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jmi

December 15, 2013

REVIEW® OF OPTOMETRY

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15th Annual Diabetes Report

Moving the Needle: Can We Influence the Course of Diabetes?

Evidence suggests nutritional supplements really can make a difference in diabetic retinopathy.
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†The sixth measure was conjunctival staining.

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Reference: 1. Morgan P, Chamberlain P, Moody K, et al. Ocular physiology and comfort in neophyte subjects fitted with daily disposable silicone hydrogel contact lenses. *Cont Lens Anterior Eye.* 2013;36(3):118-125.

VOL. 150 NO. 12 ■ DECEMBER 15, 2013

IN THE NEWS

Optometry mourns the loss of **Paul E. Berman, OD**, a sports vision specialist and the founder and global clinical director of the Special Olympics' Lions Club International Opening Eyes and Healthy Athletes programs. He was also the team optometrist for the New Jersey Devils hockey team. Dr. Berman unexpectedly passed away on November 10, 2013, at age 62.

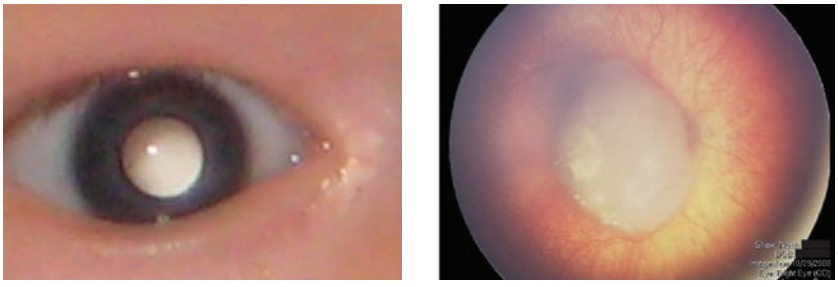
Cataract surgery is highly **cost effective**, according to a cost-utility study published in *Ophthalmology*. Cataract surgeries performed over one year eventually save $123.4 billion over 13 years in direct health care costs and lost productivity, and deliver a 4,567% return on investment to society. The study also found that the overall cost of cataract surgery in 2012 was 34.4% less than in 2000 and 85% less than in 1985, after adjusting for inflation.

The **American Board of Optometry** announced its newly elected officers: James M. Vaught, OD as chairman; David A. Heath, OD, EdM, as vice-chairman; Chelsea L. Miller, OD, as secretary; and John P. McGuire, CPA, as treasurer. Also, Jackson Lau, OD, was elected as the new director representing the AOA, and Michael D. Gerstner, OD, was elected as a new member-at-large.

There is no association between **AMD** and **Alzheimer's disease or dementia**, contrary to prior research indicating a connection, a new study suggests. Published online in *JAMA Ophthalmology*, the study reported that the genetic risk factors for the two types of diseases show no evidence of linkage.

Baby Photos Can Detect Retinoblastoma Early

This study also found that a brighter 'white eye' signals a larger tumor. **By John Murphy, Executive Editor**



Photos: Brian F. Shaw, PhD, Baylor University

Leukocoria or "white eye" has been assumed to be a sign of advanced retinoblastoma. But a new study shows that it can appear in infants as young as a few days old.

Baby pictures are perhaps the best method for early detection of retinoblastoma, a new study found.

"In a majority of retinoblastoma cases, it is the parents that initiate the diagnosis based on seeing leukocoria or 'white eye' in photos of their children," says the study's lead author Bryan F. Shaw, PhD, who is not an eye researcher but an assistant professor of chemistry and biochemistry at Baylor College.

Dr. Shaw initiated the study after his own son was diagnosed and treated for retinoblastoma.

Researchers already knew that children with retinoblastoma often display persistent leukocoria in photographs. Despite this, digital photography hasn't been intentionally used to screen for retinoblastoma because "white eye" is assumed to be a symptom of advanced retinoblastoma, not early stage retinoblastoma.

Dr. Shaw's study dispelled this assumption. It found that leukocoria can be a sign of retinoblastoma in its earliest stages—even in an infant as young as 12 days old, as in the case of Dr. Shaw's son. Early detection and treatment would increase the chances of survival and reduce loss of vision.

The study, published in the online journal *PLoS One*, also determined that the brightness and the color saturation of the leukocoria eye can indicate the retinoblastoma's severity. The brighter the white eye, the larger the tumor, Dr. Shaw says.

The researchers' next step: "If we can create software that can detect leukocoria and alert a parent when it begins to occur persistently, then I believe digital photography can eradicate metastatic retinoblastoma from this world and prevent most of the deaths that occur," Dr. Shaw says.

Abdolvahabi A, Taylor BW, Holden RL, et al. Colorimetric and longitudinal analysis of leukocoria in recreational photographs of children with retinoblastoma. PLoS One. 2013 Oct 30;8(10):e76677.

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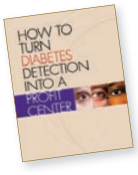

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Does 'the Pill' Cause Glaucoma?

Women who have taken oral contraceptives may be twice as likely to be diagnosed with glaucoma. But whether contraceptives actually cause glaucoma remains unclear.

Researchers with the University of California, San Diego, Duke University School of Medicine and Third Affiliated Hospital of Nanchang University in Nanchang, China, gleaned three-year data from the Center for Disease Control's National Health and Nutrition Examination Survey (NHANES) and found that women age 40 and older who had used oral contraceptives for three years or longer are twice as likely to be diagnosed with glaucoma. The findings were presented at the annual meeting of the American Academy of Ophthalmology in November.

"The message is that long-term use of oral contraceptives may be considered an additional risk factor associated with increased incidence of primary open-angle glaucoma in women," says Sherry Bass, OD, of SUNY College of Optometry.

Dr. Bass notes that the current study reflects similar results from a 2011 Nurses' Health Study, which found a 25% higher glaucoma risk among women who used birth control pills.

However, more study is needed, "since the information is preliminary at best," says Kathy Yang-Williams, OD, who practices in Seattle with an emphasis on glaucoma.

"This study shows an associative, but not necessarily causal, relationship between oral contraceptives and glaucoma," she says. "These findings should not affect ODs in their practice with regards to the diagnosis of glaucoma. If a patient takes oral contraceptives, then this should be noted as part of the review of systems and this factor added to the basic risk profile."

The study's researchers say they hope it will serve as an impetus for further research to prove potential causative effects.

Premature Birth Linked to Higher Chance of Retinal Detachment

Infants born extremely prematurely are up to 19 times more likely to experience a retinal detachment later in life than babies who are carried to full term, according to a study in the November issue of *Ophthalmology*.

A Swedish research team evaluated more than three million individuals born between 1973 and 2008. The subjects were separated into two groups: those born in 1973 to 1986 (before the mandate of Sweden's national screening program for retinopathy of prematurity), and those born in 1987 to 2008.

Within these groups, the researchers further classified subjects born at less than 28 weeks gestation as "extremely premature," those born between 28 and 31 weeks gestation as "very premature" and those born between 32 and 36 weeks gestation as "moderately preterm."

The researchers determined that extremely premature infants born from 1973 to 1986 were 19 times more likely to experience a retinal detachment during childhood, adolescence or young adult life than their full-term peers. Additionally, those born between 1987 and 2008 were nine times more likely to experience a retinal detachment.

The overall risk of retinal detachment in very premature infants fell significantly between the two groups—four times more likely for those in the older group (born 1973 to 1986) compared with three times more likely for those in the younger group (born 1987 to 2008). Interestingly, the researchers noted that moderately preterm infants in both groups were no more likely to experience retinal detachment than full-term infants.

"We may just be seeing the tip of the iceberg of late ophthalmic complications after preterm birth," says lead author Anna-Karin Edstedt Bonamy, MD, PhD, pediatrician at Karolinska Institutet in Stockholm. "Not only does the risk of retinal detachment increase with age, but there has also been an increase in survival among people born prematurely since the 1970s. This provides opportunities for future research to address if the increased risk persists among those born prematurely as they age."

Bonamy AK, Holmström G, Stephansson O, et al. Preterm birth and later retinal detachment: a population-based cohort study of more than 3 million children and young adults. Ophthalmology. 2013 Nov;120(11):2278-85.

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Lack of Eye Contact Signals Autism

A new study has found the earliest sign of autism ever observed—a steady decline in eye contact within a child's first months of life.

Autism is usually diagnosed after age two, when delays in a child's social behavior and language skills become apparent. This new study found that babies as young as two to six months old can start to show a decrease in eye contact—a clear sign of autism.

This research, published online in *Nature*, also suggests that there's a window of opportunity to possibly prevent some disabilities associated with the disorder.

Photo: Kay Hinton, Emory University

Using eye-tracking technology, researchers found that infants later diagnosed with autism showed a decline in attention to others' eyes by two to six months of age.

Lack of eye contact has been a hallmark diagnostic sign of autism since the condition was initially identified. But no one knew how early this deficit began. To find out, researchers at the Marcus Autism Center in Atlanta used eye-tracking equipment to measure eye movements in babies who watched video scenes of a caregiver.

Followed from birth to three years, the infants were divided into two groups based on their risk for developing an autism spectrum disorder. Those in the high-risk group had an older sibling already diagnosed with autism; the low-risk group did not. The researchers calculated the percentage of time each child fixated on the caregiver's eyes, mouth and body, as well as the non-human spaces in the images.

By age three, nearly all the children in the high-risk group had received a clinical diagnosis of an autism spectrum disorder. The researchers then reviewed the eye-tracking data to determine which factors differed between children who received an autism diagnosis and those who did not.

"In infants later diagnosed with autism, we see a steady decline in how much they look at mom's eyes," says Warren Jones, PhD, lead author of the study.

This drop in eye fixation began between two and six months and continued throughout the course of the study. By 24 months, the children who were later diagnosed with autism focused on the caregiver's eyes only about half as long as did their typically developing counterparts. Also, those infants whose levels of eye contact diminished most rapidly were those who were most disabled later in life.

Importantly, these results suggest that social engagement skills are intact after birth in children with autism. This finding challenges a long-standing theory—that social behaviors are entirely absent in children with autism. In other words, the observation of a decline in eye fixation—rather than an outright absence—offers a promising opportunity for early intervention.

"This insight—the preservation of some early eye-looking—is important," Dr. Jones says. "In the future, if we were able to use similar technologies to identify early signs of social disability, we could then consider interventions to build on that early eye-looking and help reduce some of the associated disabilities that often accompany autism."

In the meantime, the investigators' next step is to translate this research into a viable tool for use in the clinic.

"Most kids on the autism spectrum are not identified until later, so looking early is helpful," says Glen T. Steele, OD, professor of pediatric optometry at Southern College of Optometry and chair of the AOA's InfantSEE Committee.

Optometrists who examine babies and very young children aren't expected to make the diagnosis of autism, Dr. Steele says. "But we might be able to notice these issues much earlier in life, and a caution flag should go up." If you suspect autism, refer the child to a developmental specialist who regularly works with children with special needs, he says.

Jones W, Klin A. Attention to eyes is present but in decline in 2-6-month-old infants later diagnosed with autism. Nature. 2013 Nov 6. [Epub ahead of print.]

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Novel Topical Compound Restores Endothelial Cells

A small group of patients with Fuchs' corneal dystrophy were successfully treated with a Rho-associated kinase (ROCK) inhibitor topical medication—a technique that could have far-reaching clinical implications, according to researchers from Japan who presented their findings at the annual meeting of the American Academy of Ophthalmology in November.

The preliminary study, conducted by investigators at Kyoto Prefectural University of Medicine, reported that a one-week treatment of the ROCK inhibitor Y-27632 stimulated the proliferation of corneal endothelial cells in four test patients with Fuchs' corneal dystrophy.

Patients showed corneal healing and restored visual acuity, as well as reduced corneal thickness from 700 cells/mm^2 to 563 cells/mm^2 by three months after treatment.

"Overall, it's intriguing and, if it proves to be viable, may reduce the number of surgeries required for Fuchs' and other endothelial diseases," says Joseph Shovlin, OD, of Scranton, Pa. "ROCK inhibitors would represent the first successful medical treatment using a topical agent for certain forms of endothelial disease."

The technique involves transcorneal freezing to remove damaged endothelial cells, and then applying the eye drops to promote proliferation in the remaining functional cells. This small study treated eight patients—four with Fuchs' and four with pseudophakic bullous keratophy. Although the technique was not effective for pseudophakic bullous keratophy, it could pave the way for minimally invasive surgery for Fuchs' and other forms of corneal problems, the researchers say.

While more research must be done before such a topical drop becomes available, "it's crucial that ODs are aware of such potential non-surgical treatments in order to render the very best care possible, and also field questions that may arise in the course of patient care," Dr. Shovlin says.

Retinal Thickness May Help Diagnose Alzheimer's

The loss of cells in the inner nuclear layer of the retina may be a predictor of Alzheimer's disease, according to findings presented in November at the annual meeting of the Society for Neuroscience.

A team of researchers from Georgetown University Medical Center and the University of Hong Kong studied the retinal thickness of mice genetically engineered to develop Alzheimer's and compared them to a group of healthy, age-matched mice.

During the study, the researchers observed a significant loss of thickness in both the retinal ganglion cell layer and the inner nuclear layer of the retina. When compared with control mice, inner nuclear layer in the mice with Alzheimer's exhibited a 37% loss of neurons and the retinal ganglion cell layer had a 49% loss of neurons.

The researchers say that eye care providers may be able to diagnose or predict Alzheimer's by simply examining the thickness of these retinal layers with OCT. Additionally, new Alzheimer's treatments may even prove useful for future glaucoma management. ■

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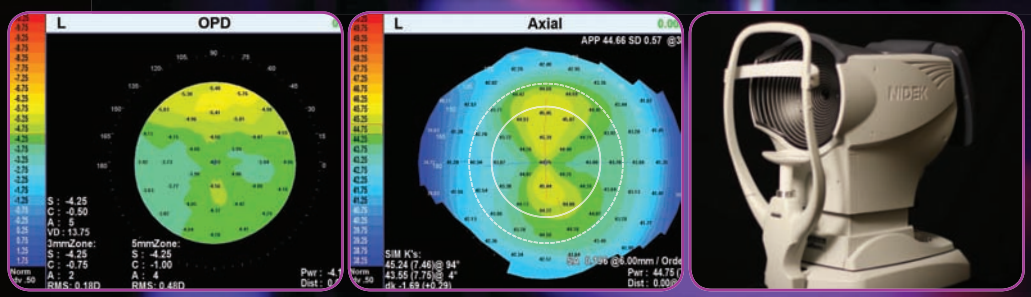

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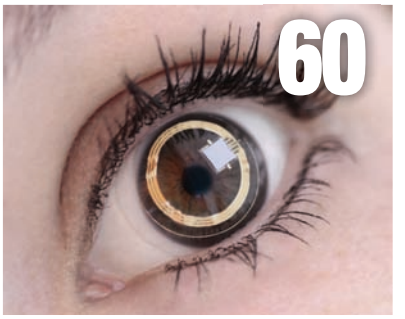

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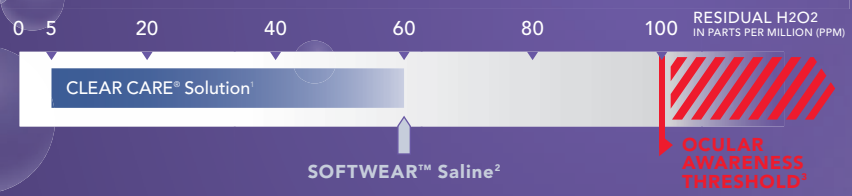

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Destined for Diabetes

With the disease's prevalence at epidemic levels, now is our moment to shine.

By Paul M. Karpecki, OD, Chief Clinical Editor

America's diabetes epidemic, like its citizens' waistlines, is growing. Data from the 2011 *National Diabetes Fact Sheet* show that nearly 26 million Americans—8.3% of the population—have been diagnosed with diabetes. The prevalence increases by 6.5% annually, according to some estimates. By the year 2020, one out of three people over age 65 will have diabetes; 27% already do.

Worse still is the sobering news that more than seven million people suffer from the disease but remain undiagnosed, and that another 79 million people are considered pre-diabetic. Among adults, either manifest or incipient diabetes will ultimately become more common than its absence.

This is borne out in our clinics. Diabetes is the leading cause of new cases of blindness in US adults. A little over four million, or 28.5%, of people with diabetes age 40 or older had a diagnosis of diabetic retinopathy, and 4.4% have the proliferative form.

Literally millions more are waiting for appointments right now.

There are over 100 million eye exams performed annually (most commonly by optometrists) but only about 40 million visits to primary care providers for annual check-ups. Unfortunately, many patients—even those at high risk—are not compliant with annual physicals. So, there are at least twice as many opportunities for us to diagnose diabetes as there are for GPs or FPs in the course of one year. Furthermore, type 2 diabetes occurs when patients are most likely to seek an eye examination, which is in the early 40s, around the age of presbyopia.

It is within our power to dramatically alter the course of diabetic eye disease, and diabetes itself—a systemic disease with multi-organ morbidity that may be first discovered in your chair.

We Set the Pace

This crisis highlights the profound importance of optometry's role as the health care providers who initiate and coordinate diabetes care in collaboration with endocrinologists, primary care physicians, retina specialists and diabetes educators. As we all know, the only anatomical site where one can directly examine the human vasculature is the eye. This gives us unprecedented opportunity to initiate care for many patients.

Of course, changes in blood glucose might be identified prior to any sort of retinopathy, but improved diagnostic capabilities are helping optometrists to identify diabetes even prior to any retinopathy findings and now even prior to changes in A1C.

New technology that can measure autofluorescence of the lens (*see this month's 'Research Review,' page 72*) could enhance our ability to diagnose diabetes as much as six to seven years in advance of other clinical manifestations. Furthermore, detecting and timely treatment of diabetic retinopathy with laser can reduce the development of neovascularization by an estimated 50% to 60%. And the Diabetes Control and Complication Trial showed that earlier diagnosis with well controlled blood glucose in patients with type 1 diabetes reduced the incidence of diabetic retinopathy by more than 75%.

Diabetes patients require an annual dilated examination; those diagnosed with nonproliferative diabetic retinopathy may be seen every six months to ensure that it is stable. Progression to proliferative diabetic retinopathy would then warrant involving the retina specialist.

In short, we set the pace of patient care.

Something Old, Something New

This patient population's care requirements also dovetail nicely with traditional optometry.

Diabetes patients have a higher risk of glaucoma and greater propensity to develop cataracts prematurely; they also have dry eye in about 50% of cases, and over two-thirds of adults with diabetes and poor vision have a refractive error that can be improved with corrective lenses.

Let's rely on our strengths in vision and eye health to serve existing diabetes patients' needs while embracing our new responsibilities in not merely primary *eye* care but primary care, period, as we remain vigilant for those at risk. ■

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2014 NEW TECHNOLOGIES AND TREATMENTS IN VISION CARE

...*REVIEW* MEETINGS OF CLINICAL EXCELLENCE

SAVE THESE DATES:

ARUBA	January 16-19
SAN DIEGO, CA	May 2-4
ORLANDO, FL	June 19-22
MINNEAPOLIS, MN	July 17-20
TYSONS CORNER, VA (Washington DC area)	September 12-14

REVIEW® OF OPTOMETRY

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Jingle Bells, Christmas Sells

It's that time of year when everyone has visions of sugarplums! Too bad, because our scope of practice doesn't include that, and we can't bill for it. **By Montgomery Vickers, OD**

I am thrilled that: (a) I have survived my first foray into Obamacare; and (b) Christmas is right around the corner. I look at both issues with a 60-year-old jaded eye (ICD-10 has a code for this).

Christmas, like health care, has evolved. It's now perhaps the biggest driver of our economy. If retailers are successful at Christmas, it keeps our country afloat for another year. We do this by borrowing money from China and spending it on stuff made in China. Did you notice that Christmas and China both start with "ch"? That might not be an accident. By the way, so does Chia Pet and chalazion, either of which you can order for your loved ones with free shipping from Amazon this season.

And that brings us back to eyes. For Christmas, amid the glitz and glamour of politically correct Barbies and Canadian mayoral bobbleheads, we should sit back and remember the real reason for the season: selling second pairs of glasses.

Seriously, I love when my optical lab rep comes in all full of Christmas cheer (or could it be one hot toddy over the line?) and tells me how we can improve this/his holiday season by convincing our patients that they should give glasses as a Christmas gift. But, I have a hard time believing that any eight-year-old (or even any 80-year-old) would be thrilled with spectacles in the stocking.

Instead, here are some gift ideas that are sure to please:

- Easy-Bake Contact Lens Sterilizer (ah, the good ol' days of contact lens care)
- Magic Melting Spectacles (guaranteed to melt within two years)
- See Your Soul Contact Lenses (when you peer inward, you should be 20/20)
- Vodka Eye Drops (heard about this from a frat brother)
- My Little Glaucoma Treatment Kit (contents should be planted only in Colorado or California)
- Genuine Pope Hat (has nothing to do with eye care—I just want one)
- Play Money (as minted by the US Treasury Department—has no real value but you have to send back a third anyway)
- Doctor Income Multiplier (it's a copy of *How to Sell Old Sweaters on eBay*)
- Box O' Glasses (you already have one stuck away and the grandchildren will be thrilled!)
- Dr. Dandy's Subconjunctival Hemorrhage Maker (a rubber band and a 12-year-old boy)
- LASIK Mommy Doll (comes with arm extenders for reading after surgery)
- Super Politician (includes lifetime supply of baloney—bull manure sold separately, but available in all states)

I hope that helps.

Now, if Christmas is not your thing, that's OK. I'm not here to judge. You can always fall back on Obamacare. That's what I call a reason to celebrate! ■

Personal note: Thanks to my readers, friends and colleagues for the outpouring of prayer and support for my new little granddaughter, Grace Annette Vickers, who had heart surgery at two weeks of age. She is recovering, but has a long way to go and more surgeries to come.

Please visit www.facebook.com/Gifts4Grace *for updates and information about how you can assist her and her family.*

New DAILIES TOTAL1® Water Gradient Contact Lenses: Comfort Redefined

A new era in contact lenses for a new era in comfort. — **Mile Brujic, OD**

When I graduated from optometry school in 2002, silicone hydrogel lenses had been available for several years, but most of the lenses we fit were still hydrogels. Over the last decade we have seen a major transition in soft contact lens prescribing, motivated by the hope that increasing oxygen flow to the cornea would enhance ocular health and comfort.

Oxygen Permeability

Unique among tissues, the avascular cornea gets much of its oxygen directly from the air, and, to varying degrees, contact lenses can impede that process. Over time, diminished corneal oxygen flow can result in physiological changes, including edema, epithelial microcysts, limbal hyperemia, and neovascularization.[1]

The demand for greater oxygen transmissibility led to the addition of silicone, an extremely oxygen permeable material, to the hydrogel lens matrix. Silicone hydrogel solved the oxygen transmissibility problem, and the incidence of serious hypoxia-related complications was reduced to almost zero.[1,2]

Silicone and Comfort

Unfortunately, while silicone is highly oxygen permeable, it is also extremely hydrophobic. Even embedded in a hydrogel matrix, hydrophobic silicone moieties can migrate to the lens–air interface. At the lens surface, tiny hydrophobic areas can form and coalesce, reducing surface lubrication and potentially creating discomfort during blink.

To address this challenge, material scientists tried surface treatments to encapsulate the silicone and added wetting agents to the lens matrix to improve surface moisture. These strategies have worked well, but a subset of patients continues to remain uncomfortable.

A New Approach: The Water Gradient

The novel material (delefilcon A), from which DAILIES TOTAL1® contact lenses are made, has brought a new era in contact lens comfort. The first and only water gradient contact lenses, DAILIES TOTAL1® contact lenses are 33% water at their core, but over 80% water in the 6 microns between the core and the surface.[4]* The result is that DAILIES TOTAL1® contact lenses combine outstanding surface lubricity for comfort throughout the day with high oxygen transmissibility (Dk/t of 156 at –3.00 D), and essentially no silicone at the surface.

Thanks to the water gradient, the remarkable surface of DAILIES TOTAL1® contact lenses is exceptionally lubricious, offering a smooth, wet surface for the lids to slide over during blink. Indeed, DAILIES TOTAL1® contact lenses have the lowest coefficient of friction of any daily disposable contact lenses tested.[5] The result is outstanding comfort from beginning to end of day.

In an ongoing multicenter European clinical study (n = 280), patients preferred DAILIES TOTAL1® contact lenses to their habitual lenses by a ratio of 13 to 1.[6]** That startlingly high level of preference was replicated in my own patients' enthusiastic reactions to these lenses.

A High-performance Product

When I introduce DAILIES TOTAL1® water gradient contact lenses, patients are naturally curious about what makes them different from the ones they currently wear. I describe the revolutionary water gradient concept, emphasizing that the low water content core makes the lenses highly breathable, while the highly lubricious surface makes them exceptionally comfortable.

COMFORT COUNTS

Comfort issues are surprisingly common among contact lens wearers—even ones who never complain about discomfort. Industry studies show us that the overwhelming majority of patients with discomfort symptoms simply don't tell us about them—even when we ask. I have found that when I ask patients about their lens-wearing experience, they typically answer "good" or "fine." But when I ask them to rank it on a scale of zero to 10, they will rate it as a 6 or 7.

To me, 6 or 7 out of 10 is an opportunity to improve a patient's wearing experience. We know that lack of comfort is the number one reason patients give up on contact lens wear.[3] I want my patients to truly enjoy contact lens wear and to be happy with the lenses I prescribe. Their health, and that of my practice, depends on it.

* In vitro measurement of unworn lenses.
** Percentage of wearers agreeing with statement "I prefer these lenses to my previous contact lenses."

Mile Brujic, OD, is a partner of Premier Vision Group, a four location optometric practice in Northwest Ohio.

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Revolution or Evolution?

Changes in health care delivery affect everyone. Now, what are you going to do about it?

By John Rumpakis, OD, MBA, Clinical Coding Editor

As you're certainly aware, health care is undergoing a massive upheaval. Change is occurring in the medical fee-for-service system, in the upcoming (ongoing) adoption and rollout of accountable care organizations, in refractive carrier policies, in revised rules and regulations, and more—and all are valid reasons to seriously question how we're doing what we're doing.

So, how are you going to address these stresses, these changes, these current and nonstop issues that you now must deal with on a daily basis?

