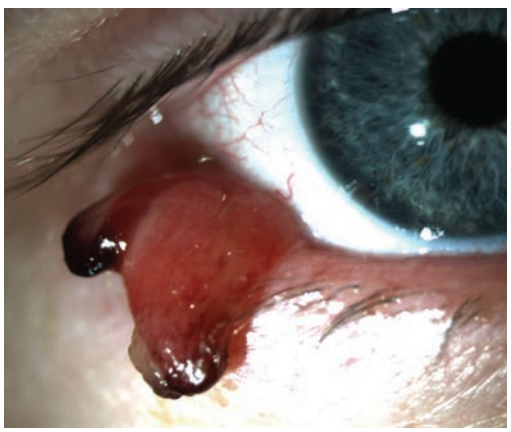

Fig. 1. Atypical lower lid granuloma.

Anterior Segment Considerations

Most anterior segment structures can be associated with pain. The cornea is especially sensitive due to its high concentration of sensory nerves, particularly in the center of the cornea—the most sensitive of all anterior segment structures. In fact, a recent study noted the cornea is the most densely innervated tissue in the body, due to its thick trunks of nerves that enter the stroma directly from the sclera, episclera and conjunctiva and send a large plexus through Bowman's membrane and just beneath the basal epithelial layer.[1] Any defect involving the cornea and its array of nerves, such as a recurrent corneal erosion (RCE) or extensive ocular surface disease, can be extremely painful. These and other corneal conditions can produce pain that varies in duration. Management options to control this pain may range from mild palliative agents to strong prescription opioid medications.

Several anterior segment conditions are associated with ocular pain (*Table 1*). Often, patients will

Release Date: January 2016
Expiration Date: January 1, 2019
Goal Statement: When patients present with ocular pain in either the anterior or posterior segment, the best way to alleviate it is to follow a specific protocol, based in part on the underlying pathology. This course provides an overview of that protocol and the associated pathologies. Additionally, it reviews the use of several specific pain medications and their indications and associated risks.

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tolerate minor anterior segment problems until they experience corneal involvement. For example, a 43-year-old white male presented with complaints of a red, irritated right eye. He noted a lid "bump" that had changed significantly in the previous 24 hours. Within the last day, the lesion, which had been growing slowly for at least two weeks, had "flipped" and was now outside the lid, and starting to rub against the conjunctiva and cornea (*Figure 1*).

While the patient had noted puffiness and increasing size for approximately two weeks, the onset of discomfort and bleeding finally brought him into the clinic. His ocular history was significant for a previous history of a "stye" that had been unresolved, despite a prescription, provided elsewhere, for oral amoxicillin. His visual acuity was 20/25 OD, OS with normal preliminary test results. The anterior segment exam revealed a large, vascularized, lobed and stalked lesion with associated diffuse staining of the conjunctiva and temporal cornea. We diagnosed an atypical granuloma.

A granuloma tends to be a relatively small nodular inflammatory lesion that may be triggered by infectious or noninfectious entities, such as a hordeolum or a small foreign body (e.g., sand), respectively. These localized changes most commonly develop from the palpebral conjunctival tissue and result in mild foreign body sensation. Due to the large size of this lesion, the discomfort and findings were greater than typical. To confirm the source of the patient's pain, we used a drop of proparacaine 0.5% in office. The patient experienced relief from most of his symptoms, which further confirmed the etiology; unfortunately, proparacaine has dose limitations, as it is short acting and results in an unstable epithelium when used chronically.

The patient was provided with the steroid/antibiotic combination medication Tobradex (tobramycin and dexamethasone, Alcon) QID, to reduce the inflammatory response and pain mediators within the granuloma, as well as provide protection against secondary infection.

The patient responded excellently to the management with the lesion shrinking and symptoms subsiding within 18 hours of initiation of topical therapy.

Had the patient developed a secondary anterior uveitis, a cycloplegic agent would have decreased the inflammatory response and secondary pain triggered by the normal pupillary constriction to light; the same intervention is appropriate for patients with primary uveitis.

Initial Pain Management

When managing ocular pain, follow this rule of thumb: first, treat the cause; then, adequately and effectively treat the pain.

Once a treatment regimen for the underlying condition is established, initial pain management can begin. In mild cases, this can involve using palliative measures and topical pain medications, such as cool compresses and artificial tears. If you recommend artificial tears, consider the length of anticipated patient use, necessity of clear vision, drop formulation and likelihood of pain recurrence. For patients with recurrent corneal erosion *(Figure 2)*, recommend use of an ointment prior to bedtime to decrease the risk of overnight adherence of the most superficial layers of the cornea to other ocular surfaces. Consider an ointment that does not contain medications per se (e.g., Refresh Lacri-Lube, Allergan) or a more targeted recommendation such as hypertonic ointment (Muro 128, Bausch + Lomb). Sodium chloride drops and ointment may reduce physiologic epithelial edema and secondarily reduce the risk of painful re-erosions in the morning.

Table 1. Differential Diagnosis of Nontraumatic, Noninfectious Primary Anterior Segment Pain

- Dry eye syndrome
- Limbal stem cell deficiency
- Anterior uveitis
- Epithelial basement membrane dystrophy
- Recurrent corneal erosion
- Significant hypoxia/CL associated red eye
- Corneal hydrops associated with keratoconus
- Iatrogenic/medicomentosa-induced corneal damage
- Post-surgical irregularities
- Shield ulcer secondary to vernal/atopic conditions
- Episcleritis (less likely)
- Scleritis
- Secondary angle closure
- Bullous keratopathy

Proposed general benefits of hyperosmotic agents are demonstrated in a study on the effects of these agents on epithelial disruptions during LASIK, resulting in decreased epithelial edema—especially in patients older than 34 years.[2] However, in a separate study with 26 participants, there was no difference in the occurrence of objective signs of recurrent erosion between hypertonic saline ointment vs. tetracycline ointment or lubricating ointment.[3] In short, prophylactic lubrication is needed, but the exact management remains unclear for best reduction of repeat erosions.

Steroidal Agents

Both topical and oral corticosteroids can influence the inflammatory cascade early within the response

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and help decrease production of pain modulators. All steroids act by blocking most pain-mediating prostaglandin pathways. Steroids can be highly effective in the management of patients with uveitis, scleritis, acute dry eye symptoms and various other noninfectious ocular conditions associated with inflammation.

Common ocular side effects of steroids include increased intraocular pressure (IOP), risk of secondary infection and risk of cataract formation. Steroids may also reduce the cornea's ability to heal quickly due to reduced time for collagen formation, making topical steroids a less-than-ideal option for patients with already increased collagenase activity.

Finally, prescribing may be more complicated for steroids than some other pain modulators because dosing options and relative risk of side effects vary for different topical steroids (*Table 2*). Treatment regimens for different conditions can vary significantly based on the ability of a specific corticosteroid to penetrate different ocular surfaces. Each specific steroid carries its own benefits and risks of complications.

Table 2. Review of Topical Steroids, Indications, Relative Risks

Strong Steroids	Indications/Benefits	Specific Relative Risks
Durezol (difluprednate 0.05%, Alcon)	Strong anti-inflammatory agent; Does not need to be shaken; Dosing approximately ½ than with traditional prednisolone acetate	Quick, significant rise in IOP; Initial cost to patient
Lotemax (loteprednol etabonate 0.5%), gel or ointment, Bausch + Lomb	Good for chronic, recurrent inflammatory conditions; Less likely to increase IOP than other "strong steroids"	Blur associated with instillation; Less posterior penetration
Pred Forte (prednisolone acetate 1%), Allergan and generic	All-purpose steroid for significant inflammatory conditions such as anterior uveitis	Generic formulation requires significant shaking
Generic prednisolone sodium phosphate 1%	Potent, relatively inexpensive; Use for anterior surface inflammation and postoperative management	No shaking necessary
Mild/Moderate Steroids	**Indications/Benefits**	**Specific Relative Risks**
Alrex (loteprednol etabonate 0.2%), Bausch + Lomb	Chronic allergy; Good for long-term use due to mild strength and less likely increase in IOP	Cost to patient
Flarex (fluorometholone acetate 0.1%, Alcon); FML (Allergan)	Mild inflammatory conditions: pingueculitis, allergy	Some variable penetrance and limitations for management

Nonsteroidal Anti-Inflammatory Drugs

Another class of topical and oral agents for pain management, the non-steroidal anti-inflammatory drugs (NSAIDs), work slightly further down the inflammatory cascade than steroids to decrease inflammation and diminish pain by blocking the cyclooxygenase (COX) pathways that lead primarily to prostaglandin formation.[4] Some newer-generation topical NSAIDs have better penetration into the posterior chamber than older versions and require less frequent dosing, making them more effective in posterior segment penetration.[5] That is why these agents continue to be used routinely and are so effective for pain following cataract surgery.

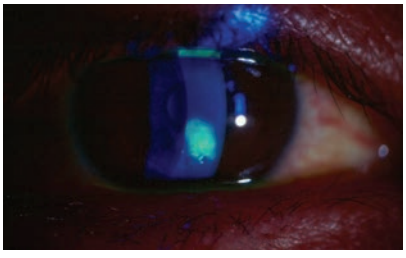

Fig. 2. Sodium fluorescein staining helps diagnose recurrent corneal erosion.

Historically, there was an 'idiosyncratic' risk of corneal melt reported in multiple case reviews with various NSAID medication formulations.[6,7] Since the initial reports, various mechanisms for the corneal melt have been proposed, including an uncommon collagen disorder adversely affected by COX enzyme inhibition, activation of MMPs, or due to decreased corneal sensitivity associated with topical NSAIDs complicated in patients with dry eye and identifiable, pre-existing epitheliopathy.[8] Thus, topical NSAIDs may be disruptive to patients with significant dry eye.

Cyclosporine

Medications that are classified as immunomodulators, such as cyclosporin-A, may be used as an adjuvant for pain management. These medications act to modify the effects of other agents by blocking several different cytokines involved in the inflammatory process; however, cyclosporin-A does not directly block pain-causing prostaglandins as effectively as do either steroids or NSAIDs. For patients with chronic dry eye associated with rheumatologic diseases, where underlying systemic inflammation contributes significantly to ocular pain, cyclosporin-A may be beneficial. Nevertheless, these patients will often only find immediate pain relief with topi-

cal steroid pulse-therapy treatment.[9]

Patients with severe dry eye may also find some assistance and chronic pain relief with the use of oral omega dietary supplementation.[10]

Case Consideration

A 54-year-old black female presented with a history of a mildly red eye for the past six months. She reported a sudden onset of concurrent increased redness and pain in the left eye for the previous three days. The patient denied additional ocular symptoms or significant ocular history. However, she had a complicated medical history that included hypertension, hypercholesterolemia and rheumatoid arthritis (RA)—all for seven years. The patient was on multiple systemic medications, including lisinopril, lovastatin, meloxicam, folic acid, prednisone (5mg, QID), and methotrexate (2.5mg, BID).

Her visual acuity was 20/20-1 OD and 20/40 OS. Slit lamp findings revealed deep scleral injection and thickening 360 degrees in the left eye without blanching upon instillation of phenylephrine 2.5% (*Figure 3*). Blood pressure measured 132/87mm Hg with Goldmann measured IOP of 16mm Hg OD and OS. The diagnosis was diffuse non-necrotizing anterior scleritis in her left eye secondary to poorly controlled RA.

Pain is a common complaint in patients with scleritis—and changes in associated systemic conditions, management protocols or both, often precede ocular flare-ups.[11,12] Initial topical management (e.g., steroids) may be beneficial to quell some symptoms, but true management requires oral anti-inflammatory and pain comanagement with the rheumatologist/managing physician. In this case, the rheumatologist increased the oral prednisone from 5mg QID to 20mg QID while the patient was also prescribed topical

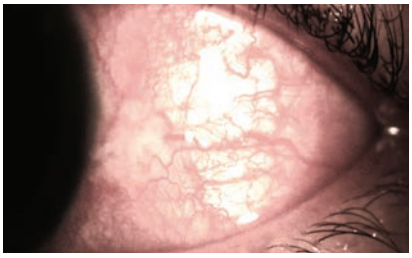

Fig. 3. Initial presentation of scleritis in the left eye.

Durezol (difluprednate, Alcon) QID OS.

One study reported that nearly 60% of scleritis patients require oral steroids or immunosuppressive agents to control the disease (oral steroids ~ 31.9%, systemic immunosuppressive agents ~ 26.1%).[13]

At the one-week follow-up, the patient reported overall improvement of symptoms and VA with residual, moderate scleral injection and thickening. As demonstrated in this patient, it is imperative to comanage the patient's underlying condition in cases where the patient presents with both acute pain and a contributing underlying systemic conditions for complete, long-term pain resolution.

Oral Medications

In many cases, non-prescription oral medications may be suitable to assist in pain management. For example, over-the-counter (OTC) NSAIDs, such as ibuprofen, can be quite helpful in alleviating patients' pain; at higher dosages, it may help reduce inflammation. Ibuprofen is an analgesic, antipyretic and potential anti-inflammatory. Analgesic dosing is 200mg to 400mg every four to six hours whereas an anti-inflammatory therapeutic dosing is 600mg to 800mg every six to eight hours. Ibuprofen may be used to assist in ocular surface injuries, moderate-to-severe episcleritis, mild scleritis, uveitis and postoperative cataract surgery regimens.[14,15] However, ibuprofen should be recommended/prescribed with caution in women of childbearing age, as it falls into the historic FDA pregnancy category C.

Another OTC medication that may be used for pain relief is naproxen sodium, branded as Aleve, Anaprox and Naprosyn. The OTC formulation of 220mg naproxen sodium actually contains 200mg of naproxen. Normal adult dosing for the OTC formulation is 220mg every eight hours, not to exceed two caplets in any eight- to 12-hour period. As a prescription formulation, it is available in a large variety of dosing options ranging from 250mg to 750mg (once daily dosing).

Prescription NSAID medications include Mobic (meloxicam, Boehringer Ingelheim) and Celebrex (celecoxib, Pfizer). Mobic is typically used for patients with arthritis—both osteo and rheumatoid. Children older than two years who have juvenile rheumatoid arthritis may also use Mobic.[16] This drug can be used daily as either 7.5mg or 15mg tablets or a 7.5 mg/5ml suspension. The NSAID celecoxib is a COX-2 inhibitor that is available in prescription formulations of 50mg, 100mg, 200mg and 400mg options. A typical adult dose is 400mg initially for pain and then 200mg every 12 hours.

NSAID Risks

While all NSAID medications may be beneficial for pain relief, they are accompanied by a variety of risks, warnings and contraindications. All NSAIDs have cardiovascular risks, including an increase propensity for myocardial infarction and stroke. Gastrointestinal risks include bleeding, ulceration and gastric or intestinal perforation. Prescription NSAIDs should be used with caution, especially in patients with congestive heart failure, hypertension, asthma, GI ulcers and renal impairment. The negative association with asthma and oral NSAID use is due to an increased risk of allergic reactions to

the class of medications in patients with asthma. Additional contraindications include a potential for cross-reactivity in individuals with aspirin allergy and complications for individuals with chronic hepatitis. Also, avoid NSAID use in patients who complain of pain from coronary artery bypass graft surgery, as they may face bleeding complications. All oral NSAIDs discussed are historically pregnancy category C.

Aspirin is the final OTC NSAID that warrants discussion for pain management. The usual dose for pain and fever in adults is 325mg to 650mg every four to six hours, with a total daily dosage that should not exceed four grams per day, with some health care practitioners recommending even less total daily. Like the other NSAID medications, aspirin is contraindicated for individuals with recent stomach or GI bleeds and allergy to the other NSAIDs because of possible cross-reactivity. However, due to the excellent blood thinning capabilities of aspirin, it is also contraindicated with concurrent Coumadin use, bleeding disorders or heavy alcohol use. Aspirin should not be used in pregnant or breastfeeding women. Finally, due to the risk of death associated with Reye's syndrome—a condition that has occurred when aspirin was used to treat flu-and cold-like symptoms in children—the FDA has recommended that aspirin and aspirin-containing products not be used to treat patients younger than 19 years.

An over-the-counter medication that is not considered an NSAID but is used to treat fever and pain is Tylenol (acetaminophen, Johnson & Johnson). While useful in the treatment of ocular pain, acetaminophen is an especially complicated pain medication to manage because it is available in so many single medication and combination formulations. A total maximum adult intake per day—including all medications containing acetaminophen, like aspirin—should not exceed four grams daily. The main contraindication for use of acetaminophen is liver damage, as it is the leading cause of acute liver failure in the United States.[17] In 2011, the FDA asked drug manufacturers to limit the strength of acetaminophen to 325mg/tablet in prescription drug products, which are predominantly combinations of acetaminophen and opioids.[18]

Acute Angle Closure Glaucoma

While many topical and oral analgesic and anti-inflammatory agents may be beneficial in the management of certain types of ocular pain, understanding the etiology of an inciting event and treating the direct cause is imperative in most cases.

For example, a 68-year-old Asian female presented with severe constant pain and primarily frontal headache with concurrent blurred vision. She reported recently visiting the emergency room for headache complaints, for which she was given a diagnosis of "migraine" and provided with a prescription analgesic without relief of her symptoms. Instead, her headache got worse and she began to experience vomiting associated with the pain. She denied any ocular history prior to her visit and was not taking any ocular medications. Uncorrected visual acuity was 20/30 OD and 20/50 OS with normal ocular motility and confrontation fields but a mid-dilated pupil in her left eye. Slit lamp examination revealed grade three conjunctival injection and corneal edema with compromised views in the anterior chamber of her left eye. IOP was 24mm Hg OD and 48mm Hg OS. Gonioscopy revealed a closed angle in the left eye and peripheral anterior synechiae consistent with signs of chronic angle closure and acute angle closure at present.