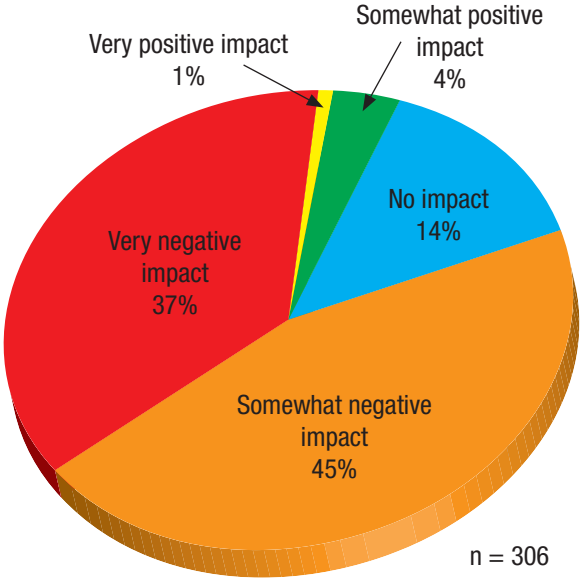
Here's What You Think

Some say that this is just a natural evolution of America's capitalistic health care system. Some would have you believe that it is unsustainable, while others tout our financially incentivized system as being the only sustainable model for delivering high-quality, professional services. Still others say that the Affordable Care Act is a revolution—a complete tipping of the cart toward socialized medicine.

No matter what camp you're in, as health care providers, change is upon us. More importantly, though, is how you plan on responding to this change that is thrust upon you—because if you don't respond to changes within the marketplace, you may not have the luxury of being around in future years.

Today's system isn't as flexible. And policy makers are taking a harder line, both in what they allow us to do professionally and in how we are compensated for it. So, pretending that change doesn't affect your ability to provide appropriate clinical care to your patients is not a sound strategy in today's world.

What kind of impact will managed vision care plans' consolidation/'product restriction' have on your practice?



In eye care, we're seeing change in separate areas. We have the area of prepaid managed vision care plan benefits (which include optical materials), and we have the world of medical eye care (which is limited to professional encounters, special ophthalmic procedures and surgical services). For the average optometrist's practice, the bulk of patient encounters, and income, comes through managed vision care plans (MVCP).

Within the last year, these plans have proposed and implemented a significant number of changes, causing disruption within the average practice. To find out about the average practitioner's perception of these changes, we recently conducted a brief survey to gauge optometrists' perspectives on the recent changes that managed vision care plans have implemented within their networks. The survey went out to *Review of Optometry*'s entire readership, and some 350 optometrists responded.

The results found:

- 72% of the ODs who responded to the survey indicate that they are aware of the changes in the MVCP models and channeling of products.
- 90% of all respondents say that they are concerned—either "very concerned" (67%) or "somewhat concerned" (23%)—about these MVCP developments.
- 82% of ODs report that the changes would have a somewhat (45%) or very negative impact (37%) on their practices.
- 51% say that VSP is the MVCP that has the most impact on their practice, followed by EyeMed

If only you could predict how ocular inflammation will behave.

DUREZOL® Emulsion has head-to-head data vs prednisolone acetate in patients with endogenous anterior uveitis.[1]

Scan the QR code with your smartphone or log on to **www.inflammationhappens.com** to see the results for yourself.

INDICATIONS AND USAGE: DUREZOL® Emulsion is a topical corticosteroid that is indicated for:

- The treatment of inflammation and pain associated with ocular surgery.
- The treatment of endogenous anterior uveitis.

Dosage and Administration

- For the treatment of inflammation and pain associated with ocular surgery instill one drop into the conjunctival sac of the affected eye 4 times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the postoperative period, followed by 2 times daily for a week and then a taper based on the response.
- For the treatment of endogenous anterior uveitis, instill one drop into the conjunctival sac of the affected eye 4 times daily for 14 days followed by tapering as clinically indicated.

IMPORTANT SAFETY INFORMATION

Contraindications: DUREZOL® Emulsion, as with other ophthalmic corticosteroids, is contraindicated in most active 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. If this product is used for 10 days or longer, IOP 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 beyond 28 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.
- Bacterial infections – Prolonged use of corticosteroids may suppress the host response and thus increase the hazard of secondary ocular infections. In acute purulent conditions, steroids may mask infection or enhance existing infection. If signs and symptoms fail to improve after 2 days, the patient should be re-evaluated.
- 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.
- Contact lens wear – DUREZOL® Emulsion should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of DUREZOL® Emulsion. The preservative in DUREZOL® Emulsion may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of DUREZOL® Emulsion.

Most Common Adverse Reactions

- Post Operative Ocular Inflammation and Pain – Ocular adverse reactions occurring in 5-15% of subjects included corneal edema, ciliary and conjunctival hyperemia, eye pain, photophobia, posterior capsule opacification, anterior chamber cells, anterior chamber flare, conjunctival edema, and blepharitis.
- In the endogenous anterior uveitis studies, the most common adverse reactions occurring in 5-10% of subjects included blurred vision, eye irritation, eye pain, headache, increased IOP, iritis, limbal and conjunctival hyperemia, punctate keratitis, and uveitis.

For additional information about DUREZOL® Emulsion, please refer to the brief summary of prescribing information on adjacent page.

DUREZOL®
(difluprednate ophthalmic emulsion) 0.05%

The results you want. The relief they need.

Alcon®
a Novartis company

Reference: 1. DUREZOL® Emulsion package insert.

DUREZOL®
(difluprednate ophthalmic emulsion) 0.05%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE
Ocular Surgery
DUREZOL® (difluprednate ophthalmic emulsion) 0.05%, a topical corticosteroid, is indicated for the treatment of inflammation and pain associated with ocular surgery.
Endogenous Anterior Uveitis
DUREZOL® Emulsion is also indicated for the treatment of endogenous anterior uveitis.

DOSAGE AND ADMINISTRATION
Ocular Surgery
Instill one drop into the conjunctival sac of the affected eye 4 times daily beginning 24 hours after surgery and continuing throughout the first 2 weeks of the postoperative period, followed by 2 times daily for a week and then a taper based on the response.

Endogenous Anterior Uveitis
Instill one drop into the conjunctival sac of the affected eye 4 times daily for 14 days followed by tapering as clinically indicated.

DOSAGE FORMS AND STRENGTHS
DUREZOL® Emulsion contains 0.05% difluprednate as a sterile preserved emulsion for topical ophthalmic administration.

CONTRAINDICATIONS
The use of DUREZOL® Emulsion, as with other ophthalmic corticosteroids, is contraindicated in most active 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 disease of ocular structures.

WARNINGS AND PRECAUTIONS
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 beyond 28 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.

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

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 culture should be taken when appropriate.

Topical Ophthalmic Use Only
DUREZOL® Emulsion is not indicated for intraocular administration.

Contact Lens Wear
DUREZOL® Emulsion should not be instilled while wearing contact lenses. Remove contact lenses prior to instillation of DUREZOL® Emulsion. The preservative in DUREZOL® Emulsion may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of DUREZOL® Emulsion.

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

Ocular Surgery
Ocular adverse reactions occurring in 5-15% of subjects in clinical studies with DUREZOL® Emulsion included corneal edema, ciliary and conjunctival hyperemia, eye pain, photophobia, posterior capsule opacification, anterior chamber cells, anterior chamber flare, conjunctival edema, and blepharitis. Other ocular adverse reactions occurring in 1-5% of subjects included reduced visual acuity, punctate keratitis, eye inflammation, and iritis. Ocular adverse reactions occurring in < 1% of subjects included application site discomfort or irritation, corneal pigmentation and striae, episcleritis, eye pruritis, eyelid irritation and crusting, foreign body sensation, increased lacrimation, macular edema, sclera hyperemia, and uveitis. Most of these reactions may have been the consequence of the surgical procedure.

Endogenous Anterior Uveitis
A total of 200 subjects participated in the clinical trials for endogenous anterior uveitis, of which 106 were exposed to DUREZOL® Emulsion. The most common adverse reactions of those exposed to DUREZOL® Emulsion occurring in 5-10% of subjects included blurred vision, eye irritation, eye pain, headache, increased IOP, iritis, limbal and conjunctival hyperemia, punctate keratitis, and uveitis. Adverse reactions occurring in 2-5% of subjects included anterior chamber flare, corneal edema, dry eye, iridocyclitis, photophobia, and reduced visual acuity.

USE IN SPECIFIC POPULATIONS
Pregnancy
Teratogenic Effects
Pregnancy Category C. Difluprednate has been shown to be embryotoxic (decrease in embryonic body weight and a delay in embryonic ossification) and teratogenic (cleft palate and skeletal) anomalies when administered subcutaneously to rabbits during organogenesis at a dose of 1–10 mcg/kg/day. The no-observed-effect-level (NOEL) for these effects was 1 mcg/kg/day, and 10 mcg/kg/day was considered to be a teratogenic dose that was concurrently found in the toxic dose range for fetuses and pregnant females. Treatment of rats with 10 mcg/kg/day subcutaneously during organogenesis did not result in any reproductive toxicity, nor was it maternally toxic. At 100 mcg/kg/day after subcutaneous administration in rats, there was a decrease in fetal weights and delay in ossification, and effects on weight gain in the pregnant females. It is difficult to extrapolate these doses of difluprednate to maximum daily human doses of DUREZOL® Emulsion, since DUREZOL® Emulsion is administered topically with minimal systemic absorption, and difluprednate blood levels were not measured in the reproductive animal studies. However, since use of difluprednate during human pregnancy has not been evaluated and cannot rule out the possibility of harm, DUREZOL® Emulsion should be used during pregnancy only if the potential benefit justifies the potential risk to the embryo or fetus.

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

Pediatric Use
DUREZOL® Emulsion was evaluated in a 3-month, multicenter, double-masked, trial in 79 pediatric patients (39 DUREZOL® Emulsion; 40 prednisolone acetate) 0 to 3 years of age for the treatment of inflammation following cataract surgery. A similar safety profile was observed in pediatric patients comparing DUREZOL® Emulsion to prednisolone acetate ophthalmic suspension, 1%.

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

NONCLINICAL TOXICOLOGY
Carcinogenesis, Mutagenesis, and Impairment of Fertility
Difluprednate was not genotoxic *in vitro* in the Ames test, and in cultured mammalian cells CHL/IU (a fibroblastic cell line derived from the lungs of newborn female Chinese hamsters). An *in vivo* micronucleus test of difluprednate in mice was also negative. Treatment of male and female rats with subcutaneous difluprednate up to 10 mcg/kg/day prior to and during mating did not impair fertility in either gender. Long term studies have not been conducted to evaluate the carcinogenic potential of difluprednate.

Animal Toxicology and/or Pharmacology
In multiple studies performed in rodents and non-rodents, subchronic and chronic toxicity tests of difluprednate showed systemic effects such as suppression of body weight gain; a decrease in lymphocyte count; atrophy of the lymphatic glands and adrenal gland; and for local effects, thinning of the skin; all of which were due to the pharmacologic action of the molecule and are well known glucocorticosteroid effects. Most, if not all of these effects were reversible after drug withdrawal. The NOEL for the subchronic and chronic toxicity tests were consistent between species and ranged from 1–1.25 mcg/kg/day.

PATIENT COUNSELING INFORMATION
Risk of Contamination
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 emulsion. Use of the same bottle for both eyes is not recommended with topical eye drops that are used in association with surgery.

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

Contact Lens Wear
DUREZOL® Emulsion should not be instilled while wearing contact lenses. Patients should be advised to remove contact lenses prior to instillation of DUREZOL® Emulsion. The preservative in DUREZOL® Emulsion may be absorbed by soft contact lenses. Lenses may be reinserted after 10 minutes following administration of DUREZOL® Emulsion.

Revised: May 2013
U.S. Patent 6,114,319

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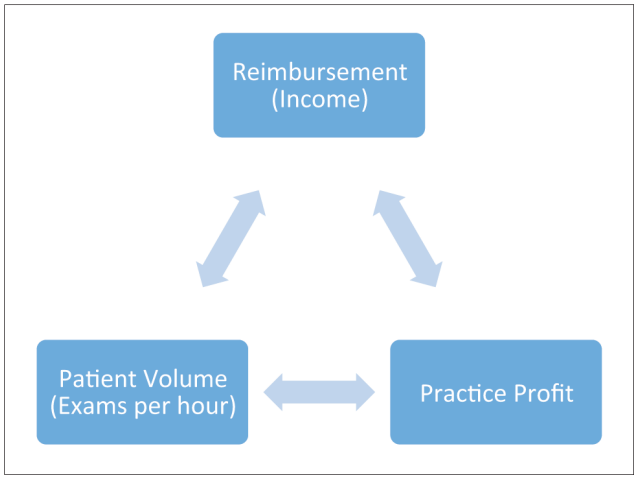
(31%), Davis Vision (9%) and Spectera (5%).

• 78% of ODs say that they would be changing their practice strategy either somewhat (51%) or significantly (27%) in response to MVCPs' channeling of products.

• 89% of respondents indicated that they are looking for resources that would help to reduce their practices' dependency on MVCPs.



The profit triangle: If reimbursements go down, then a practice's patient volume must go up to maintain the same profit.

How Will You Respond?

So, most of you indicated that you're not happy with MVCPs' changes, and that these changes affect your ability to provide the quality of care that you want to provide to your patients.

Additionally, we also know that reimbursements from managed vision care plans are on the decline, and the premium dollars for those plans continue to get challenged in the consumer marketplace. The question is, of course, how are you going to respond to those decreased reimbursements?

Let's take a look at a classic profit triangle. If reimbursement per exam is decreasing and patient volume stays the same, then the only way that your profitability can move is down. Because you don't have the power to increase your reimbursement, the only other variable that you can change in this system is the volume of patients per hour.

That means that the days of the 30-minute exam are over. If you want to keep your profitability intact, you're going to have to look at alternative ways that you can still deliver quality care in 15 minutes or less per exam.

Of course, if this isn't what you want to do, then you have another choice: quit the plan. While on the surface that may seem scary, our survey shows that many of you are contemplating this very action. Personally, I've been first party to many practitioners who have done this, and done it successfully, by replacing their low-paying refractive examinations with higher-paying refractive and medical eye care visits.

Prepare to Adapt

Optometrists have long enjoyed a significant portion of their practices' profitability from sales of retail products. While being able to sell and profit from what you prescribe is generally not allowed in medicine due to self-referral rules (the Stark laws), optometry and ophthalmology are currently exempt from these restrictions. That said, market forces today are dictating change in our retail strategies as well.

Refractive carriers that restrict practitioner choice in exchange for better pricing, or to simply participate in the plan, as well as greater challenges from other retail models (e.g., online sellers such as Warby Parker, Zenni Optical, etc.) are putting greater pressure on our traditional profit model.

And to top it off, our responsibility to provide and maintain the standard of care to our patients is increasing, which is putting our survival as an independent practice model in the crosshairs of sustainability.

As dire as all of this sounds, remember that these are all potential consequences if you ignore the changes in the health care landscape around you or if you delay taking action to these changes until it is far too late to respond.

Many practitioners are very successful in being proactive and keeping themselves and their staff on top of both federal and local issues that are affecting their chosen way of practice. These practitioners are the models for us to all follow; we know who they are in our communities, we wonder at their continued success and are often stumped at why they excel at something that we may struggle with. Like them, we have to be perpetual students, always learning, always adapting to the challenges that lie before us.

I have no doubt that 2014 will be a pivotal year for the profession of optometry and how eye care is delivered. I also have no doubt that we are and will continue to be the primary eye care providers in any health care system of the future. Is it a health care revolution or simply evolution? Adapting to change is required to be part of either. ■

Please send your questions and comments to CodingAbstract@gmail.com.

Besivance®
besifloxacin ophthalmic suspension, 0.6%

By Agustín L. González, OD

A Good Choice for Treating Bacterial Conjunctivitis

When it comes to managing bacterial conjunctivitis, this fluoroquinolone antibiotic has proven efficacy. Find out why.

More than four million Americans suffer from bacterial conjunctivitis each year,[1] with patients most often seeking consultation for complaints of secretions and red, inflamed eyes. The initial infection usually manifests itself unilaterally and typically spreads to the fellow eye within a 48-hour time span. Patients often complain of mucous discharge with lid crusting, tearing and foreign body sensation.

Microorganisms associated with bacterial conjunctivitis include *Staphylococcus aureus*, *Streptococcus pneumonia*, *Pseudomonas aeruginosa* and *Haemophilus influenza*.

From 2000 to 2005, there has been an increasing incidence of methicillin-resistant *S. aureus* (MRSA) in serious ocular infections in the United States.[2] It is unquestionable that bacteria develop various degrees of tolerance and susceptibility to the agents designed to control them. This fact has been well documented in the medical literature.[2,3] Not surprisingly, cases of MRSA and other resistant organisms, such as methicillin-resistant *Staphylococcus* epidermidis (MRSE), have become a serious potential complication and a concern for optometrists who manage bacterial conjunctivitis.

BESIVANCE® INDICATION

BESIVANCE® is a quinolone antimicrobial indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following bacteria: *Aerococcus viridans**, CDC coryneform group G, *Corynebacterium pseudodiphtheriticum**, *Corynebacterium striatum**, *Haemophilus influenzae*, *Moraxella catarrhalis**, *Moraxella lacunata**, *Pseudomonas aeruginosa**, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis**, *Staphylococcus lugdunensis**, *Staphylococcus warneri**, *Streptococcus mitis* group, *Streptococcus oralis*, *Streptococcus pneumoniae*, *Streptococcus salivarius**.

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

THE CONTACT LENS CONNECTION

P. aeruginosa is a Gram-negative bacteria that is a habitual contaminant of aqueous solutions. Because of the structure of the microorganism itself, it is particularly virulent. The bacterial cell surface is hydrophobic and contains pili, which aid the bacteria in adhering to host cells. The presence of flagella on the cell surface increases the mobility of the bacteria, and extracellular proteases promote the ability of the bacteria to digest its substrate. All of these factors make contact lens-related *P. aeruginosa* bacterial conjunctivitis a challenging concern that is difficult to eradicate.[4–6]

As with any bacterial infection, antibiotics are helpful for eliminating the bacteria. Most often, treatment of bacterial conjunctivitis is accomplished with the use of topical antibiotic eye drops and/or eye ointments and can take from one to two weeks, depending on infection severity.[7,8]

ANTIBIOTIC POTENCY & FORMULATION

The potency of an antibiotic is an important metric for antibiotics and is used to evaluate potential bacterial resistance. When talking about antimicrobial efficacy, the minimum inhibitory concentration (MIC) is the metric by which antibiotic activity and potency is evaluated. It is a descriptive measurement of the concentration at which a specific molecule inhibits *in vitro* growth of a specific bacterial culture.[9]

MIC_{90} and MIC_{50} are the metrics used to describe the lowest amount of drug concentration that inhibits the growth of 90% or 50% of in vivo isolates of cultured microorganism. A lower MIC value indicates a more powerful drug and, in turn, a lower chance for the development of resistance (the higher the amount of microorganisms killed, the lower the risk of resistance to the molecule).[9]

We can use MIC values to help determine the ability of an antibiotic to eradicate organisms. Besivance has a very low MIC against ocular pathogens. Because bacterial conjunctivitis is often treated in an empirical manner, a low MIC value is important. BESIVANCE® has demonstrated success in the elimination of common ocular pathogens, including MRSA, in preliminary microbiological studies.[8,10] One *in vitro* study of 2,690 clinical isolates from 40 species of bacteria showed that the MICs for besifloxacin were at least two to four times lower than the other antibiotics tested.[8] Most notably, besifloxacin had demonstrated *in vitro* activity against

Important Risk Information for BESIVANCE®

- 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.
- As with other anti-infectives, prolonged use of BESIVANCE® may result in overgrowth of non-susceptible organisms, including fungi. If superinfection occurs, discontinue use and institute alternative therapy.
- 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% to 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 the full prescribing information for BESIVANCE® on page 28.

both Gram-positive and Gram-negative bacterial isolates deemed widely resistant to fluoroquinolones, including MRSA.[11]

Halogenation has long been used in antibiotic drug design to improve penetration and activity. Besides the fluorine atom common to all fluoroquinolones, a second halogen substitution in the form of a chlorine atom is added to the besifloxacin molecule. The additional 7-azepinyl ring distinguishes it from other fluoroquinolones and is believed to contribute to its potency. The clinical significance of *in vitro* data has not been established. The unique molecular design of the 7-azepinyl ring and the double chloro-fluoro halogenation contributes to potency by increasing affinity for topoisomerase IV.[12]

Fluoroquinolones work by inhibiting two critical bacterial enzymes: DNA gyrase and topoisomerase IV. Quinolones efficiently bind to DNA gyrase, but generally have less effect on topoisomerase IV, which explains why early quinolone antibiotics are more active against Gram-negative microbes.[8,12–14] BESIVANCE® is unique because in addition to having a C6-fluoro-substituent, which is common to all fluoroquinolones, it also has a distinct chloro-substituent at the C8 position, which has demonstrated potency against Gram-positive activity. Its dual halogenation derives from its combination of these two substituents.

BESIVANCE® is only available as an ophthalmic suspension and is formulated with the DuraSite vehicle (InSite Vision Inc.). DuraSite is a biocompatible polymer used to deliver therapeutic drug dosages by suspending the drug molecule in the polymer matrix. The polymer matrix is designed to increase contact time on the ocular surface after instillation. Even 12 hours following instillation, BESIVANCE® tear concentrations were greater than the MIC_{90}s for *Staphylococcus epidermidis*, *S. aureus*, *Streptococcus pneumoniae*, *Haemophilus influenzae*, *P. aeruginosa* and ciprofloxacin-resistant MRSA/MRSE.[15, 16]

In the ARMOR study, besifloxacin, the only dual-halogenated chloro-fluoroquinolone, was shown to be the most potent fluoroquinolone against staphylococci, specifically the ciprofloxacin resistant staphylococci.[14,15] There are two forms of resistant *Staphylococcus*: MRSA/MRSE and QRSA/QRSE (quinolone-resistant *S. aureus* and *S. epidermidis*). However, quinolone-resistant *Staph* is really ciprofloxacin-resistant, since that is what is tested. This dual-halogenated chloro-fluoroqinolone has balanced ability to inhibit topoisomerase IV and DNA gyrase with nearly equal potency. *In vitro* studies demonstrated cross-resistance between BESIVANCE® and some fluoroquinolones.[10,17,18]

Research has also proven besifloxacin to be effective in the treatment of the most common bacteria that cause bacterial conjunctivitis such as *Staphylococci*, *Streptococci* and *Corynebacterium*.[14,19] Similarly, it has been shown to be effective in contact lens-related bacterial conjunctivitis caused by *P. aeruginosa*.[14,19]

Antimicrobial efficacy in the treatment of bacterial conjunctivitis is important. The standard of care has been to provide patients with a seven-day treatment with a broad-spectrum antibiotic. The quick initiation of treatment helps reduce the time of contagion, thus helping to reduce the spread of the bacterial conjunctivitis. Since its release in 2009, I've been making a decision to choose BESIVANCE® to treat bacterial conjunctivitis.

CONCLUSION

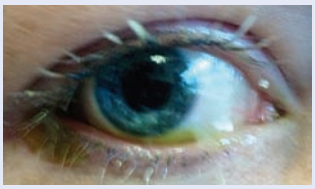
The reported rise of drug-resistant organisms and the spectrum and virulence of offending microorganisms are factors that pose increased concern for clinicians who treat bacterial conjunctivitis. In these cases, ocular anti-infective strategy is aimed to deliver higher drug levels early in the course of infection when the bacterial burden is likely highest.

Because empirical treatment is the norm, and cultures are not routinely performed in most clinical settings, clinicians must choose an antimicrobial therapy with a broad spectrum of activity. With empirical treatment of bacterial conjunctivitis, a potent and broad-spectrum antibiotic is an appropriate weapon. BESIVANCE® is a molecule designed with dual halogenation for potency and balanced activity against bacterial DNA gyrase and topoisomerase IV.

Bacteria can easily and rapidly mutate and form bactericidal-resistant strains; therefore, effective agents are always in high demand. BESIVANCE® is a good choice for the treatment of bacterial conjunctivitis.

Dr. González is a licensed optometric glaucoma specialist and therapeutic optometrist in Richardson, Texas, specializing in the treatment of eye diseases, conditions and infections. He is a nationally recognized expert in optometric public health and serves as an industry expert on dry eye and ophthalmic medications. Additionally, Dr. González lectures extensively to both optometry and ophthalmology groups and is a consultant for various pharmaceutical and contact lens companies.

PATIENT CASE STUDY



A 27-year-old white female showed up in our office with complaints of profuse mucous secretions with crusting and "sticky, glued" eyelids of the right eye when she woke up in the morning. She claimed to have a mild, tender foreign-body feeling the previous day with no light sensitivity or other relevant history.

Exam Findings: Physical examination revealed a unilateral red eye and mild lid edema, + 2 bulbar conjunctiva injection, mild papillary reaction and evident mucous discharge. No notable meibomian gland dysfunction, cells/flare or anterior inflammatory entity was observed. Nicox RPS testing was negative for adenoviral etiology and there was no evidence of preauricular lymphadenopathy. History was negative for pharyngitis, fever or any respiratory infection.

Diagnosis: Bacterial conjunctivitis; pathogen identity and resistance profile unknown.

Treatment: Considering the lack of immediate information about the identity and susceptibility of the causative pathogen, I immediately prescribed BESIVANCE® (besifloxacin ophthalmic suspension 0.6%, Bausch + Lomb). With prolonged contact time, a t.i.d.-dosing regimen and potency against both Gram-positive and Gram-negative pathogens, it is a good choice.

Proper antibiotic therapy will lead to quicker remission and decreased transmission. Because bacterial conjunctivitis is a contagious condition and contagion time is unpredictable, I suggested the patient stay home for the next two days and follow proper hygiene, including hand washing multiple times a day. I also advised the patient to call the office if no signs of resolution where seen by the third day.

Outcome: The patient reported improvement in signs and symptoms after initiating topical antimicrobial therapy. She also noted that both conjunctival injection and secretions resolved quickly after the second day. I instructed her to continue the use of BESIVANCE® t.i.d. (four to 12 hours apart) for the complete seven-day treatment cycle.

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BAUSCH+LOMB

Besivance®

besifloxacin ophthalmic suspension, 0.6%

HIGHLIGHTS OF PRESCRIBING INFORMATION

These highlights do not include all the information needed to use Besivance safely and effectively. See full prescribing information for Besivance.