The patient required multiple pressure lowering agents—both oral and topical—starting with in-office Iopidine 0.5% (apraclonidine), a beta-blocker and eventually oral acetazolamide due to the chronicity of her condition.

When ocular pain is associated with increased IOP, use of topical pressure-lowering agents is essential to start to manage the patient's symptoms. In-office Iopidine (a topical alpha-agonist), topical carbonic anhydrase inhibitors and a topical beta-blocker may be initiated to try to reduce aqueous production. Pilocarpine may also be effective in angle closure patients with an IOP lower than 40mm Hg—used to physically move the iris away from the angle structures; however, at higher pressures (as in the case presented) it is not effective.

In patients like the one discussed, where the condition is chronic, it is usually necessary to use oral or IV medications such as Diamox (acetazolamide, Barr) PO (2 x 250mg tablets). Upon resolution of the acute crisis and when IOP "control" is obtained, long-term management options can be discussed with the patient.

Posterior Segment/ Neurological Conditions

Conditions beyond the anterior segment that may be associated with ocular pain can be acute, like optic neuritis associated with multiple sclerosis (MS), or may be dull, constant and longstanding, such as the pain associated with ocular ischemic syndrome (*Table 3*).

The nature of the pain is generally different than that noted in the anterior segment, which is often accompanied by a clear inciting event. The pain associated with posterior segment diseases in particular may be less acute and more difficult for the patient to localize and describe.

Unlike the cornea, the retina has no pain receptors and any posterior segment pain is due to neurologic symptoms or associations, or ischemic-related disease.

A particularly challenging presentation of bilateral, persistent eye-related pain with foreign body sensation was recently described as ocular neuropathic pain that developed in a patient with vitamin B12 deficiency.[19] The patient responded well with vitamin B12 therapy—which may make this a differential in cases of persistent ocular pain going forward.

Another, more common, but equally challenging, ocular-related pain occurs in the prodrome phase associated with herpes zoster ophthalmicus (HZO). Patients with this neurologic condition are often in severe pain and only a detailed history and description of the location and pattern of the pain may allow for early diagnosis, as initial findings are limited. The pain associated with HZO is generally significant enough to require management with opioids.

Medications for Severe Pain

Opioid drugs may be indicated for moderate-to-severe ocular pain, but they have several contraindications and potential side effects. When considering these medications, assess the likely efficacy vs. potential side effects and choose an option that best suits the patient. This class is contraindicated in patients who have depression and severe respiratory disease, due to the likelihood of exacerbation of symptoms.

Opioids should be used with caution in patients who use alcohol chronically, have Addison's disease, renal dysfunction, a history of drug abuse, impaired lung function, psychosis, hypotension or cardiovascular disease. Side effects include itching, rash, constipation, seizures and cardiotoxicity.

Table 3. Differential Diagnosis of Nontraumatic, Noninfectious Posterior Segment Pain

- MS/retrobulbar optic neuritis
- GCA symptoms associated with CRAO, A-AION
- Posterior uveitis
- Posterior scleritis
- HZO prodrome phase
- OIS
- Panuveitis

Ultram (tramadol, Janssen), an opioid class medication used to manage moderate to moderate-severe pain, is available as a 50mg tablet or 100mg, 200mg or 300mg extended-release capsules. The typical adult dose is between 50mg and 100mg every four to six hours, not to exceed 400mg per day. A modification of dosage is recommended for patients with kidney or liver problems. Ultram has two mechanisms of action—a weak mu-opioid receptor agonistic effect, leading to induced serotonin, and the ability to inhibit reuptake of norepinephrine. Ultram was recently moved from a non-scheduled to a Schedule IV medication due to the clinical recognition of risk for drug addiction.

Tylenol 3 (Johnson & Johnson) is a combination of 30mg codeine with 300mg acetaminophen that is categorized as a Schedule III drug. Tylenol 4 contains a higher dosage of codeine (60mg), but is currently also listed as a Schedule III drug. Tylenol 3 is usually dosed one to two tablets every four hours. Both Tylenol 3 and Tylenol 4 may be used to manage post-surgical pain or corneal hydrops, and may be used for severe trauma, abrasions and erosions. A primary concern in patients using Tylenol 3 or Tylenol 4 is the risk of depressed respiratory function. The side effects and contraindications are typical for opioid class medications with cautions against prescribing to anyone with a hypersensitivity to narcotics or substance abuse risk.

Oxycontin (oxycodone, Purdue), a Schedule II medication, has a high potential for abuse. It is available in 5mg, 10mg, 15mg, 20mg and 30mg tablets. Additionally, it is available in other doses/formulations for extended release to decrease the risk of abuse. Generally, Oxycontin is prescribed 5mg to 30mg every four to six hours for significant pain.

A final notable pain medication is hydrocodone, which is also a Schedule II class medication. Hydrocodone is available in combination with several other products (e.g., acetaminophen, ibuprofen) with a variety of different brand names and specific indications depending on the combination. For example, hydrocodone combined with Vicodin (hydrocodone bitartrate and acetaminophen, Abbvie) would be used for pain, whereas hydrocodone combined with guaifenesin would be indicated for cough suppression.

When patients are suffering from a painful ocular condition, they often have comorbidities that contribute to that pain. It is necessary for optometrists to look beyond the eye to consider the overall welfare and health status of the patient. For patients experiencing pain due to underlying systemic inflammation, oral steroids or methotrexate may be warranted to manage an underlying systemic condition, but these require careful comanagement. Other adjuvant medications may include muscle relaxers, anti-anxiety medications or antidepressants. Regardless, effectively managing pain is essential to the well-being and recovery of the patient. Counsel the patient about appropriate expectations and the value of communicating with their physicians—both primary care and specialists, including optometrists. ■

9th Annual Pharmaceuticals Report

Dr. Tyler is a module chief of primary care for The Eye Care Institute at Nova Southeastern University in Davie, Fla.

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1. Which of these is a Schedule IV drug?
a. Hydrocodone with ibuprofen.
b. Lortab.
c. Oxycodone.
d. Tramadol.

2. Which of these is a Schedule III drug?
a. Tylenol 3.
b. Tramadol.
c. Oxycodone.
d. Hydrocodone with guaifenesin.

3. What is the leading cause of acute liver failure in the United States?
a. Stevens-Johnson syndrome.
b. Steroid abuse.
c. Acetaminophen overuse.
d. Cardiovascular disease.

4. What effect do opioids have on the respiratory system?
a. Depress/lower function.
b. Increase function.
c. No effect on respiration.
d. Depression only in those who are drug abusers.

5. Vicodin contains which ingredients?
a. Acetaminophen with oxycodone.
b. Acetaminophen with hydrocodone.
c. Ibuprofen with oxycodone.
d. Ibuprofen with hydrocodone.

6. What is the safe upper limit for one day for acetaminophen?
a. 300mg.
b. 60mg.
c. 1g.
d. 4g.

7. Advil, Aleve, and other oral NSAIDs are classified for pregnancy as:
a. Category A.
b. Category B.
c. Category C.
d. Category D.

8. What is the minimum dose of Ibuprofen that is considered to be anti-inflammatory and not just analgesic?
a. 200mg.
b. 300mg.
c. 400mg.
d. 600mg.

9. Reye's syndrome is a risk with aspirin use for which patients?
a. Patients older than 65 years with GI ulcers.
b. Patients younger than 19 years with fever or viral illness.
c. Patients with cardiovascular disease.
d. Patients with liver failure.

10. What section of the eye has the most highly concentrated area of sensory nerves?
a. Central cornea.
b. Peripheral cornea.
c. Eyelid.
d. Conjunctiva.

11. When managing a patient with ocular pain, whenever possible:
a. Use a Schedule II medication in lieu of a non-scheduled medication for a patient with a history of drug abuse.
b. Start with a Schedule II medication and then treat the underlying cause of the pain.
c. First treat the underlying cause and second treat the pain.
d. Consider prescription medications first, then, if unresponsive, consider palliative management.

12. You should reccommend a nighttime lubricating agent for patients with:
a. Acute angle closure.
b. Recurrent corneal erosion.
c. Ocular ischemic syndrome.
d. Anterior uveitis.

13. Corticosteroids are associated with causing/worsening which ocular complications?
a. Cataracts.
b. Granuloma.
c. Anterior uveitis.
d. Dry eye.

14. NSAIDs work at which point in the inflammatory pathway?
a. At the exact same point in the inflammatory cascade as steroids.
b. Slightly further down the inflammatory cascade than steroids.
c. Before the initiation of the inflammatory

OSC QUIZ

cascade flow.
d. Within the cornea to modify the IOP.

15. Patients with severe dry eye may find some relief from chronic pain with the use of:
a. Proparacaine every 30 minutes while awake.
b. Oral omega dietary supplements.
c. Pallative management with increased use of oral and topical antihistamines.
d. Viroptic supplements.

16. Which of the following is a common side effect of all NSAID medications?
a. Reye's syndrome.
b. Addiction.
c. Increased risk of bleeding.
d. Increased prostaglandins and pain.

17. A granuloma can be defined as:
a. A growth, most likely seen within the bulbar conjunctiva.
b. A lesion that started as an infection of the meibomian gland.
c. A relatively small nodular inflammatory lesion.
d. A lesion that is elevated on the iris along the pupil margin.

18. What is the best option for treatment of a symptomatic conjunctival granuloma?
a. Topical steroid.
b. Topical antibiotic.
c. Topical prostaglandin.
d. Topical antiviral.

19. When a patient is in angle closure and the pressures are excessively high (>40), what oral medication would be most beneficial for management?
a. Diamox PO, 2 x 250mg tablets.
b. Ibuprofen PO 600mg.
c. Acetaminophen PO 325 caplets.
d. Omega 3 supplement PO 1600mg.

20. What information will be helpful in making a diagnosis of HZO in the prodrome phase?
a. Assessment of the angle for neovascularization and visual field.
b. Amsler grid and macular pigment density.
c. Type of trauma to the eye.
d. Location, pattern and severity of pain.

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18.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
19.	Ⓐ	Ⓑ	Ⓒ	Ⓓ
20.	Ⓐ	Ⓑ	Ⓒ	Ⓓ

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Sharpen Your Subjective Refraction Technique

Minimize chair time, avoid frustration and help patients see better with this standardized protocol. **By Mark E. Wilkinson, OD**

Using a standardized protocol allows clinicians to approach each refraction in a logical and sequential manner, eliminating simple mistakes that lead to clinician and patient frustration, and longer chair time. The protocol below was developed for the University of Iowa as its standard refraction technique and we have had great success with it in minimizing mistakes and delays. We want to share it so that our fellow optometrists can be more efficient in their refractions and enjoy the positive impact it will have in the office.

We encourage you to download, print and place this protocol in your office for easy reference. Look online at www.reviewofoptometry.com for a downloadable PDF of this article.

Taking a Baseline

Prior to starting your refraction, baseline visual acuities (OD, OS and OU) must be determined. For individuals with near vision complaints, and all presbyopes, near acuity should also be documented using M-notation, and testing distance should be documented if it is different than 16in, or 40cm.

To view a downloadable PDF of this article, scan this QR code or visit www.reviewofoptometry.com.

Accurately assessing visual acuity is important for many reasons. It allows the clinician to:

- Determine best-corrected acuity with refraction.
- Monitor the effect of treatment or disease progression.
- Estimate the dioptric power of optical devices needed for reading regular-sized print.
- Verify eligibility for tasks such as driving.
- Verify eligibility as legally blind.

When measuring distance acuity, measuring visual acuity in a darkened room is no longer necessary. In the past, when projected charts were used, the room lights had to be lowered for better contrast on the chart. Now, with high-definition LCD monitor acuity charts and ETDRS charts, contrast is no longer an issue. Additionally, for some patients, particularly those who have difficulty adjusting to low-light conditions, taking them from a normally-lit waiting room into a darkened clinic or workup room will artificially lower their acuity. Because clinical decisions are based on these acuity measurements, accurate assessment of each person's acuity is critically important.

With this in mind, all acuity testing should be done with the overhead lights on in the exam or workup room; however, if the patient you are working up complains of photophobia and asks you to lower the lights or asserts the need to put on their sunglasses, accom-

modate them accordingly. Simply note that the recorded acuities were taken in conditions that deviated from the standard.

"Lights on" During Retinoscopy

When doing retinoscopy, you will want the lights lowered; but, once you start your refraction, you will achieve greater accuracy when you refract with the lights on. Keeping the lights on during your refraction is important to avoid over-minusing your patients. When someone is over-minused, the chart will look darker, which can be mistakenly thought of as looking clearer.

Pinhole Visual Acuity

For individuals without ocular disease, a pinhole aperture is a useful tool for determining if a refractive error is present or if a refractive change is needed. The most useful pinhole diameter for clinical purposes is 1.2mm. This pinhole size is effective for refractive errors of +/-5.00D. A pinhole improves visual acuity by decreasing the size of the blur circle on the retina, resulting in an improvement of the individual's visual acuity; however, if the pinhole aperture is less than 1.2mm, the blurring effects of diffraction around the edges of the aperture will increase the blur circle and cause worsened vision.

Because the reduced amount of light entering through the pinhole makes the chart less clear for individuals with macular disease and other ocular diseases that affect central vision, they may have the same, or even reduced, acuity when looking through a pinhole. It can also be difficult to use eccentric fixation through a pinhole. For this reason, individuals with ocular disease may still benefit from a spectacle correction change and should not be told otherwise based solely on their acuity when looking through a pinhole. Careful retinoscopy, along with trial frame refraction, is needed to determine whether an individual with pathology-induced vision loss will benefit from a spectacle correction change.

Photo: Marc B. Taub, OD

Pinhole acuity is useful for patients without underlying ocular disease.

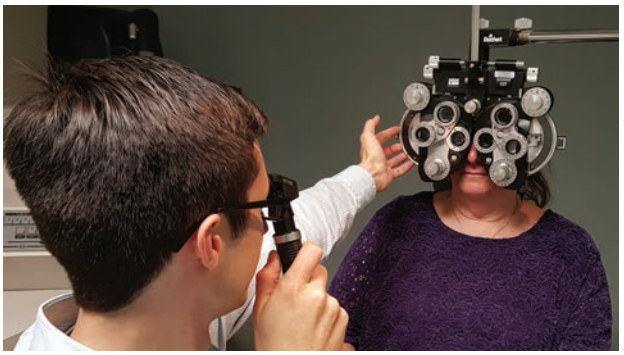

Photo: Marc B. Taub, OD

Start off right with an objective determination of refractive error by retinoscopy.

Standard Subjective Refraction Techniques

The goal of the subjective refraction is to achieve clear and comfortable binocular vision.

The clinician's ability to maintain control during the refraction is directly related to their ability to communicate clearly with the patient.

The subjective refraction starts after retinoscopy or autorefraction, which provide the clinician with an objective assessment of refractive error. It is possible to start with the patient's previous prescription; however, this is the least desirable way to begin, as there is no objective information about the patient's current refractive error. Thus, the best starting point is from the objective determination of refractive error by retinoscopy.

Whether you start your refraction after retinoscopy, or with autorefraction findings, you will first check acuity in each eye separately before the Initial Maximum Plus to Maximum Visual Acuity (MPMVA) step.

Set up for Retinoscopy—Minus Cyl Phoropter

- ❏ Before putting the phoropter in front of the patient, clear the phoropter, set the cylinder axis at 180 degrees and unocclude both eyes.
- ❏ After positioning the phoropter in front of the patient, level the phoropter and make sure the interpupillary distance is properly adjusted.
- ❏ Put either a group of letters or a fixation dot on the chart and direct the patient to look at the chart, not at you or your light.
- ❏ Ask the patient to tell you if your head blocks their view of the chart.

Retinoscopy

- ❏ For patients with an unknown refractive error, start with a vertically-oriented Plano mirror streak (sleeve up on Copeland and sleeve down on Welch-Allyn) to streak the horizontal meridian.

- ❏ As you begin streaking the horizontal meridian, if your retinoscopic streak does not line up with the retinal reflex, rotate your streak until the streak and the reflex are aligned. Continue streaking along this meridian.
- ❏ Neutralize this meridian by adding plus lenses for "with motion" or minus lenses for "against motion."
- ❏ Once neutralized, rotate your retinoscope's streak 90 degrees from where your streak was previously aligned with the retinal reflex.
- ❏ Now, with this streak more horizontally oriented, streak the more vertically-oriented meridian.
  - ❍ If your patient has *no astigmatism*, there will be no motion. Retinoscopy is completed for this eye.
  - ❍ If your patient has *with-the-rule* astigmatism, you will see "against motion," which you will neutralize by adding minus cylinder axis 90 degrees away from the initial meridian you neutralized.
  - ❍ If your patient has *against-the-rule* astigmatism, you will see "with motion." If this is noted, neutralize it by adding plus spherical power.
    - □ For against-the-rule astigmatism, after neutralizing this second meridian with sphere power, rotate the cylinder axis 90 degrees, back to the initial meridian.
    - □ Next, rotate your retinoscope's streak back to this more vertically-oriented position. You should now see "against motion" in the more horizontal meridian, which you will neutralize by adding minus cylinder.
- ❏ Once you have neutralized the right eye, do the same for the left eye.
- ❏ When you have neutralized both eyes by retinoscopy, remove your working distance lens from each eye (1.50D for a 66cm working distance or 2.00D for a 50cm working distance).