Besivance® (besifloxacin ophthalmic suspension) 0.6%
Sterile topical ophthalmic drops
Initial U.S. Approval: 2009

---------- RECENT MAJOR CHANGES ----------
Indications and Usage (1) 09/2012

---------- INDICATIONS AND USAGE ----------

Besivance® (besifloxacin ophthalmic suspension) 0.6%, is a quinolone antimicrobial indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following bacteria:
*Aerococcus viridans**, CDC coryneform group G, *Corynebacterium pseudodiphtheriticum**, *Corynebacterium striatum**, *Haemophilus influenzae*, *Moraxella catarrhalis**, *Moraxella lacunata**, *Pseudomonas aeruginosa**, *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Staphylococcus hominis**, *Staphylococcus lugdunensis**, *Staphylococcus warneri**, *Streptococcus mitis* group, *Streptococcus oralis*, *Streptococcus pneumoniae*, *Streptococcus salivarius**
*Efficacy for this organism was studied in fewer than 10 infections. (1)

---------- DOSAGE AND ADMINISTRATION----------

Instill one drop in the affected eye(s) 3 times a day, four to twelve hours apart for 7 days. (2)

---------- DOSAGE FORMS AND STRENGTHS----------

7.5 mL size bottle filled with 5 mL of besifloxacin ophthalmic suspension, 0.6% (3)

----------CONTRAINDICATIONS----------

None (4)

----------WARNINGS AND PRECAUTIONS ----------

Topical Ophthalmic Use Only. (5.1)

Growth of Resistant Organisms with Prolonged Use. (5.2)

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. (5.3)

---------- ADVERSE REACTIONS ----------

The most common adverse reaction reported in 2% of patients treated with Besivance was conjunctival redness. (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: 09/2012

FULL PRESCRIBING INFORMATION: CONTENTS*

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

FULL PRESCRIBING INFORMATION

1 INDICATIONS AND USAGE

Besivance® (besifloxacin ophthalmic suspension) 0.6%, is indicated for the treatment of bacterial conjunctivitis caused by susceptible isolates of the following bacteria:
*Aerococcus viridans**
CDC coryneform group G
*Corynebacterium pseudodiphtheriticum**
*Corynebacterium striatum**
Haemophilus influenzae
*Moraxella catarrhalis**
*Moraxella lacunata**
*Pseudomonas aeruginosa**
Staphylococcus aureus
Staphylococcus epidermidis
*Staphylococcus hominis**
*Staphylococcus lugdunensis**
*Staphylococcus warneri**
Streptococcus mitis group
Streptococcus oralis
Streptococcus pneumoniae
*Streptococcus salivarius**
*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.

3 DOSAGE FORMS AND STRENGTHS

7.5 mL bottle filled with 5 mL of besifloxacin ophthalmic suspension, 0.6%.

4 CONTRAINDICATIONS

None

5 WARNINGS AND PRECAUTIONS

5.1 Topical Ophthalmic Use Only

NOT FOR INJECTION INTO THE EYE.

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.

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)]*.

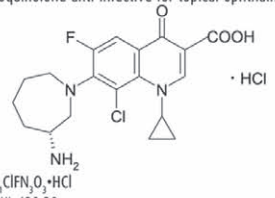
There is no evidence that the ophthalmic administration of quinolones has any effect on weight bearing joints, even though systemic administration of some quinolones has been shown to cause arthropathy in immature animals.

8.5 Geriatric Use

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

11 DESCRIPTION

Besivance (besifloxacin ophthalmic suspension) 0.6%, is a sterile ophthalmic suspension of besifloxacin formulated with DuraSite®† (polycarbophil, edetate disodium dihydrate and sodium chloride). Each mL of Besivance contains 6.63 mg besifloxacin hydrochloride equivalent to 6 mg besifloxacin base. It is an 8-chloro fluoroquinolone anti-infective for topical ophthalmic use.



$C_{19}H_{21}ClFN_3O_3 \cdot HCl$
Mol Wt 430.30

Chemical Name: (+)-7-[(3R)-3-aminohexahydro-1H-azepin-1-yl]-8-chloro-1- cyclopropyl-6-fluoro-4-oxo-1,4-dihydroquinoline-3-carboxylic acid hydrochloride.

Besifloxacin hydrochloride is a white to pale yellowish-white powder.

Each mL Contains:
Active: besifloxacin 0.6% (6 mg/mL);
Preservative: benzalkonium chloride 0.01%
Inactives: polycarbophil, mannitol, poloxamer 407, sodium chloride, edetate disodium dihydrate, sodium hydroxide and water for injection.

Besivance is an isotonic suspension with an osmolality of approximately 290 mOsm/kg.

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.

12.4 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.

16 HOW SUPPLIED/STORAGE AND HANDLING

Besivance® (besifloxacin ophthalmic suspension) 0.6%, is supplied as a sterile ophthalmic suspension in a white low density polyethylene (LDPE) bottle with a controlled dropper tip and tan polypropylene cap. Tamper evidence is provided with a shrink band around the cap and neck area of the package.

5 mL in 7.5 mL bottle
NDC 24208-446-05

Storage:

Store at 15°-25°C (59°-77°F). Protect from Light. Invert closed bottle and shake once before use.

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

Besivance® is a registered trademark of Bausch & Lomb Incorporated.

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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9142705(folded)

Art in Practice

Turning a blank canvas into a winning look.

By Erin Kelly, Senior Associate Editor

When you commit to building a new practice or improving your current one, you need perseverance, vision and a plan of attack. A blank canvas offers you limitless possibility, but it also means starting from scratch—a potentially overwhelming proposition when faced with unexpected costs, logistical snags, late deliveries and failed design concepts. The weight and responsibility can be daunting, but the rewards are ultimately vast. The three winners of this year's annual Office Design Contest all attest to that.

These featured practices were chosen from numerous entries as reflecting the best overall approach based on design, efficiency, style and technological integration. Using feedback from our trio of qualified judges, we crowned one winner and two runners-up, all of which have enjoyed the rewards of a new build.

We called on last year's winners to judge the entries for 2013. Using their own field experience and eye for design, they scored entries based on pictures and detailed entry forms in which applicants explained how each new build improved functionality, incorporated new optometric equipment, considered ergonomics in the layout and achieved an aesthetically pleasing new look.

So, let's meet our winners!

Meet the Judges

Shaun Golemba, OD
2012 Office Design Contest Winner

Dr. Golemba is the owner of Valley Vision Optometry in Port Alberni, British Columbia.

Sonja Franklin, OD
2012 Office Design Contest Winner

Dr. Franklin is the owner of Modern Eyes in Austin, Texas.

Tom Wilson, OD
2012 Office Design Contest Winner

Dr. Wilson is the owner of Pine Creek Vision Clinic in Colorado Springs, Colo.

WINNER

Michael Hung, OD
and
Teri Hung, OD
Dunwoody, Ga.

Eye Elements

When you have a creative project on your hands, inspiration can come from anywhere. And looking beyond optometry sometimes offers a fresh approach. For Teri Hung, OD, owner of Eye Elements in Dunwoody, Ga., inspiration came from the luxury, efficiency and creative beauty of the restaurant industry. She searched for interior design photos from restaurants all over the world and pinned her favorites to a Pinterest board. Atlanta designer James Beaty brought that board to life in a new office space of more than 3,500 usable square feet.

Patients who walk into this L-shaped office hear ambient music from the integrated in-ceiling speaker system and can easily browse the optical area without creating a logistical logjam with people waiting for eye exams. A centralized pre-testing area and contact lens area allows multiple doctors and multiple patients to be examined and escorted to any of the exam rooms in this large practice.

"This is a very nice 'open concept' office with good use of an accent color," contest judge Sonja Franklin, OD, says. "The office has great curb appeal and the use of window displays create interest to pedestrians."

Indeed, Dr. Hung says some people walk into the new office just to enjoy the aesthetics.

Getting in Good Shape

At first, the owners were concerned that their L-shaped office would pose a design challenge.

"Many office spaces are linear, but our office space was more unique," Dr. Hung says. Turns out, the L shape was ideal: "It works perfectly for our needs. Our L-shaped space allows us to differentiate the optometric clinic from the optical."

With a centralized pre-testing and contact lens area, patients can move easily throughout the practice.

"Placing the optical near the front entry allows walk-in shoppers to browse products, and the front desk is conveniently positioned to serve both patients in the clinic and buyer in the optical, with an open view to the entire front office," she says.

"Any time you put a lot of time, money and effort into something, you hope that it will be successful. We created a practice of our dreams and are thrilled that we have a space for all of our patients and staff to enjoy," Dr. Hung says. "New patients are intrigued by the space, while established patients are pleasantly surprised. The design of the office represents who we are and that we pay careful attention to details."

The office expansion includes upgraded computer and clinical equipment, a new exam lane and server integration that connects Dunwoody to another location in Roswell.

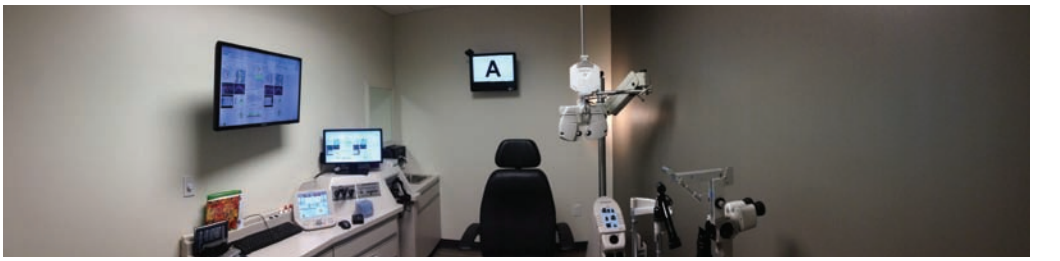
"Nice open concept office with good use of color."

1st RUNNER-UP

Sharokh Kapadia, OD
Ponte Vedra, Fla.

St. John's Eye Associates

"All of the elements coordinate! High-end feel."



Every inch of the 1,900 square feet of St. John's Eye Associates was designed with patients in mind, from the pleasant office environment to the flat-screen exam room TVs that allow for easy patient viewing, according to owner Sharokh Kapadia, OD. The office layout includes a walk-through between the inner business office and contact lens room, with ergonomically designed seating in the exam rooms for better comfort and posture.

"Patients really like the clean, neat look to the practice," says Dr. Kapadia, who also owns a practice in St. Augustine, Fla. "The LED lighting in the optical really enhances the way the eyewear looks when it's on the frame boards."

For contest judge Shaun Golemba, OD, the remarkable lighting was one of the most notable features of Dr. Kapadia's entry.

"I like the high-end feel," Dr. Golemba says. "I think all of the elements coordinate. Everything is cohesive. I like the contrast of the dark cabinets from the white walls and light floor, and the big-screen TV in the exam room would be very practical for viewing the various imaging devices we use these days."

Dr. Kapadia also invested in dry-air technology that releases fragrance without sprays, aerosols or heated oils, so one of the first things his patients notice is the smell.

He says he spent more than a year planning and building the practice, but watching it grow over the past 12 months has been its own reward, especially as the first eye care provider at his second location.

When you're the first ECP, "it's slower at first, but patients appreciate the fact that you have spent your time and resources to open a practice to take care of their needs."

Better, Brighter Refractions

One of Dr. Kapadia's goals was to offer the best technology possible, so he invested in two automated refracting lanes that allow for quick and more accurate refractions.

"Patients also benefit because they don't have to be asked the same, 'What's better, one or two?' as much," he says.

The refractions are done in a well-lit room, rather than a darkened one, which makes for a better atmosphere.

2nd RUNNER-UP

Eye Columbus

Craig Miller, OD
Columbus, Ohio

Some patients of Eye Columbus have visited the practice ever since it was originally founded in 1967. Craig Miller, OD, felt it was time for a substantial redesign that rewarded the loyalty of older patients and met the expectations of the newer ones. He delivered on that vision with the recent overhaul of Eye Columbus's 3,760-square-foot location.

Dr. Miller drew inspiration from eye-catching retail spaces and input from his staff to create an atmosphere that seamlessly married the optical retail experience with the optometric clinical experience.

"Although it was a great challenge, I feel we accomplished that completely," Dr. Miller says.

The use of dark wood and shades of orange accents create the foundation for the warm, welcoming environment of Eye Columbus.

Contest judge Tom Wilson, OD, said Eye Columbus was notable for its "creative look and open feeling."

The practice moved from a single exam

room office with two dispensing desks to a three exam room office with four dispensing desks, which dramatically improved quality of care. Dr. Miller also incorporated an open design lab with multiple entrance points to improve the flow for opticians.

During this process, Dr. Miller also kept the future in mind, trying to predict how the practice will change over the next 10 years so he can continue offering updated service.

"Patients and guests are truly wowed when they walk into the front door, which is great, but the best compliment is when patients acknowledge that the level of care is top-notch," he says.

Ergonomically Sound Practice

In the exam rooms, a single monitor is attached to a wall-mounted swivel so that the doctor or scribe can use it. A single computer controls the letter chart, EHR, interactive patient education software and Internet.

"Dual keyboards enable the doctor and the scribe to input material, allowing the doctor to face the patient most of the exam and verbalize what needs to be written down," Dr. Golemba says.

New drawers in the exam rooms improve ease of access to equipment and make it easier to keep the space tidy:

- The first drawer holds pretest tools.
- The second contains the doctor's tools.
- Trial frames are found in the third drawer, which is positioned at arm's length when standing, so the doctor doesn't have to bend to access them.
- Brochures and other information materials are located in the fourth drawer.

The business office comfortably holds five workstations and an overhead projector for business meetings and distance-education webinars.

15th Annual Diabetes Report

Moving the Needle:

Can We Influence the Course of Diabetes?

Evidence suggests nutritional supplements really *can* make a difference in diabetic retinopathy. **By A. Paul Chous, MA, OD**

As most readers probably know, the landmark Age-Related Eye Disease Study (AREDS) demonstrated that a nutritional supplement could positively influence progression of AMD.[1] Since that 2001 study appeared, a big question has been: might nutritional supplements also have a similar effect on diabetic retinopathy (DR)? Because vitamins, minerals and other micronutrients serve a variety of biological functions potentially beneficial in diabetes, there has been renewed interest in the possibility of these supplements treating a host of diabetes complications.

Long-term administration of AREDS antioxidants has yielded exciting results in preventing the pathogenesis of DR in rodent models. "These results suggest the merit of testing the AREDS antioxidants in a clinical trial to prevent the development and/or progression of diabetic retinopathy, with the possibility of reducing the impact of this common vision-threatening disease," wrote prominent retinal biologists in a 2011 *Investigative Ophthalmology & Visual Science* paper.[2]

Factors Contributing to Diabetic Retinopathy

- Hyperglycemia
- Hypertension
- Inflammatory dyslipidemia
- Oxidative stress
- Release and suppression of growth factors
- Hormonal influences
- Apoptosis
- Upregulation of inflammatory cytokines
- BRB breakdown and hypoxia

We can safely say there is a plausible epidemiological basis for thinking that dietary supplementation might correct nutritional deficiencies common in diabetes. Studies suggest that patients with diabetes are more likely to suffer from deficiencies of potassium, calcium, magnesium, zinc, manganese, chromium, vitamin D and serum carotenoids.[3-8] Such deficiencies may negatively affect glucose control, cell repair and survival, and may ultimately contribute to diabetes complications. Moreover, long-term use of the most widely prescribed oral anti-diabetic agent, metformin, has recently been linked with vitamin B12 deficiency, a risk factor for diabetic retinopathy.[9,10]

But will merely correcting micronutrient deficiencies make a meaningful difference in terms of the development and progression of DR in humans? Another, related question: might additional preventative micronutrients be helpful?

Of course, only a large, well-designed clinical trial would give us the answer. In the meantime, however, we combine our knowledge of the complex biological pathways that lead to diabetic retinopathy with evidence that shows how targeted micronutrients block these pathways to make scientifically rational recommendations to our patients with diabetes.

Current clinical algorithms for diabetic eye disease call for earlier diagnosis of diabetes, tighter metabolic control, annual dilated retinal examinations and treatment (e.g., laser, anti-VEGF drugs, steroids) if DR threatens vision. There is no doubt this "reactive" strategy has protected the vision of millions of diabetes patients, but we also know there is room for improvement. For example, despite the

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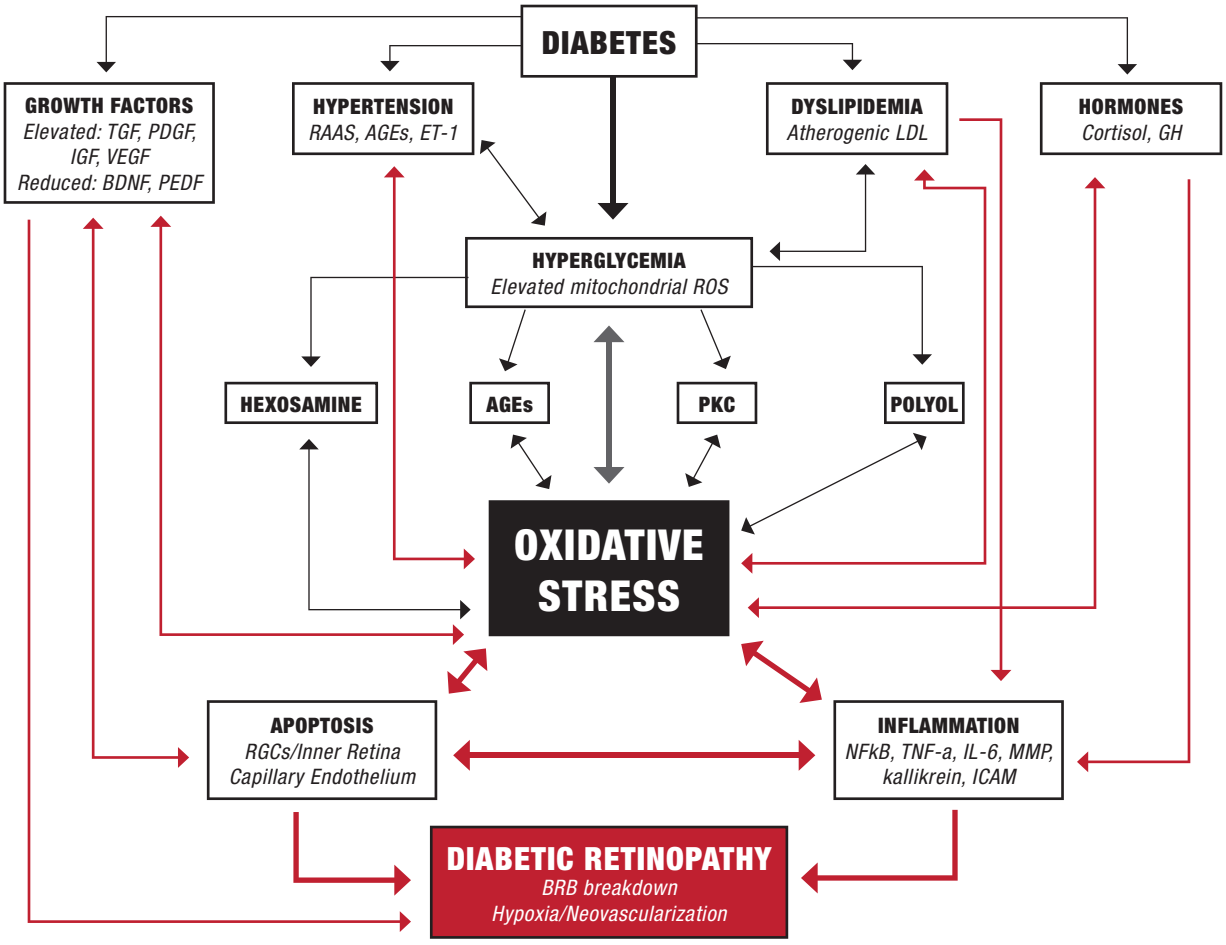
enormous effort put into education, many patients with diabetes do not undergo dilated exams or achieve their metabolic targets—and, furthermore, even those who strictly follow these guidelines may still develop sight-threatening diabetic retinopathy (STR).

A major strength of the targeted nutritional supplements discussed in this article is their ability to offer a proactive, rather than reactive, strategy in fighting this disease—an ounce of prevention that might ultimately be worth the proverbial pound of cure.

A Continuous Climb

Diabetic retinopathy remains the leading cause of new cases of blindness in Americans under age 74. This may be surprising to many practitioners who have noticed a long-term trend towards reduced rates of severe DR over the last several decades. Despite evidence that tighter control of blood glucose and blood pressure reduces the risk of microvascular diabetes complications, as well as tremendous advances in the clinical management of diabetic eye disease, rates of DR in the US have increased by 89% over the last decade (probably due to better detection and increasing rates of diabetes).[11]

Importantly, significant visual impairment associated with diabetes remains high, and recent estimates show that nearly 5% of US adults with diabetes have STR—with significantly higher rates amongst African, Latino and Native American populationss.[12] Moreover, global estimates of DR and STR based on pooled analysis of population-based studies show 93 million cases of DR and 28 million cases of STR, which suggests that nearly 2.8 million



The biology of diabetic retinopathy. A number of factors cause the small blood vessel damage that leads to diabetic retinopathy, including high blood sugar, high blood pressure, high and abnormal cholesterol, production of harmful free-radical molecules and inflammation. Complex interactions among metabolic abnormalities characteristic of diabetes lead to activation of abnormal biochemical pathways (hexosamine, AGE, PKC, Polyol), oxidative stress, apoptosis and inflammation, in addition to breakdown of the blood/retinal barrier, hypoxia and neovascularization.

Americans may have sight-threatening diabetic retinopathy today.[13]

Increasing the rates of dilated eye exams among patients with diabetes reduces blindness, yet nearly 40% of patients failed to have one performed in 2010.[14] We also know that improving blood glucose and blood pressure control significantly reduces rates of DR and STR. Nonetheless, 12% of diabetes patients had HbA1c levels >9% in 2004, while more than 30% had HbA1c levels >8%.[15] Although improving blood glucose control lowers risk, evidence shows that there is no level of average blood glucose that fully protects against DR.

Perhaps the single most important step we can take to combat DR is to reduce the incidence of diabetes (especially type 2) by addressing complex environmental factors like obesity, sedentary lifestyle and even sleep deprivation.[16,17] Rates of diabetes continue to climb, and projections are that one in three American adults will have it by 2050.[18]

Working Model of DR

To better understand how and why nutritional supplements might benefit diabetic retinopathy, it is helpful to have a working model of the biology underlying the disease.

Diabetes causes a number of metabolic abnormalities, including hyperglycemia, dyslipidemia, hypertension and oxidative stress. These factors interact in a variety of ways to cause increased production of singlet oxygen (also known as reactive oxygen species [ROS]) by mitochondria, especially within the retina and other insulin-independent tissues (small-caliber neurons, renal glomeruli and aorta). These mitochondrial ROS activate specific and well-established biochemical pathways within retinal cells that directly lead to vascular and retinal ganglion cell damage (polyol, PKC, hexosamine flux and advanced glycation endproduct pathways).[19,20]

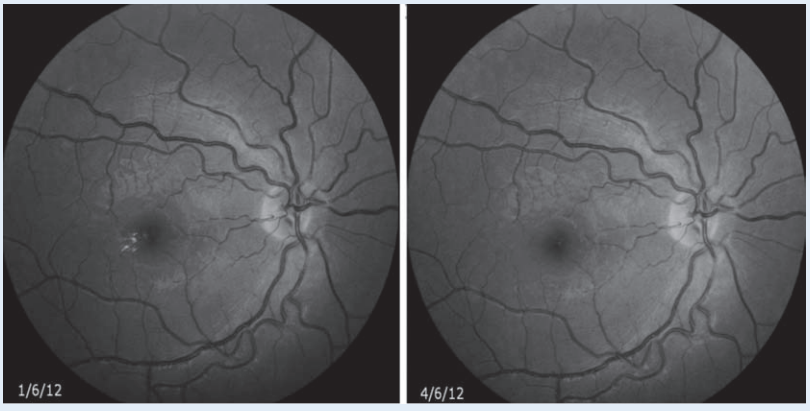
Release of inflammatory proteins and programmed destruction (apoptosis) of capillary endothelial cells and retinal ganglion cells may lead to breakdown of the blood/retinal barrier, resulting in vascular leakage, hypoxia and retinal neovascularization—the hallmarks of diabetic retinopathy. Accompanying deficits in visual function, including contrast sensitivity, visual field sensitivity and color vision, are common.

Elevated blood glucose plays a central role in DR, worsening dyslipidemia and hypertension, and driving oxidative stress that damages the retina. This is why control of blood sugar (as well as blood pressure and blood lipids) constitutes the foundation of preventing diabetes complications, including retinopathy. However, a number of biological processes that occur further downstream from hyperglycemia also can affect progression and thus give us additional targets for intervention.

Pills, Not Pulses

A 27-year-old male with type 1 diabetes presented with new retinal exudates and macular edema that did not qualify as CSME by ETDRS criteria (left). He was first diagnosed 13 years earlier.

The patient was offered focal laser treatment by the local retinal specialist, but declined. After three months of nuritional supplementation with benfotiamine and pycnogenol, the hard exudates and macular edema resolved (right).



The Benefits of Nutritional Supplementation

When considering evidence for micronutrient intervention in DR pathobiology, bear in mind that effects demonstrated in a laboratory, or associations seen in human beings, do not necessarily translate into clinical efficacy. A summary of these supplements' potential biological activity (*see "Biological Activity of Micronutrients in DR," p. 41*) and their site of action in the diabetic retinopathy pathway are described below.

• ***Benfotiamine.*** A synthetic, lipophilic analog of vitamin B1 (thiamine), benfotiamine has been shown to elevate intracellular levels of transketolase—an enzyme that redirects glucose and the harmful glucose metabolites, fructose-6-phosphate and glyceraldehyde-3-phosphate, to the pentose phosphate shunt pathway. Increased transketolase levels reduce intracellular formation of protein kinase C, sorbitol, advanced glycation (AGE) and advanced lipo-oxidation (ALE) endproducts—

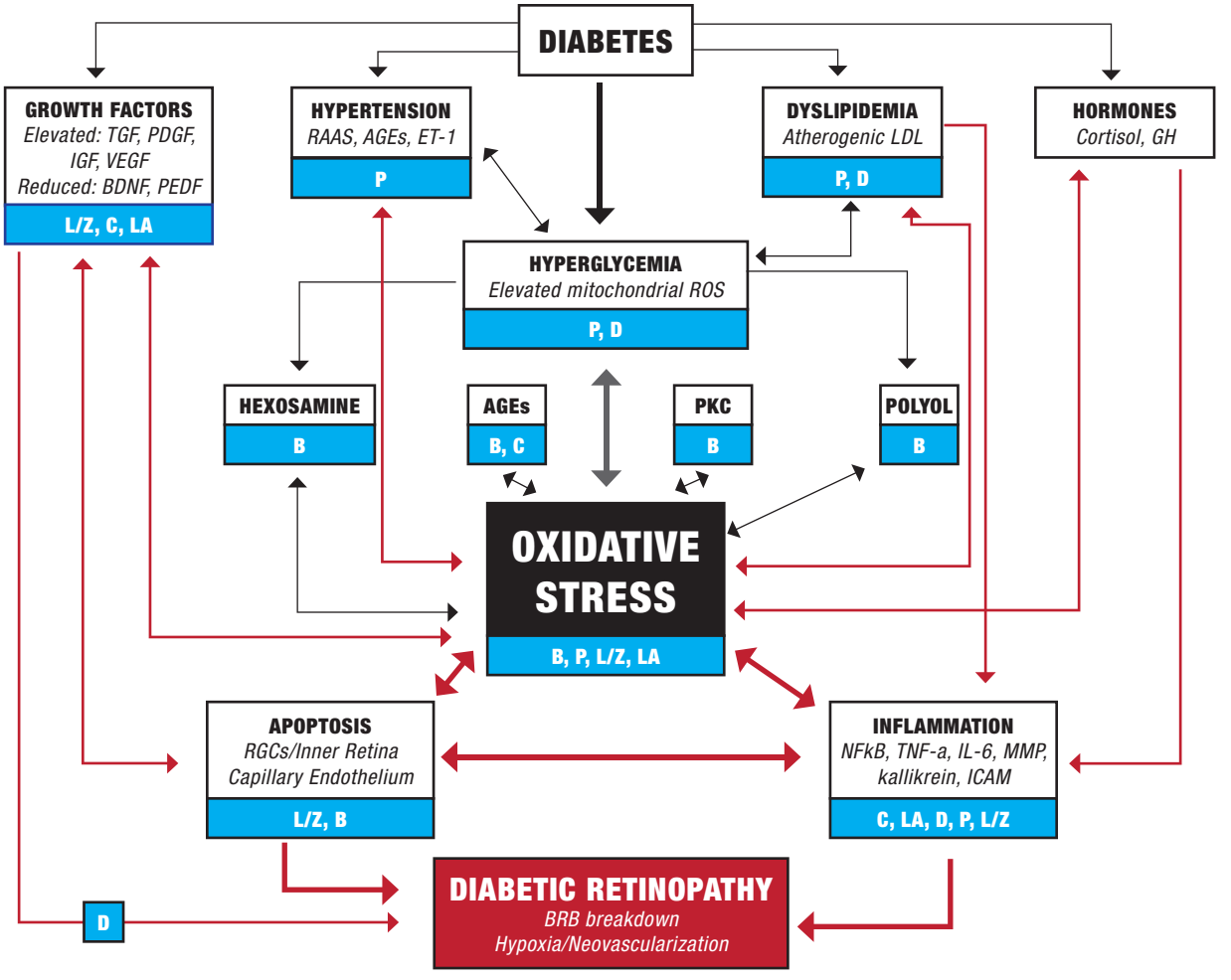
substrates directly involved in the pathogenesis of diabetic microvascular damage, including diabetic retinopathy.[21]

Benfotiamine has been shown to block activity in the polyol, hexosamine flux, protein kinase C and advanced glycation endproduct pathways, helping to prevent diabetic retinopathy in a murine model of the disease.[22] It also prevents glucose-dependent apoptosis of human retinal pericytes.[23]

Multiple studies have shown that benfotiamine improves vibratory sensation, nerve conduction and pain scores in patients with diabetic neuropathy.[24,25] When combined with slow-release alpha-lipoic acid, benfotiamine normalized activity in the polyol, hexosamine and AGE pathways in patients with type 1 diabetes, as well as reduced levels of prostacyclin synthase—a protein implicated in atherosclerosis.[26] Benfotiamine also prevented endothelial dysfunction and oxidative stress in patients with type 2 diabetes following a provocative high-AGE meal.[27]

• ***Pycnogenol.*** A patented extract of bark from the French Maritime Pine, *Pinus pinaster*, pycnogenol contains a number of polyphenolic procyanidins (anthocyanidins)—antioxidants that inhibit inflammation and selectively bind to collagen and elastin fibers to improve capillary fragility.[28,29] Pycnogenol inhibits nuclear factor kappa beta (NF-kβ) and secretion of MMP-1, MMP-2 and MMP-9, of which the latter two have been implicated in breakdown of the blood/retinal barrier in diabetic retinopathy.[30, 31]

Pycnogenol also inhibits the digestive enzyme alpha-glucosidase, delaying the intestinal absorption of sugars to ameliorate post-prandial hyperglycemia.[32] More than 30 randomized, controlled clinical trials have shown that pycnogenol



Legend: **B** = *benfotiamine,* **C** = *curcumin,* **D** = *vitamin D,* **L** = *lutein,* **LA** = *lipoic acid,* **P** = *Pycnogenol,* **Z** = *zeaxanthin*

Sites of action of micronutrients in DR. See "Biological Activity of Micronutrients in DR" on page 41 for additional details.

improves a number of health conditions, ranging from tinnitus to chronic venous insufficiency to kidney dysfunction.[33-35] In patients with type 2 diabetes, Pycnogenol improved glycosylated hemoglobin, blood pressure and dyslipidemia.[36,37]

Several studies suggest that Pycnogenol improves capillary leakage and retards retinopathy progression in patients with diabetes.[38,39] Pycnogenol was shown to improve retinal blood flow, reduce retinal thickening and improve visual acuity in patients with early diabetic macular edema.[40]

• ***Non-provitamin A carotenoids.*** Lutein and zeaxanthin are the primary components of the macular pigment, which filters short-wavelength blue light, scavenges free radicals and suppresses inflammation in a number of disease models, including streptozotocin-induced diabetes and retinal ischemia.[41]

Type 2 diabetes patients with a higher ratio of serum non-pro-vitamin A carotenoids (lutein, zeaxanthin, lycopene) to pro-vitamin A carotenoids (alpha-carotene, beta-carotene and beta-cryptoxanthin) were associated with a 66% reduction in risk for diabetic retinopathy after adjustment for confounding variables.[42] Moreover, macular pigment optical density (MPOD) has been reported to be lower in patients with type 2 diabetes than in age-matched controls, lower still in patients with type 2 diabetes and retinopathy, and inversely correlated with glycosylated hemoglobin.[43]

Lutein supplementation reduced retinal oxidative stress and activation of NF-kβ, and increased the neuroprotective cytokine brain-derived neurotrophic factor (BDNF) in a mouse model.[44] Diabetic mice supplemented with lutein/zeaxanthin-rich wolfberry demonstrated normalized retinal thickness, RPE integrity and number of retinal ganglion cells via initiation of adenosine monophosphate-activated protein kinase and reduction of endoplasmic reticulum stress compared with controls.[45]

Biological Activity of Micronutrients in DR

Micronutrient	*Potential Biological Activity in DR*
Benfotiamine	Blocks polyol, protein kinase C (PKC), hexosamine and advanced glycation endproduct (AGE) pathways; reduces oxidative stress; inhibits retinal pericyte apoptosis.
Pycnogenol	Inhibits MMPs and retinal capillary leakage; lowers HbA1c and blood pressure; reduces retinal thickening and improves retinal blood flow in DME.
Lutein & Zeaxanthin	Higher serum ratio associated with 2/3 less DR; preserve RGCs in animal models; reduce oxidative damage, inflammation and VEGF; improve MPOD, VA, contrast and foveal thickness in subjects with NPDR.
Vitamin D	Deficiency associated with presence and severity of DR in both type 1 and type 2 diabetes; improves insulin sensitivity; reduces inflammatory dyslipidemia; inhibits retinal neovascularization.
Alpha-lipoic Acid	Quenches mitochondrial free radicals; prevents harmful metabolic memory in retinal mitochondria; reduces inflammation, VEGF and DR in animal models; improves endothelial dysfunction in humans.
Curcumin	Decreases inflammation; reduces VEGF and AGE cross-linking in animal models; improved DME in a small human trial; lowest rates of DR in countries where turmeric intake is highest after adjusting for other factors.

Supplementation with zeaxanthin also prevented oxidative damage and reduced production of VEGF and intracellular adhesion molecule (ICAM-1) in diabetic rats.[46] Lutein (6mg per day) and zeaxanthin (0.5mg per day) supplementation over three months increased MPOD, improved visual acuity, contrast sensitivity and foveal thickness in subjects with non-proliferative diabetic retinopathy compared to controls.[47]

• ***Vitamin D.*** Low serum levels of vitamin D have been implicated in the development of both type 1 and type 2 diabetes.[48-50] Vitamin D insufficiency also is a risk factor for atherosclerosis and cancer—both of which are more common in patients with diabetes.[51,52] Recently, serum vitamin D status has been linked to the presence and severity of diabetic retinopathy in patients with both type 1 and type 2 diabetes; vitamin D deficiency also proved more predictive of DR than diabetes duration or glycosylated hemoglobin in Australian adolescents with type 1 diabetes.[53,54]

Vitamin D supplementation reduced both vascular endothelial growth factor (VEGF) and transforming growth factor beta-1 (TGF-β1) in a murine model of diabetic retinopathy, giving insight into its possible mechanism of action affecting DR.[55] In a murine model of oxygen-induced ischemic retinopathy, supplementation with the active metabolite of vitamin D3 (1,25-dihydroxyvitamin D3) significantly inhibited retinal neovascularization without reducing ocular VEGF levels.[56] Vitamin D also appears to block foam cell

formation in serum samples from subjects with type 2 diabetes, suggesting improvement of the inflammatory dyslipidemia that contributes to DR.[57,58]

• ***Alpha-lipoic acid.*** Also known as thioctic acid, alpha-lipoic acid (ALA) is a naturally occurring compound synthesized by mitochondria that serves as a cofactor for enzymes producing ATP via the citric acid cycle.[59] In addition to being a potent antioxidant, ALA stimulates synthesis of glutathione and regenerates other antioxidants by reducing their oxidized forms—including vitamin C, vitamin E and coenzyme Q10—an attribute that has given ALA a reputation as the "antioxidant of antioxidants."

Because alpha-lipoic acid crosses the blood/brain barrier and distributes to mitochondria where its reduced form, dihyrolipoic acid (DHLA), is capable of regenerating other antioxidants, it may be particularly well-suited to pathologies characterized by excess mitochondrial production of reactive oxygen species, such as diabetes.[19]

ALA has been shown to reduce both small and large blood vessel complications of diabetes in animal models.[60,61] ALA treatment reduced retinal capillary damage, oxidative stress, nuclear factor kappa-beta activation and VEGF in an animal model of diabetic retinopathy. [62] Also, long-term use prevented the development of retinopathy in diabetic rats.[63]

Human RPE cells are protected from hyperglycemic oxidative stress and mitochondrial dysfunction when treated with ALA.[64] Recent evidence suggests ALA prevents deleterious "metabolic memory" (i.e., worsening of diabetic retinopathy after an initial period of poor blood glucose control, despite subsequent improved blood glucose control) by improving mitochondrial homeostasis.[65] ALA supplementation improved "endothelial dysfunction" (flow-mediated vasodilation) in patients with metabolic syndrome and impaired fasting glucose.[66] Though administration to human subjects with type 2 diabetes over two years did not result in statistically significant reductions in clinically significant macular edema, subjects in the treatment arm had a 14% lower relative risk of developing it.[67]

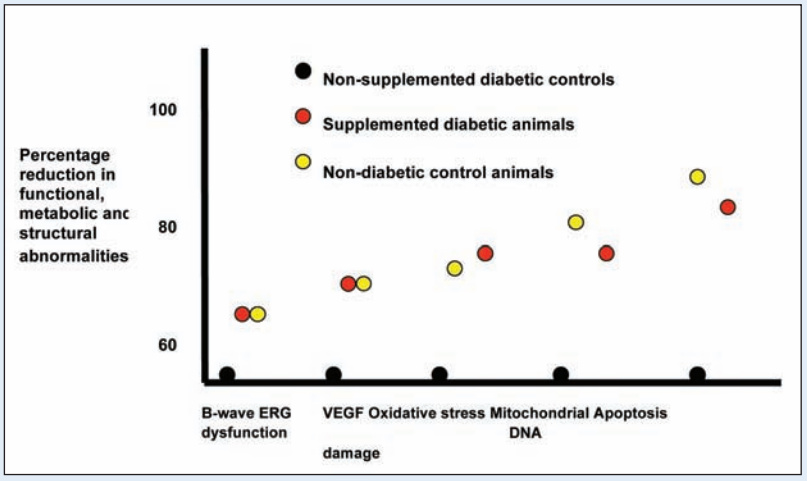
• ***Curcumin.*** This is a component of the Indian spice turmeric. It contains a number of polyphenolic molecules believed to modulate inflammation. Curcumin inhibited diabetes-induced elevation in levels of the retinopathic proteins IL-1β, VEGF and NF-kβ in a murine model of diabetes, without inducing amelioration of hyperglycemia, and prevents AGE-collagen cross linking in diabetic rats.[68,69] Curcumin also was shown to normalize elevated VEGF and tumor necrosis factor-alpha (TNF-α), the inflammatory cytokine, as well as to prevent early basement membrane changes associated with diabetic retinopathy in an animal model.[70]

Additionally, lecithinized curcumin was shown to improve retinal blood flow, retinal edema and visual acuity in subjects with DR over four weeks of supplementation.[71] It is

Beneficial Effects of Supplementation with the DiVFuSS Formula

An animal model prevented or normalized the following diabetes-induced retinal changes:

- **Dysfunction, as measured by b-wave ERG** (supplemented diabetic animals' ERG equivalent to non-diabetic controls and 30% better than non-supplemented diabetic controls).
- **VEGF expression** (supplemented diabetic animals' VEGF levels equivalent to non-diabetic controls and 40% lower than non-supplemented diabetic controls).
- **Oxidative stress** (supplemented diabetic animals produced 50% less reactive oxygen species [ROS] than diabetic controls and 20% less ROS than non-diabetic controls).
- **Damage to mitochondrial DNA** (supplemented diabetic animals had 50% less damage than non-supplemented diabetic controls).
- **Retinal capillary cell apoptosis** (supplemented diabetic animals had 70% less apoptosis than non-supplemented diabetic controls).



Data courtesy of Renu A. Kowluru, PhD, Kresge Eye Institute, Wayne State University.

noteworthy that DR rates are lower in Southern India—where turmeric consumption is highest—than in European and North American populations, after controlling for established risk factors.[72]

Yes, But Does Dietary Supplementation Work?

I have seen beneficial effects with some of these micronutrients in my practice (*see "Pills, Not Pulses," page 39*). This, of course, proves nothing. Only a large clinical trial will tell, but I am currently undertaking a small trial in my office using a combination of these supplements in patients with diabetes and mild to moderate non-proliferative diabetic retinopathy. The study aims to determine effects on visual function, spectral-domain optical coherence tomography results, and serum markers of inflammation (the Diabetes Visual Function Supplement Study – DiVFuSS; ClinicalTrials.gov Identifier: NCT01646047; Sponsored by ZeaVision, LLC).

In a 2013 ARVO poster, the test formula was shown to improve or normalize retinal structure, metabolism and function in an animal model of DR.[73] Specifically, it reduced mitochondrial damage, oxidative stress, activation of NF-kβ—as well as production of VEGF, ICAM-1 and MMP. Retinal function as assessed by β-wave ERG was preserved and, most significantly, apoptosis of retinal capillary cells was prevented without causing significant difference in blood glucose levels in treated and untreated animals.

Diabetic retinopathy continues to be a leading cause of vision loss, despite improvements in metabolic control and advancements in treatment. Though annual dilated eye exams make a tremendous difference in detecting and treating sight-threatening disease, many patients are still falling through the cracks. Though tighter blood sugar and blood pressure control certainly lowers patient risk, many do not achieve these goals, and some patients develop severe DR despite excellent control.

Use of targeted micronutrients may give us the opportunity to offer patients with diabetes something more than warnings about good disease control and regular dilated eye exams. It may give us a chance to do more than simply monitor for vision threatening diabetic retinopathy and eventual referral to retinal specialists for treatment. It offers an

opportunity to be proactive, rather than merely reactive, by addressing some of the biological mechanisms underlying the disease. ■

Dr. Chous specializes in diabetes eye care and education in Tacoma, Wash. He is a consultant to several diabetes-related companies and is receiving support for DiVFuSS from ZeaVision, LLC.

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Do Your Patients' Contact Lenses Match Their Lifestyle?

Many patients desire the freedom of constant vision correction without resorting to surgery; however, we find that many optometrists are reluctant to prescribe contact lenses for extended wear (EW) or continuous wear (CW). This gap between what the prescribing doctor believes and what the patient wants often results in a failure to fit patients in the best lens for their lifestyle.

Cause for Redirection

A recent survey of 141 offices in the U.S. revealed that 31% of contact lens wearers admitted to some amount of EW.[1] In fact, 64% of the patients who admitted to sleeping in their lenses for seven or more consecutive nights weren't sleeping in a lens FDA-approved for CW.[1]

If we can't break patients of this habit, perhaps we should instead consider prescribing these patients a contact lens designed for their lifestyle.

Educating patients on what it means to sleep in a contact lens and prescribing AIR OPTIX® NIGHT & DAY® AQUA contact lenses when appropriate are our best weapons for promoting successful contact lens wear for these patients.

The Cold Hard Facts

In 1981, the FDA approved low-Dk soft contact lenses for up to 30 days of EW.[2] Unfortunately, a sudden increase in presumed microbial keratitis (MK) followed, and the agency had to scale back the recommended EW period to seven consecutive days.[2] With the introduction of silicone hydrogel lenses in 2001, there was a resurgence of the concept of CW.

An extensive post-market surveillance study of more than 6,200 patients demonstrated the safety of 30-night CW of original NIGHT & DAY® contact lenses.[2] It established that there was no increase in the rate of MK in patients sleeping in their silicone hydrogel contact lenses for up to 30 continuous nights as compared with previous studies (18 per 10,000).[2]

A different post-market clinical trial revealed that patients who wore original NIGHT & DAY® contact lenses as CW had less signs and symptoms of dryness during and at the end of the day, redness, photophobia, lens awareness and blurred vision than patients fit in low-Dk hydrogels for daily wear only.[3]

"64% of patients who sleep in their lenses for 7+ consecutive nights weren't sleeping in a lens approved for continuous wear.[1]"

Identifying Your Sleepers

Knowing that CW is an appropriate alternative for the right patient, the next step is to reveal who the sleepers are in your practice. (The "typical" sleeper is a female established contact lens wearer in her mid-30s with more than 3 D of myopia.[1]) ***Surprisingly, only 44% of ECPs are asking every patient if they sleep in their lenses.[1]*** A piece of advice: don't bluntly ask a patient if they sleep in their lenses; ask how many nights they sleep in their lenses.

I strive for all of my patients to have a symptom-free wearing experience, and I keep the conversation simple: "Sleeping in contact lenses increases the risk of infection and requires a more advanced technology lens. I am prescribing you AIR OPTIX® NIGHT & DAY® AQUA contact lenses, which are approved for up to 30 nights of CW.** It is the most breathable* soft lens available[4] and has a plasma surface treatment that resists deposits, but you need to replace it on the first of each month. You are approved for a one-year supply and our staff can help you understand your insurance and any available rebates."

A Clear Choice for Sleepers

The AIR OPTIX® NIGHT & DAY® AQUA contact lens is the number-one lens recommended by eye care practitioners for sleepers.[5] It's also the lens I prescribe for all my contact lens patients who desire the convenience and freedom of uninterrupted vision correction.

*Dk/t = 175 @ -3.00D. **Extended wear for up to 30 continuous nights, as prescribed by an eye care practitioner.

References: 1. A survey of 2,115 daily and extended wear contact lens patients. Alcon data on file, 2012. **2.** Schein O, McNally J, Katz J, Chalmers R, et al. The incidence of microbial keratitis among wearers of a 30-day silicone hydrogel extended-wear contact lens. Ophthalmology. 2005;112(12):2172-79. **3.** Bergenske P, Long B, Dillehay S, et al. Long-term clinical results: 3 years of up to 30-night continuous wear of lotrafilcon A silicone hydrogel and daily wear of low-Dk/t hydrogel lenses. Eye & Contact Lens. 2007;33(2):74-80. **4.** Based on the ratio of lens oxygen transmissibilities; Alcon data on file, 2009, 2010. **5.** In a survey of 203 optometrists in the U.S. Alcon data on file, 2011.

See product instructions for complete wear, care, and safety information.

Rx only

Important information for AIR OPTIX® NIGHT & DAY® AQUA (lotrafilcon A) contact lenses: Indicated for vision correction for daily wear (worn only while awake) or extended wear (worn while awake and asleep) for up to 30 nights. **Relevant Warnings:** A corneal ulcer may develop rapidly and cause eye pain, redness or blurry vision as it progresses. If left untreated, a scar, and in rare cases loss of vision,may result. The risk of serious problems is greater for extended wear vs. daily wear and smoking increases this risk. A one-year post-market study found 0.18% (18 out of 10,000) of wearers developed a severe corneal infection, with 0.04% (4 out of 10,000) of wearers experiencing a permanent reduction in vision by two or more rows of letters on an eye chart. **Relevant Precautions:** Not everyone can wear for 30 nights. Approximately 80% of wearers can wear the lenses for extended wear. About two-thirds of wearers achieve the full 30 nights continuous wear. **Side Effects:** In clinical trials, approximately 3-5% of wearers experience at least one episode of infiltrative keratitis, a localized inflammation of the cornea which may be accompanied by mild to severe pain and may require the use of antibiotic eye drops for up to one week. Other less serious side effects were conjunctivitis, lid irritation or lens discomfort including dryness,mild burning or stinging. **Contraindications:** Contact lenses should not be worn if you have: eye infection or inflammation (redness and/or swelling); eye disease, injury or dryness that interferes with contact lens wear; systemic disease that may be affected by or impact lens wear; certain allergic conditions or using certain medications (ex. some eye medications). **Additional Information:** Lenses should be replaced every month. If removed before then, lenses should be cleaned and disinfected before wearing again. Always follow the eye care professional's recommended lens wear, care and replacement schedule. Consult package insert for complete information, available without charge by calling **(800) 241-5999** or go to **myalcon.com**.

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Diabetic Eye Disease:

Lessons from a Telemedicine Reader

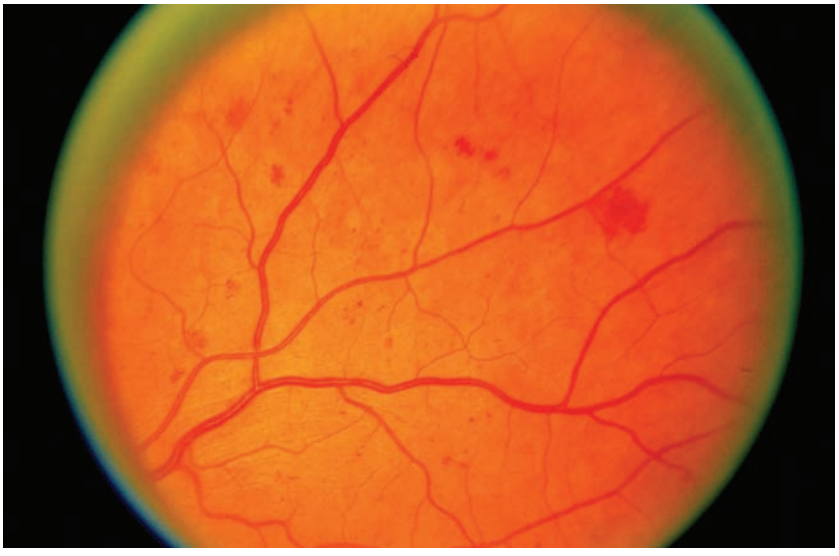
A remote reader sees dozens of retinas in a day. Here's how to put a reader's knowledge to practical use for your patients. **By Erin Giles, OD**

The pandemic of diabetes is on the rise in the United States and across the globe, resulting in growing numbers of new-onset blindness in working-age adults. The National Eye Institute reports that nearly half (40% to 45%) of Americans with diabetes have diabetic retinopathy. The NEI estimates that 7.7 million Americans ages 40 and older have some degree of diabetic eye disease. That represents an 89% increase since 2000, and projections anticipate another jump of 75%, to 13.5 million, by 2020.

In short, we can expect a huge influx of diabetes patients requiring eye care over the next few years. But how can we handle all of them?

Standardized diagnostic protocols will help. So can telemedicine. (*See "Telemedicine is Good Medicine," page 50.*) I've seen evidence of this with my own eyes. For the past seven years, I've been fortunate to be part of the Indian Health Service-Joslin Vision Network (IHS-JVN) Diabetic Retinopathy Telemedicine Program. My experience with this innovative technology has shown me that it's also relevant in conventional clinic-based eye care.

This article offers some clinical insights for better diagnosing and managing diabetic eye disease, which I've learned through my experiences reading the images of more than 20,000 patients from across the country.



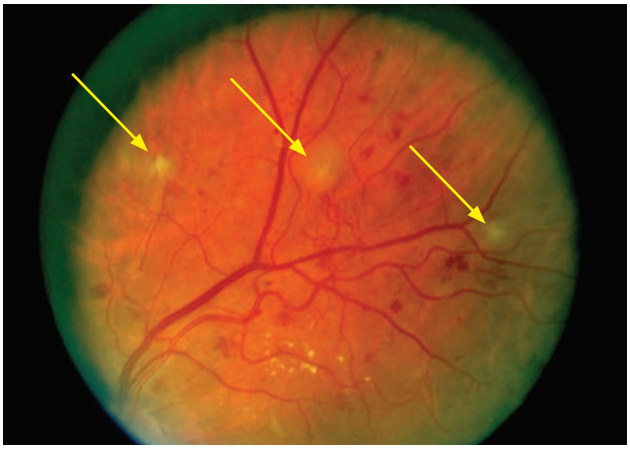
Photos: Early Treatment Diabetic Retinopathy Study Research Group. Fundus photographic risk factors for progression of diabetic retinopathy. ETDRS report number 12. Ophthalmology. 1991 May;98(5 Suppl):823-33. Used with permission.

Telemedicine readers use ETDRS standard photographs, such as this one showing hemorrhages and microaneurysms (HMAs), as a basis for comparision. A patient who has equal or lesser amounts of HMAs in any retinal quadrant, with no other diabetic retinopathy, would be diagnosed with mild nonproliferative diabetic retinopathy. However, a patient with four retinal quadrants greater than this would be diagnosed with severe nonproliferative diabetic retinopathy.

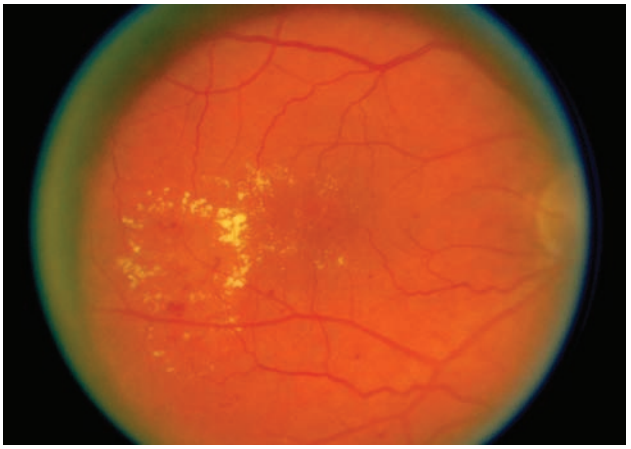
Have Some Standards

Most of us were trained to diagnose diabetic retinopathy (DR) by clinical impression; however, the science of DR diagnosis was developed in a standardized fashion. Many of the features of the IHS-JVN standardized approach to diagnosis and management of DR can be easily implemented in a typical eye clinic.

While the scope of this article doesn't allow a detailed discussion



Cotton-wool spots (soft exudates). This finding elevates the level of diabetic retinopathy to at least moderate nonproliferative diabetic retinopathy.