Initial Maximum Plus to Maximum Visual Acuity

- ❏ Next, occlude the left eye, put several lines of letters on the eye chart, such as 20/20 to 20/50 or 20/15 to 20/40, and ask the patient to read the smallest line they can.
- ❏ Assuming the patient can read the letters being presented, begin by adding +0.75D to the phoropter. This should result in the loss of two to three lines of vision.
- ❏ If there is no loss of vision, add another +0.75D and make sure there has been a decrease in vision by two to three lines from your starting point.
- ❏ Next, slowly decrease the power in the phoropter (less plus or more minus), in 0.25D steps, until the patient is able to see the 20/20 or 20/15 lines, or until there is no further improvement in vision. Expect about a one-line improvement on the eye chart for every -0.25D added.
- ❏ Once you have achieved the initial maximum plus to maximum visual acuity, the patient's cylindrical correction can be refined.

Refining Cylinder/Axis and Power

- ❏ Swing the Jackson cross-cylinder (JCC) in front of the patient's eye to refine cylinder axis and power.
- ❏ As a general rule, if the patient's refractive error is primarily cylindrical, or if by retinoscopy or autorefraction you found 1.00D of cylinder or more, start by checking the cylinder axis first. Otherwise, start by checking the cylinder power.
- ❏ To check the cylinder axis first, position the JCC so that the white and red dots straddle the cylindrical axis by 45 degrees on either side.
- ❏ Have the patient look at either a single line of letters one line larger than their best visual acuity found during the initial MPMVA, or the same grouping of letters you started with.

Reading the Fine Print

It is important to know that when doing near acuity testing, reduced Snellen acuity is only accurate at a fixed testing distance, which is 40cm for most near acuity cards.

You should also know that Jaeger numbers have no precise meaning. Jaeger numbers refer to item numbers in a printing catalog in Vienna in the 1850s. The International Council of Ophthalmology has stated that the lack of external definition of Jaeger numbers makes them extremely variable. With this in mind, Jaeger numbers should not be used for near vision testing.

The preferred method for near acuity testing uses the M-unit, which is the only letter size unit that is well defined. A 1M letter subtends five minutes of arc at 1M. For reference purposes, a 1M-sized letter is equivalent in size to newsprint, while 2M is equivalent in size to standard 18-point large print and 0.5M is equivalent in size to print half the size of newsprint.

When measuring near visual acuity, the patient will use their reading correction. Have the patient hold the reading card at their normal reading distance. The clinician should note errors related to scotomas and visual field loss. Near acuity is recorded as M-units at the testing distance (e.g., 1.25M at 40cm).

Measuring visual acuity at each clinic visit is standard of care. Documentation of visual acuity is important to defend against an accusation that a procedure or treatment harmed vision.

ALREX®:

TREATS THE ITCH AND MORE.

SHORT-TERM TREATMENT FOR THE FULL SPECTRUM OF SAC* SIGNS AND SYMPTOMS[1-3]

*Seasonal allergic conjunctivitis.

INDICATION

ALREX® (loteprednol etabonate ophthalmic suspension) is indicated for the temporary relief of the signs and symptoms of seasonal allergic conjunctivitis.

IMPORTANT SAFETY INFORMATION

ALREX® 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 the ocular structures. ALREX® is also contraindicated in individuals with known or suspected hypersensitivity to any of the ingredients of this preparation and to other corticosteroids.

Prolonged use of ALREX® is associated with several warnings and precautions, including glaucoma with optic nerve damage, defects in visual acuity, cataract formation, secondary ocular infections, and exacerbation or prolongation of viral ocular infections (including herpes simplex).

If this product is used for 10 days or longer, intraocular pressure should be monitored. The initial prescription and renewal of the medication order beyond 14 days should be made by a physician only after reexamination of the patient with the aid of magnification. Fungal infections of the cornea may develop with prolonged use of corticosteroids.

Ocular adverse reactions occurring in 5-15% of patients treated with loteprednol etabonate ophthalmic suspension (0.2%-0.5%) in clinical studies included abnormal vision/blurring, burning on instillation, chemosis, discharge, dry eyes, epiphora, foreign body sensation, itching, infection, and photophobia.

Please see brief summary of full Prescribing Information on the following page.

References: 1. ALREX [package insert]. Tampa, FL: Bausch & Lomb Incorporated; 2013. **2.** Dell SJ, Lowry GM, Northcutt JA, Howes J, Novack GD, Hart K. A randomized, double-masked, placebo-controlled parallel study of 0.2% loteprednol etabonate in patients with seasonal allergic conjunctivitis. *J Allergy Clin Immunol.* 1998;102(2):251-255. **3.** Shulman DG, Lothringer LL, Rubin JM, et al. A randomized, double-masked, placebo-controlled parallel study of loteprednol etabonate 0.2% in patients with seasonal allergic conjunctivitis. *Ophthalmology.* 1999;106(2):362-369.

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Alrex®
loteprednol etabonate
ophthalmic suspension 0.2%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

This Brief Summary does not include all the information needed to use Alrex® (loteprednol etabonate ophthalmic suspension 0.2%) safely and effectively. See full prescribing information for Alrex.

Alrex®

loteprednol etabonate
ophthalmic suspension 0.2%

Sterile Ophthalmic Suspension

Rx only

INDICATIONS AND USAGE
ALREX Ophthalmic Suspension is indicated for the temporary relief of the signs and symptoms of seasonal allergic conjunctivitis.

CONTRAINDICATIONS
ALREX, 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. ALREX is also contraindicated in individuals with known or suspected hypersensitivity to any of the ingredients of this preparation and to other corticosteroids.

WARNINGS
Prolonged use of corticosteroids may result in glaucoma with damage to the optic nerve, defects in visual acuity and fields of vision, and in posterior subcapsular cataract formation. Steroids should be used with caution in the presence of glaucoma.

Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In those diseases causing thinning of the cornea or sclera, perforations have been known to occur with the use of topical steroids. In acute purulent conditions of the eye, steroids may mask infection or enhance existing infection.

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

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

If signs and symptoms fail to improve after two days, the patient should be re-evaluated.

If this product is used for 10 days or longer, intraocular pressure should be monitored.

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.

Information for Patients: This product is sterile when packaged. Patients should be advised not to allow the dropper tip to touch any surface, as this may contaminate the suspension. If redness or itching becomes aggravated, the patient should be advised to consult a physician.

Patients should be advised not to wear a contact lens if their eye is red. ALREX should not be used to treat contact lens related irritation. The preservative in ALREX, benzalkonium chloride, may be absorbed by soft contact lenses. Patients who wear soft contact lenses **and whose eyes are not red,** should be instructed to wait at least ten minutes after instilling ALREX before they insert their contact lenses.

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, (1500 and 750 times the maximum clinical dose, respectively) prior to and during mating did not impair fertility in either gender.

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 (85 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 (15 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 postimplantation 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 (15 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. ALREX Ophthalmic Suspension 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 ALREX is administered to a nursing woman.

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

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

Ocular adverse reactions occurring in 5-15% of patients treated with loteprednol etabonate ophthalmic suspension (0.2% - 0.5%) in clinical studies included abnormal vision/blurring, burning on instillation, chemosis, discharge, dry eyes, epiphora, foreign body sensation, itching, injection, and photophobia. Other ocular adverse reactions occurring in less than 5% of patients include conjunctivitis, corneal abnormalities, eyelid erythema, keratoconjunctivitis, ocular irritation/pain/discomfort, papillae, and uveitis. Some of these events were similar to the underlying ocular disease being studied.

Non-ocular adverse reactions occurred in less than 15% of patients. These include headache, rhinitis and pharyngitis.

In a summation of controlled, randomized studies of individuals treated for 28 days or longer with loteprednol etabonate, the incidence of significant elevation of intraocular pressure (≥10 mm Hg) was 2% (15/901) among patients receiving loteprednol etabonate, 7% (11/164) among patients receiving 1% prednisolone acetate and 0.5% (3/583) among patients receiving placebo. Among the smaller group of patients who were studied with ALREX, the incidence of clinically significant increases in IOP (≥10 mm Hg) was 1% (1/133) with ALREX and 1% (1/135) with placebo.

DOSAGE AND ADMINISTRATION
SHAKE VIGOROUSLY BEFORE USING.
One drop instilled into the affected eye(s) four times daily.

Revised: August 2013.

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- ❏ Tell the patient, "I am going to give you two choices. Neither will be perfectly clear; however, I want you to tell me which lens choice is clearer: choice one or choice two; choice three or choice four? And so on."
- ❏ Be sure to use fresh choices and new numbers with each pair you present.
- ❏ Move the axis in the direction of the red dot, initially in 15-degree increments, for individuals with 2.00D of cylinder or less. You will decrease the increment size following a reversal by 15-10-5-3-1 degrees as the axis is refined.
- ❏ For individuals with more than 2.00D of cylinder, start with 5-degree increments, decreasing the increment size following a reversal by 5-3-1 degrees until the axis is refined.
- ❏ To check cylinder power, adjust the position of the JCC so that the white or red dots correspond with the cylinder axis.
- ❏ Ask the patient, "Which lens choice is clearer: choice one or choice two?"
  - ❍ If the patient chooses the *white dot*, subtract -0.50D of cylinder power while remembering to add -0.25D of spherical power to maintain the spherical equivalent.
  - ❍ If the patient chooses the *red dot*, add -0.50D of cylinder power and add +0.25D of spherical power to maintain the spherical equivalent.
  - ❍ Once the patient reverses (i.e., chooses the red dot after previously choosing the white or vice-versa) adjust the cylinder power by 0.25D in the opposite direction of your previous change. The spherical power does not need to be adjusted for this 0.25D change.
- ❏ Once more, check the cylindrical power with the JCC to see if the patient wants more or less power. The goal is to give the least amount of cylindrical power that provides the clearest vision.
- ❏ When the cylindrical power and axis have been refined with the JCC, remove the JCC from in front of the patient's eye and ask the patient to read the smallest line they can.
- ❏ Remember, if the starting cylinder power is 1.00D or greater, check the cylinder axis first. You will only check the cylinder power first for cylinder powers less than 1.00D.

Cylinder Power Search

If retinoscopy or autorefraction indicated no cylinder was needed and you suspect otherwise, do a cylinder power search.

- ❏ With your JCC oriented for power at 90 and 180 degrees, ask the patient, "Which is better: choice one or two?"
  - ❍ If the patient indicates *no preference*, repeat at 45 and 135 degrees.
  - ❍ If the patient indicates *a preference*, add -0.50 cylinder at the axis where the red dot is oriented, along with +0.25D sphere power to maintain the spherical equivalent.
- ❏ Using the standard JCC technique described above, refine the cylinder power and axis.

Favorite Phrases

- During the subjective portion of the refraction say, "I am going to have you look through two different lenses. Although neither lens may be perfect, I want you to tell me which one looks clearer."
- When the patient becomes indecisive, remember to add, "…or do they look the same?" Reassure them that it is OK to think the choices look about the same.

Second Maximum Plus to Maximum Visual Acuity

This step is performed when the cylinder power has changed by 0.50D or more, or if the cylinder axis has changed by 10 degrees or more during cylinder power and axis refinement.

- ❏ Begin by adding +0.50D to the phoropter. The patient should lose about two lines of vision. If the acuity is the same or better, add another +0.50D until the vision is blurred by one to two acuity lines.
- ❏ Next, slowly decrease the power in the phoropter in 0.25D steps until the patient is able to see the 20/20 or 20/15 line, or until there is no further improvement in vision.
- ❏ Occlude the right eye while unoccluding the left. Repeat the same process for the left eye, beginning with the Initial MPMVA.

Binocular Balance

Once the monocular subjective refraction has been completed for each eye, it is time for the binocular balance. Binocular balancing is only done when the visual acuity is relatively equal between the two eyes.

Binocular balancing can be accomplished in two different ways: using the Risley prism on the phoropter or by alternate occlusion (described on the next page).

- ❏ In either case, you should start the binocular balancing procedures by adding +0.75D sphere to both eyes so that the patient's visual acuity is blurred to the 20/30 to 20/40 levels. By slightly blurring vision in this way, eye dominance is effectively neutralized during the balancing process. It is important to

make sure the patient is mildly blurred before using the Risley prism or alternate occlusion binocular balancing techniques.

Risley Prism Binocular Balancing Technique

- ❏ Using the Risley prisms, apply three prism diopters base up in front of the right eye and three prism diopters based down in front of the left eye. This will result in the right eye seeing the lower image and the left eye seeing the upper image.
- ❏ Asking the patient to ignore brightness differences (this can be confusing for some patients), have them tell you which image appears clearer. Add +0.25D to the clearer eye to fog it further.
- ❏ Again ask the patient which image is clearer and add +0.25D to the clearer eye.
- ❏ The endpoint is reached when either both sets of letters look the same or when the dominant eye appears slightly clearer than the non-dominant eye.

Alternate Occlusion Technique

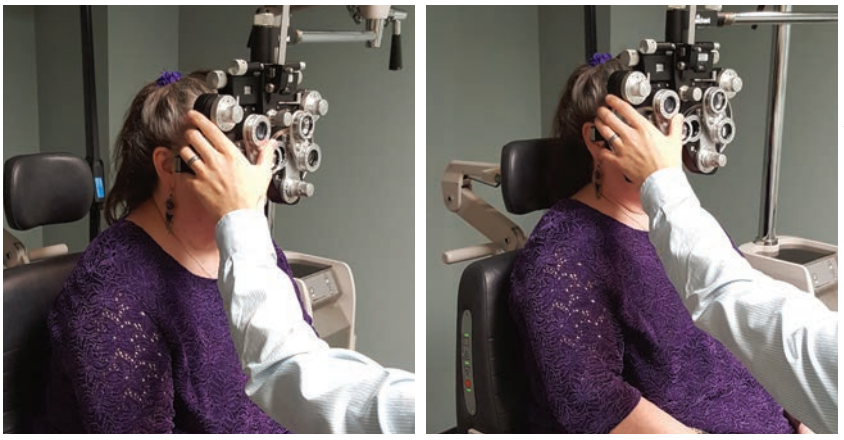
- ❏ After fogging the patient, alternately cover one eye and then the other, while asking the patient which eye sees the chart more clearly, eye one or eye two. To avoid confusion, say "eye one" or "eye two" rather than "right eye" or "left eye" while you alternately occlude. Add +0.25D to the clearer eye to fog it further.
- ❏ The endpoint is reached when both sets of letters look the same or when the patient's dominant eye appears slightly clearer than their non-dominant eye.

Determining the Final Correction

- ❏ Once the binocular balance is completed, add -0.25D OU one step at a time to bring the patient back to their best visual acuity. Remember, you should expect about one line of improvement in vision with each -0.25D addition.
- ❏ Do not give additional minus spherical power without an improvement in acuity.

Duochrome Test

The duochrome (red-green) test can be used as a monocular or binocular test to determine the proper spherical power.



Photos: Marc B. Taub, OD

Leaning to see the chart better while in a 10-foot exam room can be equivalent to a one-line or more improvement in vision. For the sake of accuracy, the patient should sit back in the exam chair—no leaning forward.

- ❏ If the letters on the green side of the chart appear blacker, add +0.25D. If the letters on the red side of the chart appear blacker, add -0.25D.
- ❏ The endpoint is reached when the letters appear equally black on both the red and green side. It is important to ask the patient to tell you on which side the letters look "blacker," not on which side they look "clearer" on.

Refracting in a Shorter Room

Shorter examination rooms are common outside of pediatric practices. A shorter room is considered a room less than optical infinity, which is 20 feet or 6m. It is important to recognize that when refracting in a shorter lane, vergence and accommodation are in play.

To calculate vergence, use the formula *1/x (m)*, or *100/x (cm)* or *40/x (in)*. Given this, the vergence demand in a 10-foot exam room is 40/120 = 0.33D. Therefore, when testing acuity in a 10-foot lane, the patient is effectively getting an extra -0.33D of refracting power from the shorter room. With this in mind, for every patient refracted and focused at infinity in a shorter exam room, additional minus power needs to be added to what was found in the phoropter. For example, add -0.25D for a 10-foot exam room. Add -0.50D for a six-foot exam room.

Consider what happens when testing visual acuity in a shorter exam room. In a shorter room, the patient is getting, at the least, an extra -0.25D of improvement in their vision on the eye chart. This is why someone can have 20/20+2 entrance acuity and still need an extra -0.50D in his or her final prescription to see with 20/15 acuity. Be aware that the acuity charts in shorter exam rooms are adjusted to the correct letter height for the

room's testing distance, so the visual acuity measured in a shorter exam room is the correct acuity.

Finally, with respect to visual acuity testing, it is important to understand that when a patient leans in to see the chart better, the testing distance can be 12 to 20 inches less. A lean of 16 inches while in a 10-foot exam room is equivalent to a one-line improvement in vision. For the sake of accuracy, it is important to have the patient sit back in the exam chair—there should be no leaning forward in an attempt to see the chart better.

Cardinal Rules of Refraction

Our ultimate goal is to make both images looked the same, yet we continually are asking the patient to determine which is better, knowing that the decision gets harder as we get closer to our goal of equality. The principles below will help avoid frustration for both doctor and patient:

- Refraction is both an art and a science. Given this, it is important to know that patients do not always respond accurately during testing with the Jackson cross cylinder and during duochrome testing. This is why starting with an objective assessment of the patient's refractive error will help you stay on target with your refraction.
- Keep it simple—avoid needless detail or jargon when describing what you are doing.
- Maintain your patience—to avoid frustration, go slowly when needed and try to make the choices as easy as possible.
- Provide encouragement—particularly when working with patients who are hard to refract.
- Proceed with a purpose—do not offer more choices than are necessary to establish your endpoint. Boredom and fatigue can result in poor subjective responses.

Though optometry has made enormous strides in expanding its scope of practice, refraction is its lifeblood. Such an inherently subjective experience is never going to be as precise as we may hope, but adopting a standardized protocol such as this will help remove some the variables that lead to suboptimal results. ■

Dr. Wilkinson is a clinical professor in the department of ophthalmology and visual sciences at the University of Iowa's Carver College of Medicine. He is also director of the institution's vision rehabilitation service.

20 Troubleshooting Tips for 'Eyeglass Checks'

What do you check for when a patient complains that their new glasses are not as good as their previous pair? Consider these 20 tips.

1. Ask about complaint specifically. Is it distance? Near? Asthenopia? Diplopia? Pain behind the ears or at the bridge of the nose from ill-fitting glasses?
2. Read the new and old glasses on the lensometer and compare.
3. If you feel the prescription is reading differently than prescribed on an automated lensometer, check the prescription on a manual lensometer to be sure.
4. Remember that digital lenses, particularly digital progressive lenses, will not measure exactly to the power prescribed. This is because digital lenses are designed to adjust to the different vertex distances the patient will have when viewing through different parts of the lens.
5. Make sure the old glasses did not have any prism.
6. Check the patient for undetected strabismus with cover testing.
7. Refract the patient again, possibly with a cycloplegic agent, if the symptoms warrant.
8. Check the optical centers in comparison to the pupillary centers.
9. Check whether the reading segments are in the correct position.
10. Make sure the new glasses fit the patient correctly.
11. Check whether the old glasses were made in a plus cylinder design using the Geneva lens clock.
12. Check whether the base curve was changed using the Geneva lens clock.
13. Evaluate the patient for dry eye.
14. If the patient has a high prescription, check the vertex distance. Often, it is easier to refract such patients over their old pair of glasses to keep the vertex distance the same.
15. Check the pantoscopic tilt. Normally the tilt is 10 to 15 degrees, so that when the patient reads, the eye is perpendicular to the lens. The patient may be noticing that the tilt is different compared to the old glasses.
16. With postoperative glasses, evaluate for diplopia in down gaze due to anisometropia.
17. The add may be too strong or too weak. Check the patient using trial lenses and reading material.
18. Sometimes, if the diameter of the lens is much larger in the newer frame, the patient may be noticing distortion in the periphery of their lenses. In this situation, encourage a smaller frame. Conversely, if the new frame is significantly smaller, the patient may notice the edges of the lenses, or the reading area of their multifocal lens may be too small to use efficiently. In this situation, encourage the use of a larger frame.
19. Above all, try to test the new prescription in a trial frame with a walk around the office; you do not want to go through this process again.
20. If you can find nothing wrong with the Rx and the optics of the lenses, encourage the patient to give the glasses another try. An adaptation period may be necessary, especially for progressives.

Get Laser Focused on the Appropriate Glaucoma Treatment

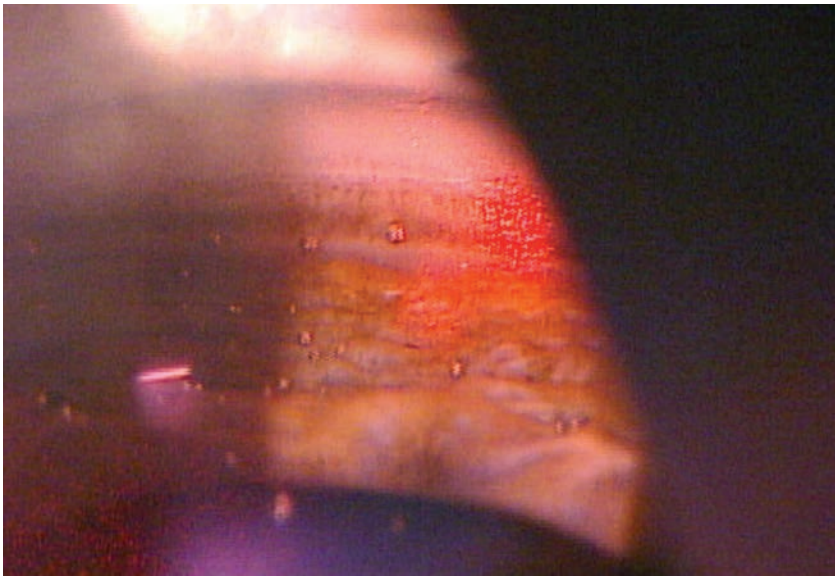
SLT—once the exclusive domain of ophthalmology—is becoming a first-line treatment as multiple states allow optometrists to perform it. **By Nathan Lighthizer, OD**

Laser therapy in glaucoma, particularly selective laser trabeculoplasty (SLT), is moving closer to being embraced as a first-line treatment. This installment of our ongoing "Essential Procedures" print-and-video series explains just how to perform it.

We've heard plenty of excuses from noncompliant glaucoma patients in our practices:

- "I am really going to struggle taking my glaucoma drops."
- "I can't afford the medications."
- "I get more of the drop on my cheek than in my eye."
- "I get the drops in three or four days per week."

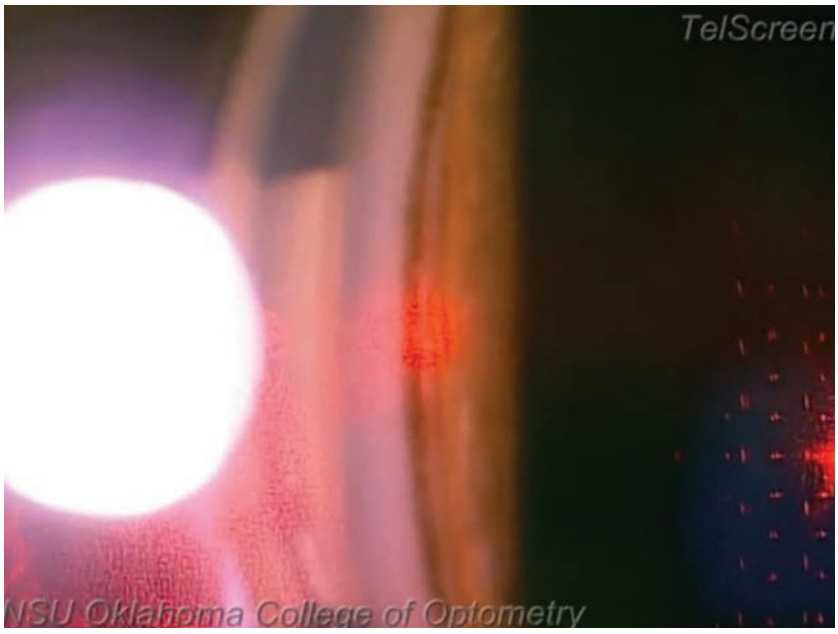
Compliance with topical medications is one of the biggest issues doctors face when treating patients with primary open angle glaucoma (POAG). In the United States, the standard of care for the past few decades has been to follow a straightforward tier system when selecting the right glaucoma treatment: drops first, laser second, surgery third. Treatment should always



The SLT procedure tends to be effective in most patients—approximately 80% to 90% of patients will have an effective outcome. The more pigment the patient has in the trabecular meshwork, the better the likelihood of success.

To see a narrated video of this procedure, visit www.reviewofoptometry.com, or scan this QR code.

be tailored patient-by-patient, based on factors such as disease severity, the patient's age and testing results. But the aforementioned tiered-treatment protocol has largely been the standard for years. In many instances, doctors will try two or three drops before moving up to the second treatment tier. Recent evidence is challenging this thinking and forcing treating optometrists and ophthalmologists to ask themselves: when should I consider laser?[1] It's an intriguing question, especially considering the fact that eye care providers in many European countries have long considered SLT a first-line therapy.[2]

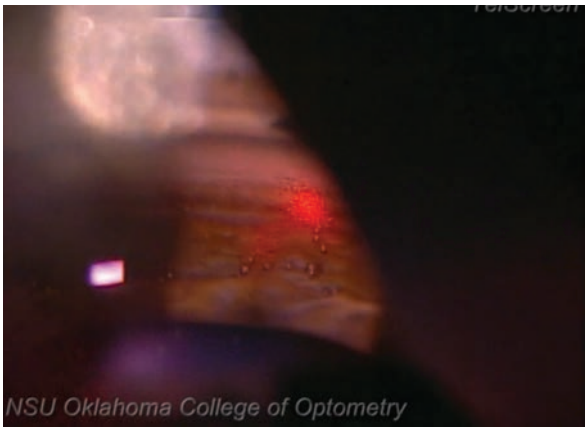


A critical element of laser therapy is to prepare the eye by performing a gonioscopy exam first to confirm that the patient's eye provides enough room to perform the procedure and the trabecular meshwork is clearly visible. It will also help to determine the amount of pigment in the angle, which will dictate the energy setting.

Laser History

SLT, introduced in 2001, is an improvement in the mechanism of action over its predecessor, argon laser trabeculoplasty. ALT uses laser energy to cause a thermal, or coagulative, burn upon the trabecular meshwork (TM), which mechanically opens up adjacent areas (a so-called "mechanical effect"). SLT uses a shorter duration of laser energy than ALT to cause a sub-lethal stress reaction in the TM cells, which causes inflammatory cells to travel to the meshwork and clean out the cellular debris, enhancing aqueous outflow (a so-called "biologic effect").[3] The structural damage to the TM is far less in SLT compared with ALT, and this may be one factor in its more favorable repeatability.[4]

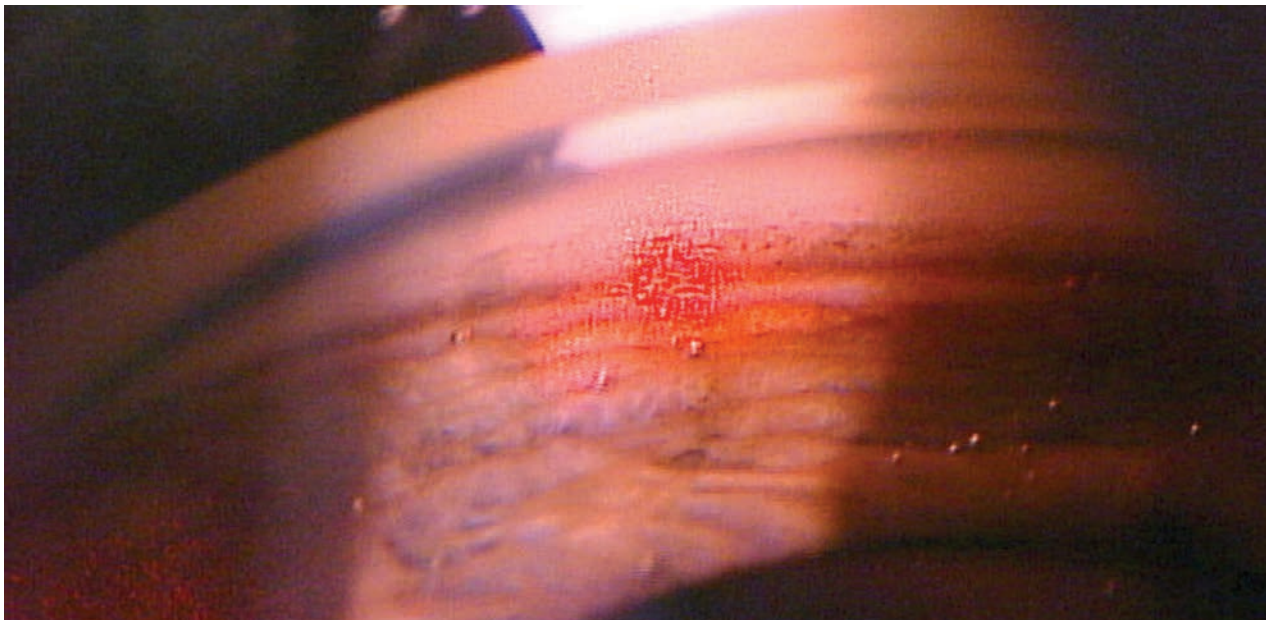
The "selective" in SLT is named so because the procedure selectively targets the melanin-containing cells in the TM, which absorb the laser energy and cause the desired tissue changes to enhance outflow. To that effect, the more pigmented the TM, the more effective the laser.



Because SLT creates no pits, craters or blanching of the tissue, doctors performing the procedure won't be able to rely on visual landmarks to show them where they started. Always start in the same place to ensure you remember where the first laser was fired.

The effectiveness of SLT depends on numerous factors. On average, 80% to 90% of patients will experience intraocular pressure (IOP) lowering of 15% to 30%.[3] In my clinical experience, when patients present with heavy pigment in the TM, success rate is even higher due to all of the pigment that the laser can select. Patients with higher initial IOPs and no prior treatment often have more significant IOP reduction. This effect is similar to topical glaucoma drops, which have a greater IOP-lowering effect the first time (25% to 35%), compared with the later drops (which may only lower IOP 10% to 15%).[5]

The area of treatment often will significantly affect the IOP lowering effect. Scientific studies and clinical experience has shown that a larger area of the angle often packs a much bigger punch in terms of IOP lowering effect than if a smaller amount of the angle is treated.[6]



The cavitation bubbles or "champagne" bubbles that can be seen throughout the trabecular meshwork as the procedure is performed lets the physician know that the laser is properly interacting with the tissue.

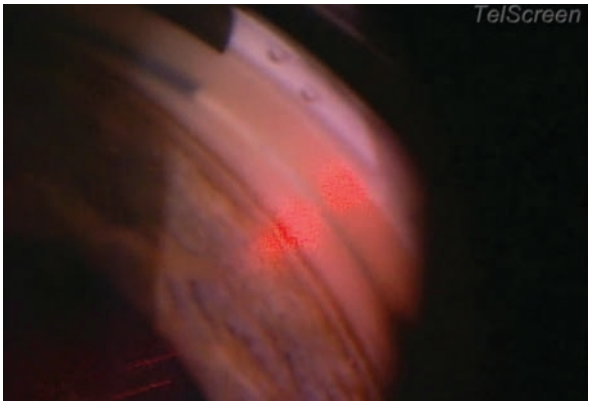
Indications and Contraindications

Indications for performing SLT are numerous. The five most common entities for which you may consider SLT are:

- POAG.
- Low-tension glaucoma.
- Pigment dispersion syndrome/glaucoma.
- Pseudoexfoliative glaucoma.
- Ocular hypertension.

Even in these cases, the standard of care remains one or two glaucoma drops first and then, once the patient has reached maximum medical therapy, consider laser. However, this view is changing and many are now shifting laser to the top of the list in their treatment approaches, due to numerous studies, including the SLT/MED study, which shows a favorable comparison between SLT and prostaglandin therapy for first-line treatment.[1,2,7]

SLT is contraindicated for patients who have an angle that is not open enough to clearly visualize the TM. Evidence of any secondary glaucoma, such as neovascular, inflammatory, angle recession or congenital glaucoma, are also either absolute or relative contraindications, depending on the case. Complete failure of a prior laser trabeculoplasty, either ALT or SLT, should also give reason for pause when considering an additional SLT.



The SLT procedure requires approximately 25 shots per quadrant, which is about 50 shots per 180 degrees, or, in this case, if you're going all the way around, 100 shots for 360 degrees.

Other surgical procedures, such as valves or stents, should be considered in preference to SLT when dealing with particularly advanced glaucoma, as in the case of severe, central VF defects, advanced cup-to-disc ratio greater than 0.8 in the vertical meridian or severe thinning on the OCT.

Side effects of the SLT procedure include transient IOP elevation after the procedure, inflammation, peripheral anterior synechiae, floaters, transient blurred vision, angle bleeding and possible corneal edema from endothelial cell loss.[1] The two most common, albeit still rare, are transient IOP elevation and inflammation.[1] Both of these can be easily controlled in most cases with pre- and postoperative topical medications.[3]

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The SLT Procedure

Prior to the SLT, perform a comprehensive exam, including a best-corrected visual acuity, entrance skills testing, IOP evaluation and a slit lamp examination. A fundus, macula and optic nerve head evaluation should also be performed prior to SLT. Since patients are usually not dilated on the day of the SLT, a dilated fundus examination often takes place on a prior visit.

Take a careful health history, including allergies, current medications, pulse and blood pressure.

It is critical to review the patient's specific glaucoma diagnosis, current glaucoma treatments, as well as any history of past laser or surgical treatments.

Review with the patient a consent form detailing indications, contraindications, risks and benefits and alternative treatments and have the patient sign the form.

After you've completed the examination and obtained the proper consent, the steps of an SLT treatment are as follows:

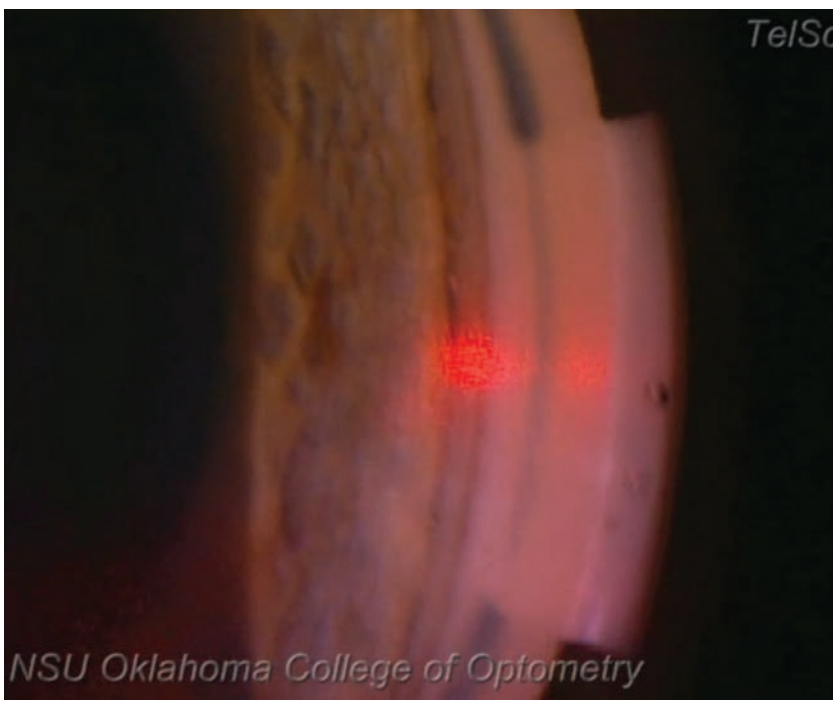
1. ***Perform Gonioscopy.*** This should be done as part of the comprehensive workup before every SLT procedure. It is a critical step to determine how widely open the angle is, which determines how much room you will have to work in the angle during the procedure. It also will let you know how much pigment the patient has in the TM, which directly affects the energy level setting. A clinician who is particularly skilled in gonioscopy will have a tremendous advantage when performing the actual SLT procedure.