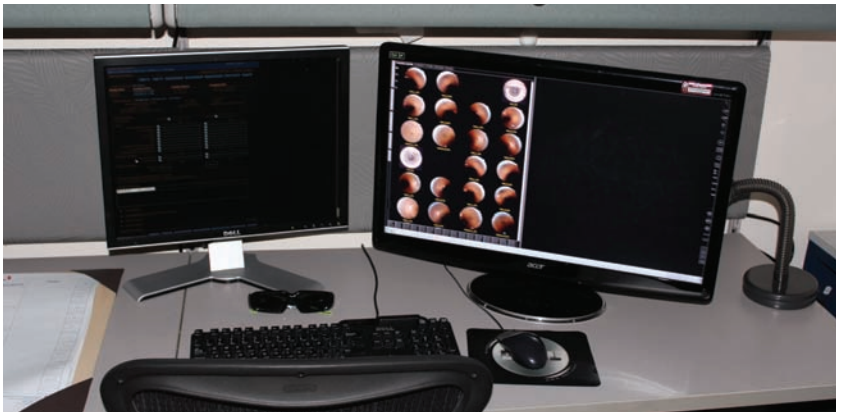


This photo shows hard exudates in the macula, which can be used to substantiate the diagnosis of clinically significant macular edema.

of the evidence basis for risk stratification of DR, we can easily refer to the Early Treatment Diabetic Retinopathy Study (ETDRS) and its standardized photographs to assist in standards-based clinical diagnosis of DR.[1]

The key is the quantification/localization of critical features, such as hemorrhages/microaneurysms (HMA), exudates, intraretinal microvascular anomalies (IRMA), venous caliber changes (as seen in venous beading) and neovascularization. A few of the ETDRS standard photographs, shown here, provide examples of these features and how they can be used for comparison to support your clinical diagnosis.

Although sophisticated telemedicine technology—using computer image enhancement and computer-assisted decision support—provides considerable diagnostic advantages for IHS-JVN readers, reliable and reproducible clinical diagnosis can be achieved without these digital enhancements. Of course, it takes careful study and repeated use of these slides to become proficient in standards-based diagnosis of DR, but improving these skills improves diagnostic accuracy and consistency, and enhances patient management and referrals.



One of the retina telemedicine reading stations at the IHS-JVN National Reading Center in Phoenix. The glasses are used to view stereoscopic images.

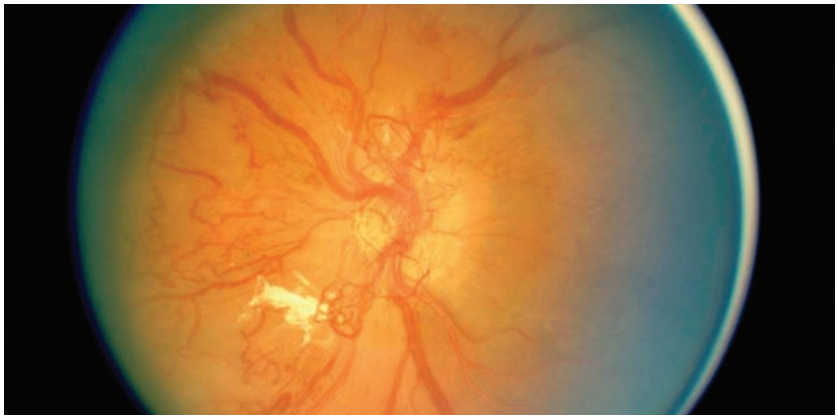
Here are some observations and lessons I've learned from my IHS-JVN telemedicine experience that you can use in conventional clinical practice.

Lesson 1: Small Pupils Can Cause Big Problems

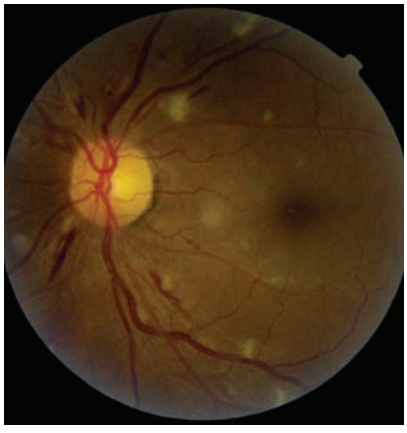
In both nonmydriatic telecapture and mydriatic live-eye exam, small pupil size can cause difficulty for clinicians. Because patients with diabetes often dilate poorly, at slower rates and often have media opacities, be certain to allow adequate time for patients to dilate. This simple pearl is often forgotten in busy practice.

Lesson 2: Hone in on High-Risk Areas

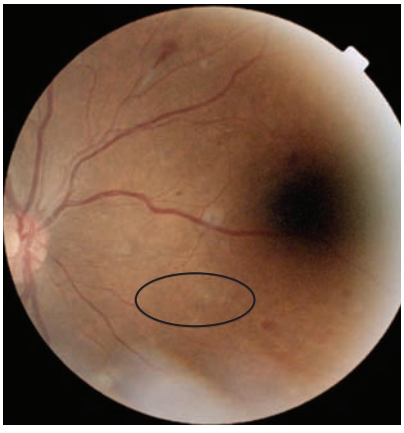
Certain retinal locations—i.e., the posterior pole, the area immediately nasal to the optic disc and the areas superior and superior temporal to the optic disc—are more likely to demonstrate high-risk characteristics of DR. The JVN validation studies document the value of special scrutiny of these locations.[2]



This photo illustrates neovascularization of the disc (NVD). A patient who shows a comparable level of disc neovascularization is considered to have proliferative diabetic retinopathy with high-risk characteristics.



Flame-shaped hemorrhages and cotton-wool spots, characteristic of hypertensive or renal/nephrophathy-associated changes, encircle the optic disc 360°.



The oval shows a subtle area of "featureless retina"—a focal area of capillary dropout—at risk for proliferative and pre-proliferative diabetic changes.

Although diabetic retinopathy certainly exists outside of these defined parameters, it's unusual that the level of pathology in other locations would be greater than those within these three areas. This can be clinically useful for patients in which viewing the fundus proves difficult, such as those with media opacity, light sensitivity or poor fixation.

Lesson 3: Know the Risks

A careful review of systems can quickly reveal important data to help better define the patient's risk of onset and progression of diabetic retinopathy:

- Age of onset and duration of diabetes mellitus (DM)
- Control of hemoglobin A1C, blood pressure and lipids
- Presence of peripheral neuropathy
- Renal failure
- Amputation(s)

For example, knowing the patient's *duration of diabetes*, HbA1C and other health conditions, such as hypertension, is of utmost importance. Specifically, the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) found that the prevalence of diabetic retinopathy varied from 28.8% in adults (age 30 and older) who had diabetes for fewer than five years to 77.8% in adults who had diabetes for 15 or more years.[4]

Clinically, I've observed that the duration of diabetes seems to be the greatest single risk factor for the development of diabetic retinopathy, particularly if the patient has poor glycemic control. Patients with other comorbidities, such as cardiovascular disease, will have earlier demonstration and progression of diabetic retinopathy and other vascular changes, so they may require more frequent follow-up.

Coexisting hypertensive retinopathy can often confound the diagnosis of diabetic retinopathy, but some clinical features help distinguish the predominant factor driving the clinical presentation. Flame-shaped retinal hemorrhages are suggestive of hypertensive retinopathy, but the cotton-wool spots that encircle the optic disc can also represent renal/nephropathy-associated changes. Cotton-wool spots that have a homogenous distribution throughout the posterior pole are most likely of diabetic origin.

Capillary nonperfusion of the retina, or "featureless retina," is another subtle finding that assists in risk stratification of the diabetic retina, yet remains a point of controversy in the literature. In addition to capillary dropout, no overlying hemorrhages or cotton-wool spots can be observed in a retina that is otherwise pathologic for diabetic retinopathy. This appearance can represent an underlying ischemic zone, which increases the risk for neovascular progression.

Handle these cases with caution and be vigilant to rule out neovascular disease. These patients should

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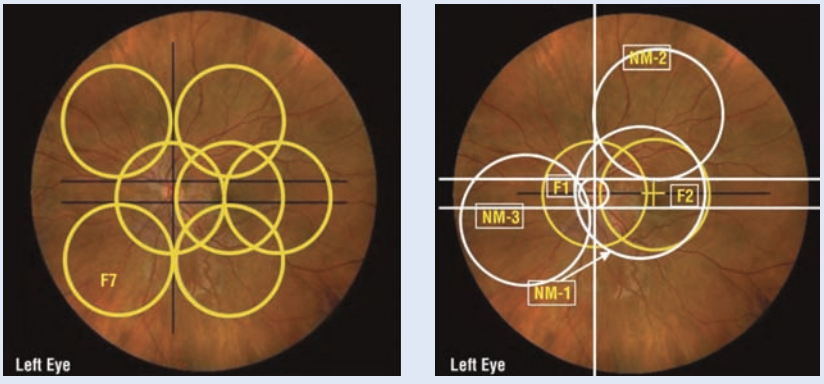
Telemedicine is Good Medicine

Remote diagnosis and management of diabetic retinopathy (DR) is a great departure from the current community practice. The Joslin Vision Network (JVN) was developed as a collaborative effort between the Joslin Diabetes Center (an affiliate of Harvard Medical School in Boston), the Veterans Administration (VA) and the Indian Health Service (IHS).

The impetus for JVN's DR telemedicine program was the sustained failure of conventional eye clinic-based programs to provide more than 50% of diabetes patients with DR surveillance that met the standard of care.[3] This is likely a large contributor to underutilization of timely treatment, with DR remaining the leading cause of new blindness among working-age adults—even though a method for significantly reducing serious vision loss due to DR has been known for almost four decades.

Although nonmydriatic photographic surveillance intuitively may seem to be of lesser quality than a conventional dilated retinal examination, the evidence and my personal experience argues otherwise in the case of diabetic retinopathy.

From the start, this program was designed to provide reliable and cost-effective diagnosis of DR in a setting that meets, and even improves upon, DR standards of care. IHS-JVN uses innovative imaging techniques and software that allow the reader to appreciate retinal stereopsis, which is critical for the evaluation of diabetic macular edema and other retinal and optic disc anomalies. The program has demonstrated a diagnostic sensitivity and specificity commensurate with ETDRS, and therefore equal or superior to a conventional DR examination.[2,3]



Images of the same eye show different methods to evaluate the retina—the Early Treatment Diabetic Retinopathy Study (ETDRS, *left*) and the Joslin Vision Network Diabetes Eye Care Program (JVN, *right*). ETDRS photos encompass a broad retinal area, whereas JVN imaging focuses primarily on the posterior pole (NM-1), superior temporal retina (NM-2) and nasal (NM-3) retinal fields. Interestingly, studies have proven JVN imaging to be equally efficacious in the grading of diabetic retinopathy against dilated eye exams by retinal specialists and the gold standard of imaging, 35mm stereo slides.[2,3]

My experience over the past seven years as an IHS-JVN reader is that this program is a highly reliable method for diagnosing the specific level of DR and diabetic macular edema among American Indians and Alaska Natives; when combined with access to the patient's general health record, it enables DR management equivalent to or better than a live dilated diabetic retinopathy evaluation. In addition, the IHS-JVN has been validated for a broad range of non-DR pathology, expanding its clinical versatility.[2]

Telemedicine allows surveillance of DR in a primary care setting with the opportunity to markedly improve the annual DR examination rate in a cost-effective manner—providing nearly 12,000 imaging exams annually in the Indian Health Service population alone.[5,6] The IHS-JVN has been successful in the IHS, and similar experiences are evident in other programs such as at the VA and the Joslin Diabetes Center.

have a more careful biomicroscopic evaluation of suspicious areas in question, using a contact fundus lens to rule out subtle IRMA and neovascularization elsewhere (NVE).

Depending on the degree of presumed capillary dropout, consider fluorescein angiography to better quantify the degree of nonperfusion, rule out macular ischemia (especially in such patients who also have reduced best acuity), as well as delineate areas suspicious for neovascular disease.

Lesson 4: A Picture is Worth a Thousand Words

One of the advantages of the telemedicine program is the ability to use the patients' fundus photographs as the platform for educating them about DR. Some diabetes patients have a hard time understanding how they are being affected by their condition, but a picture—particularly of their own fundus—provides compelling, intuitive instruction.

If you're unable to take a photo of the patient's own fundus, another photo showing DR can be used instead.

Take time to explain your diagnosis, recommendations and follow-up plan thoroughly. Make appropriate referrals to primary care practitioners for optimal glycemic, BP and lipid management.

Building contacts with primary care physicians will also increase patient recruitment for diabetic eye exams.

Nearly 27% of Americans 65 or older have diabetes, the American Diabetes Association reports. If current trends continue, perhaps as many as one in every three Americans will have diabetes by 2050, according to the Centers for Disease Control and Prevention.

Improving the quality and standardization of the diabetic retinal exam will help to build your practice and better serve this growing and already underserved population.

Even so, long-standing trends suggest that the conventional eye clinic-based exams may not be effective in reaching all the patients with diabetes. Telemedicine in a primary care medical setting has shown the ability to help.

Be aware that telemedicine is not in competition with clinical optometry, because it often reaches a different sector of patients who are not receiving eye care. In fact, the future may hold a place for using telemedicine in small optometric practices in much the same way the IHS-JVN has, by coordinating care with primary care providers through electronic medical record referrals. Telemedicine has great potential to expand the boundaries of evidence-based DM eye care and to close established barriers to care.

Our ultimate goal is the same as yours: to provide the best available care we can to help diagnose and manage these patients. ■

In addition to being a certified telemedicine reader at the IHS-JVN National Reading Center in Phoenix, Dr. Giles is a clinical optometrist practicing at the Phoenix Indian Medical Center.

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15th Annual Diabetes Report

Evolving Therapies for Diabetic Macular Edema: Options Abound

Here's a primer on the great strides eye care has made in fighting this common cause of visual disability. **By Marta C. Fabrykowski, OD**

The visual toll exacted by diabetic macular edema (DME) is steep. One in four patients will lose 15 letters of acuity within three years if the disease remains untreated.[1] For decades, DME patients had few options beyond laser photocoagulation—an imprecise intervention that poses risks of its own while also failing to offer much improvement in the worst cases of vision-impairing DME, where the need for improvement is most acutely felt.

Fortunately, recent years have witnessed considerable progress in our understanding of the pathophysiology of DME, which has in turn led to growth in the development of new therapies. The once-subdued field of DME treatment is suddenly flourishing.

The goal of this review is to briefly discuss our understanding of DME, as well as to elucidate the current state of ocular treatment options—from mainstays to the most recent clinical trials for this complex condition. As diabetes rates continue to rise, we will likely see more of these patients in our offices, so it is in our professional interest to stay informed about current developments.

DME 101

The Early Treatment Diabetic Retinopathy Study (ETDRS) defined DME as "any retinal thickening within 500µm of the center of the macula; hard exudates within 500µm of the center of the macula with adjacent retinal thickening; retinal thickening at least one disc area in size, any part of which is within one disc diameter of the center of the macula."[1] For the purposes of this article, we will consider DME as essentially equivalent to clinically significant macular edema (*figure 1*).

Diabetic macular edema is the most frequent cause of vision loss related to diabetes.[2-4] The Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) found the 14-year incidence of DME in patients with type 1 diabetes to be 26%.[5] Similarly, the Diabetes Control and Complications Trial (DCCT) reported that nearly 27% of type 1 diabetes patients develop DME within nine years of onset.[6] For type 2 insulin-dependent patients, the 10-year incidence is 25.4% and for type 2 non-insulin dependent individuals that figure is 13.9%. Because almost 26 million children and adults in the US have diabetes—a staggering 8.3% of the population—a large number of patients are at risk for DME.[7]

The pathogenesis of diabetic macular edema is multifactorial. It occurs primarily through a disruption of the blood/retinal barrier (BRB) and subsequent accumulation of fluid, inflammatory material and growth factors within the layers of the macula (*figure 2*).[2,8] The breakdown of retinal integrity and leakage of vasoactive factors may lead to the storage of pro-inflammatory factors in the vitreous.[8]

Laser Photocoagulation

For the first 25 years following the publication of the ETDRS trial in 1985, thermal laser was the mainstay treatment for DME.

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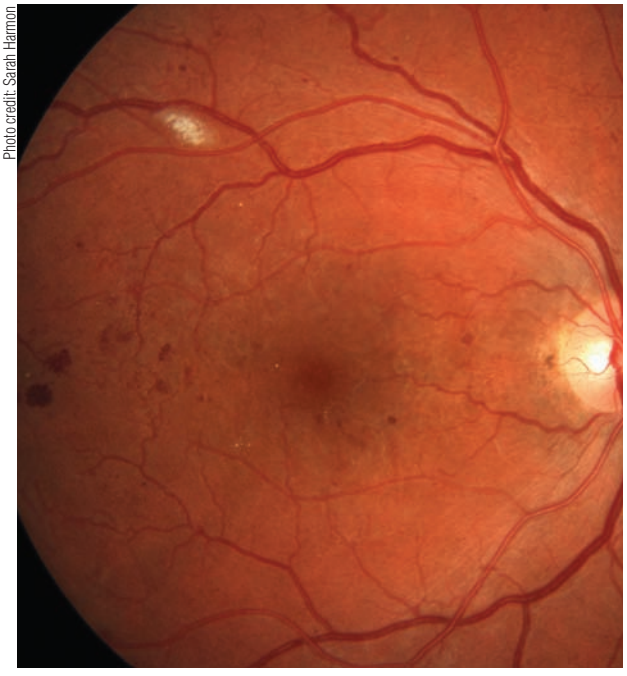

1. Diabetic retinopathy with suspected macular edema. Note the hard exudates located within 500µm of the fovea's center.

Specifically, the indication was for "prompt, focal/grid laser to microaneurysms or areas of macular edema."[1] Success following such laser treatments was defined as reducing by half the number of patients who experienced a doubling of the visual angle (i.e., going from 20/40 to 20/80 visual acuity).

Although panretinal photocoagulation, as performed during the ETDRS trial, was successful in reducing rates of visual loss due to DME, there were a few problems. Many patients did not recover lost vision, and a subset of patients were unresponsive to therapy.[9] In addition, a subset of patients exhibited diabetic pathology near the fovea, where laser would cause permanent structural damage and potentially dense central scotomas.

Anti-VEGF Therapy

The need for a treatment for patients whose macular edema involved the fovea ignited the search for non-structurally damaging intraocular pharmacologic agents. The Diabetic Retinopathy Clinical Research Network (DRCR.net) compared standard laser therapy with combination therapy (laser plus intravitreal anti-VEGF), and laser therapy against intravitreal anti-VEGF alone. The researchers found superior visual outcomes among patients who received combined injection and focal laser vs. those who received focal laser alone. Further, they suspect anti-VEGF agents decrease the release of prostaglandins (thus curbing inflammation) and inhibit expression of the VEGF gene, thereby decreasing neovascularization.[9]

• ***Lucentis.*** In August 2012, ranibizumab (Lucentis, Genentech)—previously FDA-approved for intravitreal injection in patients with AMD—gained FDA approval to treat DME. Two subsequent trials, RESTORE and REVEAL, demonstrated the usefulness of ranibizumab.[4]

The RESTORE trial indicated that ranibizumab as monotherapy or in combination with macular laser provided superior visual acuity over patients treated with only macular laser.

The REVEAL trial was similar to the RESTORE, except that it followed an Asian cohort. It also validated the superior outcome of ranibizumab and ranibizumab plus laser when compared to laser monotherapy.

• ***Avastin.*** Another anti-VEGF therapy, bevacizumab (Avastin, Genentech)—approved for intravenous use in cancer patients—has been used off-label as an intravitreal injection to treat both AMD and macular edema.[10] Bevacizumab performed well in the RIDE, RISE and RESTORE trials.[10,11] Additionally, in the Bevacizumab or Laser Therapy (BOLT) study, patients who received bevacizumab injections every six weeks exhibited superior visual acuity compared to those who received macular laser therapy every four months.[12]

• ***Eylea.*** The newest addition to the ocular anti-VEGF injection family is aflibercept (Eylea, Regeneron). The agent features the same mechanism of action as ranibizumab and bevacizumab, but has a higher binding affinity for VEGF that can maintain therapeutic effect for up to three months.[9] In some patients, the injection provides extended action, meaning that less frequent dosing may be possible compared to other anti-VEGF agents.

The DME and VEGF Trap-Eye: Investigation of Clinical Impact (DAVINCI) trial demonstrated that at six months post-injection aflibercept produced better visual outcomes than laser photogoagulation.

Currently, the VISTA (VEGF Trap-Eye In Vision Impairment Due to DME) study is ongoing. It is a three-year trial comparing aflibercept to laser monotherapy, and the manufacturer hopes the FDA will approve it for DME.[11]

Among anti-VEGF injectables, side effects are rare but include retinal detachment and endophthalmitis. More unlikely side effects include raised intraocular pressure and accelerated cataract formation.[3]

Corticosteroids

Another category of ocular injectables is the corticosteroids. There is mounting evidence that inflammation may play a significant role in the development of DME.[2,9] It is suspected that activation of inflammatory mediators in the vitreous causes subsequent adhesion and endothelial cell damage.[2] Endothelial cell death then contributes to the breakdown of the BRB and can lead to fluid accumulation in the macula.[2,9] The use of steroids is thought to curb the inflammatory breakdown of the BRB, inhibit the expression of VEGF and decrease the release of prostaglandins.[2,8,9,13]

Most injectable corticosteroids are administered intravitreously. Triamcinolone acetonide (Kenalog, Bristol-Myers Squibb) is the most widely used, and was studied as the primary treatment for DME by the DRCR.net researchers. Results showed that while triamcinolone acetonide may be less effective than laser photocoagulation as a primary treatment, it may benefit eyes that are otherwise unresponsive to laser treatment.[8] Side effects of intravitreal corticosteroids include accelerated development of cataracts and elevated intraocular pressure—the latter of which may lead to glaucomatous optic nerve damage.[3]

A newer formulation of intravitreal corticosteroid, a preservative-free version of triamcinolone called Triesence (Alcon), was approved by the FDA to treat sympathetic ophthalmia, temporal arteritis, uveitis and ocular inflammatory conditions unresponsive to topical corticosteroids.[13] Triesence could be used off-label to treat DME. Its advantage over Kenalog lies in the preservative issue: triamcinolone acetonide contains benzyl alcohol, which could be toxic to the eye. Triesence obviates such concerns.

Intravitreal corticosteroids also may be delivered via sustained-release implant. The two primary technologies—fluocinolone (Retisert, Bausch + Lomb) and dexamethasone (Ozurdex, Allergan)—reduce injection frequency, but are relatively expensive. This approach may be too aggressive for many DME patients, however. The application of Retisert requires intraocular surgery, including a 4mm sclerotomy. Potential adverse effects of such a surgery include endophthalmitis, accelerated cataract formation, retinal detachment, vitreous hemorrhage and hypotony.

It is worth noting that these agents are FDA approved for different indications. Retisert, purported to last approximately 30 months, is approved for chronic non-infectious uveitis. Ozurdex, whose sustained release is thought to last one to three months, is approved for macular edema following branch retinal vein occlusion or central retinal vein occlusion, and for the treatment of non-infectious uveitis in the posterior segment.

The potential injection-related adverse effects of these corticosteroid implants are similar to those of the anti-VEGF agents. However, steroids appear to increase risks for both elevated intraocular pressure and formation of cataracts. Short-term, the side effects are well tolerated, but a three-year follow-up of dexamethasone implants demonstrated high rates of cataract and glaucoma requiring surgical intervention.[8]

Finally, some intraocular steroids can be delivered as a sub-Tenon's injection (e.g., triamcinolone). In this instance, because the drug enters the ocular environment through a periocular route, the side-effect profile is much safer. However, patients are at risk for infection, discomfort and subconjunctival hemorrhage.

Vitrectomy

Although it does not receive the level of attention that new therapies like anti-VEGF and steroids garner, surgical intervention still has a place in the treatment algorithm. There are a number of arguments in favor of vitrectomy when photocoagulation and intravitreal injections prove ineffective.

The role of the vitreous in DME is thought to be twofold: (1) mechanical traction on the vitreoretinal interface, and (2) an accumulation of factors altering vascular permeability (e.g., VEGF) in the vitreous.[3,8,9] One study indicated that vitreomacular separation was associated with an increased rate of spontaneous resolution of macular edema.[9]

Pars plana vitrectomy with membrane peel is the primary surgical option. This

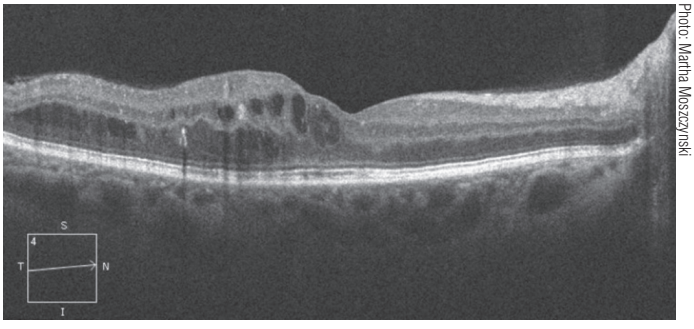

Photo: Martha Moszczynski

2. Optical coherence tomography scan of a patient with diabetic macular edema. Of significance are the focal cystic changes, with secondary disorganization of the sensory retinal layers.

is an outpatient procedure in which the vitreous gel is removed from the eye, most often including an internal limiting membrane peel, thus removing both potential culprits. Sometimes macular surgery might include injection of a gas, either C_3F_8 or SF_6, which may require patients to remain face-down for a few days, in some rare cases for more than a week. Though patients may experience varying levels of postoperative discomfort, success rates are fairly high.

In the DRCR.net research, vitrectomy for DME was studied in patients with moderate vision loss and vitreomacular traction. Postoperatively, 68% had a 50% reduction in macular thickness at six months.[14] Visual acuity improved by 10 letters in 38% of patients and deteriorated by 10 letters in 22%. Preliminary studies by the DRCR network reported six-month and one-year outcome results after vitrectomy. At six months, both visual acuity and macular thickening improved in 28% to 49% of patients and worsened in 13% to 31%.

Postoperative complications after vitrectomy include retinal detachment, endophthalmitis, vitreous hemorrhage, elevated intraocular pressure and cataract progression.[9]

At two-year follow-up, the researchers determined that focal/grid laser produced visual acuity gains of two lines or more in one-third of eyes with center-involved DME. However, one-fifth of the laser-treated eyes lost two or more lines of visual acuity over the same time period—thus, the search for more effective therapies continues.[9]

Pharmacologic means can also achieve vitreolysis. Ocriplasmin (Jetrea, ThromboGenics) is a proteolytic enzyme that targets fibronectin and laminin, components of the vitreoretinal interface.[16] In October 2012, the FDA approved Jetrea as an intravitreal injection for symptomatic vitreomacular adhesion (VMA). Approval was based on two clinical studies that collectively found VMA resolved in 26% of patients treated with Jetrea compared to 10% of those treated with placebo. Side effects were similar in both groups and included floaters, subconjunctival hemorrhage (from injection site), eye pain and blurred vision. At this time, no clinical trials of Jetrea in DME or diabetic retinopathy are underway. However, ThromboGenics is working with Bicycle Therapeutics to develop novel DME therapies that use bicyclic peptides to reduce vascular permeability.