2. ***Instill preoperative medications.*** One drop of brimonidine or Iopidine is instilled 10 to 20 minutes prior to the procedure. Occasionally, pilocarpine is instilled preoperatively to give a more open view of the angle and TM; however, this is not usually needed. Proparacaine is instilled in both eyes to eliminate the blink reflex during the procedure.

3. ***Select the appropriate laser settings.*** Typical starting energy for an SLT is 0.8mJ to 1.0mJ per shot. The more pigment that is present in the angle, the more effective the laser will potentially be, since the SLT selectively targets pigment. With this in mind, turn the energy down to 0.5mJ to 0.7mJ/shot in heavily pigmented angles, as the laser will still be effective at this energy level while, at the same time, minimizing potential complications. In cases with little pigment in the angle, turn the energy up to 1.1mJ to 1.3 mJ/shot. Laser burn size for the SLT is 400µm, and laser burn duration is three nanoseconds (10^{-9} seconds). Both of these settings are fixed with the SLT laser and cannot be adjusted.

4. ***Insert the SLT lens.*** Performing an SLT requires insertion of an SLT laser lens on the eye. Starting placement for the mirror can occur anywhere. My preference is putting the mirror at the 9 o'clock position. This will allow a clockwise rotation of the mirror to cover the first 180 degrees (from 9 o'clock to 3 o'clock) in the superior quadrant view, which in actuality is the anatomic inferior quadrant. It is nearly always preferable to do the inferior 180 degrees first, since that is usually the most open angle with the heaviest amount of pigment. In a practical sense, it does not matter where you start, as long as you remember where you started so you know where to finish the procedure.

5. ***Fire the laser.*** Starting at 9 o'clock, or your chosen starting location, place the single aiming helium-neon (he-ne) laser beam on

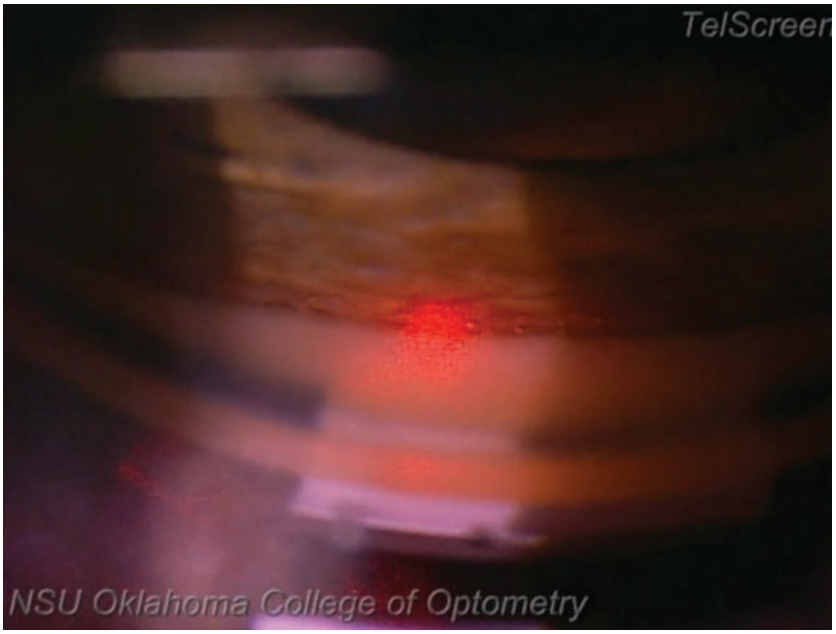


At this point in the procedure, the laser is approximately at the 3 o'clock position, or 180 degrees from the starting point. Notice the champagne bubbles forming in the area where the laser has interacted with the tissue.

the TM, covering it entirely. Fire laser spots one right next to the prior one, so that they are not overlapping while, at the same time, not spaced apart. Each shot should fall directly next to the previous shot. During the laser shots, minimal to no change in the tissue is seen other than the typical champagne bubbles. No charring, blanching, pits or craters are seen where previous laser spots have been placed, which again, makes it critical to remember where you started the procedure to avoid double treating areas of the TM. The typical number of laser pulses during the procedure is approximately 45 to 60 per 180 degrees for a half treatment, and 90 to 120 pulses per 360 degrees for a full treatment. Anatomically speaking, if the laser burns are placed too far anterior, nearing Schwalbe's line or even anterior to that, the procedure is less likely to be effective, since the TM is no longer being treated. If the laser burns are placed too far posterior, in the area of the scleral spur or ciliary body, the patient is much more likely to feel discomfort during the procedure.

6. ***Determine whether you are performing 180 degrees or 360 degrees.*** Due to the findings of the SLT/MED study, among others, our standard is to perform a 360 degree SLT in one eye on the first visit, unless the patient has pigment dispersion syndrome/glaucoma with heavy pigment in the TM, in which case we will only perform 180 degrees. The second eye can be performed at a follow-up visit in the coming weeks.

7. ***Instill postoperative medications.*** Remove the SLT lens from the eye and instill postoperative medications. Brimonidine or Iopidine should be instilled again immediately after the procedure to reduce the risk of a transient IOP spike.



Notice how this laser sticks to the trabecular meshwork exclusively. When performing the SLT procedure, it is cruical to fire the laser only within the trabecular meshwork. Hitting too far anterior, into Schwalbe's line, will likely result in decreased effectiveness, while hitting too far posterior will result in patient discomfort.

8. ***Check IOP.*** Check the IOP 30 to 60 minutes after the procedure to ensure it has not elevated significantly. IOP is typically lower 30 to 60 minutes after the procedure, due to the brimonidine that was instilled before and after. If the IOP is elevated by more than five points from the start of the exam, consider bringing the patient back the following day for an IOP check.

9. ***Prescribe NSAIDs.*** Dispense or prescribe a topical nonsteroidal anti-inflammatory agent for residual pain and inflammation after the procedure. Patients can expect the eye to be mildly red and sore for two to three days after the procedure, and often find that a few drops of topical NSAID in the days after the procedure help to alleviate the redness and soreness. Protocols vary depending on the individual patient and doctor preference, but many doctors find it preferable to have the patient use a topical NSAID PRN for two to three days following the procedure.

10. ***Schedule a follow up.*** Perform a follow-up visit one to two weeks and six to eight weeks after the initial SLT laser. It typically takes six to eight weeks to see the full effect of the treatment. So, if you are only performing a half treatment or 180 degrees, wait six to eight weeks after the initial procedure to determine if the other 180 degrees needs to be done.

Retreatment

It is widely known that the effects of laser trabeculoplasty, both ALT and SLT, tend to wane with time. Evidence suggests that treatment effectiveness tends to last two to five years for most patients.[8]

SLT has been shown to be more repeatable than ALT in recent studies.[8] Repeated treatments may not work quite as well, or last quite as long, but they are still largely

successful in many patients. SLT can also be performed on top of prior ALT.[8]

SLT has been around for longer than a decade now. Enough clinical and scientific evidence has been obtained to move this protocol to closer to the top of our treatment armamentarium.[1-7]

This quick and safe laser procedure frequently has an effect that lasts years and will often leave your patient's mind at ease knowing they don't have to worry about when and if they can get their next drop instilled. ■

Dr. Lighthizer is assistant dean for clinical care services, director of continuing education, and chief of the specialty care clinic and the electrodiagnostics clinic at NSU Oklahoma College of Optometry.

This image shows the laser returning to the 9 o'clock position, indicating the completion of the procedure. This patient had a significant enough reduction in IOP that he was able to discontinue one of his medications as a result of SLT.

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Eyes Wide Shut

Changes are happening all around you—are you embracing them or burying your head in the sand? **By John Rumpakis, OD, MBA, Clinical Coding Editor**

I think it would be fair to say that most health care professionals in the United States understand that health care reform is more about politics than it is about health care. I see new statistics rolling out daily about either the success or failure of the Affordable Care Act (ACA) and its impact on the US populace.

Whether you support it or not, one thing is for certain: the changes are affecting how we deliver care to patients. While these changes seem to have accelerated since the January 1, 2014 implementation of the ACA, they have been going on for some time. What worries me the most is that, while these things have been in plain sight, most practitioners have their eyes shut and are either believing the changes don't apply to them or are simply not aware these changes are happening.

Top 10 Changes

My concern is that the list of top 10 changes that have been happening in parallel over the past decade is astounding. I am hopeful many will sound familiar—if not, then my concerns are even greater:

1. Mandatory use of electronic health records
2. PQRS/QRUR
3. Meaningful Use (1, 2 and 3)
4. Narrow Networks (ACOs)
5. ICD-10
6. Diagnosis Related Groups
7. Hierarchical Care Categories
8. Value-Based Modifier
9. MIPS Score (Merit Incentive-Based Payment System)
10. Outcome-Based Care

The problem? They are all going to converge in health care practices between 2016 and 2019.

While most have viewed these as isolated programs, they are, in fact, intractably intertwined, and current forecasts indicate they are going to affect your practice with complete implementation by 2020. More changes will take place within the next three years than there have been in the past 50—since the implementation of Medicare.

Where We Are Heading

While a complete explanation of the impact of this convergence is beyond the scope of this column, it is imperative that you understand that these changes can, and most likely will, affect the economics of your practice, your ability to participate in health care plans you have taken for granted and, most of all, your access to your patients.

Here is a simple illustration: Outcome-based care is where our payment system is moving—where we will get compensated based upon how quickly and effectively we are able to provide the best outcome for our patients. That means that there needs to be a feedback mechanism that allows the monitoring of quality and outcomes in terms of costs. This is what the PQRS/QRUR and ICD-10 will facilitate.

We have already seen, with the October 2015 release of the CMS Comparative Billing Report, how we are being compared to our peer group in caring for patients, both on a state and national basis. Now expand this one example to your entire patient base, for both refractive care and medical eye care. These outcomes may be a significant factor in determining your ability to be part of a care network and how much you are compensated for a particular disease state management. And this is only a small illustration of where things are heading.

Preparing Your Practice

In presenting my Eyes Wide Shut curriculum around the country, I have noticed many optometrists are receptive to making formative changes in their practices. Some of these changes are easy, while others are much more difficult; yet they are all critical and you must realize how they will impact your individual practice. They are not just for practice owners, but for every licensed health care provider who is actively providing patient care in any setting.

The perception that 2015 was a busy year in health care reform may ring true to many. I see it as just the beginning of the onslaught of changes heading our way. Many say it is just too hard to keep up—likening it to drinking from a fire hose. Unfortunately, the hose just got bigger and with more pressure behind it, so we have to either learn to drink faster or drown. Whether you provide primarily refractive care or are a full-scope practitioner, these changes will apply to you. Stay tuned—we will take this wild ride together. ■

Send questions and comments to ROcodingconnection @gmail.com.

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Which Lens for KCN?

Despite their recent resurgence, scleral lenses may not always be the best choice. The tried-and-true corneal GP might be better. **Edited by Joseph P. Shovlin, OD**

Q In which cases would you still use a corneal gas permeable (GP) lens, rather than a scleral lens, to fit an irregular cornea with ectasia?

A "Corneal GP lenses were the standard of care for over 50 years in [cases of] corneal ectasia and keratoconus," says Jeffrey Sonsino, OD, of Optique Eyecare in Nashville, Tenn. Recent research, however, including the Collaborative Longitudinal Evaluation of Keratoconus (CLEK) studies, changed that benchmark. "[Following the studies,] we agreed that flat-fitting GP lenses were associated with higher risk of corneal scarring, which ultimately led to corneal transplant. In fact, around 40% of keratocones are still undergoing some form of either partial thickness or penetrating keratoplasty," explains Dr. Sonsino.[1-3]

Newer vaulting lenses (i.e., sclerals and hybrids) alleviate this problem by offering a safer apical clearance type fit; they are expected to significantly reduce the prevalence of corneal transplants among patients.

That being said, corneal GP lenses still maintain an important role for managing keratoconus, despite the advantages of scleral lenses, says Gregory DeNaeyer, OD, of Arena Eye Surgeons in Ohio. "Corneal GP lenses center where the cornea is steep and therefore can be ideal for nipple topographies that have centered apices," he explains. Patients with small apertures and deep-set eyes may also benefit from corneal GP lens wear, as these physical characteristics can impede success of a scleral lens fit.

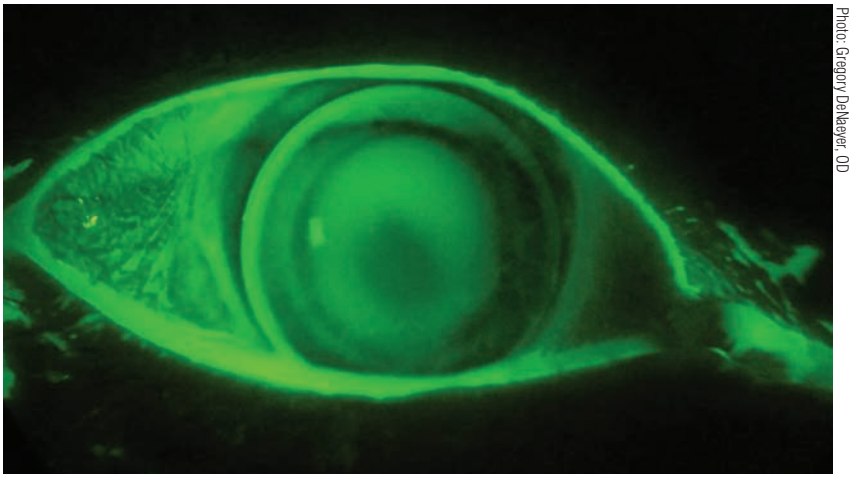

Photo: Gregory DeNaeyer, OD

Corneal gas permeable lenses offer keratoconic patients a range of benefits despite their irregular corneal topography.

Christine W. Sindt, OD, of the University of Iowa, points out that corneal GP lenses also offer higher tear exchange than scleral lenses, so patients with lid colonization or inflammatory product build-up may benefit from the reduced risk of infection. Additionally, significant scleral irregularity or toricity may make scleral lens use impossible, she adds.

Cost factors must also be considered when selecting a lens: GP lenses are significantly less expensive than scleral lenses.

If maintaining endothelial cell count is a concern, corneal GP lenses are preferable over scleral lenses, as the latter can result in corneal edema due to reduced oxygen permeability, says Dr. Sindt. Research shows that at five years following corneal transplant surgery, average endothelial cell counts are only 786 cells/mm^2, Dr. Sonsino notes.[4]

In closing, Dr. DeNaeyer offers some additional advice regarding stabilizing corneal GP lenses on these types of patients: fit corneal GP lenses with diameters larger than 9.5mm and consider piggybacking corneal GP lenses on a soft disposable lens for better comfort. ■

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See You at the (Neuromuscular) Junction: Part 2

What should you do when you suspect an autoimmune disease with ophthalmic complications such as myasthenia gravis? **By Carlo J. Pelino, OD, and Joseph J. Pizzimenti, OD**

Neuromuscular junction (NMJ) disorders result from destruction, malfunction or absence of one or more key proteins involved in neuromuscular transmission. The most common pathology is antibody-mediated damage or down regulation of ion channels or receptors, resulting in myasthenia gravis (MG), Lambert-Eaton myasthenic syndrome and acquired neuromyotonia (Isaac's syndrome).[4] These three conditions share many common features. Then, there are congenital myasthenic syndromes, which are caused by mutations in neuromuscular junction proteins.

The most common and most important NMJ disorder, particularly for optometrists, is MG.

Myasthenia Gravis

MG most commonly affects young adult women and older men. These patients often present with characteristic fluctuating muscle deficits and fatigue.[1,2]

The prevalence of MG in the United States has risen over the past two decades to an estimated 14 to 20 per 100,000.[3] However, MG remains under-diagnosed and the prevalence is probably higher. MG can be divided into ocular and generalized forms. Among patients presenting with ocular symptoms only, 20% to 50% remain ocular, while the remaining patients will progress to generalized disease.[5] For those with ocular MG, there is no reliable way to predict progression to generalized MG. However, if MG remains ocular for one year, the progression rate is 16% and drops to 6% if the disease remains localized for three years.[5]

Diagnostic Challenges

Diagnosing MG can be difficult because the disease may mimic almost any pupil-sparing pattern of ocular misalignment. The fluctuating nature of MG can also create diagnostic confusion. Diagnostic testing for fatigue is not part of the routine ophthalmic exam, so you often have to think of MG before you can find it; added to that, not all patients who are dealing with fatigue have MG, and not all MG patients clearly fatigue.

To read Part 1, go to www.reviewofoptometry.com or scan the QR code.

Testing

Although no test for MG is 100% sensitive or specific, the ice pack test is simple, fast and relatively helpful.[3] Other clinical signs to look for include orbicularis weakness, Osher's "peek sign," and Cogan's lid twitch.[4] Tests you should consider ordering include:

- ***Thyroid studies.*** Thymic abnormalities are associated with MG, but the nature of the association is uncertain. The thymus contains all the necessary elements for the pathogenesis of MG: myoid cells that express the acetylcholine receptor (AChR) antigen, antigen-presenting cells and immunocompetent T-cells. MG patients with thymoma usually have more severe disease and electromyographic abnormalities, and higher levels of AChR antibodies than those without thymoma.

Approximately 10% of MG patients have a thymoma, while

The Thymus in MG

The importance of T-cells in the pathogenesis of MG is increasingly apparent. The thymus is the central organ in T-cell mediated immunity, and abnormalities such as thymic hyperplasia or thymoma are well recognized in myasthenic patients.

Most patients with MG have either thymic hyperplasia (70%) or thymoma (10-15%).[5]

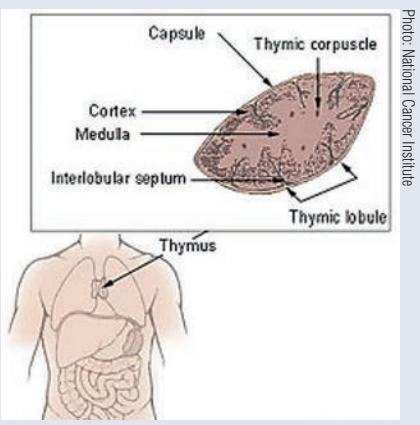

Photo: National Cancer Institute

For allergic conjunctivitis[1]

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INDICATION AND USAGE

BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% is a histamine H_1 receptor antagonist indicated for the treatment of itching associated with signs and symptoms of allergic conjunctivitis.

IMPORTANT RISK INFORMATION

BEPREVE® is contraindicated in patients with a history of hypersensitivity reactions to bepotastine or any of the other ingredients. BEPREVE® is for topical ophthalmic use only. To minimize risk of contamination, do not touch the dropper tip to any surface. Keep the bottle closed when not in use. BEPREVE® should not be used to treat contact lens–related irritation. Remove contact lenses prior to instillation of BEPREVE®.

The most common adverse reaction occurring in approximately 25% of patients was a mild taste following instillation. Other adverse reactions occurring in 2%-5% of patients were eye irritation, headache, and nasopharyngitis.

Please see the accompanying prescribing information for BEPREVE® on the following page.

Reference: 1. BEPREVE [package insert]. Tampa, FL: Bausch + Lomb, Inc; 2012.

BAUSCH + LOMB

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

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BEPREVE®
(bepotastine besilate ophthalmic solution) 1.5%

BEPREVE® (bepotastine besilate ophthalmic solution) 1.5%

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% safely and effectively. See full prescribing information for BEPREVE®.

BEPREVE® (bepotastine besilate ophthalmic solution) 1.5%
Initial U.S. Approval: 2009

----------RECENT MAJOR CHANGES----------
Contraindications (4) 06/2012

----------INDICATIONS AND USAGE----------
BEPREVE® is a histamine H1 receptor antagonist indicated for the treatment of itching associated with allergic conjunctivitis. (1)

----------DOSAGE AND ADMINISTRATION----------
Instill one drop into the affected eye(s) twice a day (BID). (2)

----------DOSAGE FORMS AND STRENGTHS--------
Solution containing bepotastine besilate, 1.5%. (3)

----------CONTRAINDICATIONS----------
Hypersensitivity to any component of this product. (4)

----------WARNINGS AND PRECAUTIONS----------
- To minimize the risk of contamination, do not touch dropper tip to any surface. Keep bottle tightly closed when not in use. (5.1)
- BEPREVE should not be used to treat contact lens-related irritation. (5.2)
- Remove contact lenses prior to instillation of BEPREVE. (5.2)

----------ADVERSE REACTIONS----------
The most common adverse reaction occurring in approximately 25% of patients was a mild taste following instillation. Other adverse reactions which occurred in 2-5% of subjects were eye irritation, headache, and nasopharyngitis. (6)

To report SUSPECTED ADVERSE REACTIONS, contact Bausch & Lomb Incorporated. at 1-800-323-0000, or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.
See 17 for PATIENT COUNSELING INFORMATION

Revised: 10/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

*Sections or subsections omitted from the full prescribing information are not listed

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE
BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% is a histamine H_1 receptor antagonist indicated for the treatment of itching associated with signs and symptoms of allergic conjunctivitis.

2 DOSAGE AND ADMINISTRATION
Instill one drop of BEPREVE into the affected eye(s) twice a day (BID).

3 DOSAGE FORMS AND STRENGTHS
Topical ophthalmic solution containing bepotastine besilate 1.5%.

4 CONTRAINDICATIONS
Bepreve is contraindicated in patients with a history of hypersensitivity reactions to bepotastine or any of the other ingredients *[see Adverse Reactions (6.2)]*.

5 WARNINGS AND PRECAUTIONS
5.1 Contamination of Tip and Solution
To minimize contaminating the dropper tip and solution, care should be taken not to touch the eyelids or surrounding areas with the dropper tip of the bottle. Keep bottle tightly closed when not in use.

5.2 Contact Lens Use
Patients should be advised not to wear a contact lens if their eye is red. BEPREVE should not be used to treat contact lens-related irritation.

BEPREVE should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of BEPREVE. The preservative in BEPREVE, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of BEPREVE.

5.3 Topical Ophthalmic Use Only
BEPREVE is for topical ophthalmic use only.

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

The most common reported adverse reaction occurring in approximately 25% of subjects was a mild taste following instillation. Other adverse reactions occurring in 2-5% of subjects were eye irritation, headache, and nasopharyngitis.

6.2 Post Marketing Experience
Hypersensitivity reactions have been reported rarely during the post-marketing use of BEPREVE. Because these reactions are reported voluntarily from a population of unknown size, it is not always possible to reliably estimate their frequency or establish a casual relationship to drug exposure. The hypersensitivity reactions include itching, body rash, and swelling of lips, tongue and/or throat.

8 USE IN SPECIFIC POPULATIONS
8.1 Pregnancy
Pregnancy Category C: Teratogenicity studies have been performed in animals. Bepotastine besilate was not found to be teratogenic in rats during organogenesis and fetal development at oral doses up to 200 mg/kg/day (representing a systemic concentration approximately 3,300 times that anticipated for topical ocular use in humans), but did show some potential for causing skeletal abnormalities at 1,000 mg/kg/day. There were no teratogenic effects seen in rabbits at oral doses up to 500 mg/kg/day given during organogenesis and fetal development (>13,000 times the dose in humans on a mg/kg basis). Evidence of infertility was seen in rats given oral bepotastine besilate 1,000 mg/kg/day; however, no evidence of infertility was observed in rats given 200 mg/kg/day (approximately 3,300 times the topical ocular use in humans). The concentration of radio-labeled bepotastine besilate was similar in fetal liver and maternal blood plasma following a single 3 mg/kg oral dose. The concentration in other fetal tissues was one-third to one-tenth the concentration in maternal blood plasma.

An increase in stillborns and decreased growth and development were observed in pups born from rats given oral doses of 1,000 mg/kg/day during perinatal and lactation periods. There were no observed effects in rats treated with 100 mg/kg/day.

There are no adequate and well-controlled studies of bepotastine besilate in pregnant women. Because animal reproduction studies are not always predictive of human response, BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

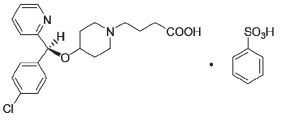
8.3 Nursing Mothers
Following a single 3 mg/kg oral dose of radiolabeled bepotastine besilate to nursing rats 11 days after delivery, the maximum concentration of radioactivity in milk was 0.40 mcg-eq/mL 1 hour after administration; at 48 hours after administration the concentration was below detection limits. The milk concentration was higher than the maternal blood plasma concentration at each time of measurement.

It is not known if bepotastine besilate is excreted in human milk. Caution should be exercised when BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is administered to a nursing woman.

8.4 Pediatric Use
Safety and efficacy of BEPREVE (bepotastine besilate ophthalmic solution) 1.5% have not been established in pediatric patients under 2 years of age. Efficacy in pediatric patients under 10 years of age was extrapolated from clinical trials conducted in pediatric patients greater than 10 years of age and from adults.

8.5 Geriatric Use
No overall difference in safety or effectiveness has been observed between elderly and younger patients.

11 DESCRIPTION
BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is a sterile, topically administered drug for ophthalmic use. Each mL of BEPREVE contains 15 mg bepotastine besilate.
Bepotastine besilate is designated chemically as (+) -4-[[(S)-p-chloro-alpha -2-pyridylbenzyl]oxy]-1-piperidine butyric acid monobenzenesulfonate.
The chemical structure for bepotastine besilate is:



Bepotastine besilate is a white or pale yellowish crystalline powder. The molecular weight of bepotastine besilate is 547.06 daltons. BEPREVE® ophthalmic solution is supplied as a sterile, aqueous 1.5% solution, with a pH of 6.8.
The osmolality of BEPREVE (bepotastine besilate ophthalmic solution) 1.5% is approximately 290 mOsm/kg.
Each mL of BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% contains:
Active: Bepotastine besilate 15 mg (equivalent to 10.7 mg bepotastine)
Preservative: benzalkonium chloride 0.005%
Inactives: monobasic sodium phosphate dihydrate, sodium chloride, sodium hydroxide to adjust pH, and water for injection, USP.

12 CLINICAL PHARMACOLOGY
12.1 Mechanism of Action
Bepotastine is a topically active, direct H_1-receptor antagonist and an inhibitor of the release of histamine from mast cells.

12.3 Pharmacokinetics
Absorption: The extent of systemic exposure to bepotastine following topical ophthalmic administration of bepotastine besilate 1% and 1.5% ophthalmic solutions was evaluated in 12 healthy adults. Following one drop of 1% or 1.5% bepotastine besilate ophthalmic solution to both eyes four times daily (QID) for seven days, bepotastine plasma concentrations peaked at approximately one to two hours post-instillation. Maximum plasma concentration for the 1% and 1.5% strengths were 5.1 ± 2.5 ng/mL and 7.3 ± 1.9 ng/mL, respectively. Plasma concentration at 24 hours post-instillation were below the quantifiable limit (2 ng/mL) in 11/12 subjects in the two dose groups.

Distribution: The extent of protein binding of bepotastine is approximately 55% and independent of bepotastine concentration.

Metabolism: *In vitro* metabolism studies with human liver microsomes demonstrated that bepotastine is minimally metabolized by CYP450 isozymes.

In vitro studies demonstrated that bepotastine besilate does not inhibit the metabolism of various cytochrome P450 substrate via inhibition of CYP3A4, CYP2C9, and CYP2C19. The effect of bepotastine besilate on the metabolism of substrates of CYP1A2, CYP2C8, CYP2D6 was not studied. Bepotastine besilate has a low potential for drug interaction via inhibition of CYP3A4, CYP2C9, and CYP2C19.

Excretion: The main route of elimination of bepotastine besilate is urinary excretion (with approximately 75-90% excreted unchanged in urine).

13 NONCLINICAL TOXICOLOGY
13.1 Carcinogenesis, Mutagenesis and Impairment of Fertility
Long-term dietary studies in mice and rats were conducted to evaluate the carcinogenic potential of bepotastine besilate. Bepotastine besilate did not significantly induce neoplasms in mice receiving a nominal dose of up to 200 mg/kg/day for 21 months or rats receiving a nominal dose of up to 97 mg/kg/day for 24 months. These dose levels represent systemic exposures approximating 350 and 200 times that achieved with human topical ocular use. The no observable adverse effect levels for bepotastine besilate based on nominal dose levels in carcinogenicity tests were 18.7 to 19.9 mg/kg/day in mice and 9.6 to 9.8 mg/kg/day in rats (representing exposure margins of approximately 60 and 20 times the systemic exposure anticipated for topical ocular use in humans).

There was no evidence of genotoxicity in the Ames test, in CHO cells (chromosome aberrations), in mouse hepatocytes (unscheduled DNA synthesis), or in the mouse micronucleus test.

When oral bepotastine was administered to male and female rats at doses up to 1,000 mg/kg/day, there was a slight reduction in fertility index and surviving fetuses. Infertility was not seen in rats given 200 mg/kg/day oral bepotastine besilate (approximately 3,300 times the systemic concentration anticipated for topical ocular use in humans).

14 CLINICAL STUDIES
Clinical efficacy was evaluated in 2 conjunctival allergen challenge (CAC) studies (237 patients). BEPREVE (bepotastine besilate ophthalmic solution) 1.5% was more effective than its vehicle for relieving ocular itching induced by an ocular allergen challenge, both at a CAC 15 minutes post-dosing and a CAC 8 hours post dosing of BEPREVE.

The safety of BEPREVE was evaluated in a randomized clinical study of 861 subjects over a period of 6 weeks.

16 HOW SUPPLIED/STORAGE AND HANDLING
BEPREVE® (bepotastine besilate ophthalmic solution) 1.5% is supplied in a white low density polyethylene plastic squeeze bottle with a white controlled dropper tip and a white polypropylene cap in the following size:
5 mL (NDC 24208-629-02)
10 mL (NDC 24208-629-01)

STORAGE
Store at 15º – 25ºC (59º – 77ºF).

17 PATIENT COUNSELING INFORMATION
17.1 Topical Ophthalmic Use Only
For topical ophthalmic administration only.

17.2 Sterility of Dropper Tip
Patients should be advised to not touch dropper tip to any surface, as this may contaminate the contents.

17.3 Concomitant Use of Contact Lenses
Patients should be advised not to wear a contact lens if their eye is red. Patients should be advised that BEPREVE should not be used to treat contact lens-related irritation.

Patients should also be advised to remove contact lenses prior to instillation of BEPREVE. The preservative in BEPREVE, benzalkonium chloride, may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of BEPREVE.

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US/BEP/13/0028 4/13

early-onset disease (before the age of 40) is associated with thymic hyperplasia. A CT thorax scan is mandatory in all anti-AChR antibody positive patients.[1-3,6] Thyroid studies should always be obtained because of the concomitant presence of thyroid dysfunction in up to 13% of patients with MG.[5]

• ***The Tensilon (edrophonium) test.*** This test has been largely superceded by the anti-AChR antibody assay in the diagnosis of MG, although it is still useful when the diagnosis needs to be confirmed with urgency.[6] Note that the test carries a small, but not insignificant, risk of respiratory arrest and cardiac arrhythmias and should be used with caution in patients with a history of these conditions.

• ***Anti-AChR antibody assay.*** Because the positive predictive value of this test is extremely high, a positive anti-AChR antibody titer in a patient with fatigue and weakness is enough to confirm an MG diagnosis. However, the negative predictive value is low; thus, a negative assay does not rule out myasthenia gravis.[5]

About 50% of patients with purely ocular signs of MG, and 15% of those with generalized disease, do not have antibodies against the AChR.[6] In the remainder of patients, practitioners must rely on clinical symptoms, signs and the results of detailed neurophysiology.[6]

• ***Neurophysiological studies.*** Repetitive nerve stimulation involves supra-maximal stimulation at 3Hz of a peripheral nerve (often the ulnar nerve), and recording the compound motor action potential from the relevant muscle. A decrement of more than 10% over five responses is considered consistent with MG.[6] Unfortunately, the test is unreliable if the limb is cold or if the patient has taken anticholinesterase (AChE) inhibitors, and it is often normal in patients with ocular myasthenia.

• ***Single fiber electromyography.*** SFEMG is a more sensitive test where recordings are made from two muscle fibers in a single motor unit. Increased variability in the interval between paired action potentials, termed *jitter*, or occasional blocking of one of the potentials is considered evidence of a defect in neuromuscular transmission.[6] However, because increased jitter can be found in conditions other than MG, it needs to be carefully interpreted.

Treatment Strategies

MG is one of the most treatable neurologic disorders, even though no clear consensus exists on treatment strategies (*Table 1*). Consider factors such as severity, distribution and rapidity of disease progression. Pharmacologic therapy includes AChE medication and immunosuppressive agents such as corticosteroids, azathioprine, cyclosporine, plasmapheresis and intravenous immune globulin.[6]

A thymoma should be removed because of the risk of metastatic spread, although this will not result in disease remission. Consult a cardiothoracic surgeon whenever discussing thymectomy.[3,7,8]

In patients with persistent ptosis, eyelid taping or a ptosis crutch may be beneficial. For patients who remain diplopic even after medical treatment, prism or occlusion therapy is a viable option. Strabismus surgery may be effective in patients whose deviation is too large to correct with prism and who show no change for up to 12 months.[5]

Myasthenia gravis is a chronic disease that may worsen acutely over days or weeks. Proper optometric management requires scheduled re-evaluation, a close doctor-patient relationship, and close follow-up care cordinationed with primary care and neurology. ■

Table 1. Systemic Therapy[3,6,7]

- ***Anticholinesterase (AChE) inhibitors:*** Initial treatment for mild MG
- Immunomodulating agents: Moderate and severe cases; usually prescribe corticosteroids earlier
- ***Intravenous immune globulin:*** Moderate to severe MG, worsening into crisis; elderly patients; patients with complex comorbid diseases; patients with severe weakness poorly controlled with other agents
- ***Plasmapheresis:*** Myasthenic crisis and refractory cases; long-term treatment; if other treatments are ineffective
- ***Thymectomy:*** Standard of care for all patients with thymoma and for patients between 10 and 55 without thymoma but with generalized MG; should be delayed in ocular MG at least two years to allow for spontaneous remission; not recommended in patients with antibodies to muscle-specific kinase

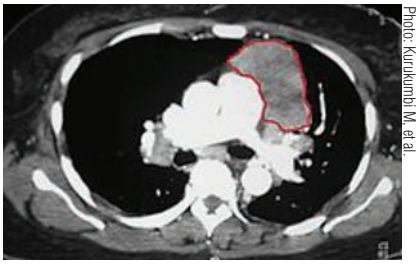

Photo: Kurukumbi M, et al.