Metabolic Considerations

Although we've chiefly focused on ocular therapeutic options for DME, it would be remiss not to mention another crucial topic regarding the diabetic patient: metabolic control. The DCCT study of patients with type 1 diabetes and the WESDR established that a higher level of glycosylated hemoglobin is a significant risk factor for DME.[9] It has also been well established that tight control of hyperlipidemia and systemic hypertension lead to a lower rate of micro-vascular complications.[9,16] Working with the patient to achieve optimal systemic medical control allows for the best prognosis following ophthalmic therapy.

The ocular effects of diabetes resound loudly in terms of vision impairment. In our fight against these afflictions, focal or grid laser photocoagulation remains the first-line treatment in a majority of patients with non–center-involving DME.[3] For the latter scenario, intravitreal injection of anti-VEGF or corticosteroids is more commonly used.[9] For those unresponsive to injections, vitrectomy may be a viable option. Early detection and treatment of diabetic macular edema is vital in preserving vision in the diabetes patient. As new and improved interventions are developed, treatment regimens will also change, and so will our conversations with our patients. ■

Dr. Fabrykowski is on staff at the Manhattan Eye, Ear and Throat Hospital Faculty Ophthalmology Practice, operated by Lenox Hill Hospital, in New York. *She thanks William Schiff, MD, for assistance with this manuscript.*

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A COMPROMISED CONTACT LENS SURFACE CAN COMPROMISE PATIENT COMFORT

BY DR. JOHN PRUITT, PHD

John Pruitt currently serves as Project Head, Biocompatibility Projects in Alcon Vision Care's Research and Development department.

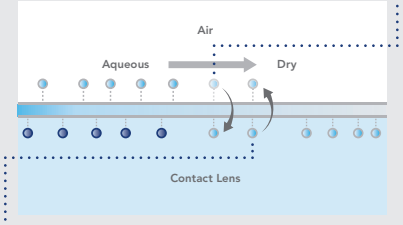
Patients don't want to think about their contact lenses. But with some silicone hydrogel materials, dehydration and deposit buildup can interrupt comfortable lens wear. A compromised lens surface can be at the root of the problem.

There's more to the surface than meets the eye

While the surface of a silicone hydrogel contact lens may seem static, it's actually quite an active component. Silicone hydrogel contact lenses contain both hydrophobic (water-repelling) and hydrophilic (water-loving) polymers that move and reorient at the surface during wear[1]—particularly when exposed to air and tear film changes between blinks.

Exposure to air sets the SiHy surface in motion

Hydrophilic (water-loving) molecules on the contact lens surface rotate inward seeking more moisture.



Hydrophobic (water-repelling) silicone sites rotate outward at the same time.

This results in **hydrophobic spots** on the surface of the contact lens that attract lipids and protein, resist rewetting and may cause discomfort.

A lot depends on the surface dynamics of a silicone hydrogel contact lens. It has been shown that some silicone hydrogel contact lens materials can attract up to 31X more deposits than other available silicone hydrogel contact lens options[2,3] (Fig.1)

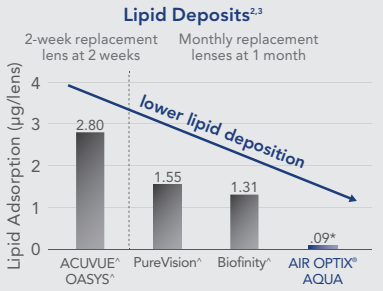
Fig. 1 – Surface defends against daily deposits

ACUVUE^ OASYS^ contact lenses
No permanent plasma treatment and an uneven surface[4]

Biofinity^ contact lenses
No permanent plasma treatment[5]

PureVision^ contact lenses
Surface made up of silicate islands that do not completely cover the surface[4]

AIR OPTIX® AQUA contact lenses
A permanent, chemically-bonded plasma treatment for a smooth, continuous surface[4]



*All differences between AIR OPTIX AQUA® contact lenses and competitive brands statistically significant (p<0.0001).

Manufacturers attempt to defend their contact lenses in different ways

Taking a closer look at silicone hydrogel contact lens technology sheds light on different manufacturers' attempts to protect lenses from dryness and deposits by masking silicone molecules on the lens surface.

ACUVUE^ OASYS^ contact lenses are made of a material containing polyvinyl pyrrolidone (PVP). This binds to water, but does not completely mask the silicone which leads to increased lipid deposits. With substantial silicone mobility, silicon levels reach approximately 10% at the surface of a dry contact lens.[6,7]

Biofinity^ contact lenses are made of a material composed of modified silicone macromers, making the lenses more wettable. However, the lens still allows silicone to be exposed at the surface—attracting lipids that decrease wettability. Silicone remains mobile with large levels of silicon present at the surface (>10%) when the contact lens is exposed to air.[6,8]

PureVision^ contact lenses undergo plasma oxidation, which converts surface silicone to silicate "glass." The surface cracks produce "glass-like" silicate islands. Exposed silicone in the cracks results in high lipid uptake.[6,9,10]

Lotrafilcon B contact lenses, such as **AIR OPTIX® brand contact lenses,** feature a unique, permanent plasma surface created by a fusion process. This permanent surface minimizes the mobility of the hydrophilic and hydrophobic sites during blinks by preventing the silicone in the lens material from being exposed to the air.[10] This smooth, protective surface allows tears to spread evenly over it, promoting moisture retention and minimal deposit buildup. With surface integrity that lasts throughout the wearing period, less than 1% silicon is measured at the surface of a dry contact lens.[8]

Conclusion

The silicone in silicone hydrogel contact lenses is highly desirable for improved oxygen transmission, but silicone can lead to poor wetting and lipid deposits. Look closer at the contact lens surface to achieve superior deposit resistance, clear vision and consistent comfort.

^Trademarks are the property of their respective owners.

Important information for AIR OPTIX® AQUA (lotrafilcon B), AIR OPTIX® AQUA Multifocal (lotrafilcon B) and AIR OPTIX® for Astigmatism (lotrafilcon B) contact lenses: For daily wear or extended wear up to 6 nights for near/far-sightedness, presbyopia and/or astigmatism. Risk of serious eye problems (i.e., corneal ulcer) is greater for extended wear. In rare cases, loss of vision may result. Side effects like discomfort, mild burning or stinging may occur.

Important information for AIR OPTIX® NIGHT & DAY® AQUA (lotrafilcon A) contact lenses: Indicated for vision correction for daily wear (worn only while awake) or extended wear (worn while awake and asleep) for up to 30 nights. **Relevant Warnings:** A corneal ulcer may develop rapidly and cause eye pain, redness or blurry vision as it progresses. If left untreated, a scar, and in rare cases loss of vision, may result. The risk of serious problems is greater for extended wear vs. daily wear and smoking increases this risk. A one-year post-market study found 0.18% (18 out of 10,000) of wearers developed a severe corneal infection, with 0.04% (4 out of 10,000) of wearers experiencing a permanent reduction in vision by two or more rows of letters on an eye chart. **Relevant Precautions:** Not everyone can wear for 30 nights. Approximately 80% of wearers can wear the lenses for extended wear. About two-thirds of wearers achieve the full 30 nights continuous wear. **Side Effects:** In clinical trials, approximately 3-5% of wearers experience at least one episode of infiltrative keratitis, a localized inflammation of the cornea which may be accompanied by mild to severe pain and may require the use of antibiotic eye drops for up to one week. Other less serious side effects were conjunctivitis, lid irritation or lens discomfort including dryness, mild burning or stinging. **Contraindications:** Contact lenses should not be worn if you have: eye infection or inflammation (redness and/or swelling); eye disease, injury or dryness that interferes with contact lens wear; systemic disease that may be affected by or impact lens wear; certain allergic conditions or using certain medications (ex. some eye medications). **Additional Information:** Lenses should be replaced every month. If removed before then, lenses should be cleaned and disinfected before wearing again. Always follow the eye care professional's recommended lens wear, care and replacement schedule. Consult package insert for complete information, available without charge by calling **(800) 241-5999** or go to **myalcon.com**.

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Looks Like Glaucoma, But is It?

The patient's visual fields say glaucoma, but his optic nerves disagree. What else is going on? **Edited by Paul C. Ajamian, OD**

Q A 45-year-old black male came into my office complaining of declining, unexplained vision loss for the past two years. His best-corrected visual acuity was 20/25 OD and 20/50 OS. His visual fields looked like glaucoma, but his optic nerves appeared normal. Where do I go from here?

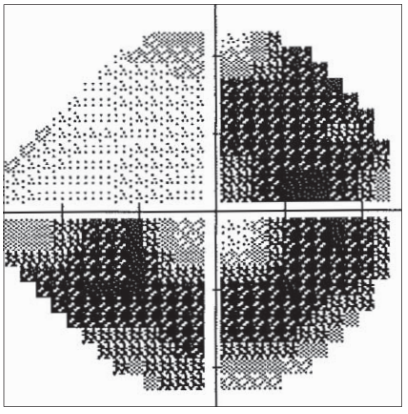
A "Take a closer look at the visual fields," says Dennis Mathews, OD, a neuro-optometrist at Eye Specialty Group, in Memphis.

On first glance, the fields might appear to represent arcuate scotomas from glaucoma. But you can see that, in the right eye at least, the defects somewhat respect the vertical midline. "In glaucoma, we expect there to be no respect to the vertical," he says. So, that's one clue that you're not dealing with glaucoma.

The second clue is that glaucoma usually doesn't begin with bitemporal field loss, as shown in this patient's visual fields, Dr. Mathews says. Glaucomatous field loss usually develops nasally and superiorly.

The third clue that this isn't a straightforward case of glaucoma is that, despite 0.80 cups, the rim tissue is intact 360° and the cupping obeys the ISNT rule. "If these fields were caused by glaucoma, one would expect a notch or other damage consistent with the disease," Dr. Mathews says.

In short, the appearance of the patient's optic nerve head doesn't correlate with the visual field loss. When that happens, it's time to look deeper.



The patient's visual fields appear glaucomatous—but also respect the midline.

Because the field defects are temporal and symmetrical, "this should make you very suspicious of a retrobulbar problem, specifically at the chiasm," Dr. Mathews says. "And the most common tumor is a non-secreting pituitary macroadenoma. Clearly, this patient requires neuro-imaging."

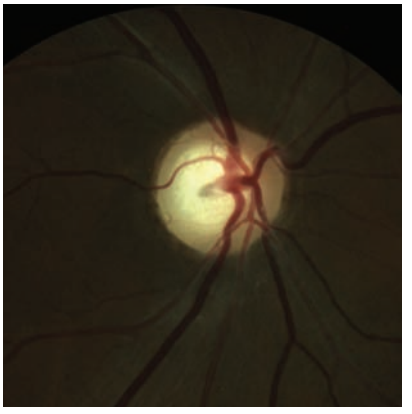
If you're comfortable managing such a case, order an MRI of the brain with and without contrast, Dr. Mathews says. If you're unable or not prepared to do that, you can refer the patient to a specialist.

In this patient's case, the MRI came back showing a large suprasellar mass lesion consistent with a pituitary adenoma.

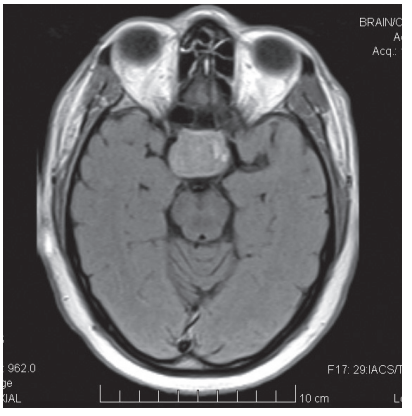
Send this patient to a neurosurgeon for decompression surgery, Dr. Mathews says. "After decompression, many times you'll see some improvement in vision, although the vision will never return to normal," he says.

Unfortunately, this patient has not recovered much of his acuity or visual field after the surgery, but time will tell. This case highlights the importance of always explaining unexplained acuity loss, Dr. Mathews says.

Last but not least, be aware that the tumor can grow back, so monitor the patient with visual fields and a dilated fundus exam every six months, Dr. Mathews says. ■



Other than slight pallor and 0.80 cupping, the patient's optic nerves appear normal.



The patient's MRI shows an adenoma by the pituitary gland.

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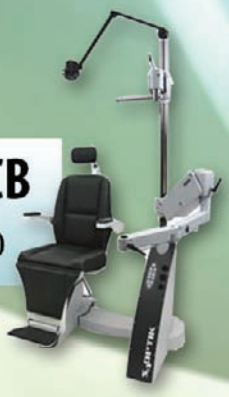

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Under Pressure

Advanced contact lenses are already making 24-hour IOP monitoring a reality for some clinicians. Will it work in your practice? **Edited by Joseph P. Shovlin, OD**

Q When assessing patients for glaucoma, knowing diurnal intraocular pressure variation—especially throughout the night—is valuable. Can you describe how the contact lens-based options actually work on the eye to measure pressure, and when they might be available?

A The ability to monitor IOP over the course of a day is considered one of the holy grails of glaucoma assessment. While the FDA has not approved any such device in the US, a number of countries, including Canada and Australia, have approved the Triggerfish system, designed by Sensimed.

Triggerfish is a soft, disposable silicone hydrogel lens that functions as a strain gauge, measuring changes in corneal curvature that are then converted to units of change.

"The system consists of a silicone contact lens that is embedded with an antenna, strain gauge and microprocessor," says Leo Semes, OD, professor of optometry at the University of Alabama in Birmingham. "This component translates choroidal pulses into a signal that is picked up by another antenna worn on the patient's orbit, which is connected by a detachable cable to a data recorder that the patient wears."

The Triggerfish system monitors IOP changes throughout the day, and provides detailed data with every recording. This data can be downloaded to a computer and used to map the patient's IOP over a 24-hour cycle.

"The instrument takes a measurement every five minutes, or 288 times per day, and obtains 300 data points at each measurement," says Ben Gaddie, OD, who practices in Louisville, Ky. "The doctor would fit and dispense the device and the patient would wear it for a few days, return it, and the doctor would then download and see the data."

Sensimed's Triggerfish lens records changes in corneal curvature that correspond with intraocular pressure.

According to Murray Fingeret, OD, who practices in New York, the lens appears to be tolerated well, and has exhibited promising results.

"Initial reports show that IOP varies throughout the 24-hour period, similar to work performed in the University of California San Diego sleep lab, which shows the IOP is highest during the nocturnal hours," says Dr. Fingeret.

"In addition, initial reports suggest that not all patients have perfectly reproducible 24-hour IOP behavior," adds Dr. Semes. "Knowing a complete 24-hour cycle of IOP and its variability may change management, or explain why some patients show progression when IOP appears in the normal or 'target' range."

The Triggerfish system may be a valuable tool, as it allows clinicians to customize IOP management based on the individual patient needs. For instance, given the differing efficacy of glaucoma medications during sleep, clinicians may be able to choose a more appropriate drug regimen for evening use based on the individual's diurnal IOP curve.

"Because some individuals show greater changes in IOP than others, this device would allow therapy to be customized to the person based upon the way their IOP varies throughout the duration of the day," says Dr. Fingeret

"Twenty-four hour IOP monitoring would allow us to gain perspective in two types of patients: those who are already progressing and any patient being staged for glaucoma treatment," adds Dr. Gaddie. "If we know that someone has a large nocturnal IOP swing, that patient's target IOP could be adjusted lower, or perhaps a surgical method might be better served to control nocturnal IOP elevation."

More information is available at: www.sensimed.ch/en/products/sensimed-triggerfishr.html. ■

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How to Tame a Steroid Response

I prescribed steroids for a patient with bilateral uveitis and central serous retinopathy—then she had an IOP increase. Now what do I do? **By James L. Fanelli, OD**

A 41-year-old white female was referred for a retinal evaluation in March 2013. She complained of blurred vision OU and an achy, "sore" feeling OS.

When I first saw her, she described a cloud-like fog in the vision of her right eye for the past two weeks. She also reported a 'spot' in her vision in the right eye, which had gotten bigger during the two weeks. She also complained of increasing photophobia (OS>OD), which began about the same time.

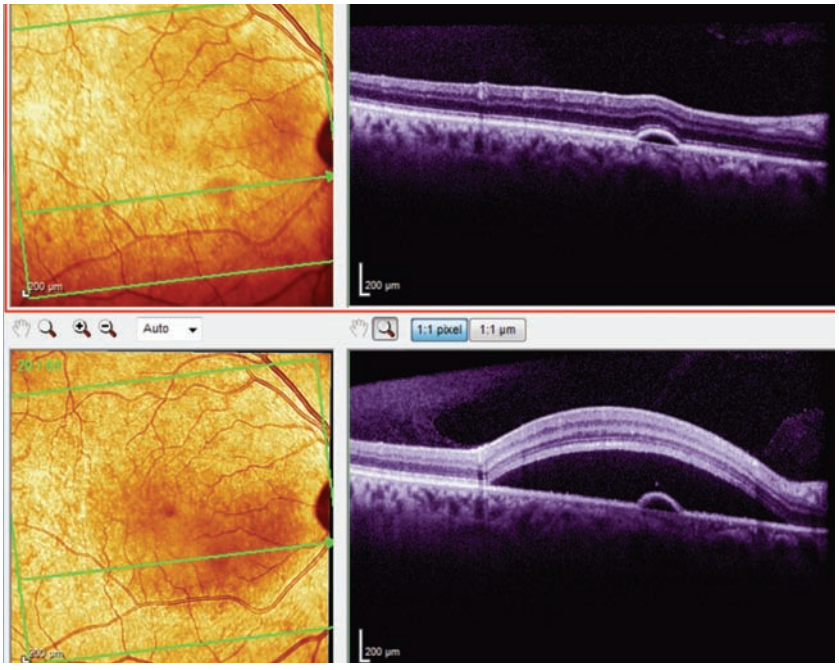
Diagnostic Data

At this initial visit, her visual acuity was 20/50 OD and 20/30 OS, with pinhole acuity of 20/40- OD and 20/20- OS. Pupils were normal with no afferent defect. Confrontation visual fields were remarkable for a central depression (OD>OS).

Slit-lamp exam showed grade 3+ cells and 2+ flare in the anterior segments OU. No keratic precipitates, iris nodules or synechiae were noted in either eye. The limbal episclera was moderately injected OU. Intraocular pressure measured 20mm Hg OU at 3:45 p.m.

Upon dilation, her crystalline lenses were clear OU. The anterior and posterior vitreous evaluations OU showed no evidence of cells. Stereoscopic disc evaluation demonstrated healthy neuroretinal rims with normal cupping in both eyes.

Macular evaluation of the right eye revealed a large area (approximately four disc diameters) of retinal thickening located adjacent to the optic nerve, just inferior to the superior temporal retinal arcades. The inferior aspect of this retinal thickening extended to the superior aspect of the foveal avascular zone. The left macula was unremarkable, as were the peripheral retinas in both eyes.



OCT image of the right eye at initial presentation (top) and first follow-up visit (bottom) shows a pigment epithelial detachment. Note the movement of the focal neurosensory detachment from a superonasal macular location (top) to a more central macular location (bottom).

Optical coherence tomography evaluation of the right macula revealed a large neurosensory retinal separation in the area of the retinal thickening, as well as a small pigment epithelial detachment (PED) in the inferior macula. The focal neurosensory retinal detachment was not centered in the macula, but was structurally characteristic of an atypical case of central serous retinopathy. Interestingly, the macular OCT of the left eye also demonstrated a small PED inferonasal to the foveal avascular zone.

Diagnosis and Management

Based upon the clinical presentation, I diagnosed atypical central serous retinopathy (CSR) OD, bilateral juxtafoveal PEDs OU and anterior uveitis OU. Given the bilaterality of the anterior uveitis and PEDs, I had to consider the possibility of a systemic etiology.

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Accordingly, I ordered the following initial labs: CBC with differential, ANA, RA latex, ESR, CRP and ACE levels.

To quiet the anterior chamber reactions, I prescribed atropine 1% BID OU, Pred Forte (prednisolone acetate 1%, Allergan) Q4H OU and Acular LS (ketorolac tromethamine 0.4%, Allergan) QID OU.

The patient returned in four days with slightly worsening vision in the right eye, and stabilization of the photophobia OU. She reported that she was compliant with her drops.

Pinhole acuity was unchanged OU. Intraocular pressure at this visit was 21mm Hg OD and 20mm Hg OS. Her anterior chambers were unchanged, still showing notable cells and flare OU. No synechiae were noted in either eye.

Her retinal evaluations, both at the slit lamp and via OCT imaging, demonstrated a gross inferior billowing shift of the focal neurosensory retinal detachment to a more central macular location, now encompassing the pre-existent PED. The PED in the left eye increased retinal thickness by 20µm. All of her lab findings were normal, except for a slightly elevated CRP level of 6.8mg/L.

Over the next several weeks, the patient remained moderately compliant with her medication schedule, although she did report on two occasions that she accelerated her steroid tapering "as my eyes felt better." At one of the follow-up visits after she decreased her dosage of steroids, her anterior chambers had re-flared, as had the CSR OD, which previously begun to clear. As a result, I directed her to increase the topical steroids to the initially prescribed level.

Unfortunately, at about this same time, IOP in both eyes began to increase. I prescribed timolol 0.5% QAM OU, and her IOP in both eyes soon dropped from the mid-30s to the upper teens.

By July 2013, her retinas were clear with no evidence of PEDs or CSR. Further labs, including thyroid function studies and chest films, were negative. Histo and Lyme titers were also normal. The anterior chambers were relatively quiet with trace cells and flare. I told her to gradually taper the steroids, with an anticipated cessation in four to six weeks. I kept her on timolol 0.5% QAM OU, but adjusted Acular to QD OU.

Unfortunately, on follow-up in August 2013, she reported increased periocular discomfort and decreased vision. She also said that the timolol was irritating her eyes, so she discontinued that drop OU. At this visit, best-corrected visual acuity was 20/20 OU. Anterior chambers showed 1+ cells and flare, and IOP had risen to 48mm Hg OD and 51mm Hg OS. I prescribed Simbrinza (brinzolamide1%/brimonidine 0.2%, Alcon) BID OU.

At the patient's most recent visit in early November 2013, her anterior uveitis had cleared (and has remained so for 30 days), and the CSR and PEDs also remained clear OU. IOP was 18mm Hg OD and 21mm Hg OS. The patient is now medicated OU with Acular QD, Pred Forte BID, Simbrinza BID and timolol 0.5% QAM.

Our current plan: a very slow taper of topical steroids to prevent re-flare, while continuing the IOP-lowering medications to control the steroid-induced glaucoma.

Discussion

This case presents a challenge: How can we control the anterior uveitis and retinal conditions while managing the steroid-induced IOP increase?

Keep in mind that when topical steroids are used to treat anterior uveitis, an IOP rise might occur for one of two reasons. First, the IOP rise may be due to the use of the steroid itself, which is believed to increase glycosaminoglycans and reduce outflow in steroid responders. In such cases, the obvious treatment is to lower or eliminate the topical steroids.

On the other hand, an IOP rise may occur due to inflammation and inflammatory debris (originating in the anterior chamber) that clogs the trabecular meshwork. When the inflammation itself is the root of the IOP rise, topical steroids may actually need to be increased to ultimately result in lower IOP (by reducing trabecular inflammation).

Trabeculitis is nearly impossible to visualize gonioscopically. However, inflammatory debris can occasionally be seen on gonioscopy. In this patient's case, gonioscopy of the anterior chamber showed open angles with no discernable debris. Could the trabeculum be inflamed, causing her elevated IOP? Or could she simply be a steroid responder? In this case, the answer to both questions is "yes." I concluded that she was a true steroid responder because the anterior uveitis was not murky or granulomatous in appearance, which is more likely to occur with trabecular inflammation.

Managing a steroid responder is rather straightforward. While we should ideally use steroids at a minimum, it's really the inflammatory condition that dictates the steroid dosage. Consequently, elevated IOP can be reduced by a variety of pressure-lowering agents. The key is to lower IOP and keep it lowered during the duration of the elevated IOP—whether that's for days or for years. ■

Two *isn't* Better Than One

We uncovered two different retinal pathologies in this patient. What are they, and how severely will they affect her vision? **By Mark T. Dunbar, OD**

A 65-year-old Hispanic female presented with mild blur at distance and near in both eyes that had persisted for six months (OD>OS). Her ocular history was significant for episcleritis in her right eye five years earlier, which resolved uneventfully.

Her medical history was significant for high cholesterol, which was medically controlled (she couldn't remember the drug's name).

On examination, her best-corrected visual acuity measured 20/25 OD and 20/20 OS. Extraocular motility testing was normal. Her confrontation visual fields were full to careful finger counting OU. Her pupils were equally round and reactive, with no evidence of afferent defect. Her anterior segment was unremarkable. Intraocular pressure measured 15mm Hg OU.

On dilated fundus exam, the vitreous was clear OU. She exhibited moderate-sized cups, with good rim coloration and perfusion in both eyes. The peripheral retina was normal in both eyes.

Both maculae showed obvious changes (*figures 1 and 2*). Additionally, we obtained a spectral-domain optical coherence tomography (SD-OCT) scan of her right eye (*figure 3*).

Take the Retina Quiz

1. What do the yellow-white changes in both maculae represent?
   a. Drusen.
   b. Intraretinal flecks.
   c. Exudate.
   d. Crystals.

2. What does the SD-OCT scan show on her inner retina?
   a. Vitreomacular traction.
   b. Macular telangiectasia.
   c. Epiretinal membrane (ERM).
   d. Retinal striae.

3. What does the SD-OCT show in the outer retinal layers?
   a. Drusen.
   b. Choroidal neovascularization (CNV).
   c. Disruption of the inner segment/outer segment (IS/OS) junction.
   d. Pigment epithelial detachment.

4. What is the correct diagnosis?
   a. Dry age-related macular degeneration (AMD).
   b. Dry AMD and ERM.
   c. Wet AMD with CNV.
   d. Vitreomacular traction with macular edema.

5. How should this patient be managed?
   a. Observation.
   b. Intravitreal anti-VEGF injection.
   c. Intravitreal Jetrea (ocriplasmin, ThromboGenics) injection.
   d. Vitrectomy and membrane peel.

For answers, turn to page 86.

Discussion

The yellow-white deposits seen in both maculae represent drusen. Therefore, our patient has some form of macular degeneration. The SD-OCT scan detailed the irregular elevations of the drusen at the level of the retinal pigment epithelium (RPE), and revealed an intact IS/OS junction that was pushed forward from the drusen. We documented no fluid or CNV, which confirmed that the patient had dry AMD.

Aside from macular degeneration, it's important to note that the SD-OCT showed a loss of the foveal depression and a slightly thickened macula OD. Indeed, the foveal thickness in her right eye measured 336µm, compared to 254µm in her left eye.