Thymoma identified on a chest CT.

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2. Benatar M. A systematic review of diagnostic studies in myasthenia gravis. Neuromuscul Disord. 2006;16(7):459-67.
3. Keesey JC. Clinical evaluation and management of myasthenia gravis. Muscle Nerve. 2004:29(4):484-505.
4. Ajamian P, ed. Drag and Droop. Review of Optometry. 2015;152(10):32.
5. Vaphiades MS, Bhatti MT, Lesser RL. Ocular myasthenia gravis. Curr Opin Ophthalmol 2012;23:537-42.
6. Hill M. The Neuromuscular Junction Disorders. J Neurol Neurosurg Psychiatry 2003;74.
7. Gilhus NE, Verschuuren JJ. Myasthenia gravis: subgroup classification and therapeutic strategies. Lancet Neurol. 2015;14(10):1023-36.
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The Spotted-White Retina

A patient presented with irritation, but a close examination revealed much more.

By Mark T. Dunbar, OD, and Paul C. Hammond, OD

An 18-year-old male presented for evaluation of a red and irritated left eye. He had a history of brain damage and seizures from birth, and only a minimal history could be elicited.

Upon examination, his best-corrected vision was 20/20 OD and 20/60 OS. Confrontation visual fields were full to careful finger counting in both eyes; pupils were equally round and reactive to light. No afferent pupillary defect was found. Intraocular pressure (IOP) was 15mm Hg OD and 8mm Hg OS.

Slit lamp examination of the right eye was unremarkable. The left eye was positive for 3+ episcleral injection and 3+ cell and flare in the anterior chamber (*Figure 1*).

On dilated fundus exam, the right eye was completely normal. The left eye had 1-2+ vitreous cell and haze, with tortuous vasculature and mild disc edema. Mid-peripherally in the superior nasal quadrant, a white lesion was visible (*Figure 2*). The retina was attached.

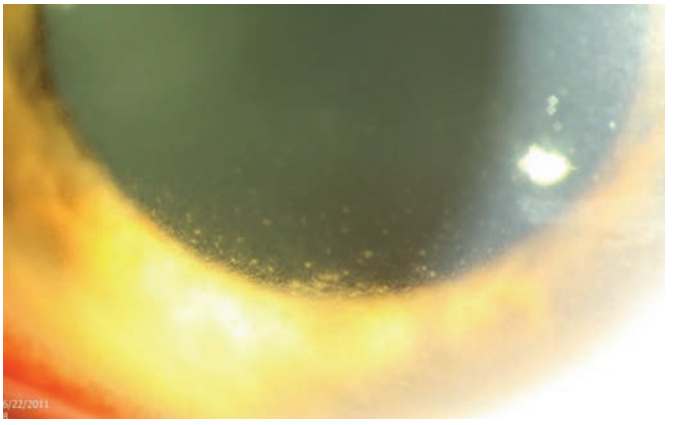

Fig. 1. An 18-year-old male's irritated left eye brought him to our office. What does his anterior segment presentation tell you about his likely diagnosis?

Take the Quiz

1. What are the findings seen on the retinal photograph of the left eye?
a. Retinal necrosis with intraretinal hemorrhage.
b. Roth spot.
c. Choroidal osteoma.
d. White without pressure.

2. What is the correct diagnosis?
a. Choroidal metastases.
b. Toxoplasma chorioretinitis.
c. Acute retinal necrosis.
d. Leukemia.

3. How should he be treated?
a. High-dose antivirals tapered to a lifetime prophylactic dose.
b. Pyrimethamine, sulfadiazine and corticosteroids.
c. Plaque radiotherapy.
d. Referral to oncology.

4. What is this patient at increased risk of developing?
a. Choroidal neovascular membrane.
b. Metastatic cancer to the liver.
c. Serous retinal detachment.
d. Rhegmatogenous retinal detachment.

For answers, see page 98.

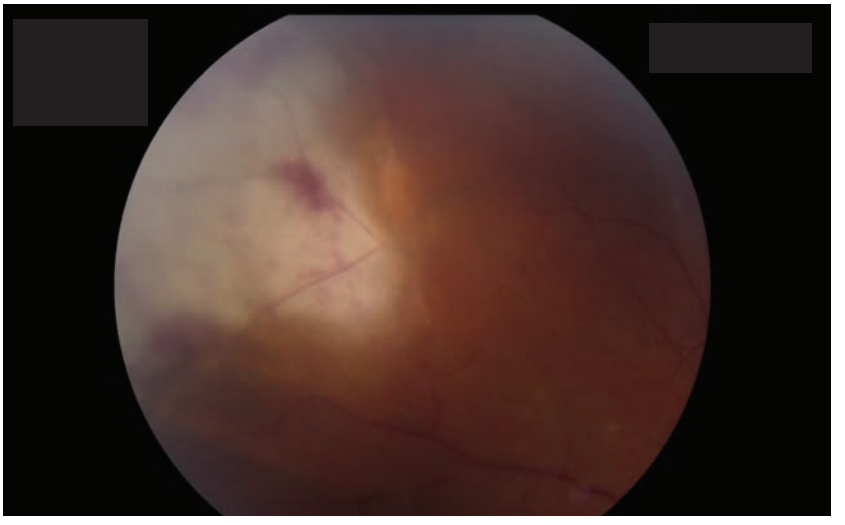

Fig. 2. What do these peripheral retinal findings represent?

Discussion

Based on the clinical findings, we suspected that our patient had acute retinal necrosis (ARN). An anterior chamber tap was performed and sent for culture. The patient was treated empirically with 900mg IV acyclovir, and started on 1g PO of valacyclovir TID. To treat his anterior segment inflammation he was started on atropine QID and prednisolone acetate QID in the left eye. At follow-up, three days later, 40mg of oral prednisone was added after consulting with the patient's pediatrician.

The diagnosis of ARN is generally made based on The clinical triad of progressive retinal necrosis, vitritis and occlusive vasculopathy in an immunocompetent individual between the ages of 20 and 60.[1] It is attributed to herpes simplex virus (HSV) or varicella zoster virus (VZV) infection. Our patient's culture was positive for HSV type 2, which was present from birth.

ARN has an acute onset with a predilection for the peripheral retina and usually self-resolves within six to 12 weeks.[1] It is followed by a late cicatrizing phase in which 30% to 50% of patients will develop a rhegmatogenous retinal detachment, usually within three to six months. The patient should be followed closely with dilated exams.[1,2]

Treatment

Historically, the standard treatment for ARN was intravenous acyclovir for five to 10 days, followed by oral acyclovir as prophylaxis for the fellow eye.[2] Since the advent of antiviral medications with better bioavailability, many physicians have adopted the protocol of one to two grams of valaciclovir TID for a minimum of six weeks, as it provides comparable efficacy with less frequent oral administration.[2]

In cases of significant vitritis or papillitis, doctors may supplement with oral prednisone.[2] You may also consider topical steroids and cycloplegics for significant anterior chamber reaction. Systemic aspirin is another option to combat the arteriolar occlusions.[1]

Generally, patients should respond in one to two weeks and experience resolution of the acute retinitis around one month after initial therapy—though doctors should perform dilated exams frequently for several months through the cicatricial phase to monitor for retinal tear or retinal detachment.[1,2]

Prophylactic laser barricade has occasionally been used to prevent subsequent retinal detachment, but the success in preventing retinal detachment is not clear at this point.[1]

Other surgical options, such as scleral buckle and vitrectomy, are reserved only for cases that progress to retinal detachment.[1]

Reports of second eye involvement range from 3% to 33% depending on treatment modality, warranting long-term prophylaxis.[1,2] Prognosis for ARN patients is dependent on the amount of retinal necrosis, presence of retinal detachment and involvement of the fellow eye.[1]

Our patient required barricade laser early on and developed a total retinal detachment 10 months after initial presentation (*Figure 3*). A pars plana vitrectomy, lensectomy, silicone oil fill, scleral buckle, endolaser and intravitreal injection of foscarnet and ganciclovir was performed. The patient remains on a prophylactic dose of 500mg valaciclovir QD. The left eye has remained stable at 20/100 and the right eye remains uninvolved. ■

Dr. Hammond is an optometric resident at the Bascom Palmer Eye Institute in Miami.

1. Vemulakonda GA, Pepose JS, Van Gelder RN. Acute Retinal Necrosis Syndrome. In: Ryan SJ ed. Retina. Vol 2, ed. V. St Louis: Mosby;2013:1523-9.
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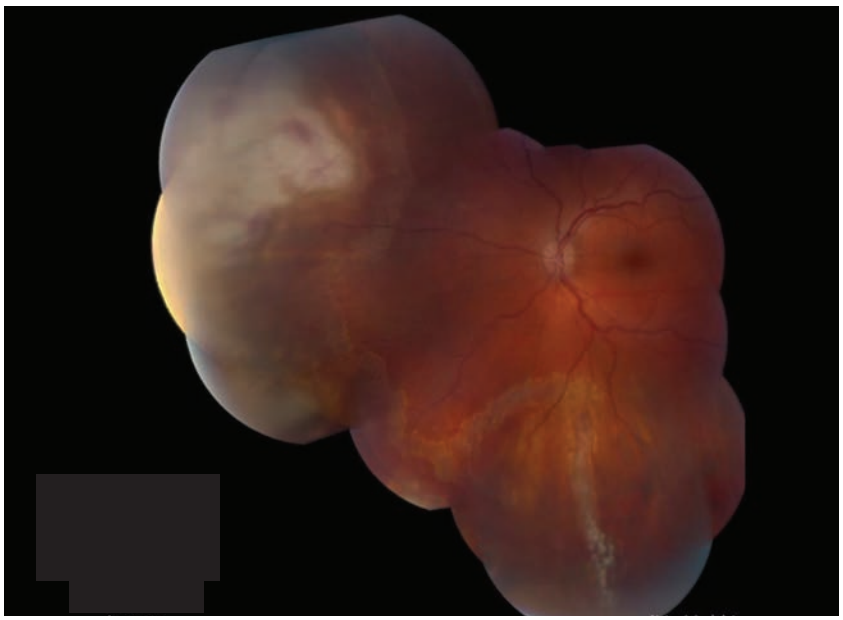

Fig. 3. Retina appearance after recent barricade laser treatment.

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The Uveitis and HLA-B27 Connection

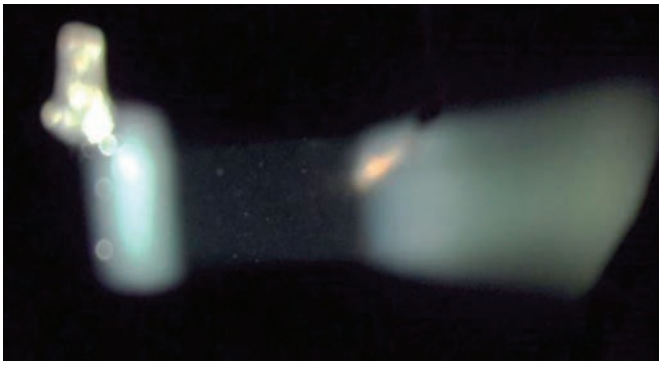
Some uveitis patients need additional monitoring.

By Alan G. Kabat, OD, and Joseph W. Sowka, OD

A 23-year-old white female presented to the office after experiencing a red, painful left eye for approximately one week. Additionally, she reported photophobia and a radiating left, frontal headache. Neither artificial tears nor acetaminophen had provided significant relief. Her ocular history included bilateral myopia as well as a small-angle, constant left esotropia with mild amblyopia in that eye.

Her best-corrected visual acuity was 20/20 OD and 20/30 OS. Pupil testing, motility testing and confrontation fields were all normal. Biomicroscopy of the right eye was essentially unremarkable, but the left eye displayed 3+ injection of the bulbar conjunctiva with a notable circumlimbal flush. Additionally, the anterior chamber demonstrated grade 2+ cells and flare. Fine keratic precipitates were also evident on the corneal endothelium, most notably inferior. Intraocular pressure (IOP) was 16mm Hg OD and 12mm Hg OS. A dilated fundus examination was unremarkable.

The patient was diagnosed with acute, idiopathic anterior uveitis in her left eye. Treatment included cycloplegia (5% homatropine twice daily in each eye) and liberal use of topical corticosteroid drops (0.05% difluprednol every two hours in the left eye for the first 72 hours). The condition was brought under control in a matter of weeks; cycloplegia was discontinued and the steroid drops were slowly tapered until cells were no longer evident in the anterior chamber.



Characteristic cells and flare presentation in a patient with acute anterior uveitis.

Although the patient responded well and the episode appeared singular, we discussed the implications of idiopathic anterior uveitis, as well as the potential for a systemic etiology.

We recommended she obtain a physical examination as a precautionary measure, with medical testing to follow as determined by her primary care physician. Several weeks later, she reported that serologic testing had come back positive for human leukocyte antigen-B27 (HLA-B27).

This column reviews some of the diagnostic and management challenges associated with uveitis, as well as with HLA-B27.

Presentation

Anterior uveitis is heralded by a constellation of clinically observable findings, typically including deep perilimbal injection of the conjunctiva and episclera, keratic precipitates along the corneal endothelium, variable corneal edema and "cells and flare" within the aqueous.[1] "Cells" represent free-floating leukocytes, liberated from the iris vasculature in response to inflammation, while "flare" refers to plasma proteins suspended in the aqueous, giving rise to a hazy or smoky appearance. The classic presentation typically involves an individual 20 to 60 years of age, complaining of unilateral ocular pain, photophobia, and tearing.[2,3]

While circumstances that spark the development of uveitis vary, its resultant events stimulate a localized inflammatory state impacting the iris, ciliary body and cornea. Cytokines mediate numerous tissue changes, among them vasodilation and increased vasopermeability.[4,5] As cellular debris and large molecular weight proteins accumulate in the aqueous, negative sequelae become increasingly likely, including synechiae, secondary glaucomas and neovascularization of the iris and angle.[4-6] Unmanaged, the condition is potentially sight-threatening from a variety of pathogenic mechanisms.

Comorbidities

Numerous etiologies may be implicated in anterior uveitis, ranging from trauma to widespread infection to generalized ischemic disorders.[7-12] Some of the more well-known systemic etiologies include rheumatoid arthritis, systemic lupus and Lyme disease.[11,12] Medical testing is generally not undertaken for isolated episodes; however, if the presentation is bilateral, severe, recalcitrant or recurrent, the patient should obtain testing to investigate for potential underlying systemic conditions (*Table 1*).

Imaging studies are also part of the medical workup. X-rays of the sacroiliac joint are useful in diagnosing ankylosing spondylitis, while a chest radiograph helps identify tuberculosis or sarcoidosis infiltration into the pulmonary system.[14] Unfortunately, these tests are time-consuming and expensive. Rather than taking a "scatter-shot" approach, we prefer to comanage patients with an internist or rheumatologist who can choose the most appropriate tests.

Human Leukocyte Antigen-B27

HLA proteins, often found on white blood cells, are encoded by genes of the major histocompatibility complex.[15-17] While their specific functions are diverse, they are principally implicated in the immune response and inflammatory pathways.[16] Researchers classify HLAs into different types (e.g., HLA-A, HLA-B, HLA-C), and those types into further, numbered versions, or alleles (e.g., HLA-A24, HLA-B13). The HLA-B27 serotype is strongly linked with the seronegative *spondyloarthropathies* group of autoimmune diseases.[15-18] In these conditions, blood tests may reveal a positive HLA-B27 result. However, rheumatoid factor and antinuclear antibody are characteristically negative. The most prevalent of these conditions is ankylosing spondylitis; other known disorders include reactive arthritis, spondylitis associated with inflammatory bowel disease (including Crohn's disease and ulcerative colitis), psoriatic arthritis and juvenile idiopathic arthritis. Additionally, HLA-B27+ individuals may manifest inflammation localized solely to the uveal tract, known clinically as isolated acute anterior uveitis.[17,19]

Table 1. Systemic Tests

Refer a patient for testing when the history or associated symptoms are suggestive of a particular disease.[13] Tests to consider include:[14]

- Complete blood count with differential and platelets.
- Erythrocyte sedimentation rate.
- Antinuclear antibody.
- Human leukocyte antigen typing.
- Rheumatoid factor.
- Angiotensin-converting enzyme.
- Purified protein derivative with anergy panel.
- Fluorescent treponemal antibody absorption.
- Rapid plasma reagin.
- Lyme immunoassay.