So, what else is going on with this patient? In addition to dry AMD, she has an ERM in her right eye. On the SD-OCT scan, the ERM can be visualized as a highly reflective entity at the level of the internal limiting membrane (ILM). More temporal to the fovea, you can see that the ILM is corrugated with focal elevations. Clinically, this is seen as retinal striae.

An ERM represents a fibrocellular membrane that grows onto the retinal surface. It is comprised of glial, RPE and collagen cells, as well as macrophages and fibrocytes.[1]

The exact mechanism by which RPE cells migrate onto the surface of the retina is not completely

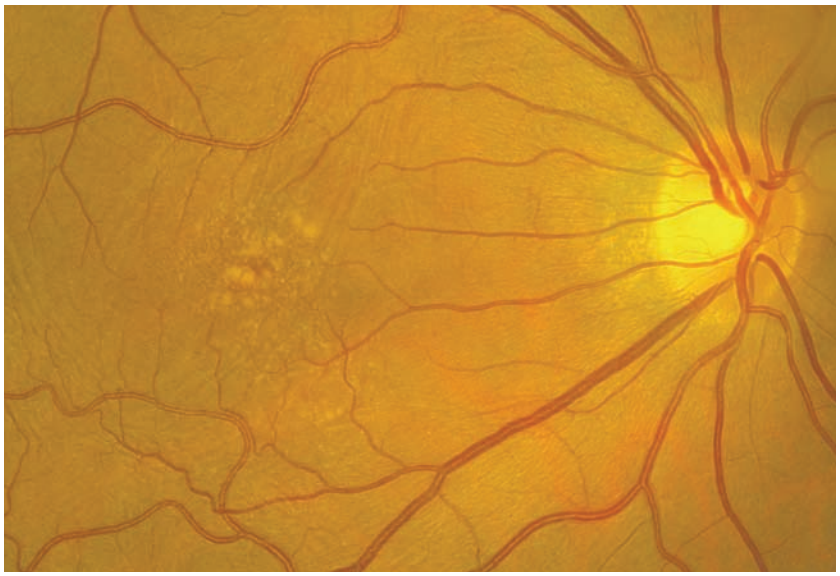
understood; however, it is believed that an ILM dehiscence might catalyze ERM development. Up to 90% of patients with ERMs also develop posterior vitreous detachments (PVDs). Thus, the process of PVD development may yield a small dehiscence in the ILM, permitting the fibrocellular membrane to form.[1]

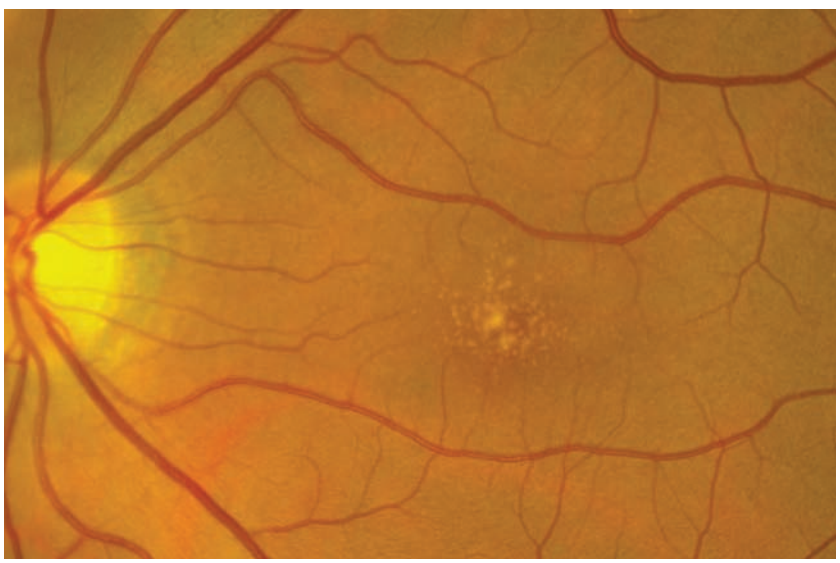
Approximately 90% of ERMs remain stable and do not affect visual acuity significantly; however, the remaining 10% typically progress.[1] For patients who develop symptomatic ERM, pars plana vitrectomy with membrane peel often is indicated. Surgical success is dependent on ERM extent and severity, as well as the level of the visual acuity.

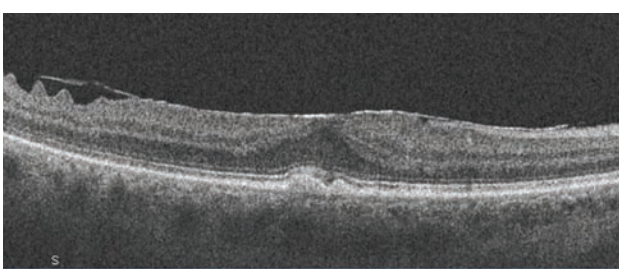
There is no definitive standard to determine when surgical intervention is necessary for ERM. Spectral-domain optical coherence tomography provides a good barometer for detecting structural changes within the retina—either at the level of the IS/OS junction, or if patients develop fluid or cystic changes within the retina. Once this occurs, most retinal specialists agree that surgery is warranted.

It is important to remember that postoperative visual acuity is dependent on the extent of retinal architecture changes. Typically, the anticipated visual recovery is approximately 50% better than the entering acuity level. In other words, ERM patients who present with an entering acuity of 20/60 can expect to achieve 20/30 or better following surgery.

Our patient's vision is still very good, and she did not report any distortion or metamorphopsia. Our hope is that she will fall into that 90% category, and won't exhibit ERM progression.







1-3. Our patient's fundus examination revealed interesting macular changes (OD top, OS middle). Additionally, what does the spectral-domain optical coherence tomography scan of our patient's right eye (bottom) reveal?

Nevertheless, she does have early dry age-related macular degeneration. So, we recommended an AREDS2 vitamin supplement that contains both lutein and zeaxanthin. We instructed her to return in six months for additional monitoring and follow-up. ■

1. Smiddy WE, Maguire AM. Idiopathic epiretinal membranes. Ultrastructural characteristics and clinicopathologic correlation. Ophthalmology. 1989 Jun;96(6):811-20.

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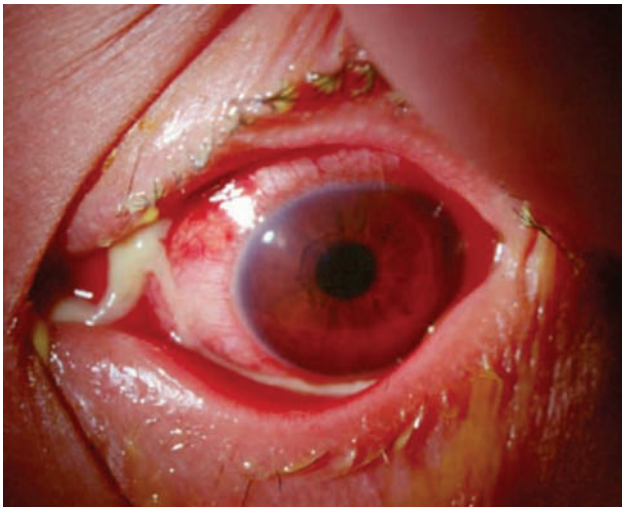
Sowka Down Under, Part III

I wrote about my previous experiences in Australasia back in 2008 and 2012. Now it's time for the hat trick. **By Joseph W. Sowka, OD**

I have always enjoyed lecturing in other countries and meeting colleagues from across the world. One of my favorite international gatherings is the Tasmania Lifestyle Congress in Hobart, Australia. It is a lovely event in a beautiful harbor town. The education is outstanding and the delegates in attendance are among the brightest I have ever encountered.

I enjoy making comparisons between the practice of optometry in Australia and the United States, and genuinely believe what happens in eye care in one country will somehow be mirrored in the other.



Interestingly, acute bacterial conjunctivitis can be diagnosed and treated independently by an Australian pharmacist—most likely with chloramphenicol.

Aussies vs. Yankees

• *Therapeutic privileges*. Optometrists gained therapeutic privileges long ago in the United States. It was a lengthy, arduous process that still presents several limitations today.

Clearly, optometrists in Australia experienced many of the same problems and growing pains that we dealt with years ago. However, it shouldn't be surmised that optometrists in other countries trail far behind their American counterparts. Actually, in several ways, they may have advantages over US optometrists.

One progressive step that Australian optometrists have made, which has yet to be taken here, is interstate parity in prescribing rights. For example—while oral prescribing laws vary from state to state in the US, the scope of optometry across Australia is now uniform. That is, the same practice standards exist in all Australian states, with consistent treatment privileges across the country.

• *Specialist referrals*. Recently, Australian optometrists took another step forward with the dissolution of the glaucoma comanagement rule. Now, Australian optometrists are able to treat open-angle glaucoma independent of ophthalmologists, and no longer have to refer out for comanagement. This significantly increases access to care for Australian citizens, as the wait time for a specialist appointment often takes several months.

It remains to be seen how the Affordable Care Act will impact the practice of optometry in the US. With increased access to insurance, more patients likely will be seeking care. Optometry has always been a gatekeeper for primary eye care. So, it is possible that the wait time for specialists could increase dramatically in the US, similar to that seen in Australia and Canada.

Now more than ever, US optometrists need to embrace the therapeutic aspect of practice. Patients

Chloramphenicol for Conjunctivitis

In Australia, the most commonly prescribed topical antibiotic is chloramphenicol. Although the agent is very effective in treating bacterial conjunctivitis, chloramphenicol has not been commonly used in the US for many years due to perceived risks of aplastic anemia.[2]

Nonetheless, the Australians have no such worries. In fact, topical chloramphenicol is an over-the-counter drug in Australia, so patients don't even need to have the medication prescribed by a doctor or pharmacist.

will need medical eye care at an unprecedented level. Longer wait times for specialist consultations means that we will need to shoulder the therapeutic burden.

Australian Pharmacists' Role in Eye Care

If these are not sufficiently compelling reasons for optometrists to embrace medical eye care, then let me share with you another change that recently occurred in Australia. Pharmacists have increased their scope of practice and now have therapeutic prescribing rights. Again, this stems from the extensive wait times for specialists in Australia.

For example, Australian pharmacists can provide a one-month supply of anti-hypertensive medications, statins and glaucoma medications without a prescription. Keep in mind that pharmacists are not diagnosing and treating these conditions, but are providing an emergency supply to patients until they can see their doctor. Of course, it remains to be seen how many patients may abuse this assistance and keep getting an "emergency supply" month after month without seeing a doctor.

What was most interesting to learn, however, is that pharmacists can now actually diagnose and prescribe for common eye conditions without the patient/customer ever having to see a doctor. The most common condition that pharmacists independently diagnose and treat is bacterial conjunctivitis. As we know, pharmacists do not typically have biomicroscopes to assist them in evaluating ocular conditions. It is very commonly accepted that bacterial, viral and allergic conjunctivitis often have some overlap in signs and symptoms, sometimes making an accurate diagnosis difficult even with a biomicroscope.

In the vast majority of cases, acute bacterial conjunctivitis is a self-limiting disease. However, most published reports indicate that despite its benign, self-resolving nature, bacterial conjunctivitis should be treated with topical antimicrobial therapy in order to shorten the disease course and improve the rate of clinical and microbiologic remission.[1] This is especially true early in the clinical course.

A primary concern associated with pharmacists prescribing for eye conditions is that many diseases present with superficial likenesses. Anterior uveitis could present early with similarities to simple conjunctivitis. Additionally, bacterial keratitis could appear similar to bacterial conjunctivitis. Therefore, a pharmacist not employing a biomicroscope could potentially under-treat a condition, leading to significant visual consequences.

To be fair, Australian pharmacists are not likely to prescribe beyond their comfort level. In fact, during my discussion with an Australian pharmacist, she said that she would refer the patient to an optometrist if there were any uncertainties (likely because she knew the difficulty in obtaining an ophthalmology appointment).

While the expanding role of Australian pharmacists may seem to have no bearing on our US practices, we have to be cognizant that patients always will require care. And, if there is a dearth of providers to deliver that care, other health care professionals must step in to fill the void.

Across the United States, pharmacists are successfully administering immunizations for influenza, pneumonia and herpes zoster. I happily get my own immunizations from a pharmacist.

As more patients flood into the health care system, it is not inconceivable that pharmacists may someday have prescribing rights for ocular diseases. In other words, what has successfully transpired in Australia could someday occur in the US if there are not enough eye care practitioners available who are willing to practice medical eye care. ■

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Over a snack, Joe and Joey compare notes on American and Austrialian eye care practices.

The Lens: Window to Diagnosis?

Research suggests that conditions such as diabetes or Alzheimer's may be best diagnosed via the crystalline lens. **By Diana L. Shechtman, OD, and Paul M. Karpecki, OD**

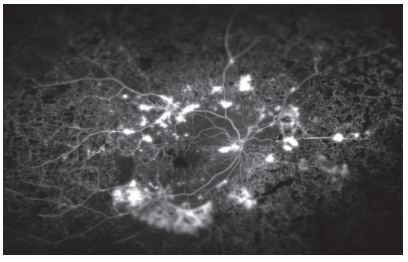
We examine the lens for cataract in all patients, but it may provide an even greater snapshot of diseases elsewhere in the body. The human lens is one of the few structures that continues to grow throughout our lifetime. As it does, it accumulates deposits that could alert practitioners to diagnose a systemic disease—not just connective tissue disorders like Weill-Marchesani syndrome in patients with microspherophakia or subluxated lenses in Marfan's syndrome, but further-reaching diseases such as Alzheimer's and diabetes mellitus.[1]

Alzheimer's Disease (AD)

An accumulation of amyloid beta plaques in the brain results in neurological effects for patients with AD. An imaging technique currently in phase II of FDA clinical trials can detect these amyloid plaques within the crystalline lens.

The technique begins with a fluorescent ligand marker applied topically in an ointment to the inner corner of one eyelid. The application is done three separate times, two hours apart, the night before Sapphire II laser imaging (Cognoptix).

For imaging, the patient fixates on a target and a low-level laser allows for fluorescent measurements of the lens, providing a score relative to the level of amyloid detected. The entire procedure takes only a few minutes with imaging equipment the size of a personal computer. This technology could be beneficial to the diagnosis of AD, but perhaps even more critical in the clinical trials of potential AD therapies. A drug that results in amyloid deposition deceleration in the lens may also show reduction of deposition in the brain. Further research is certainly warranted.



Proliferative diabetic retinopathy.

Diabetes Mellitus (DM)

Advanced glycation end products (AGEs) are lipids or proteins that become gylcated after being exposed to sugars. They are prevalent in the blood vessels of patients with diabetes, but can also contribute to lens changes as they non-enzymatically bond to the lens proteins. Although AGEs form with natural aging, the process is accelerated by hyperglycemia and thus observed sooner in DM.

The glycation or condensation of the aldehyde and ketone groups in sugars with the amino groups in proteins also leads to a Schiff base—the initial step in the formation of cataracts—and this also may be detected via autofluorescence. Although lens autofluorescence increases with age, the greater levels of fluorophores can be differentiated in diabetic disease diagnosis. This can be captured through a scanning confocal lens fluorescence biomicroscope called the ClearPath DS-120 (Freedom Meditech), which received FDA premarket clearance this year. The test is non-invasive and takes about six seconds, as the patient simply places their chin in a chin rest and looks at a target.

A study of 127 subjects between the ages of 21 and 70 showed a linear model for lens autofluorescence intensity with age that was highly statistically significant.[2] Multiple research studies have shown an increase in lens autofluorescence in patients with diabetes.[3,4] Decades-old studies show this correlation, and only recently has technology become available for optometrists to measure it accurately.[7,8]

Statistical findings can also be obtained in both young and elderly patients with diabetes and in patients with early and late onset diabetes.[7,8]

Correlation

Not only does autofluorescence of the lens help make a diagnosis of diabetes, but it can also correlate to the level of HbA1c. In one study comparing insulin-dependent diabetics with high HbA1c to another group with low HbA1c, the group with low HbA1c during the disease period showed significantly lower lens fluorescence.[9] Furthermore, lens autofluorescence provides information about long-term control of the disease, as research shows it can be delayed by good metabolic control.[10] A1c measures give a snapshot of the last two to three months in a diabetes patient, whereas lens autofluorescence measures the lifetime.

Another correlation exists with diabetic nephropathy, as one study compared 10 patients with diabetes

and kidney disease to 11 otherwise comparable patients with diabetes without kidney disease. The patients with diabetic nephropathy had significantly greater lens autofluorescence measurements and decreased lens transmittance.[11]

What makes autofluorescence of the lens even more compelling is that it can support early diagnosis. In one 14-year follow-up study, which confirmed that lens fluorescence was significantly related to mean HbA1c, researchers noted that although fluorophore accumulation in the lens of a diabetes patient was increased in proportion to glycemic control, it was not sufficient to explain the entire variation. Thus, lens fluorescence must be influenced by other factors before initiation and during the study. The study authors further concluded that it may have been affected before the onset of DM.[12] The underlying mechanism could be a variation in susceptibility to lens protein denaturation by glycation. This means that patients who are more likely to develop diabetes may have the initial effects noted in their crystalline lens.

The ability to make a diagnosis of AD or DM via the crystalline lens prior to clinical diagnosis or symptoms could solidify our role as primary eye care providers and help save the vision and lives of our patients. ■

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Product Review

Contact Lenses

PureVision2 Multi-Focal

Clear and consistent vision at all distances can be a challenge for people with presbyopia, but the newly released PureVision2 Multi-Focal lenses from Bausch + Lomb seeks to change that. Featuring a three-zone progressive design, these lenses were designed for real-world use to improve both near and intermediate vision, whether you're looking at your cell phone or sitting in a movie theater.

The lenses were also crafted to allow for predictable, quick fits for eye care professionals, the company says.

Visit www.bausch.com.

Diagnostics

Gonio and Funduscopy Lenses

A new line of diagnostic lenses offers high-quality optics without the hassles of cleaning and disinfecting, says Sensor Medical Technology. The company's wide range of lenses is inexpensive, sterile and disposable, according to the company. The line includes 3-Mirror, 4-Mirror, Single Mirror Gonioscopy, Fundus, Retina 90, Retina 165 and Retina 180 lenses.

Each lens has anti-reflective coating, according to Sensor Medical, which has also introduced a line of indirect ophthalmoscopy lenses with powers of 20D, 28D, 60D, 78D and 90D.

Visit sensormedtech.com.

Accessories

Flōt Merchandising System

If you're looking for a more interesting way to shelve your eyewear, Flōt may be what you need.

The merchandising system, crafted by Optical Displays, features a compelling combo of shelves and interchangeable accessories to visually captivate customers and improve your sales, according to the company. You can choose from a collection of various sizes and materials, from solid to Lucite, for design flexibility.

Visit www.opticaldisplays.com.

Lens Edger

Weco E.5

If you have an in-office spectacle lab, or are thinking of adding one but worry about a low-to-medium volume of prescriptions to fill, a new patternless edger may help. The Weco E.5 offers integrated drilling and wrap frame processing without compromising performance or value, according to manufacturer AIT Industries.

The Weco E.5 includes touch-screen controls, a grinding wheel capable of beveling all materials, automatic polishing, continuous 3D mapping, adjustable grooving angles and a superhydrophobic lens roughing process, among other features.

Visit www.aitindustries.com.

Diagnostics

Sjö

Because the earliest stages of Sjögren's syndrome mimic those of many other dry eye presentations, optometrists find themselves with a unique responsibility to identify this serious, progressive and underdiagnosed autoimmune disease as soon as possible. Lab testing can improve specificity, but may delay diagnosis.

Recently launched in the US by Nicox, Sjö is an advanced diagnostic panel for in-office use that combines traditional biomarkers with three novel ones as a means to detect Sjögren's early enough to manage the condition and help avoid further complications.

Nicox has also formed a partnership with the Sjögren's Syndrome Foundation to raise awareness of the disease, which is often undiagnosed until its late stages. Patients are typically diagnosed with traditional dry eye when their symptoms first manifest.

Visit www.nicox.com.

Vitamins

AREDS 2 Plus

Patients who need ocular vitamins can choose from two products updated to reflect AREDS 2. One version, called EyePromise AREDS 2 Plus with a Multi-Vitamin, incorporates the AREDS 2 elements and a multi-vitamin formulation. Patients who want to nix the zinc can

opt instead for EyePromise AREDS 2 Plus Zinc-Free.

According to parent company ZeaVision, clinical studies showed that many patients who took eye vitamins also enjoyed daily multi-vitamins, and some patients achieved better vision protection without the zinc. Hence, the new offerings, designed to encourage convenient and consistent daily use.

Visit www.eyepromise.com.

Retinal Imaging

Volk Pictor

Weighing in at just one pound, the Volk Pictor is a compact and lightweight digital imaging system that takes retinal images in either infrared or white light, as well as anterior segment photos of the eye. According to AIT Industries, this gives you the flexibility to take images in places like off-site clinics or hospitals, as well as in your office.

Pictor produces high-resolution images and video that are compatible with most imaging software, the company says. It's also adaptable to any EMR that allows JPEG files to be attached to medical records. The retinal imaging module provides a wide 45-degree field of view of the fundus.

Visit www.aitindustries.com.

High-Tech Products, High-Quality Care

Chart systems, slit lamps, OCTs and autorefractors were among many new products introduced by Topcon Medical Systems at the American Academy of Opthalmology annual meeting. Not all are yet available in the US, but here's a preview of what's coming. Check with your Topcon rep for availability or visit topconmedical.com for more details.

3D OCT-1 Maestro
This fully automated, high-resolution FD-OCT device also offers nonmydriatic retinal camera functioning, and 12mm x 9mm widefield scan that allows for measurement and topographical maps of the optic nerve and macula in one scan.

KR-800S Subjective Auto Kerato-Refractometer
This device incorporates subjective visual acuity testing with autorefraction technology to refine patient measurements. Includes a glare-testing function that assesses visual acuity under glare conditions.

IMAGEnet 5
This DICOM-compliant computerized digital system allows you to capture, view and archive images of the eye from either local or remote locations.

DRI OCT-1 Atlantis
With a 1,050nm light source and scanning speed of 100,000 A-scans/second, this next-generation OCT device uses new swept-source scanning technology. The Atlantis provides uniform scanning sensitivity, which allows for superior visualization of the vitreous and choroid in the same scan, and can even scan through cataracts, Topcon says.

Synergy ODM
Images and diagnostic data from Topcon and more than 130 other manufacturers' systems are integrated into a single, secure, digital environment in this unique software platform that allows better digital connectivity.

TRK-2P Auto Kerato-Refractometer/Tonometer
This four-in-one instrument increases efficiency by combining an autorefractor, keratometer, non-contact tonometer and pachymeter in one space.

SL-D791 and DC-4
A new LED illumination source and high-quality optics in the SL-D791 slit lamp deliver sharp, clear and bright view of ocular anatomy. Additional features include a five-magnification drum-style changer from 6x to 40x, 20° tilt for gonioscopy observation, Galileo-type parallel-converging binoculars and smooth movement by universal joystick. The DC-4 digital photo attachment allows for image acquisition in still mode, video clip and "smart capture" rapid sequence acquirement.

CC-100 LCD Acuity Chart System
This is a versatile computerized acuity chart system. The high-resolution LCD monitor ensures clear and bright chart display. All common visual acuity tests are available. You can also add your own video content.

IS-600N
An economical, yet fully featured chair and stand combination unit with phoropter arm, dual instrument sliding tabletop, halogen reading lamp and chart projector bracket.

SP-1P
The new Topcon Specular Microscope model SP-1P automatically centers, focuses and acquires the endothelial cell image. The entire operation takes a few seconds and requires minimal training, Topcon says.

MC-4S 3D Mirror Chart
This simulates a full 20' lane in a 2' to 5' range, allowing for use in very small refraction areas and features a high resolution, polarized LCD display that includes all common visual acuity charts as well as the ability to show 3D movies or to show the effects of polarization on a patient's glasses.

Meetings + Conferences

January 2014

■ **11.** *2014 Glaucoma Symposium.* Willows Lodge, Woodinville, Wash. Hosted by: Pacific University College of Optometry. CE hours: 7. Contact Marti Fredericks at frederim@pacificu.edu or (503) 352-2929. Visit www.pacificu.edu/optometry/ce.

■ **11.** *Coding Update & HIPAA & HR Compliance Training.* Doubletree Hilton, Little Rock, Ark. Hosted by: Arkansas Optometric Association. CE hours: 8. Key faculty: John A. McGreal, OD, Joe DeLoach, OD, BJ Avery. Email aroa@arkansasoptometric.org. Visit www.arkansasoptometric.org.

■ **12.** *Winter CE.* Hyatt Regency O'Hare, Rosemont, Ill. Hosted by: Illinois Optometric Association. Key faculty: Paul Karpecki, OD. CE hours: 6. Contact Charlene Marsh at ioabb@ioaweb.org or (217) 525-8012. Visit www.ioaweb.org.

■ **11-12.** *Eye Care Associates Annual Meeting and Continuing Education Program.* Williamsburg Hotel, Williamsburg, Va. Hosted by: Eye Care Associates. Presenter: Scot Morris, OD. CE hours: 12. Contact Linda Cavasos at ECA_linda@hotmail.com or (804) 356-5165. Non-members are welcome.

■ **16-19.** *New Technology & Treatments in Vision Care.* The Westin Resort & Casino, Aruba. Program Chair: Paul Karpecki, OD. Faculty: Jimmy Bartlett, OD, Ben Gaddie, OD, and Kimberly Reed, OD. Hosted by: *Review of Optometry*. CE hours: 14. Contact Lois DiDomenico at ReviewMeetings@Jobson.com. Visit www.revoptom.com/conferences.

■ **18-19.** *30th Annual Gold Coast Educational Retreat.* Hyatt Regency Pier 66, Ft. Lauderdale, Fla. Hosted by: Broward County Optometric Association. CE hours: 19. Email BCOA@browardeyes.org or visit http://www.browardeyes.com.

■ **18-20.** *Kraskin Invitational Skeffington Symposium on Vision.* Hyatt Regency Bethesda, Bethesda, Maryland. Hosted by: OEPF. CE hours: 19. Chair: Jeffrey Kraskin, OD. Contact Dr. Kraskin at jkraskin@rcn.com. Visit www.skeffingtonsymposium.org.

■ **18-20.** *Berkeley Practicum - 25th Annual.* DoubleTree Hotel, Berkeley Marina, Berkeley, Calif. Hosted by: University of California, Berkeley, School of Optometry. CE hours: 20. Email optoCE@berkeley.edu. Visit http://optometry.berkeley.edu/ce/berkeley-practicum.

■ **19-25.** *2014 Island Eyes Conference.* Grand Wailea, Maui, Hawaii. Hosted by: Pacific University College of Optometry. Contact Jeanne Oliver at jeanne@pacificu.edu or (503) 352-2740. Visit www.pacificu.edu/optometry/ce.