Diligence

For our patient, identification of the HLA-B27 serotype resulted in mixed emotions. While we were somewhat relieved at having discovered an underlying cause, we were greatly concerned about her future. Would she be likely to suffer additional recurrences of uveitis? Could she potentially develop any of the systemic illnesses mentioned? What steps can she take now to help prevent potential complications later on? While these questions are difficult to answer with absolute certainty, the reality is that individuals who are HLA-B27+ have a high tendency toward recurrent anterior uveitis; of even greater concern is the fact that about 50% will develop an associated spondyloarthropathy during their lifetime.[20] Unfortunately, the only known prophylactic measure that can lessen the severity of complications associated with HLA-B27+ disorders is diligence. Proactive care with the PCP or managing rheumatologist, as well as regular evaluations by the eye care provider, are all that we can presently recommend for individuals like our patient. ■

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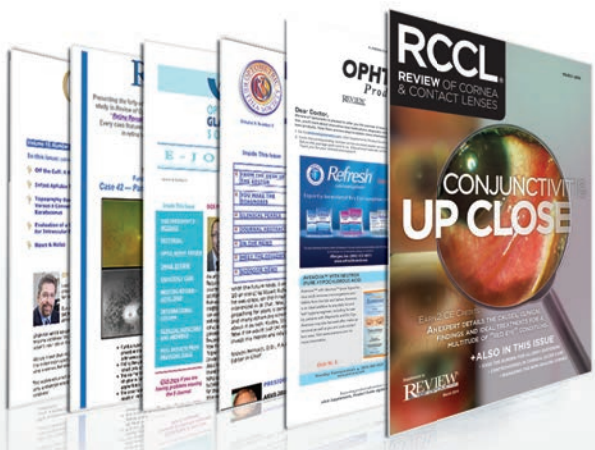

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Diagnostic Technology

Smartphone Fundus Imager

Optometrists looking for a handheld imaging option can now consider Volk optical's new iNview fundus imaging device.

Used with dilated patients, the device provides a static 50 degrees field of view, with dynamic peripheral retina views out to 80 degrees, according to the company. The device offers manual capture and a convenient auto-capture feature, which takes a rapid series of images, according to the company.

Data is encrypted with a user-defined password key, ensuring HIPPA compliance, according to the company. The JPEG images can be exported to Mac or PC. A packaged system that comes with an iPod is also available.

Visit www.volk.com/index.php/news.

Tonopachy Imaging Feature

Optometrists currently using Nidek's Tonopachy NT-530P can now look forward to new functionality. The device now offers a new anterior chamber angle mode, allowing the practitioner to view and document the anterior chamber angle using Scheimpflug imaging. The visual observation of the anterior chamber angle, along with the intraocular pressure, assists optometrists in their glaucoma assessments.

Visit www.nidek-intl.com.

Ophthalmic Lenses

New Progressive Lens

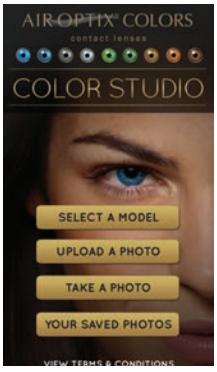
Optometrists looking to offer their patients a new progressive spectacle lens option can now consider Kodak's new DSII lens. Using a dual-sided design, the lens offers the highest level of visual performance in the Kodak Lens Professional series, according to the company. The DSII lens is available in 26 materials, and is customized to each patient by incorporating the point-of-wear measurement into the lens design, according to the company.

Visit www.kodaklens.com/pro.

Contact Lenses

Colored Lens Phone App

Optometrists now have a new app to help their patients interested in trying colored contacts. Air Optix Colors app for iOS devices allows users to upload a photo and virtually "try on" up to two colors at once. Patients can test out up to nine colors offered by Alcon's Air Optix contact lens brand, and add individual makeup items to the photo to create a custom look, according to the company.



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Practice Management

Waiting Room Video

A new waiting room video series may help optometrists educate patients and boost lens sales. The six-minute, looped video by Signet Armorlite helps to inform patients about the types of vision correction in eye wear and lens options, while providing an overview of the products offered under the Kodak name, according to the company.

The video details the range of the Kodak Lens Professional Series line of products, including:

- Anti-reflective lens coatings.
- Progressive lenses.
- Digital single vision lenses.

The video runs on six minute loop, is available online and in DVD format, and includes subtitles.

Visit www.salitonline.com. ■

January 2016

■ **24.** *IOA Winter CE Series*. Hyatt Regency O'Hare, Rosemont, IL. Hosted by: Illinois Optometric Association. Key faculty: Paul Karpecki. CE hours: 6. To register, email Charlene Marsh at ioabb@ioaweb.org or go to www.ioaweb.org.

■ **30.** *Georgia Optometric Association Super CE*. Georgia International Convention Center, College Park, GA. Hosted by: Georgia Optometric Association. CE hours: 8. To register, email Vanessa Grosso at VanessaGOA@aol.com, call (770) 961-9866 x-1 or go to http://hleachgoa.wix.com/goaeyes.

■ **31.** *VOA 1 Day CE Conference*. Richmond Marriott West, Glen Allen, VA. Hosted by: Virginia Optometric Association. CE hours: 4. To register, email Bo Keeney at Office@thevoa.org, call (804) 643-0309 or go to www.thevoa.org.

February 2016

■ **3-4.** *Michigan Optometric Association Winter Seminar*. Kellogg Hotel and Conference Center of Michigan State University, East Lansing, MI. Hosted by: Michigan Optometric Association. Key faculty: Steven Ferrucci, Marc Bloomenstein. CE hours: 12. To register, email Amy Root at amy@themoa.org, call (517) 482-0616 or go to www.themoa.org.

■ **8.** *IOP Winter CE*. The Grove Hotel, Boise, ID. Hosted by: Idaho Optometric Physicians. CE hours: 4. To register, email Randy Andregg at execdir@iopinc.org, call (208) 461-0001 or go to Idaho.aoa.org.

■ **12-14.** *Heart of America Contact Lens Society*. Sheraton Crown Center, Kansas City, MO. Hosted by: HOACLS. Key faculty: Paul Ajamian, Michael Chaglasian, Joseph Sowka, Valerie Kattouf, Jeffry Gerson. CE hours: 77 total, 15 per OD. To register, email Ron Fiegel at registration2@thehoalcls.org or go to www.hoacls.org.

■ **12-16.** *SkiVision*. Westin Snowmass Resort, Snowmass Village, CO. Hosted by: SkiVision, *Review of Optometry*. Key faculty: Murray Fingeret, John Flanagan, Ian Ben Gaddie, Jack Schaeffer, Jay Haynie, Kathy Dumbleton. CE hours: 20. To register, email Lois DiDomenico at ldidomenico@jobson.com, call (610) 492-1018 or go to www.skivision.com.

■ **13.** *OAL Mid-Winter CE Conference*. DoubleTree Hotel, Lafayette, LA. Hosted by: Optometry Association of Louisiana. CE hours: 8. To register, email Jim Sandefur at optla@bellsouth.net, call (318) 613-1392 or go to www.optla.org.

■ **13-20.** *Innovations in Eye Care*. Western Caribbean Cruise from Fort Lauderdale, FL. Hosted by: Dr. Travel Seminars, LLC. Key faculty: Robert Wooldridge. CE hours: 16. To register, email Robert Pascal at DrTravel@aol.com, call (800) 436-1028 or go to www.drtravel.com/optometristsSeminars.html.

■ **14.** *IOA Winter CE Series*. Marriott Bloomington-Normal Convention Center, Bloomington/Normal, IL. Hosted by: Illinois Optometric Association. Key faculty: Michael Chaglasian. CE hours: 6. To register, email Charlene Marsh at ioabb@ioaweb.org, call 217-525-8012 or go to www.ioaweb.org.

■ **14-24.** *AEA Cruises Canary Islands Optometric Cruise Seminar*. Aboard NCL Epic, Barcelona, Spain. Hosted by: AEA Cruises. CE hours: 10. To register, email Marge McGrath at aeacruises@aol.com, or go to www.optometriccruiseseminars.com.

■ **19-21.** *32nd Annual Palm Beach Winter Seminar.* Hilton West Palm Beach, Florida. Hosted by: Palm Beach County Optometric Association. CE hours: 20+. To register, email PBWinterSeminar@gmail.com or go to www.pbcoa.org.

■ **20-27.** *AEA Cruises Eastern Caribbean Optometric Cruise Seminar*. Aboard NCL Escape, Miami. Hosted by: AEA Cruises. CE hours: 10. To register, email Marge McGrath at aeacruises@aol.com, call (888) 638-6009 or go to www.optometriccruiseseminars.com.

■ **25-27**. *MOA Winter Educational Symposium*. Huntley Lodge, Big Sky, MT. Hosted by: Montana Optometric Association. Key faculty: Andrew Morgenstern, Maynard Pohl. CE hours: 13. To register, email Sue Weingartner at sweingartner@rmsmanagement.com, or go to www.mteyes.com.

■ **25-27.** *Third Party/Practice Management Seminar*. Embassy Suites, Portland Airport, Portland, OR. Hosted by: Oregon Optometric Physicians Association. Key faculty: John McGreal, Elizabeth Cottle, Steve Farebrother, Ronald Guerra, Shelly Sneed. CE hours: 15 total, 13 per OD. To register, email Lynne Olson at lynne@oregonoptometry.org, call (800) 922-2045 or go to www.oregonoptometry.org.

■ **28.** *OptoWest South Newport Beach*. Newport Beach Marriott Hotel and Spa, Newport Beach, CA. Hosted by: California Optometric Association. Key faculty: Leo Semes, Todd Severin. CE hours: 12 total, 6 per OD and 6 per staff member. To register, email Sarah Harbin at sharbin@coavision.org, call (916) 266-5022 or go to www.coavision.org.

■ **28.** *IOA Winter CE Series*. Tinley Park Convention Center, Tinley Park, IL. Hosted by: Illinois Optometric Association. Key faculty: Mark Dunbar. CE hours: 6 regular or TQ. To register, email Charlene Marsh at ioabb@ioaweb.org, call (217) 525-8012 or go to www.ioaweb.org.

■ **28-March 4.** *30th Annual Eye Ski Conference*. The Lodge at Mountain Village, Park City, UT. Hosted by: Timothy Kime and James Fanelli. Key faculty: Joe Pizzimenti, Alan Berman, Leonard Messner, James Fanelli. CE hours: 20. To register, email Timothy Kime at tandbkime@bex.net, call (419) 475-6181 or go to www.EyeSkiUtah.com.

■ **29-March 1.** *COVD at SECO*. Omni Hotel at CNN Center, Atlanta. Hosted by: College of Optometrists in Vision Development. Key Faculty: Carl Hillier. CE Hours: 13. To register, email penny@covd.org, or go to www.covd.org.

March 2016

■ **3-7.** *VT/Visual Dysfunctions.* 2080 Appleby Line Ste. E6, Burlington, Ontario, Canada. Hosted by: OEP Foundation. Key Faculty: Steen Aalberg. CE Hours: 35. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org/oepf_calendar.

■ **4-12.** *Tropical CE–Tahiti 2016.* Sofitel Mo'orea Resort and InterContinental Bora Bora Resort and Spa, Mo'orea and Bora Bora, French Polynesia. Hosted by: Tropical CE. Key Faculty: Paul Ajamian, Maynard Pohl. CE Hours: 20. To register, email Stuart Autry at sautry@TropicalCE.com, call (281) 808-5763 or go to www.TropicalCE.com.

■ **5.** *AZ-AAO Chapter Annual Spring Meeting 2016.* Midwestern University Arizona College of Optometry, Glendale, AZ. Hosted by: American Academy of Optometry Arizona Chapter. CE Hours: 6. To register, email Carla Engelke at arizona.aaopt@gmail.com or go to www.aaopt.org/AZChapter.

■ **5-6.** *Borish Symposium.* Bloomington, IN. Host: IU School of Optometry. CE Hours: 16. To register, email Cheryl Oldfield at coldfiel@indiana.edu, call (812) 856-3502 or go to www.opt.indiana.edu/ce/seminars.htm.

■ **11.** *ICO Resident Grand Rounds.* Illinois College of Optometry, Chicago. Hosted by: Illinois College of Optometry. CE Hours: 4. To register, email Elizabeth Grantner at continuinged@ico.edu, call (312) 949-7426 or go to www.ico.edu/alumni/continuing-education.

■ **12-13.** *Ocular Disease: Part II.* Illinois College of Optometry, Fullerton, CA. Hosted by: Illinois College of Optometry. Key Faculty: George Comer, David Sendrowski, Judy Tong. CE Hours: 17. To register, email Antoinette Smith at ce@ketchum.edu, call (714) 449-7495 or go to www.ketchum.edu/index.php/ce.

■ **13.** *ICO Winter/Spring CE Program.* Illinois College of Optometry, Chicago. Hosted by: Illinois College of Optometry. CE Hours: 6. To register, email Elizabeth Grantner at continuinged@ico.edu, call (312) 949-7426 or go to www.ico.edu/alumni/continuing-education.

■ **17-20.** *VT/Strabismus and Amblyopia.* OEP National Education Center, Timonium, MD. Hosted by: OEP Foundation. Key Faculty: Robert A. Hohendorf. CE Hours: 28. To register, email Karen Ruder at karen.ruder@oep.org, call (410) 561-3791 or go to www.oepf.org/oepf_calendar. ■

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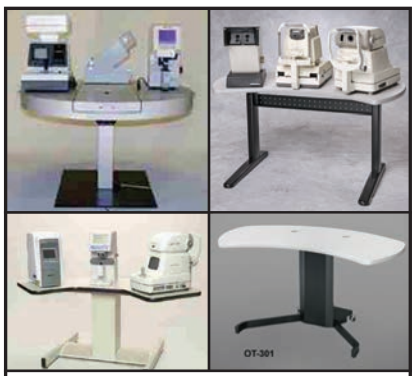

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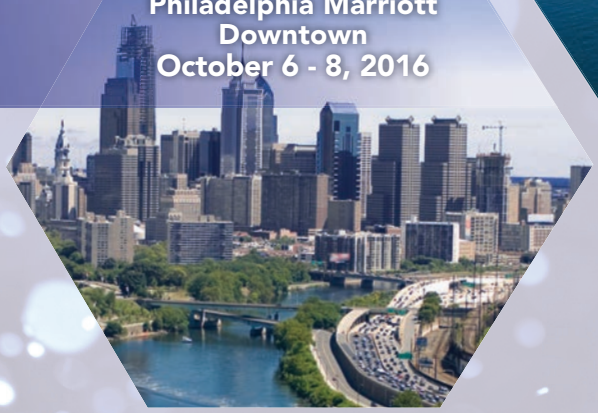

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Diagnostic **Quiz**

Many Suspects in Vision Loss

By Andrew S. Gurwood, OD

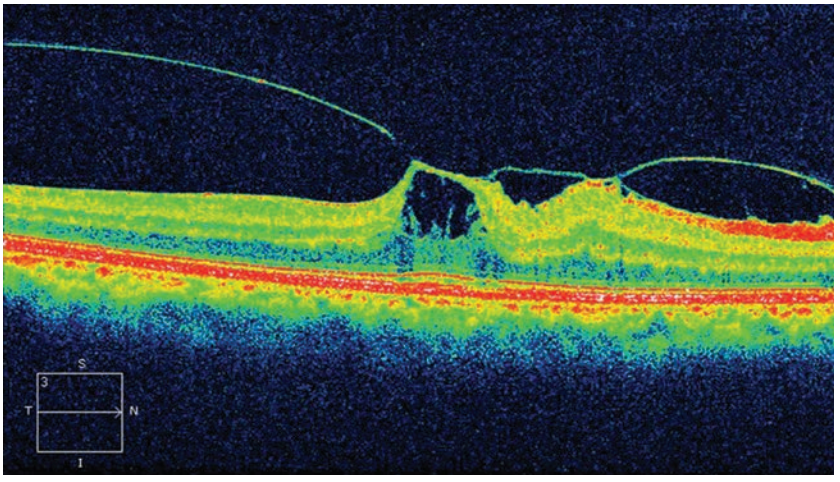
History

A 77-year-old black female presented with a chief complaint of decreased vision in her left eye beginning four weeks prior, which she first noticed while reading. She said the vision loss was progressively worsening and that her glasses did not alleviate the symptoms at distance or near. She did not note any pain or discomfort.

Her systemic history was remarkable for hypertension and chronic obstructive pulmonary disease, for which she was appropriately medicated with systemic oral preparations and a steroid inhaler. Her ocular history was remarkable for open angle glaucoma, which was controlled with a topical prostaglandin drop. She had peripheral iridotomies in both eyes, nuclear sclerosis in her right eye and was pseudophakic in her left eye.

Diagnostic Data

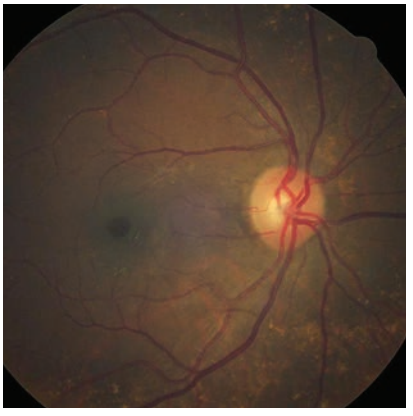
Her best-corrected entering visual acuities were 20/25 OD and 20/60 OS at distance and near with no improvement upon pinhole. Her external examination was normal, and showed no evidence of an afferent pupillary defect. Biomicroscopic examination demonstrated patent peripheral iridotomies with no new anterior segment abnormalities. Goldmann applanation tonometry measured 12mm Hg OU. The new pertinent findings in her left eye are revealed in the optical coherence tomograph (OCT).



This OCT displays findings from our 77-year-old patient's left eye. What diagnosis does the image suggest?

Your Diagnosis

Does this case require any additional tests? What does this patient's history and clinical findings tell you about her likely diagnosis? How would you manage this patient? To find out, please visit www.reviewofoptometry.com.



Can this fundus image help identify the pathology behind our patient's reported vision loss?

Retina Quiz Answers *(from page 84):* 1) a; 2) c; 3) a; 4) d.

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[1]Gabriel M, Bartell J, Walters R, et al. Biocidal efficacy of a new hydrogen peroxide contact lens care system against bacteria, fungi, and Acanthamoeba species. Optom Vis Sci. 2014; 91: E-abstract 145192. © 2015 Novartis 5/15 CCS15069AD-B