■ **22.** *Dermatology: General and Neoplastic Disease.* West Los Angeles VA, Los Angeles. Hosted by: Marshall B. Ketchum University/SCCO. Email ce@ketchum.edu or visit www.ketchum.edu/ce.

■ **23-26.** *Global Specialty Lens Symposium.* Rio Hotel and Casino, Las Vegas. Hosted by: Contact Lens Spectrum. CE hours: 30. Contact Maureen Platt at maureen.platt@pentavisionmedia.com or visit www.pentavisionevents.com.

■ **24.** *2014 Winter CE.* PCLI, Pearl District, Portland, Ore. Hosted by: Oregon Optometric Physicians Association. CE hours: 8. Email lynne@oregonoptometry.org. Visit www.oregonoptometry.org.

■ **24-25.** *High Performance Vision/Sports Vision Consulting Weekend.* Hollywood Beach Marriott, Hollywood, Fla. Hosted by: Ultimate Events. Key faculty: Don Teig, OD. CE hours: 16. Contact Dr. Teig at don@ultimateeventsllc.com. Visit www.ultimateeventsllc.com.

■ **25-26.** *Vision Training Conference II.* Embassy Suites Rockside Road, Independence, Ohio. Hosted by: College of Optometrists in Vision Development. Key faculty: W.C. Maples, OD, MS. CE hours: 12. Contact Jackie Cencer at jcencer@covd.org. Visit www.covd.org.

■ **26.** *Winter CE.* The Westin Chicago North Shore, Wheeling, Ill. Hosted by: Illinois Optometric Association. Key faculty: Ben Gaddie, OD. CE hours: 6. Email office@thevoa.org or (804) 643-0309. Visit www.thevoa.org.

■ **26.** *VOA One-Day CE Conference.* Richmond Marriott West, Glen Allen, Va. Hosted by: Virginia Optometric Association. Key faculty: Joe DeLoach, OD, BJ Avery. CE hours: 4. Contact Charlene Marsh at ioabb@ioaweb.org or (217) 525-8012. Visit www.ioaweb.org.

■ **30-February 3.** *Women of Optometry Spa Cruise.* Celebrity Constellation, Bahamas. Hosted by: AEA Cruises Optometric Cruise Seminars. Email aeacruises@aol.com. Visit www.OptometricCruiseSeminears.com.

February 2014

■ **8-9.** *Mid Winter CE Meeting 2014.* New Orleans Marriott, New Orleans. Hosted by: Optometry Association of Louisiana. Email optla@bellsouth.net. Visit www.optla.org.

■ **9-10.** *2014 Advocacy Boot Camp & Free CE.* Salem Conference Center/Grand Hotel, Salem, Ore. Hosted by: Oregon Optometric Physicians Association. Email lynne@oregonoptometry.org. Visit www.oregonoptometry.org.

■ **14-16.** *53rd Annual Heart of America Contact Lens and Primary Care Congress.* Sheraton Kansas City Hotel at Crown Center, Kansas City, Mo. Hosted by: Heart of America Contact Lens Society. Email registration@thehoacls.org. Visit www.hoacls.org.

■ **27-March 1.** *2014 Winter Educational Symposium.* Huntley Lodge, Big Sky, Mont. Hosted by: Montana Optometric Association. Faculty: Blair Lonsberry, OD, Christopher Wolfe, OD. CE hours: 13. Email sweingartner@rmsmanagement.com. Visit www.mteyes.com.

■ **28-March 1.** *2014 Third Party/Practice Management Seminar.* Eugene Hilton, Eugene, Ore. Hosted by: Oregon Optometric Physicians Association. For additional information, email lynne@oregonoptometry.org. Visit www.oregonoptometry.org.

March 2014

■ **12-16.** *SECO International 2014.* Building A, Georgia World Congress Center, Atlanta. CE hours: 400+. Email cweems@secostaff.com. Visit www.seco2014.com.

■ **22-23.** *Spring Conference.* Nova Southeastern University Ft. Myers Campus, Ft. Myers, Fla. Hosted by: Nova Southeastern University. Email oceaa@nova.edu. Visit http://optometry.nova.edu/ce/index.html.

April 2014

■ **12-13.** *2014 MOS Primary Care Spring Symposium.* Cincinnati Marriott Northeast, Mason, Ohio. Hosted by: The MidWest Optometric Society and the Ohio State University College of Optometry. Contact Marci at (513) 321-2020. Visit www.midwestoptometricsociety.com.

■ **24-27.** *Arkansas Optometric Association Spring Convention.* The Peabody, Little Rock, Ark. Hosted by: Arkansas Optometric Association. Email aroa@arkansasoptometric.org. Visit www.arkansasoptometric.org.

May 2014

■ **2.** *Berkeley Glaucoma Day – 2nd Annual.* DoubleTree Hotel, Berkeley Marina, Berkeley, Calif. Hosted by: University of California, Berkeley, School of Optometry. Email optoCE@berkeley.edu.

■ **2-3.** *Educational Meeting 2014.* Mission Inn, Howey-in-the-Hills, Fla. Hosted by: Florida Chapter of the American Academy of Optometry. Featured speakers: Leo Semes, OD, Albert Woods, OD, and Tim Underhill, OD. CE hours: 10. Contact Arthur T. Young, OD, at eyeguy4123@msn.com.

■ **3-4.** *Morgan Symposium – 29th Annual.* DoubleTree Hotel, Berkeley Marina, Berkeley, Calif. Hosted by: University of California, Berkeley, School of Optometry. Email optoCE@berkeley.edu. Visit http://optometry.berkeley.edu/ce/morgan-symposium.

August 2014

■ **1-3.** *Annual Educational Retreat 2014.* South Seas Island Resort, Sanibel Island, Fla. Hosted by: South West Florida Optometric Association. Featured speakers: Ben Gaddie, OD, Carlo Pelino, OD, April Jasper, OD, and Ron Foreman, OD. CE hours: 18. Contact Brad Middaugh, OD, at swfoa@att.net or (239) 481-7799. Visit www.swfoa.com.

To list your meeting, please send the details to:

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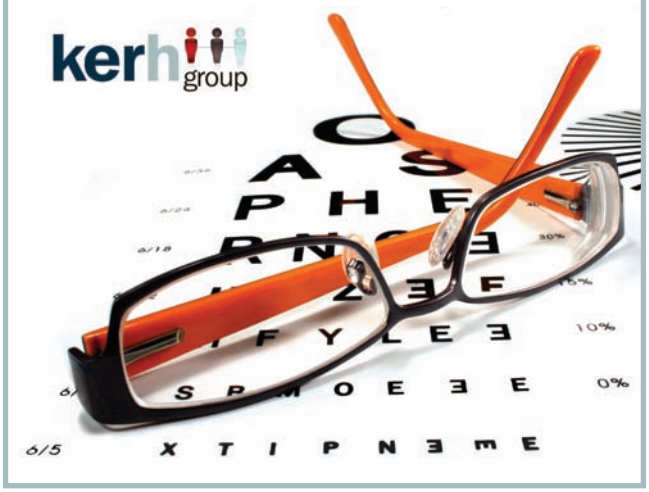



RK: The Unkindest Cut

Decades later, we are still seeing adverse events caused by one of the earliest refractive surgery procedures. **By Derek N. Cunningham, OD, and Walter O. Whitley, OD, MBA**

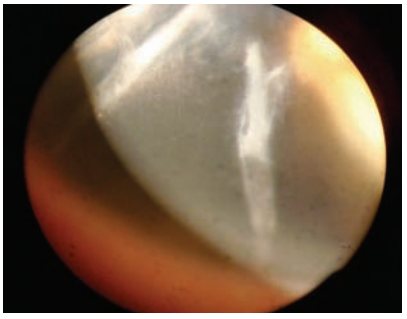
Radial keratotomy (RK), a popular procedure in the 1980s and early 1990s for the correction of low to moderate myopia (-1D to -6D) and astigmatism, seems primitive by today's exacting standards. It primarily involved creating partial-thickness incisions through approximately 90% of the cornea in a radial pattern around the mid periphery, to flatten the central cornea while steepening the periphery.

Short-term complications of RK included pain, infection, delayed healing, poor scotopic vision due to radial corneal scars, epithelial ingrowth and neovascularization of incisions, corneal erosions, epithelial defects, gaping or non-healing incisions, micropunctures of Descemet's membrane, corneal perforation and endothelial cell loss. Because RK was relatively imprecise and more risky than PRK and LASIK, it fell out of favor relatively soon after the advent of laser-based procedures.

Undoing the Damage

RK's long-term complications were never well studied before it became popular, and were largely unknown. Although most patients enjoyed relatively stable vision for years, an alarmingly high number continued to experience progressive corneal flattening as they aged, leading to significant hyperopia and irregular astigmatism.

Daily fluctuating vision—due to diurnal intraocular pressure changes causing the cornea to change shape—was a common complication experienced by RK patients.

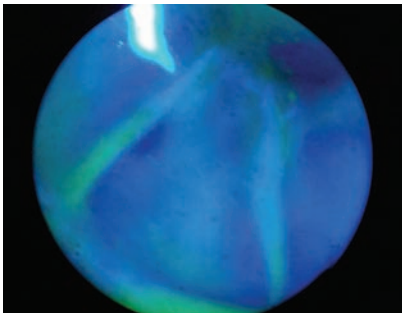


A gaping corneal RK incision.

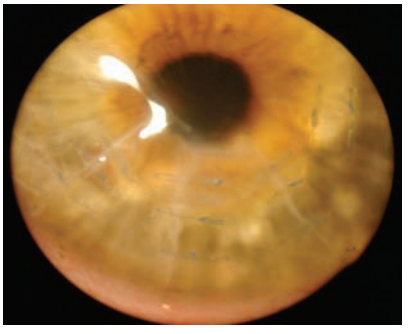
Splitting or gaping incisions are a less common complication that we still see decades later. The patient may notice a sudden onset of corneal pain or decreased vision, but can also present with mild or no symptoms. Surgical closure of these incisions is often warranted to improve anterior corneal shape, decrease risk of epithelial ingrowth, and to prevent neovascularization and permanent corneal warpage.

Gaping incision closure is typically done with non-dissolving nylon sutures. Partial corneal-depth sutures are used to close the wound, and then the knots are buried under the epithelium. Excessive tension is needed to ensure permanent wound closure; this often induces local steepening of the cornea that can temporarily reduce vision and persists until the sutures are removed at a later date.

Postoperatively, patients need to be monitored for infection, leaking suture sites and excessive inflammation that could precipitate further corneal scarring. Patients should also be counseled that while the sutures are inducing asymmetric tension to their cornea, the vision is likely to change. Sutures can be left in the cornea for months or years, until the surgeon feels comfortable that there is little risk of re-splitting the incisions upon removal. If sutures are left in for a long period of time, patients should be monitored for suture erosion and possible related GPC.



Gaping corneal RK incision taking up fluorescein.



Closure of gaping incisions using sutures.

This procedure can temporarily make vision worse, but patients should be counseled that the long-term medical risks from not closing the incisions can be more serious than the possible (and often temporary) vision changes. ■

ILEVRO™

(nepafenac ophthalmic suspension) 0.3%

BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE
ILEVRO™ Suspension is indicated for the treatment of pain and inflammation associated with cataract surgery.

DOSAGE AND ADMINISTRATION
Recommended Dosing
One drop of ILEVRO™ Suspension should be applied to the affected eye one-time-daily beginning 1 day prior to cataract surgery, continued on the day of surgery and through the first 2 weeks of the postoperative period. An additional drop should be administered 30 to 120 minutes prior to surgery.

Use with Other Topical Ophthalmic Medications
ILEVRO™ Suspension may be administered in conjunction with other topical ophthalmic medications such as beta-blockers, carbonic anhydrase inhibitors, alpha-agonists, cycloplegics, and mydriatics. If more than one topical ophthalmic medication is being used, the medicines must be administered at least 5 minutes apart.

CONTRAINDICATIONS
ILEVRO™ Suspension is contraindicated in patients with previously demonstrated hypersensitivity to any of the ingredients in the formula or to other NSAIDs.

WARNINGS AND PRECAUTIONS
Increased Bleeding Time
With some nonsteroidal anti-inflammatory drugs including ILEVRO™ Suspension, there exists the potential for increased bleeding time due to interference with thrombocyte aggregation. There have been reports that ocularly applied nonsteroidal anti-inflammatory drugs may cause increased bleeding of ocular tissues (including hyphemas) in conjunction with ocular surgery. It is recommended that ILEVRO™ Suspension be used with caution in patients with known bleeding tendencies or who are receiving other medications which may prolong bleeding time.

Delayed Healing
Topical nonsteroidal anti-inflammatory drugs (NSAIDs) including ILEVRO™ Suspension, may slow or delay healing. Topical corticosteroids are also known to slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.

Corneal Effects
Use of topical NSAIDs may result in keratitis. In some susceptible patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use of topical NSAIDs including ILEVRO™ Suspension and should be closely monitored for corneal health. Postmarketing experience with topical NSAIDs suggests that patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients.

Postmarketing experience with topical NSAIDs also suggests that use more than 1 day prior to surgery or use beyond 14 days post surgery may increase patient risk and severity of corneal adverse events.

Contact Lens Wear
ILEVRO™ Suspension should not be administered while using contact lenses.

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

Ocular Adverse Reactions
The most frequently reported ocular adverse reactions following cataract surgery were capsular opacity, decreased visual acuity, foreign body sensation, increased intraocular pressure, and sticky sensation. These events occurred in approximately 5 to 10% of patients.

Other ocular adverse reactions occurring at an incidence of approximately 1 to 5% included conjunctival edema, corneal edema, dry eye, lid margin crusting, ocular discomfort, ocular hyperemia, ocular pain, ocular pruritus, photophobia, tearing and vitreous detachment.

Some of these events may be the consequence of the cataract surgical procedure.

Non-Ocular Adverse Reactions
Non-ocular adverse reactions reported at an incidence of 1 to 4% included headache, hypertension, nausea/vomiting, and sinusitis.

USE IN SPECIFIC POPULATIONS
Pregnancy
Teratogenic Effects.
Pregnancy Category C: Reproduction studies performed with nepafenac in rabbits and rats at oral doses up to 10 mg/kg/day have revealed no evidence of teratogenicity due to nepafenac, despite the induction of maternal toxicity. At this dose, the animal plasma exposure to nepafenac and amfenac was approximately 70 and 630 times human plasma exposure at the recommended human topical ophthalmic dose for rats and 20 and 180 times human plasma exposure for rabbits, respectively. In rats, maternally toxic doses ≥10 mg/kg were associated with dystocia, increased post-implantation loss, reduced fetal weights and growth, and reduced fetal survival.

Nepafenac has been shown to cross the placental barrier in rats. There are no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, ILEVRO™ Suspension should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Non-teratogenic Effects.
Because of the known effects of prostaglandin biosynthesis inhibiting drugs on the fetal cardiovascular system (closure of the ductus arteriosus), the use of ILEVRO™ Suspension during late pregnancy should be avoided.

Nursing Mothers
ILEVRO™ Suspension is excreted in the milk of lactating rats. It is not known whether this drug is excreted in human milk. Because many drugs are excreted in human milk, caution should be exercised when ILEVRO™ Suspension is administered to a nursing woman.

Pediatric Use
The safety and effectiveness of ILEVRO™ Suspension in pediatric patients below the age of 10 years 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
Nepafenac has not been evaluated in long-term carcinogenicity studies. Increased chromosomal aberrations were observed in Chinese hamster ovary cells exposed *in vitro* to nepafenac suspension. Nepafenac was not mutagenic in the Ames assay or in the mouse lymphoma forward mutation assay. Oral doses up to 5,000 mg/kg did not result in an increase in the formation of micronucleated polychromatic erythrocytes *in vivo* in the mouse micronucleus assay in the bone marrow of mice. Nepafenac did not impair fertility when administered orally to male and female rats at 3 mg/kg.

PATIENT COUNSELING INFORMATION
Slow or Delayed Healing
Patients should be informed of the possibility that slow or delayed healing may occur while using nonsteroidal anti-inflammatory drugs (NSAIDs).

Avoiding Contamination of the Product
Patients should be instructed to avoid allowing the tip of the dispensing container to contact the eye or surrounding structures because this could cause the tip to become contaminated by common bacteria known to cause ocular infections. Serious damage to the eye and subsequent loss of vision may result from using contaminated solutions.

Use of the same bottle for both eyes is not recommended with topical eye drops that are used in association with surgery.

Contact Lens Wear
ILEVRO™ Suspension should not be administered while wearing contact lenses.

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

Concomitant Topical Ocular Therapy
If more than one topical ophthalmic medication is being used, the medicines must be administered at least 5 minutes apart.

Shake Well Before Use
Patients should be instructed to shake well before each use. U.S. Patent Nos. 5,475,034; 6,403,609; and 7,169,767.

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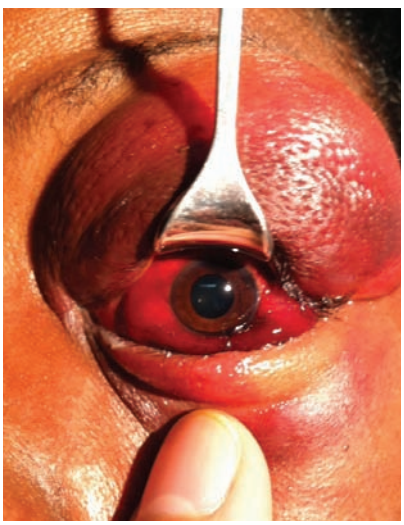
Diagnostic **Quiz**

Worst Trip Ever!

By Andrew S. Gurwood, OD

History

A 57-year-old black female reported to the office following a fall that injured her face and left orbital rim. Her systemic history was remarkable for hypertension, diabetes and dyslipidemia, which were medically controlled. Her ocular history was non-contributory. She reported no known allergies of any kind.



Diagnostic Data

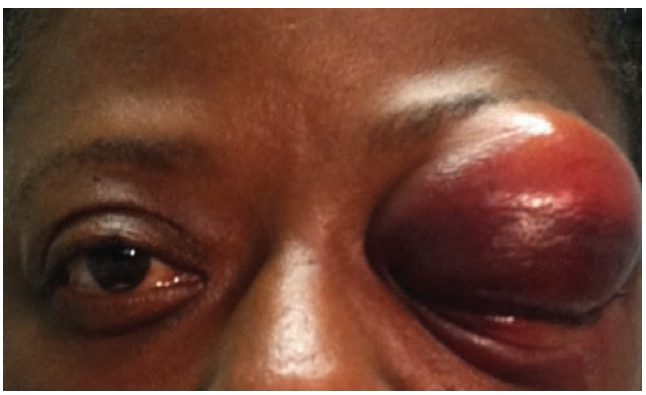
Her best-corrected entering visual acuity measured 20/20 OD and 20/30 OS at distance and near, with no improvement upon pinhole testing. We observed no evidence of afferent pupillary defect OU. The biomicroscopic examination of the anterior segment revealed mild cell and flare in her left eye.

Intraocular pressure measured 15mm Hg OD and 20mm Hg OS. There were peripheral pathologies OU. Our findings from the external evaluation are illustrated in the photographs.

Your Diagnosis

How would you approach this case? Does the patient require any additional tests? What is your diagnosis? How would you manage this patient? What is the likely prognosis?

To find out, please visit www.revoptom.com. Click on the cover icon for this month's issue, and then click "Diagnostic Quiz" under the table of contents. ■



Gross exterior photographs of our 57-year-old patient who presented with visually significant facial and orbital injuries following a fall. What is the most likely diagnosis, and how should she be managed?

Retina Quiz Answers *(from page 66):* 1) a; 2) c; 3) a; 4) b; 5) a.

Next Month in the Mag

January features our Diagnostic Skills & Techniques Report. Topics include:

- *Tricky Retinal Disease Masqueraders—Unmasked!*
- *Diagnostic Dilemmas: Give Yourself This Quiz*
- *Essential Uses of Radiologic Testing* (earn 2 CE credits)

Feedback

Review of Optometry welcomes questions and comments. E-mail Jack Persico, editor-in-chief, jpersico@jobson.com, with "Letter to the Editor" as the subject line.

Or, write to *Review of Optometry*, 11 Campus Blvd., Suite 100, Newtown Square, PA 19073.

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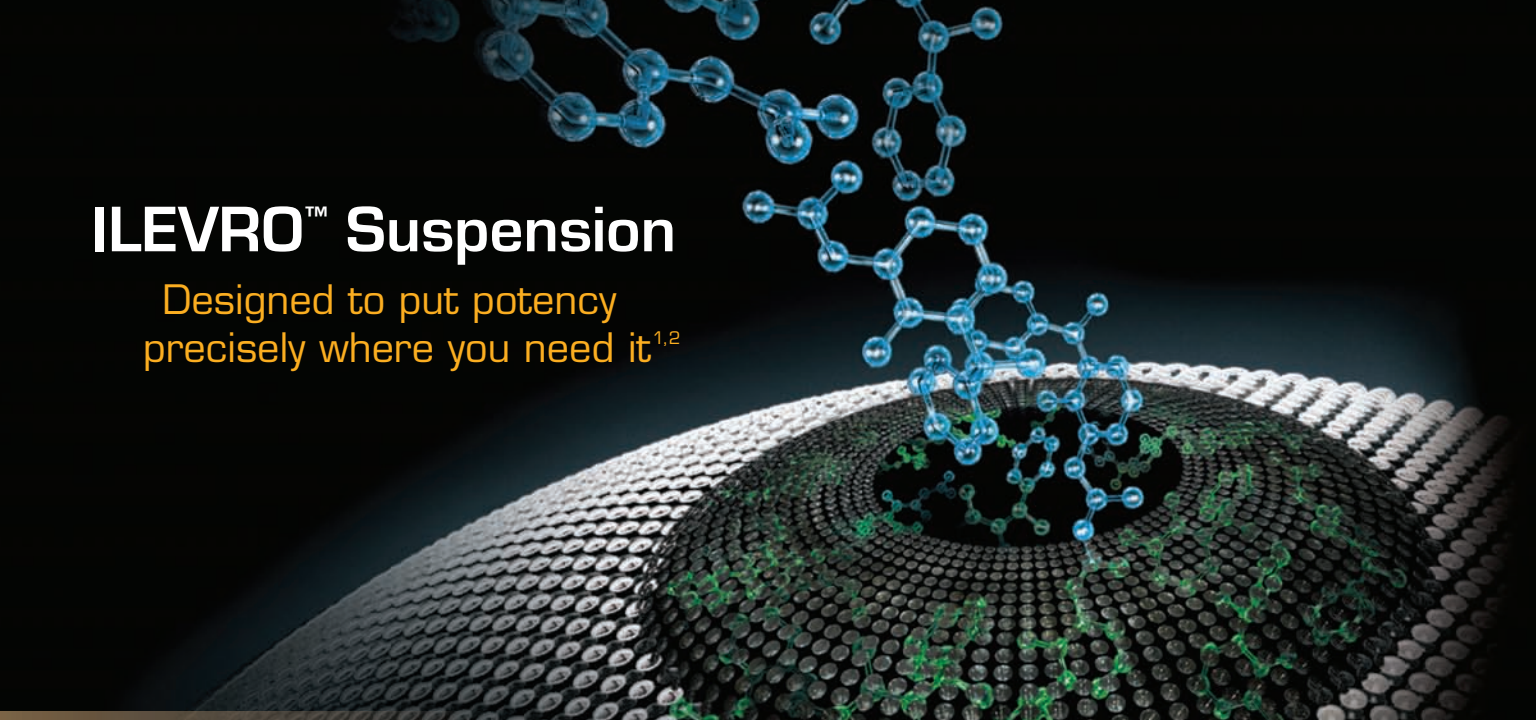

ILEVRO™ Suspension

Designed to put potency precisely where you need it[1,2]

ONCE-DAILY POST-OP

One drop should be applied once daily beginning 1 day prior to surgery through 14 days post-surgery, with an additional drop administered 30 to 120 minutes prior to surgery[3]

Use of ILEVRO™ Suspension more than 1 day prior to surgery or use beyond 14 days post-surgery may increase patient risk and severity of corneal adverse events[3]

INDICATIONS AND USAGE

ILEVRO™ Suspension is a nonsteroidal, anti-inflammatory prodrug indicated for the treatment of pain and inflammation associated with cataract surgery.

Dosage and Administration

One drop of ILEVRO™ Suspension should be applied to the affected eye one-time-daily beginning 1 day prior to cataract surgery, continued on the day of surgery and through the first 2 weeks of the postoperative period. An additional drop should be administered 30 to 120 minutes prior to surgery.

IMPORTANT SAFETY INFORMATION

Contraindications

ILEVRO™ Suspension is contraindicated in patients with previously demonstrated hypersensitivity to any of the ingredients in the formula or to other NSAIDs.

Warnings and Precautions

- Increased Bleeding Time – With some nonsteroidal anti-inflammatory drugs including ILEVRO™ Suspension there exists the potential for increased bleeding time. Ocularly applied nonsteroidal anti-inflammatory drugs may cause increased bleeding of ocular tissues (including hyphema) in conjunction with ocular surgery.
- Delayed Healing – Topical nonsteroidal anti-inflammatory drugs (NSAIDs) including ILEVRO™ Suspension may slow or delay healing. Concomitant use of topical NSAIDs and topical steroids may increase the potential for healing problems.
- Corneal Effects – Use of topical NSAIDs may result in keratitis. In some patients, continued use of topical NSAIDs may result in epithelial breakdown, corneal thinning, corneal erosion, corneal ulceration or corneal perforation. These events may be sight threatening. Patients with evidence of corneal epithelial breakdown should immediately discontinue use.

  Patients with complicated ocular surgeries, corneal denervation, corneal epithelial defects, diabetes mellitus, ocular surface diseases (e.g., dry eye syndrome), rheumatoid arthritis, or repeat ocular surgeries within a short period of time may be at increased risk for corneal adverse events which may become sight threatening. Topical NSAIDs should be used with caution in these patients.

  Use more than 1 day prior to surgery or use beyond 14 days post-surgery may increase patient risk and severity of corneal adverse events.
- Contact Lens Wear – ILEVRO™ Suspension should not be administered while using contact lenses.

Adverse Reactions

The most frequently reported ocular adverse reactions following cataract surgery occurring in approximately 5 to 10% of patients were capsular opacity, decreased visual acuity, foreign body sensation, increased intraocular pressure, and sticky sensation.

For additional information about ILEVRO™ Suspension, please refer to the brief summary of prescribing information on adjacent page.

References: 1. Ke T-L, Graff G, Spellman JM, Yanni JM. Nepafenac, a unique nonsteroidal prodrug with potential utility in the treatment of trauma-induced ocular inflammation, II: In vitro bioactivation and permeation of external ocular barriers. *Inflammation.* 2000;24(4):371-384. **2.** Data on file. **3.** ILEVRO™ Suspension package insert.

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